Advanced cross-sectional imaging in refining aircrew risk - the current and emerging role of cardiovascular CT and MRI

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Chairman, NATO HFM 251 PANEL
I have no financial relationships to disclose.
Scope

- Background – Ex ECG
- CT assessment
- RAF AMCS use of CTCA
- CMR assessment
- RAF AMCS use of CMR
- Conclusion
Detecting Plaque before the accident

• Screening for CAD
  – First line screening
  – Enhanced screening
  – Second line investigations
Military Guidelines

- US – early use of CACS and then MPS or ICA
- UK – ECG then ETT, then usually CTCA
- Germany – ETT as a baseline, early use of CTCA
- NDL – ETT as a baseline, considering CTCA routinely

- Civil approaches also variable and counter-intuitive

- Evidence in aircrew is lacking – what is the correct approach?
Test with 60% Sensitivity, 90% Specificity
Population 20,000 subjects, 5% prevalence CAD

<table>
<thead>
<tr>
<th></th>
<th>Significant CAD</th>
<th>No Significant CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal Test</td>
<td>600 (TP)</td>
<td>1,900 (FP)</td>
</tr>
<tr>
<td>Normal Test</td>
<td>400 (FN)</td>
<td>17,100 (TN)</td>
</tr>
</tbody>
</table>

\[
PPV = \frac{TP}{TP+FP} = 24\%
\]

\[
NPV = \frac{TN}{TN+FN} = 98\%
\]
Low to intermediate likelihood of CAD—role of ExECG?

Estimated likelihood of CAD is 10-29%

- If score is 0: investigate other causes of chest pain
- If score is 1-400: offer 64-slice CT coronary angiography
- If score is > 400: follow pathway for 61-99% CAD (page 14)

Significant CAD (box 9)

- Uncertain: offer non-invasive functional imaging (box 8)
- Significant angiography

- No

- Treat as stable angina
- Investigate other causes of chest pain

Box 8 Non-invasive functional testing

- Offer SPECT:
  - MPS with SPECT
  - Stress echocardiography
  - First-pass contrast-enhanced magnetic resonance (MR) perfusion
  - MR imaging for stress-induced wall motion abnormalities

- Take account of local availability and expertise and the patient’s contraindications and preferences.

- Use adenosine, dipyridamole or dobutamine as stress agents for MPS with SPECT.

- Use adenosine or dipyridamole for first-pass contrast-enhanced MR perfusion.

- Use exercise or dobutamine for stress echocardiography or MR imaging for stress-induced wall motion abnormalities.

- Do not use:
  - MR coronary angiography for diagnosing stable angina
  - Exercise ECG to diagnose or exclude stable angina in people without known CAD.
Enhanced Screening

• ExECG – poor for sig CAD assessment – **should not be used to assess for significant CAD as a sole test**
Coronary Artery Calcification

Stary Classification of Atherosclerotic Plaques

I  II  III  IV  V_{a,b,c}  VI_{a,b,c}

Normal  Early Lipid rich  Internal rupture  Calcified shell Calcified plaque Vulnerable  Rupture  Thrombus Myocardial infarction Obstructive

Fatty streaks  White blood cells  Calcium  Scar  Platelets and fibrin
Red blood cells  Lipid rich plaque  White blood cells

Inflammation and calcification Scar development with calcification

Royal Brompton & Harefield NHS Foundation Trust
Epidemiology

- 10,377 asymptomatic subjects, mean follow-up 5 years
- Calcium score independent predictor and incremental to risk factors

