

MRI evidence of cardiovascular involvement in Erdheim-Chester disease

Davide Gianfreda, Alessandro A. Palumbo, Enrica Rossi, Lorenzo Buttarelli, Gaia Manari, Chiara Martini, Massimo de Filippo and Augusto Vaglio

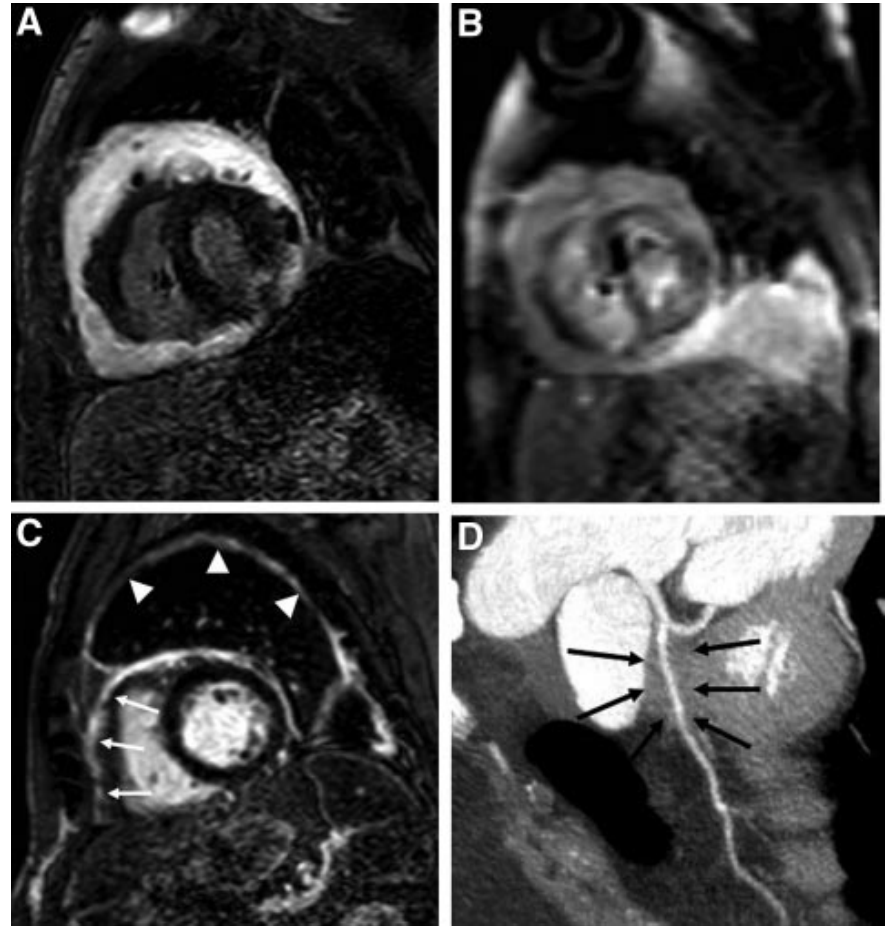
Nephrology Unit and Radiology Unit,
University Hospital of Parma, ITALY

Background

- Cardiovascular (CV) involvement occurs in 40-60% of patients with Erdheim-Chester disease (ECD). Cardiac lesions include atrial infiltration, pericardial thickening+effusion, and coronary artery infiltration
- Large-vessel involvement consists of vascular wall thickening/perivascular sheathing and involves the aorta and the epiaortic artery origin
- Patients with CV involvement are thought to have a poorer prognosis and are therefore treated more aggressively. Whether the adverse outcome is due to cardiac lesions or associated organ involvement is unknown
- Cardiac MRI is considered the most sensitive imaging method for ECD

Background

- 37 ECD patients studied with CT or MRI of the heart or large vessels
- 26 pts (70%) had abnormal heart imaging
- 30% right atrium pseudotumoral mass
- 19% infiltration of right AV sulcus
- 24% pericardial effusion
- 14% pericardial thickening
- Periarterial infiltration of the left coronary in 27% and of the right coronary in 5% (in absence of right AV sulcus infiltration)



Aims of the study

- To assess the frequency and type of cardiovascular manifestations in ECD using a standardised cardiac-MRI and angio-MRI protocol
- To compare the outcome (overall survival, progression-free survival) in CV+ vs CV- patients
- To explore the extent of organ involvement in CV+ vs CV- patients

