

Malattia di Anderson-Fabry

Caso clinico interattivo

Alessia Argirò



L.C.

Malattia di Fabry diagnosticata a fine anni 90 nell'ambito di uno screening familiare (d.n. 1946).

Analisi genetica nel 2001 per Fabry: R301P (variante classica)

acroparestesie dolorose febbrili in età giovanile, angiocheratoma corporis, cornea verticillate in OO, interessamento audio vestibolare (Ipoacusia percettiva bilaterale).

ERT (alfa) dal 2004

La paziente ha presentato numerosi ictus ischemici cerebrali di tipo lacunare. Il primo episodio è avvenuto nel 2001, con paresi dell'emisoma destro e disartria. Il secondo e terzo episodio sono sopraggiunti nel 2004, con deficit di forza dell'arto inferiore destro. Uno nel settembre 2010, caratterizzato da deficit stenico ed ipoestesia dell'emisoma destro, con disturbo dell'eloquio.

Nel 2018 breve episodio di fibrillazione atriale parossistica all'Holter.

Cosa faresti?

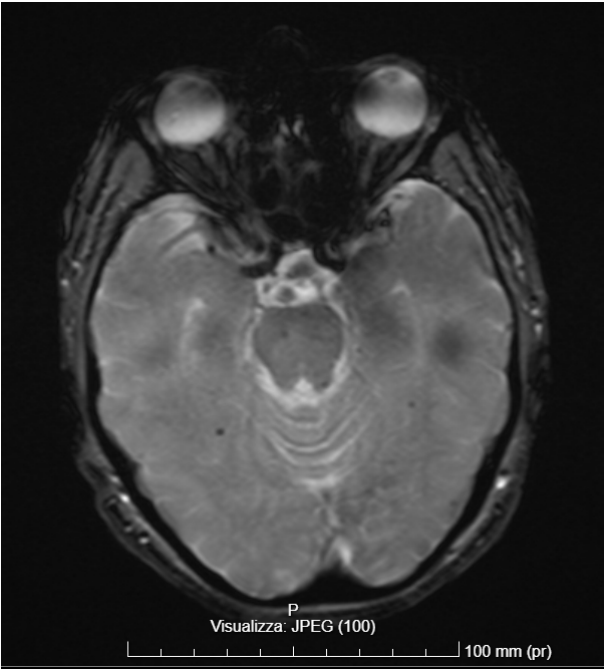
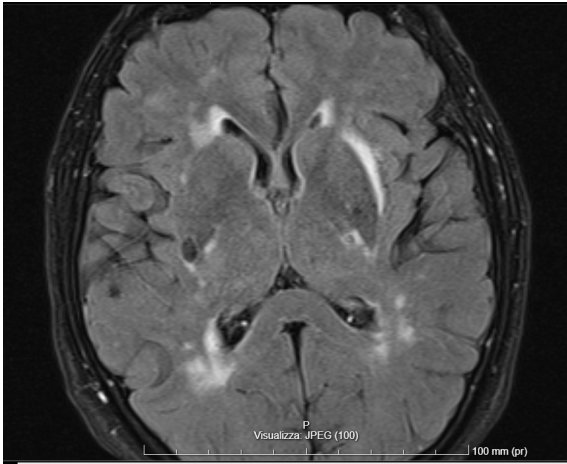
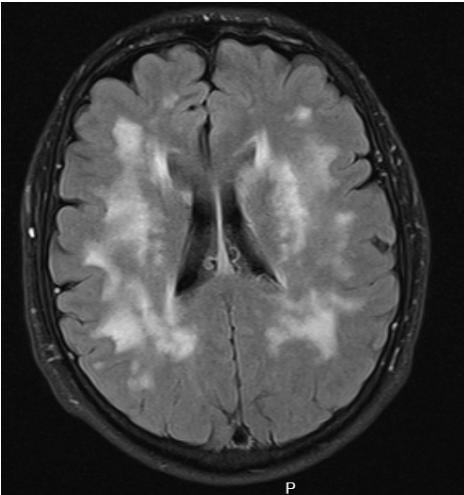
- terapia anticoagulante con warfarin
- Terapia anticoagulante con NOAC
- Non inizio terapia anticoagulante

Il 6/6/2023 accede al DEA di Careggi per ictus ischemico a sede occipitale dx (emianopsia, emineclect) in corso di FA ad elevata FVM (+ BBdx).