Shaw LJ. Radiology 2003; 228: 826
CACS

- US
  - Score <10 – unrestricted
  - >10 grounded

- UK
  - <10 not reassuring
  - >100 may be OK

<table>
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<tr>
<th>CAC Score:</th>
<th>0</th>
<th>1-9</th>
<th>10-99</th>
<th>100-399</th>
<th>400-999</th>
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<td>n</td>
<td>249</td>
<td>51</td>
<td>202</td>
<td>263</td>
<td>212</td>
<td>112</td>
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<tr>
<td>CD/MI/revasc</td>
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<td>0</td>
<td>6</td>
<td>8</td>
<td>17</td>
<td>12</td>
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<tr>
<td>Annual event rate</td>
<td>0.45%</td>
<td>0.00%</td>
<td>1.11%</td>
<td>1.14%</td>
<td>3.00%</td>
<td>4.01%</td>
</tr>
</tbody>
</table>

Rozanski, et al JACC 2007
Enhanced Screening

- CACS – indicates atheroma and has strong population level data but risks being a poor discriminator at individual level – data in aircrew?
Fig. 1. Figure comparing CT calcium score, CT coronary angiography maximal stenosis, and aggregate stenosis.
CT Coronary Angiography vs. Coronary Artery Calcium Scoring for the Occupational Assessment of Military Aircrew

Iain Parsons; Chris Pavitt; Rebecca Chamley; Jo d’Arcy; Ed Nicol

Fig. 1. Figure comparing CT calcium score, CT coronary angiography maximal stenosis, and aggregate stenosis.
Fig. 2. CT coronary angiography of a pilot with significant LAD stenosis, but a calcium score of 0, confirmed by invasive angiography (see arrows).
Fig. 1. Figure comparing CT calcium score, CT coronary angiography maximal stenosis, and aggregate stenosis.
Enhanced Screening

• CACS – indicates atheroma but poor discriminator at individual level – If performed in isolation may not predict risk on individual basis
CTCA
No Ex ECG
No CACS
No PTP assessment

1.3.4.3 Offer 64-slice (or above) CT coronary angiography if:

- clinical assessment (see recommendation 1.3.3.1) indicates typical or atypical anginal chest pain, or
- clinical assessment indicates non-anginal chest pain but 12-lead resting ECG has been done and indicates ST-T changes or Q waves.

[new 2016]
Strengths of CTCA

- Ubiquity – cardiac enabled CT
- Speed vs. ICA/MPS/CMR
- Non-invasive
- Plaque analysis
- Rapidly evolving field
- Potential for functional data
- Low dose
Weaknesses of CTCA

- Heart rate and HRV limitations
- Calcium
- Radiation – PROTECTION VI study
- EHJ Aug 2018
- DLP 200 (3mSv)
- = Annual background radiation (Europe)

- Access and cost in some nations
Deriving coronary artery calcium scores from CT coronary angiography: a proposed algorithm for evaluating stable chest pain

CCT-Comprehensive Cardiac Examination

Anatomy

Function

Coronary Plaque/Stenosis

Stress Perfusion

CT-FFR

Source: Salerno M, University of Virginia
Shear stress

Shape and regularity

Cardoso et al. J Biomech 2014

Location

Asakura et al. Circ Res. 1990

Low shear stress area

Development of plaque

Asakura et al. Circ Res. 1990

Chatzisisis et al. Circulation 2008
Vascular inflammation creates a gradient of adipocyte lipid content in perivascular fat

3D changes of PVAT attenuation can be quantified in contrast CTA

Perivascular Fat Attenuation Index: Excellent sensitivity/specificity to detect culprit lesions

Antoniades et al - Sci Transl Med. 2017

N=~1400 fat biopsies

Perivascular Fat Attenuation Index: A new way to identify vascular inflammation

Sensitivity: 90% Specificity: 85%

AUC (95% CI): 0.91 (0.80-1.00), P<0.001
CMR

• CMR provides highly accurate morphological and functional assessment
• Excellent reproducibility permitting accurate quantification, or highly sensitive exclusion, of pathology.
• ‘Gold-standard’ for ventricular volumes and mass
• Late gadolinium contrast enhancement (LGE) provides tissue characterisation
• Accurate imaging of the valves and great vessels
• BUT it’s expensive, and time-consuming
The right ventricle