Study design and eligibility criteria

Observational, prospective study including all patients with ECD diagnosed at or referred to our ECD clinic during the study period (2007-2015)

Diagnosis of ECD following Veyssier-Belot's criteria

No contraindications to Gd-enhanced MRI

MRI study protocol

MRI was performed using a 1.5T MR Scanner. MRI acquisition: ECG-gated

MRI sequences

- **b-SSFP**: balanced steady-state free precession (b-SSFP). Cine sequence, allows evaluation of myocardial function (eg, contractility, diastolic phase)(bright blood)
- **T1- or T2-weighted** (black blood): allows visualisation of morphology, tissue edema and infiltration
STIR (short-time inversion recovery): allows suppression of the fat signal (better differentiates adipose-rich tissue)
- **3D-GRE** (gradient echo)/inversion recovery T1w-sequences: performed for evaluation of delayed enhancement

Large vessel MRI: uses the above sequences but is not ECG-gated

Results

Demographics and general features

23 consecutive patients enrolled (20 M, 87%), median age at diagnosis 48 yrs (range 22-72)

16 enrolled at diagnosis, 7 after a median of 72 (19-180) months from diagnosis

All biopsy-proven ECD

Of 18 pts tested, *BRAF* V600E was found in 12 (66.7%)

MRI results

- 10 patients (43%) had evidence of cardiac involvement
Myocardial involvement in 9 and pericardial in 9
- 7 patients had large vessel involvement (of them only 1 did not have cardiac lesions)

Myocardium

Right atrial mass

Right AV sulcus infiltration
with frequent right coronary
artery involvement

No signs of diffuse
myocardial infiltrative
disease

Pericardium

Diffuse and irregular
thickening

Pericardial effusion (2
tamponade, 3
pericardiocentesis)

Pericardial nodules

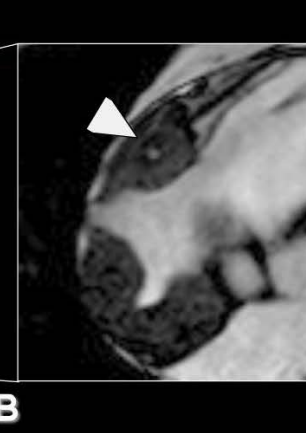
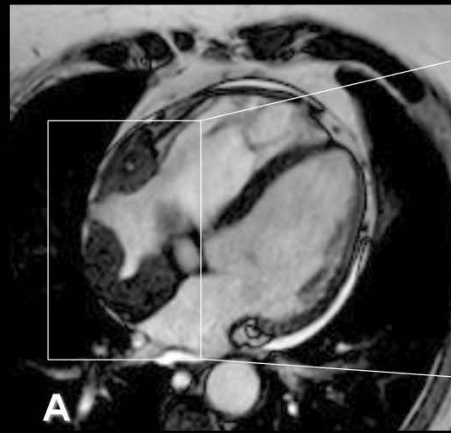
Large vessels

Diffuse thickening of
the thoracic aorta and
epiaortic artery origin

Sometimes segmental
involvement

No stenosis or
aneurysms

Frame taken from cine bSSFP sequences



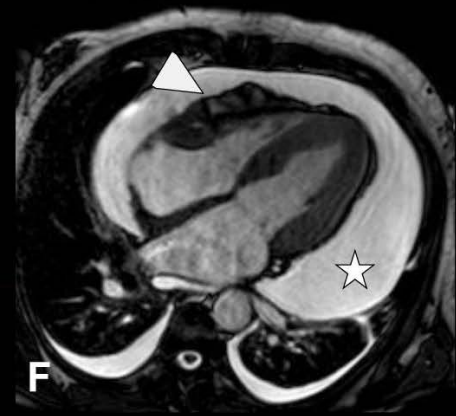
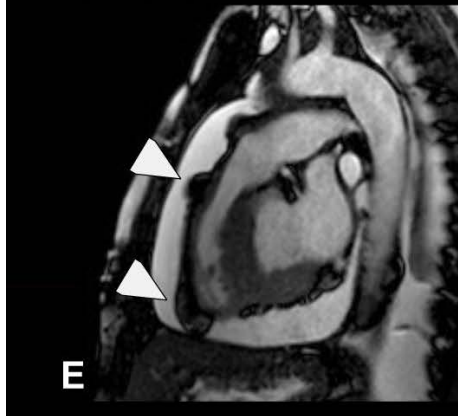
Frame taken from cine bSSFP sequences