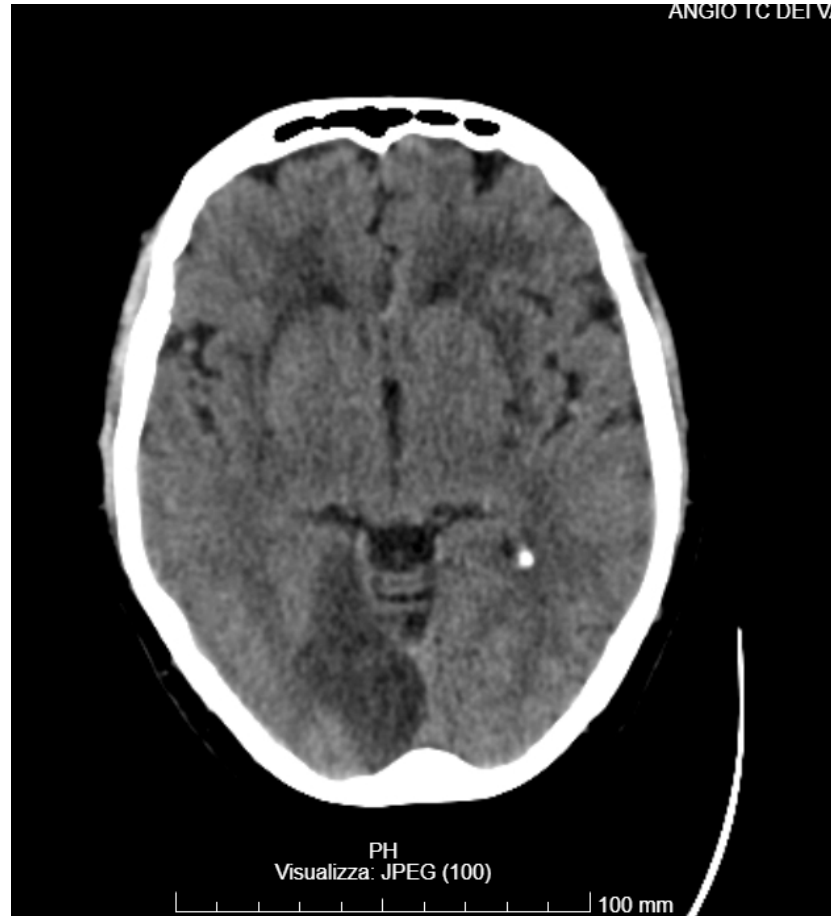
All'ecocardiografia documentazione di trombosi in auricola sn, per cui viene deciso, dopo valutazione del rischio emorragico cerebrale e della funzione renale residua, introduzione di Dabigatran 110 mg x 2