- Assessment of the right ventricle (RV) a particular strength of CMR
- Reproducible quantification of function
- Confirm/exclude dilatation and potential causes:
  - Shunt quantification
  - ASD assessment for potential closure
- Aneurysmal/dyskinetic segments for query arrhythmogenic ventricular cardiomyopathy
Hypertension vs HCM

- CMR may be able to distinguish between them (not 100% though)
- Asymmetry of hypertrophy, severity of hypertrophy, presence of myocardial crypts, presence of LVOT obstruction, presence of SAM of the MV
- Can assess the apex in query apical HCM, when echo may be affected by near-field artefact
- Can also look for fibrosis in a characteristic pattern, using LGE
  - typically seen as patchy/hazy enhancement in HCM, usually in areas of maximal hypertrophy
Myocarditis vs MI

• Chest pain & ↑ troponin may occur with both
• Angiography may not be clear-cut
• Aeromedical disposition significantly different
• Confirming myocarditis, not MI, may allow a return to the cockpit much more quickly in many – LGE pattern usually diagnostic
• In the acute stage, can assess inflammation & oedema - to confirm diagnosis, assess LV (dys)function and fibrosis with LGE
• For follow up, can also assess recovery of LV function, resolution of oedema or inflammation, and degree of fibrosis
Cardiomyopathy

- Can detect cardiomyopathy (CM) before LV dysfunction seen on echo
  - Therefore may be able to detect it earlier, and limits aeromedical risk
  - May show anatomy or specific patterns of LGE consistent with aetiology of CM
  - Can also provide reassurance in cases where suspicion arises of query CM
  - Can also be used for follow up in CM - accurate & reproducible follow up in those with CM if continued flying privileges dependent on LV/RV function
  - LGE also highly sensitive for detection of cardiac sarcoid, with characteristic pattern seen, even in those with normal ECG & echo
AMCS cohort

- From a total aircrew population of 8000, over a two-year period, 1025 personnel were referred for clinical outpatient assessment.

- Of these, 558 referrals (54%) were for further medical evaluation of suspected cardiovascular disease.

- 52/558 (9.3%) underwent a CMR scan – abnormal ECG/Holter (46%).

- 65% to exclude a CM

CMR cohort:
- median age of 43 years (range 20-62 years)
- predominantly male (96%).
- The largest occupational group was pilots (35%)
AMCS cohort

• Of the 52 subjects assessed by CMR:
  • prior to the scan
    • 30 (58%) were grounded
    • 22 (42%) were flying with occupational restrictions
  • after the scan
    • 8 (15%) remained grounded
    • 25 (48%) were returned to flying with occupational restriction
    • 19 (37%) were cleared for unrestricted flying duties
24/52 patients (46%) had confirmed pathology on CMR.

Within this group:
- 8 (33%) had dilated cardiomyopathy
- 6 (25%) had evidence of previous myocarditis
- 4 (17%) hypertrophic cardiomyopathy
- 2 (8%) bicuspid aortic valve with dilated aortic root
- 2 (8%) had significant coronary artery disease with a perfusion defect
- 1 patient had a previous myocardial infarction
- 1 congenital LV aneurysm
- 5 (21%) unclear/uncertain diagnosis (athletic heart vs. HCM) despite CMR
<table>
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<tr>
<th>Variable</th>
<th>Sub-variable</th>
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<th>Occupational restriction pre CMR</th>
<th>Occupational restriction post CMR</th>
<th>p-value for change in restriction</th>
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<tbody>
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<td>Grounded n (%)</td>
<td>Restrictions n (%)</td>
<td>Grounded n (%)</td>
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<td>All aircrew</td>
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Conclusions

• Cardiovascular CT and CMR are key investigations in the occupational assessment for cardiovascular disease.

• When compared with standard of care, CT & CMR increases the likelihood of a well-characterised cardiac diagnosis or the confident exclusion of pathology.

• This results in a significant increase in return to flying duties.
Any questions?