STIR T2-weighted image



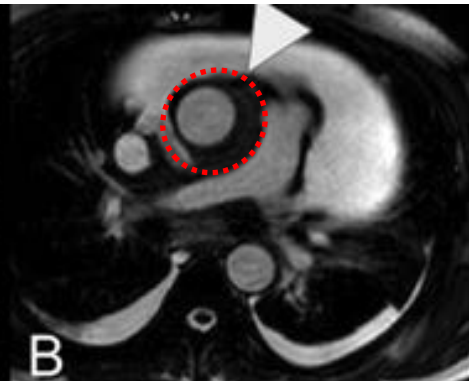
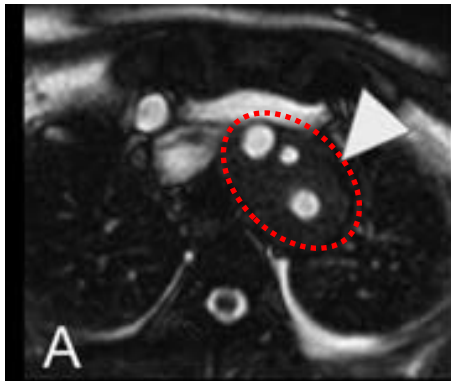
Gradient-echo T1-weighted post-Gd injection (10 minutes)

Frame taken from cine bSSFP sequences



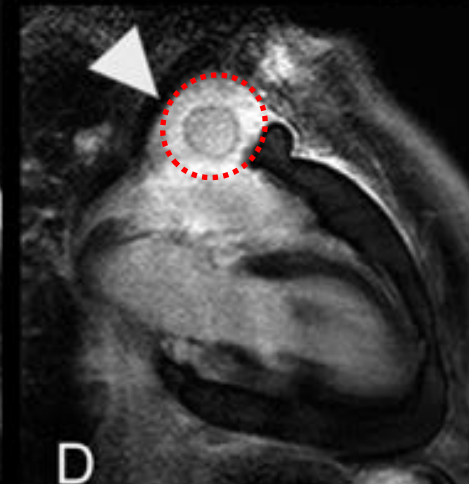
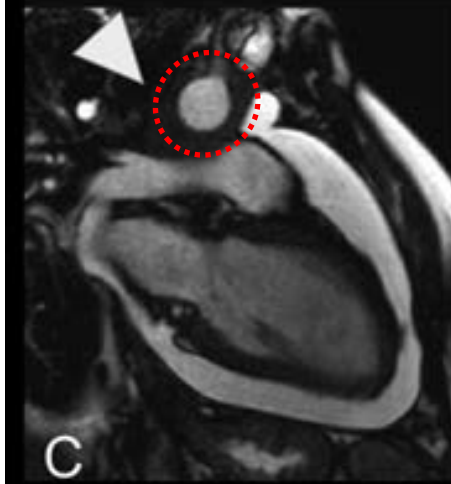
Frame taken from cine bSSFP sequences

Frame taken from
cine bSSFP
sequences



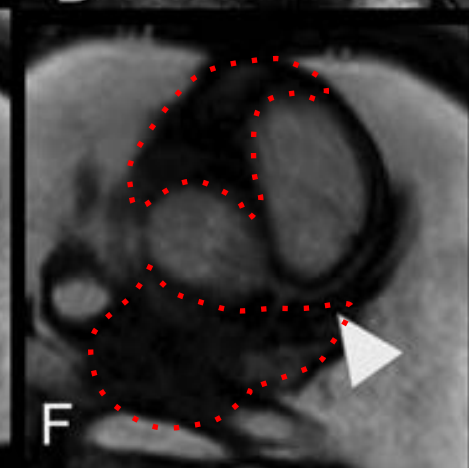
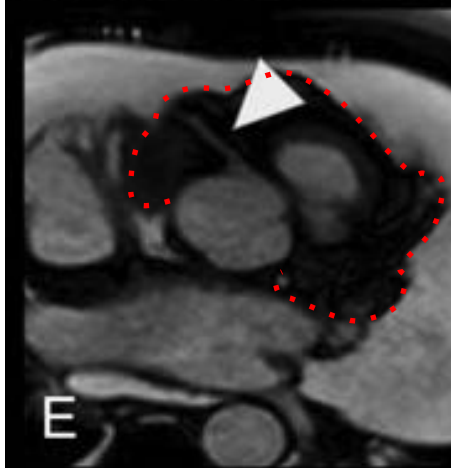
Frame taken from
cine bSSFP
sequences