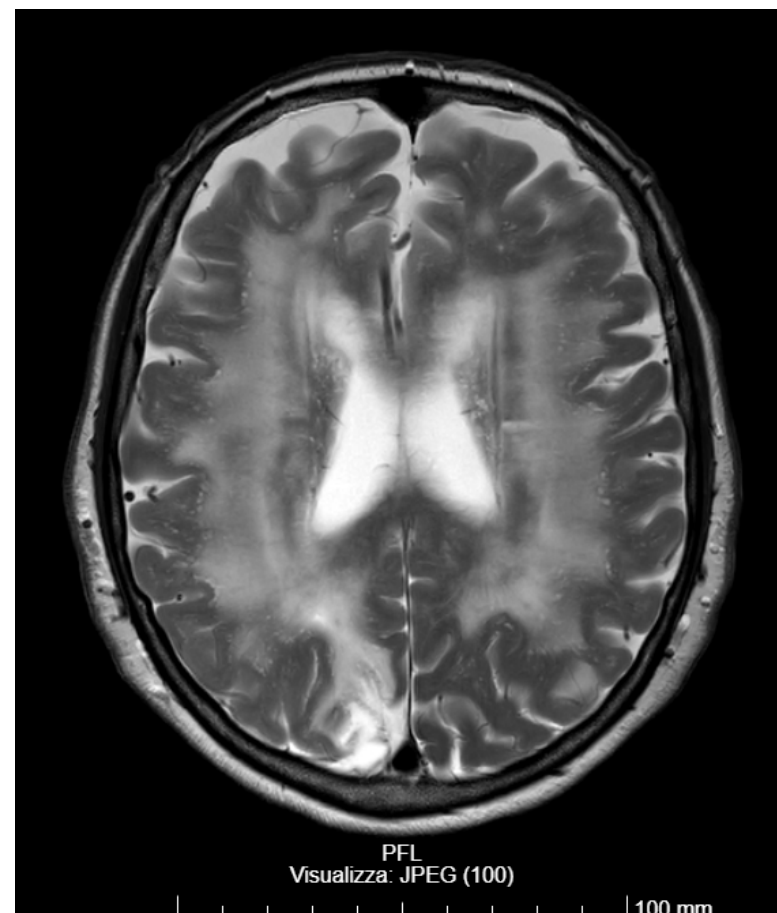
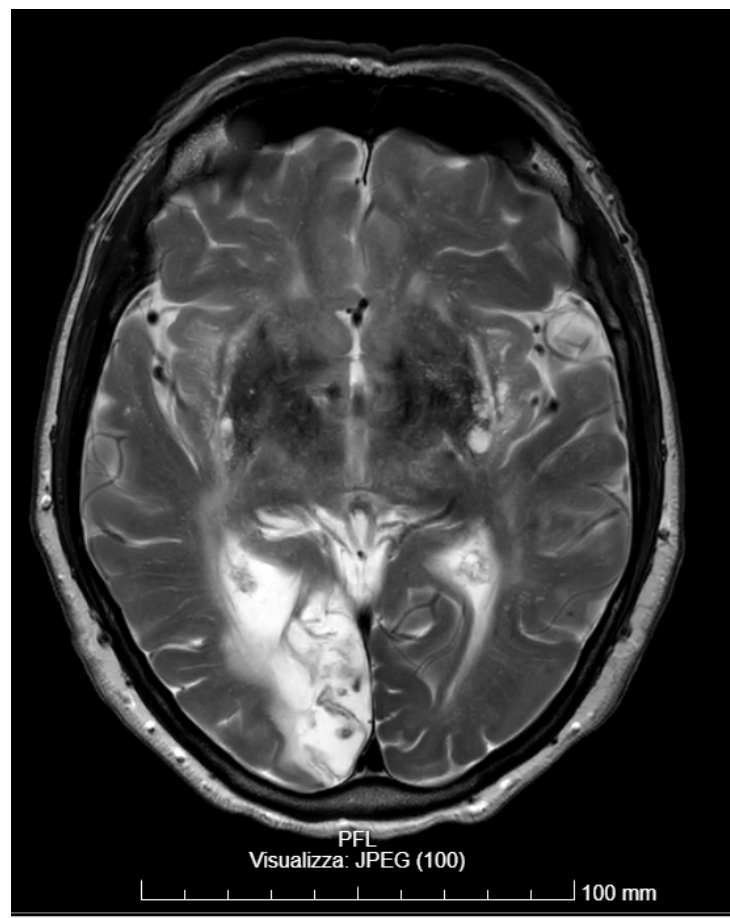
Ha eseguito RM encefalo (4/11/2025) non mostra lesioni focali di nuova insorgenza. Stabili i microbleeds e il quadro di leucoencefalopatia

2011



Stroke 2023





In anamnesi: Dolore toracico in seguito a sforzi modesti e all'esposizione con basse temperature, proposta coronarografia, sempre rifiutata. Trattata con ranolazina e nitrati al bisogno.

