ΔΙΕΡΕΥΝΗΣΗ ΙΝΩΣΗΣ ΚΑΙ ΚΛΙΝΙΚΗ ΣΗΜΑΣΙΑ

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Overview

• Pathogenesis

• Detection of myocardial fibrosis

• Clinical Implications
Myocardial fibrosis is one of the most common histological forms of the failing heart. Major independent predictive factor of adverse cardiac outcome.
Detection of Myocardial Fibrosis

Endomyocardial Biopsy

- Invasive
- Sampling error
- Cannot assess the entire heart
Detection of Myocardial Fibrosis

Echocardiographic parameters

- Backscatter
- Subclinical systolic / diastolic dysfunction (TDI, strain)

Nuclear Methods

- SPECT molecular labeling
- PET-perfusable tissue index
Detection of Myocardial Fibrosis

Cardiac Magnetic Resonance (CMR)

- Late Gadolinium Enhancement (LGE)
- T1 Mapping
- Extracellular volume (ECV) imaging
Infarct Imaging with LGE-CMR

**GADOLINIUM**
- Paramagnetic properties
- Extracellular space

**ACUTE MI**
- Ruptured cell membrane

**OLD MI**
- Scar → Interstitial space expansion

Kinetics of Gadolinium: Imaging Time Periods

- **Blood pool**: 
  - Perfusion: <10s
  - Infarct: 10-20 min

- **Normal**

- **Infarct**

[Graph showing the kinetics of gadolinium with time periods highlighted.]
Delayed Enhancement CMR

- 6 – 20 min post Gd DTPA
- Inversion recovery FLASH
- “Bright is dead”
- Normal, stunned, hibernating myocardium is dark

Kim R et al, Circulation 1999
LGE CMR and Myocardial Viability

All Dysfunctional Segments

Kim R et al
NEJM 2000

Selvanayagam J et al
Circulation 2004

Transmural Extent of Hyperenhancement (%)
Scar presence and Outcome in CAD

11,636 patients - follow-up of 32 months

857 patients follow-up 4.4 years


Circulation 2009; 120: 2069-2076
Patterns of Late Gadolinium Enhancement

Ischemic
A Subendocardial Infarct
B Transmural Infarct

Nonischemic
A Mid-wall HE
- Idiopathic Dilated Cardiomyopathy
- Myocarditis
- Hypertrophic Cardiomyopathy
- Right ventricular pressure overload (e.g., congenital heart disease, pulmonary HTN)
- Sarcoïdosis
- Myocarditis
- Anderson-Fabry
- Chagas Disease

B Epicardial HE
- Sarcoidosis, Myocarditis, Anderson-Fabry, Chagas Disease

C Global Endocardial HE
- Amyloidosis, Systemic Sclerosis, Post cardiac transplantation
Dilated Cardiomyopathy – Fibrosis

Gulati A et al. JAMA 2013
DCM Examples

Patient A: No LGE

Patient B: Midwall LGE
**LGE in DCM & Prognosis**

Primary Endpoint: All cause mortality or hospitalisation due to CV events

N= 101 DCM patients

Follow-up: 658±355 days

J Am Coll Cardiol 2006;48:1977–85
Fibrosis in HCM
LGE and Arrhythmias in HCM

87 HCM patients - AF

Papavassiliu T et al.
JCMR 2009;11:34

177 HCM patients - VEs

Adabag AS et al.
JACC 2008;51:1369-74
Prognostic Significance of LGE-CMR in HCM

For every 5% increase in fibrosis the risk of reaching the primary endpoint increases by 15%

34 of 136 (25%)

6 of 81 (7.4%)

Primary Endpoint:
cardiovascular death
unplanned CV admission
sustained VT or VF,
appropriate ICD discharge

HR: 3.4

J Am Coll Cardiol, 2010; 56:867-874
Prognostic Significance of LGE-CMR in HCM

- 220 HCM patients
- 20 patients died (9%)
  (16 cardiac death)
- 2 appropriate ICD discharges

J Am Coll Cardiol, 2010; 56:875-887
Prognostic Significance of LGE-CMR in HCM

- Relation between extent of late gadolinium enhancement (LGE) and sudden cardiac death (SCD) events in 1293 patients with HCM

- Extensive LGE provides additional information for assessing SCD event risk among HCM patients, particularly patients otherwise judged to be at low risk

Chan et al. Circulation. 2014;130:484-495
Arrhythmogenic Cardiomyopathy
LGE predicts adverse cardiovascular outcomes in nonischemic cardiomyopathy

1488 patients

*All-cause Mortality  | Hospitalization HF  | Sudden cardiac death*

\[ p = 0.01^* \] \[ p = 0.002^* \] \[ p < 0.001^* \]

*p-values are for the significance of the annualized event rate difference between LGE+ and LGE- subjects.
Limitations of Late Gadolinium Imaging

- Needs **contrast**
  - Renal dysfunction
  - Allergy

- **Diffuse, homogenously distributed fibrosis?**
Native T1 Mapping

Turbo-spin Echo: High signal on TSE

TSE Fat-Sat: Fat-suppresses

ShMOLLI T1-map: Low T1 ~ 230 – 350 ms
Native T1 Mapping in HCM and DCM

- 28 HCM, 18 DCM, and 12 normal – CMR 3-Tesla
Native T1 Mapping – Correlation with Histology

- 109 patients with moderate and severe Aortic stenosis
- 33 controls

Heart. 2013; 99: 932–937
Extracellular Volume Imaging

- Combining T1 measurements before and after contrast, and adding the Ht into the equation…
Extracellular Volume (ECV) imaging

• ECV is considered a surrogate for myocardial fibrosis

BUT

• ECV may expand with fibrosis, edema or amyloid
T1 Mapping in Clinical Context
Ongoing Research

- Publications on PubMed about T1 Mapping CMR
Take Home Messages

• **Fibrosis is common** in various heart diseases

• Associated with **adverse prognosis**

• **Imaging fibrosis – CMR**
  – LGE CMR for regional fibrosis
  – T1 Mapping techniques for diffuse fibrosis
  – Extensive ongoing research