Frame taken from
cine bSSFP
sequences
(two-chamber view,
long axis)



Gradient-echo T1-
weighted post-Gd
injection (10 minutes)

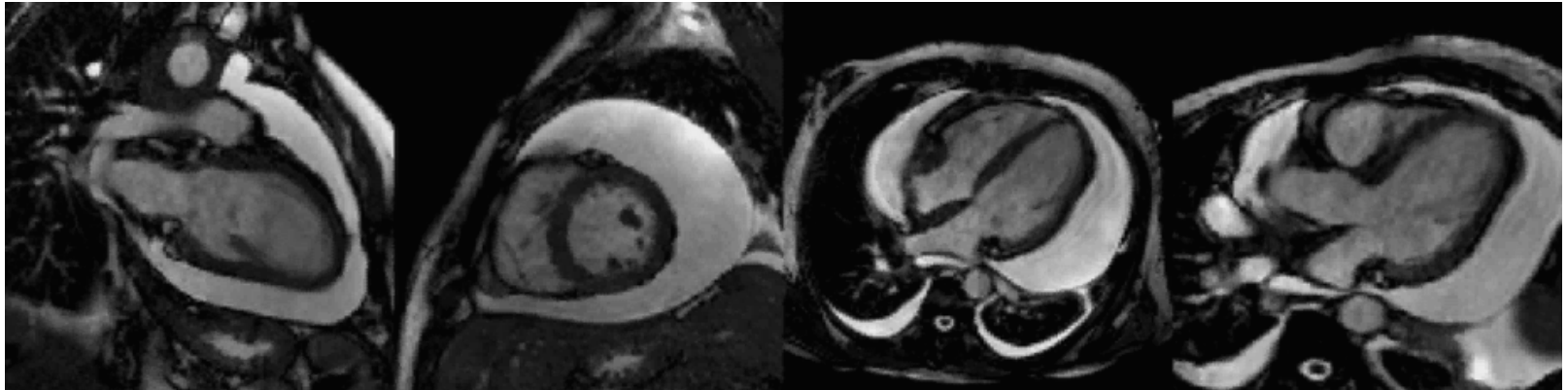
Frame taken from
cine bSSFP
sequences



Frame taken from
cine bSSFP
sequences

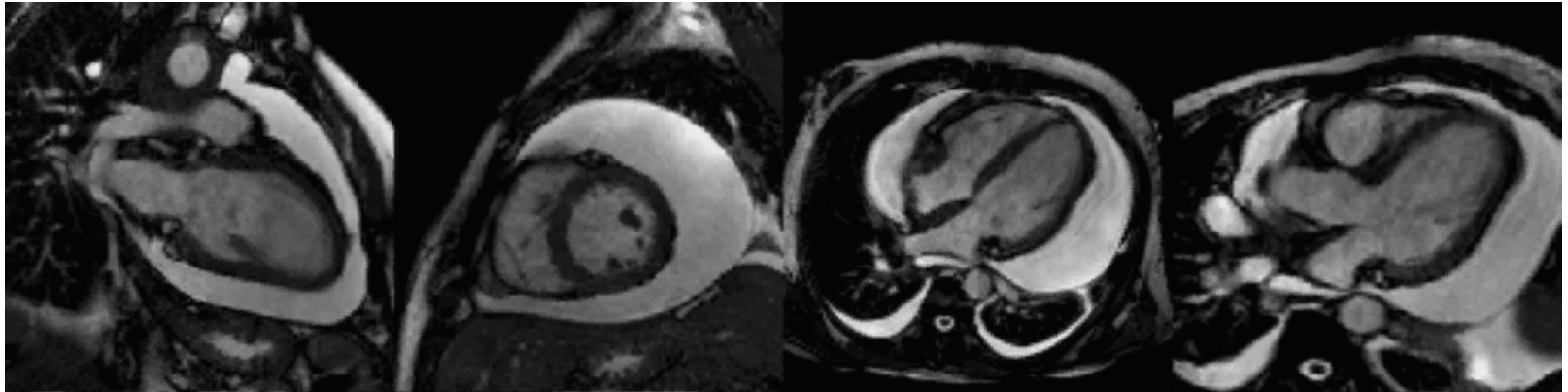
MRI results

Disease
onset

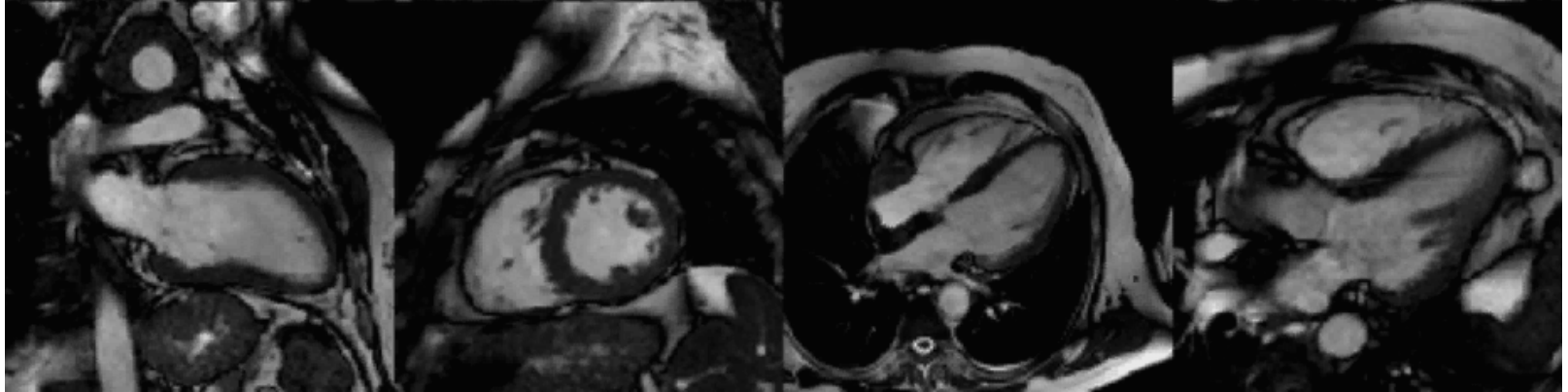


MRI results

Disease
onset



After
pericardial
drainage
and
SRL+PDN
therapy



CV complications and outcomes