In ottobre 2021 durante infusione di terapia presso ambulatori terapeutici dell'Immunoallergologia di Careggi episodio di dolore toracico con ECG invariato.

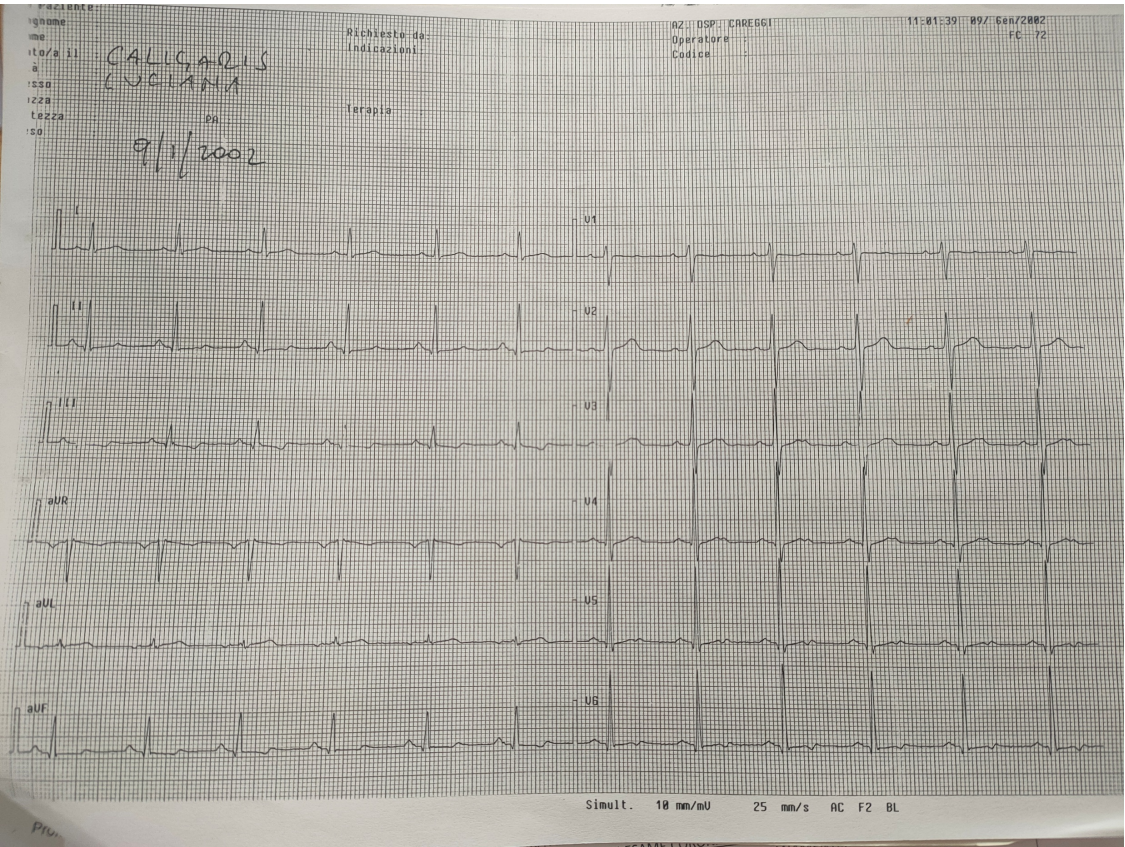
Cosa faresti?

