Imaging Calcification in Aortic Stenosis

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Aortic Stenosis
A Disease of the Valve and the Myocardium

The Valve
Pathophysiology of Aortic Valve Narrowing

Aortic Stenosis
Biphasic response

• **Inflammation / lipid deposition** = Disease Initiation
  – Markers associated with the incidence of AS
  – Atherosclerotic risk factors
  – Lp (a) SNP on genetic analysis

• **Calcification** = Disease Propagation
  – Markers of calcification emerge as the strongest predicts of disease progression and clinical outcomes
  – Less closely associated with inflammation / lipid- failure of the statin trials
Modalities for Imaging Valvular Calcium

1) Echocardiography

2) Computed Tomography

3) Positron Emission Tomography
Echocardiography
Echocardiographic Aortic Valve Calcium Score

1 = NORMAL
No calcium

2 = MILD
Isolated small spots

3 = MODERATE
Multiple bigger spots

4 = SEVERE
Extensive all cusps

Rosenhek NEJM 2000
Predicts Progression & Adverse Clinical Outcomes

• Predicts faster rate of progression in patients with mild / moderate aortic stenosis
  Rosenhek Eur Heart J 2004

• Severe calcification independent predictor of AVR / Death
  Rosenhek NEJM 2000
  Cioffi Echocardiography 2013

INCREMENTAL PREDICTIVE AND PROGNOSTIC DATA OVER AND ABOVE HAEMODYNAMIC ECHO PARAMETERS
COMPUTED TOMOGRAPHY
Computed Tomography

- Aortic Valve Calcium Score
- Same approach as calcium scoring the coronaries
  - ECG- gated, non-gated scan (120mv, 50mA)
  - Axial scans
  - Expressed as Agatston units (radiodensity + volume)
Initial Studies

- Correlates with echo parameters ($r=0.54$) but not perfect
  Cowell J Clin Radiol 2004

- In 262 patients followed up for $3.8 \pm 0.9$ years CT calcium score only predictor of aortic stenosis progression on multivariate analysis
  Messika-Zeitoun Arterioscl Thromb Vasc Biol 2007
Gender Differences

- Correlations between CT calcium score and echo parameters improve when examining males and females independently.

- Women need less AV calcium than men to develop the same degree of haemodynamic obstruction ($P<0.0001$).

- Even after adjustment for their smaller body surface area or aortic annular area (both $P<0.0001$).
Optimal Cut Off

- 460 patients with moderate or severe AS and concordant echo measures of severity

- Aimed to establish optimal cut off in AV calcium score that defines severe AS

- Higher in males than females
  - AVC 2,065 AU in men and 1,275 AU in women
Does it Predict Clinical Outcomes?

- 794 patients from 3 centres

- Severe absolute AVC defined as
  - ≥1,274 AU in women
  - ≥2,065 AU in men

- Predicted overall mortality (adjusted HR: 1.71; 95% CI: 1.12 to 2.62; p = 0.01).
Should We Be Using It Now?

- Patients with discrepant echocardiographic assessments of aortic stenosis
  - Only a minority explained by low flow status

- Up to 1/3\textsuperscript{rd} of patients with moderate/severe disease

- Can provide useful discrimination as to the true severity of the aortic stenosis
PET/CT
Positron Emission Tomography
Computed Tomography
PET Tracers Used

Inflammation: 18F-Fluorodeoxyglucose (18F-FDG)
- Uptake correlates with macrophage burden

Calcification: 18F-Sodium Fluoride (18F-NaF)
- PET bone tracer for 30 years
- Adsorbs to hydroxyapatite
- Detects regions of newly developing microcalcification
18F-NaF Activity: Aortic Valve

Field of View: 780mm
512 matrix size
Voxel size: $1.5 \times 1.5 \times 3.0$mm
What Is $^{18}$F-Fluoride Telling us that is Different to Calcium Scoring?

Correlation between $^{18}$NaF and CT calcium score
R=0.80 p<0.001

Dweck et al Circulation 2012
What Is 18F-Fluoride Telling us that is Different to Calcium Scoring?
PET/CT
Different Distribution

Moderate
18F-NaF Correlates with Histological Markers of Calcification Activity

Alkaline Phosphatase

% Surface area of the valve stained

Valve $^{18}$F-NaF Activity (Mean TBR)

$\text{r}=0.65$

$p=0.04$

Dweck & Jenkins Circulation CVS Imaging 2014
**18F-NaF Predicts Aortic Stenosis Disease Progression at 1 year**

Good correlation between baseline PET activity and change in calcium score (CT) $r=0.66$, $p<0.001$

18F-FDG was not predictive of disease progression: $r=0.14$, $p=0.55$

Dweck & Jenkins Circulation CVS Imaging 2014
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