With Cardiac MRI lesions

- 3 patients had dyspnea and edema due to pericarditis
- 1 patient had acute heart failure
- 1 patient had atrial flutter
- 1 patient had acute coronary syndrome due to atherosclerotic (non ECD-related) coronary artery disease

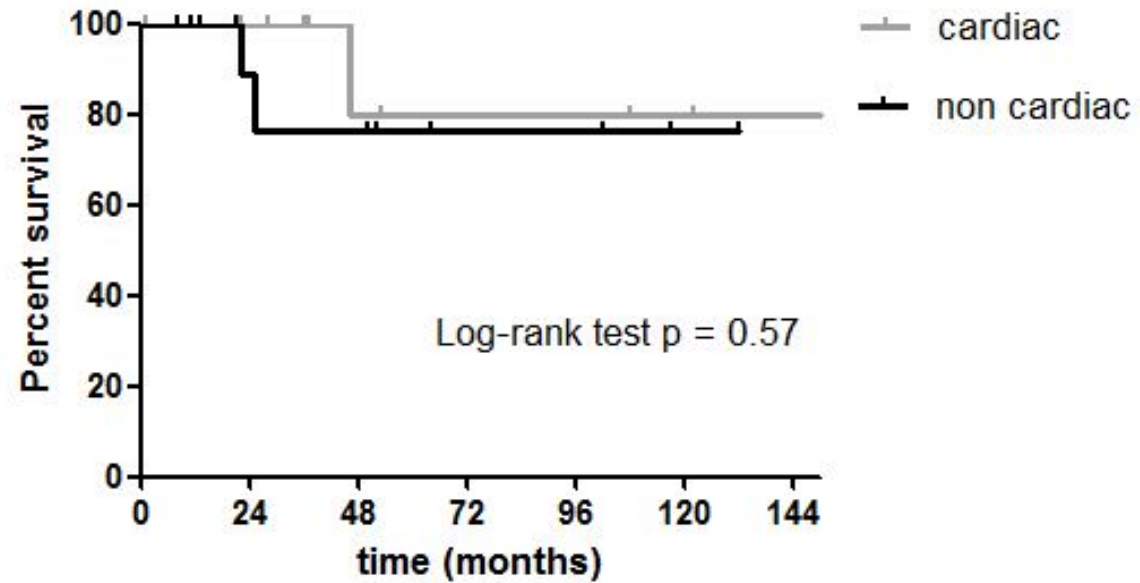
Without Cardiac MRI lesions

- 1 patient had dyspnea due to uremic pericarditis
- 2 patients had acute coronary syndrome due to atherosclerotic (non ECD-related) coronary artery disease