- Coronarografia
- TC coro
- Implement anti-angina therapy

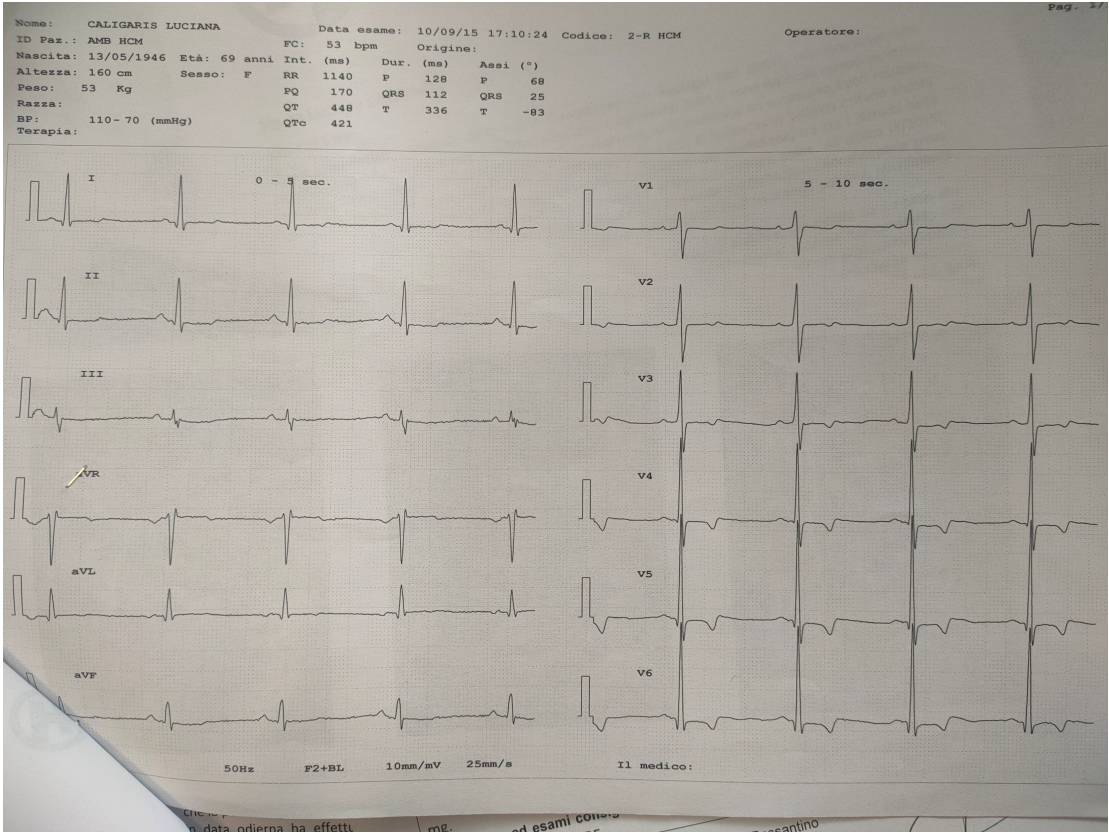
Coronarografia che ha mostrato albero esente da lesioni.

Durante il ricovero NT proBNP 780-749-1080. TnThs 248>237>221

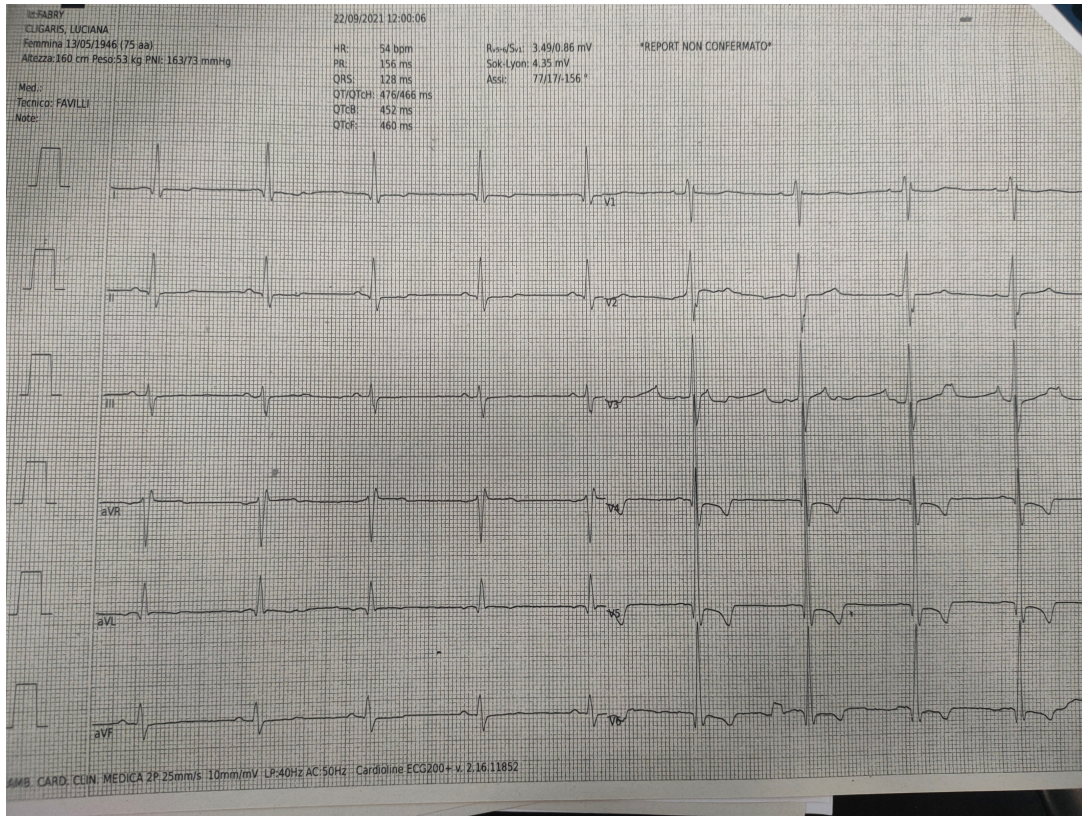
All'ecocardiogramma non evidenza di alterazioni della cinetica regionale. Veniva consigliata terapia con Nitroderm che la paziente ha mal tollerato per allergia cutanea, ritornando ad assumere Dermatrans con miglioramento degli episodi anginosi, tuttavia non scomparsi.