Survival

- 3 patients died (one in the cardiac and 2 in the non-cardiac group)

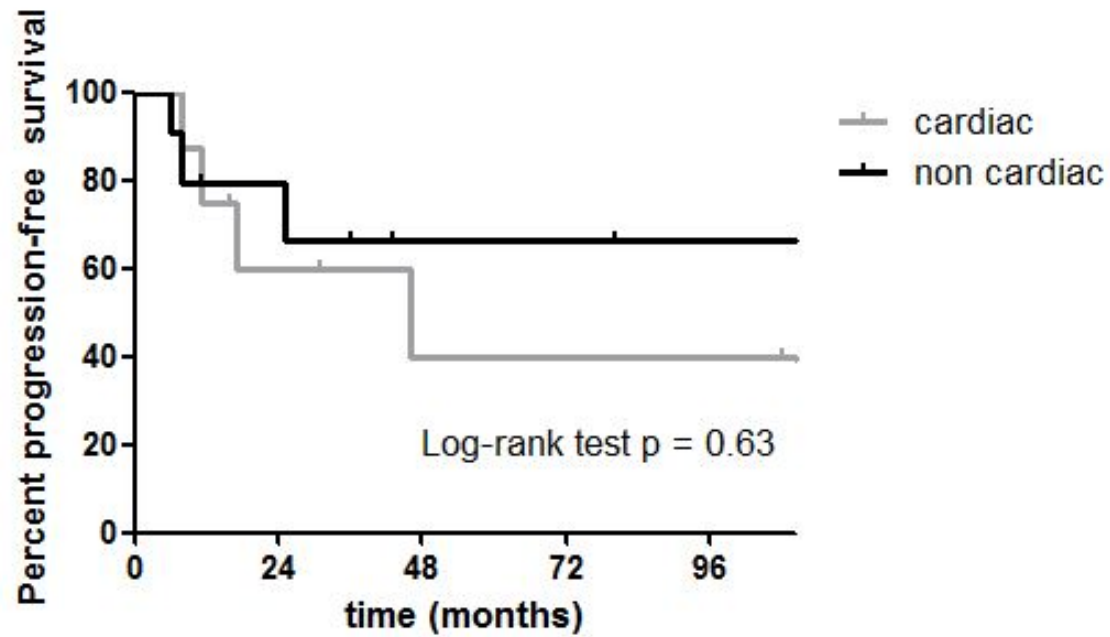
CV involvement and survival



n° patients at risks

Cardiac	10	9	5	4	4	3	1
Non cardiac	13	9	7	4	4	2	1

CV involvement and survival



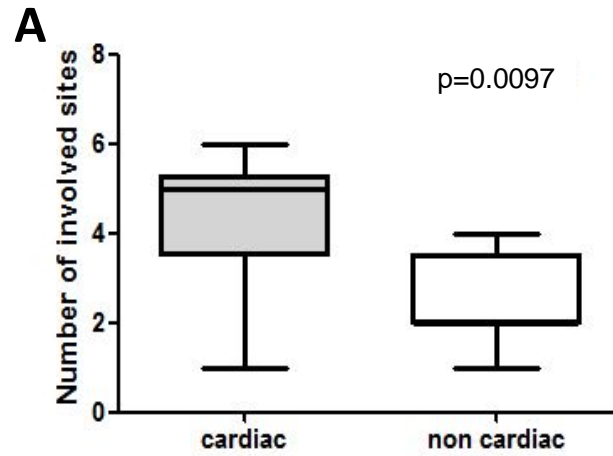
n° patients at risks

Cardiac	8	5	3	3	3
Non cardiac	11	7	3	3	2

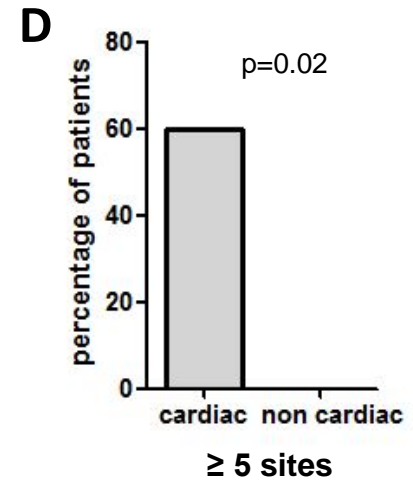
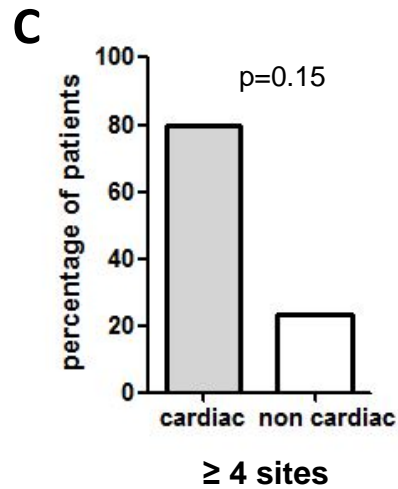
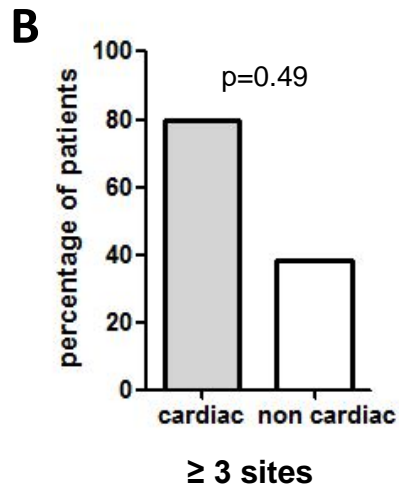
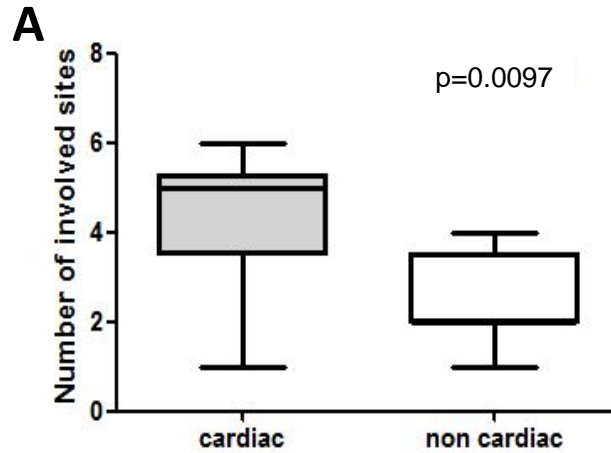
CV involvement and disease extension

	All (N=23)	Cardiac involvement on MRI (N=10)	No cardiac involvement on MRI (N=13)	<i>P value</i>
Age, median (range)- yrs	48 (22-72)	46.5 (25-70)	50 (22-72)	0.15
Time to diagnosis, median (range)- months	36 (1-180)	33 (3-126)	39 (1-180)	0.88
Bone involvement, n (%)	17 (73.9)	8 (80)	9 (69.2)	1.00
Retroperitoneal involvement, n (%)	17 (73.9)	9 (90)	8 (61.5)	0.74
CNS involvement, n (%)	5 (21.7)	2 (20)	3 (23.1)	1.00
Facial/orbit involvement, n (%)	8 (34.8)	6 (60)	2 (15.4)	0.22
Lung involvement, n (%)	5 (21.7)	4 (40)	1 (7.7)	0.32
Cutaneous involvement, n (%)	11 (47.8)	6 (60)	5 (38.5)	0.72
Endocrine involvement, n (%)	13 (56.5)	8 (80)	5 (38.5)	0.49

CV involvement and disease extension



CV involvement and disease extension



Conclusions

- CV lesions detected by MRI occur in approximately 40% of ECD patients
- Typical cardiac lesions include pseudotumoral masses mainly involving the posterior wall of the right atrium, infiltration of the right AV sulcus, pericardial thickening/nodules and pericardial effusion
- Thoracic large-vessel (mainly aortic) involvement is frequent but often asymptomatic
- Patients with CV lesions more frequently have disseminated disease forms
- Larger studies are needed to ascertain whether ECD patients with (MRI-detected) CV lesions have a worse prognosis