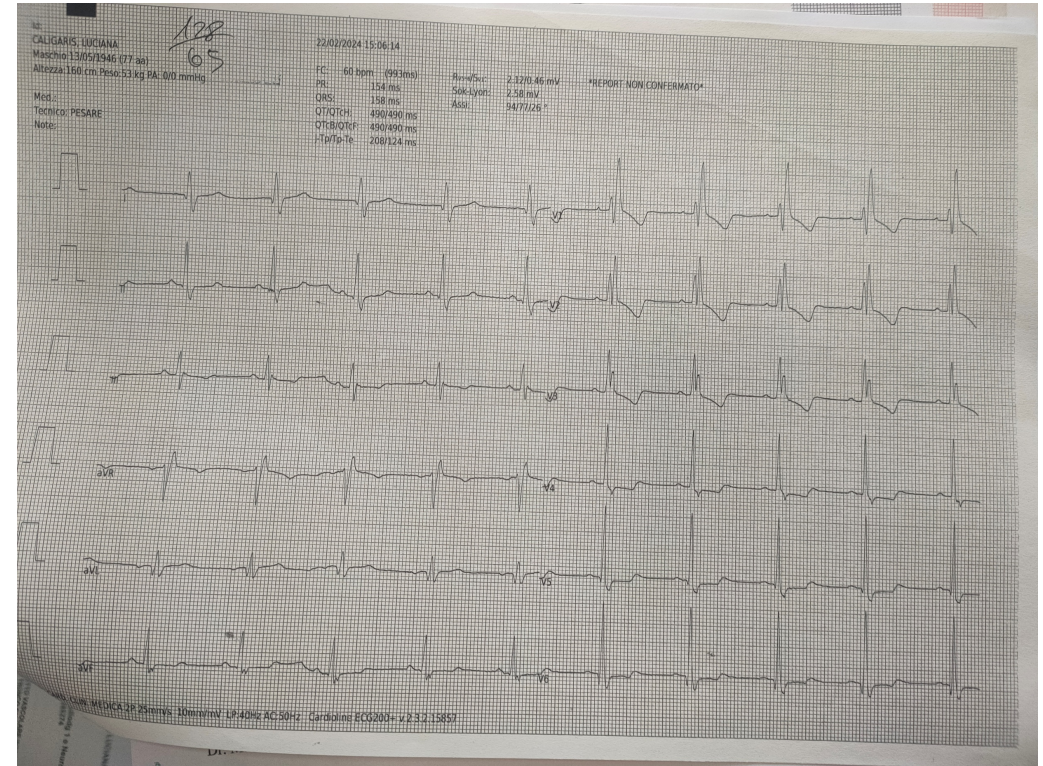
2002



2015

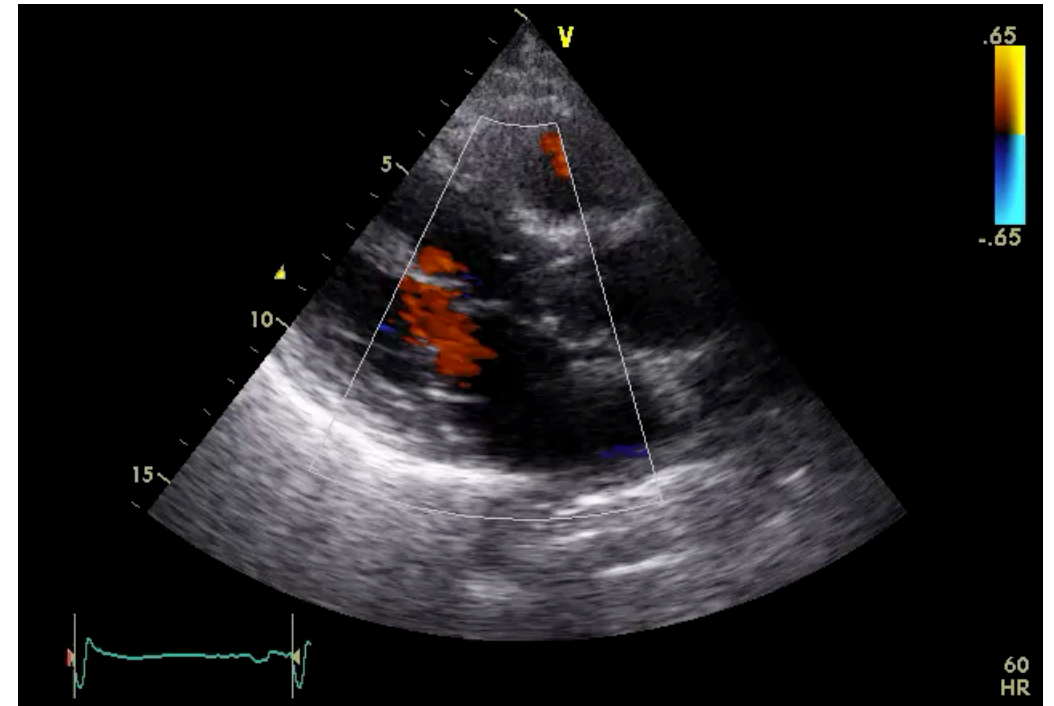
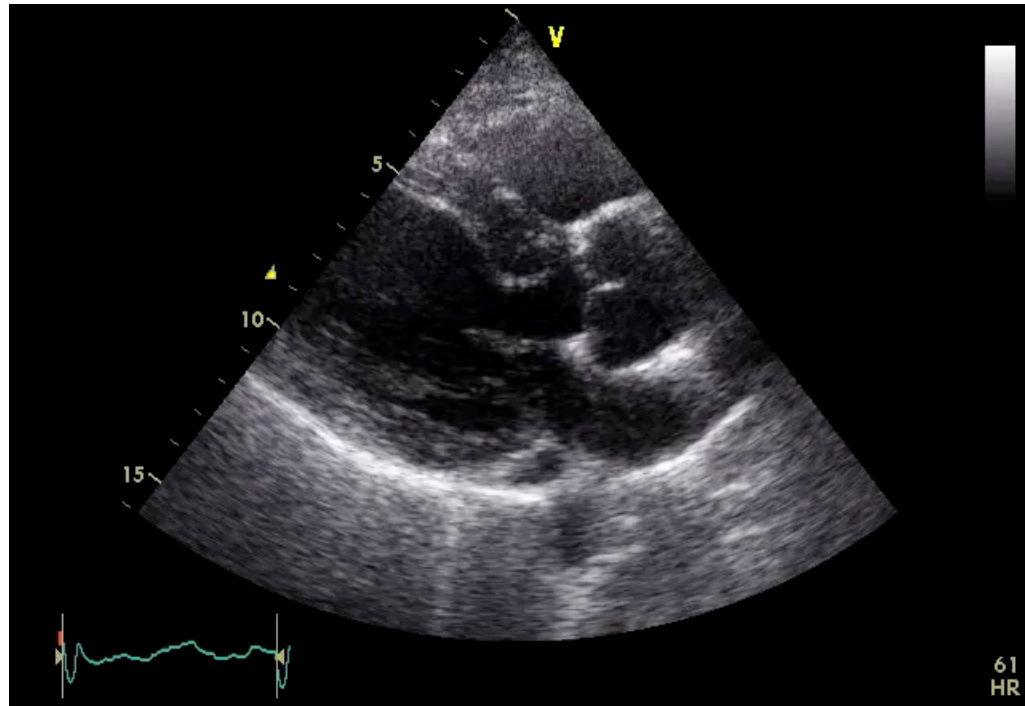


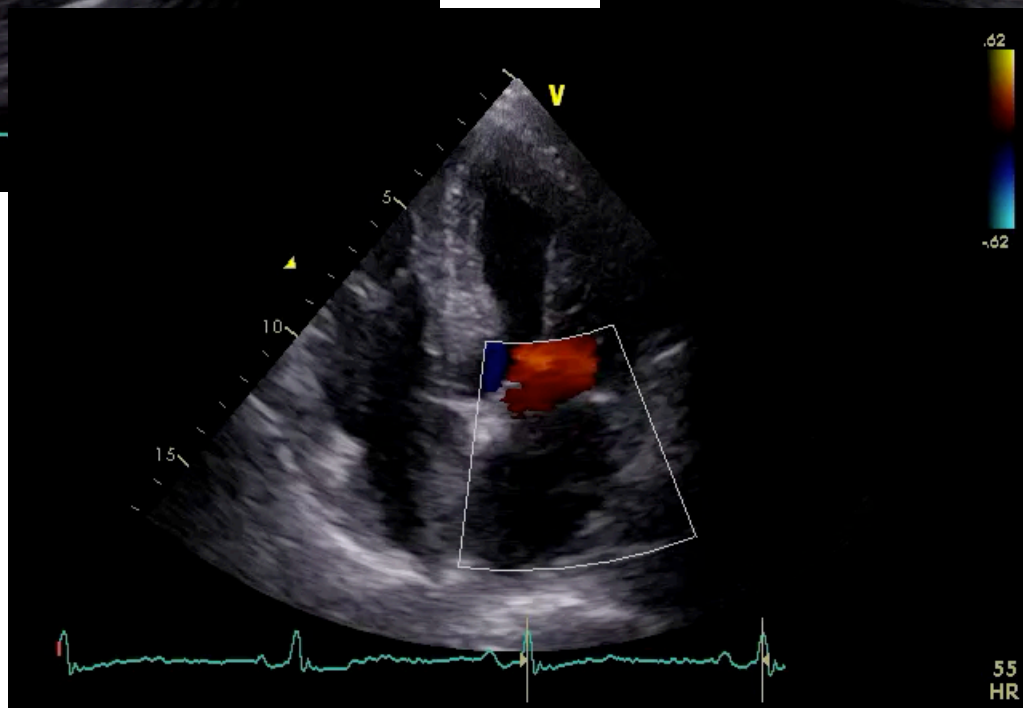
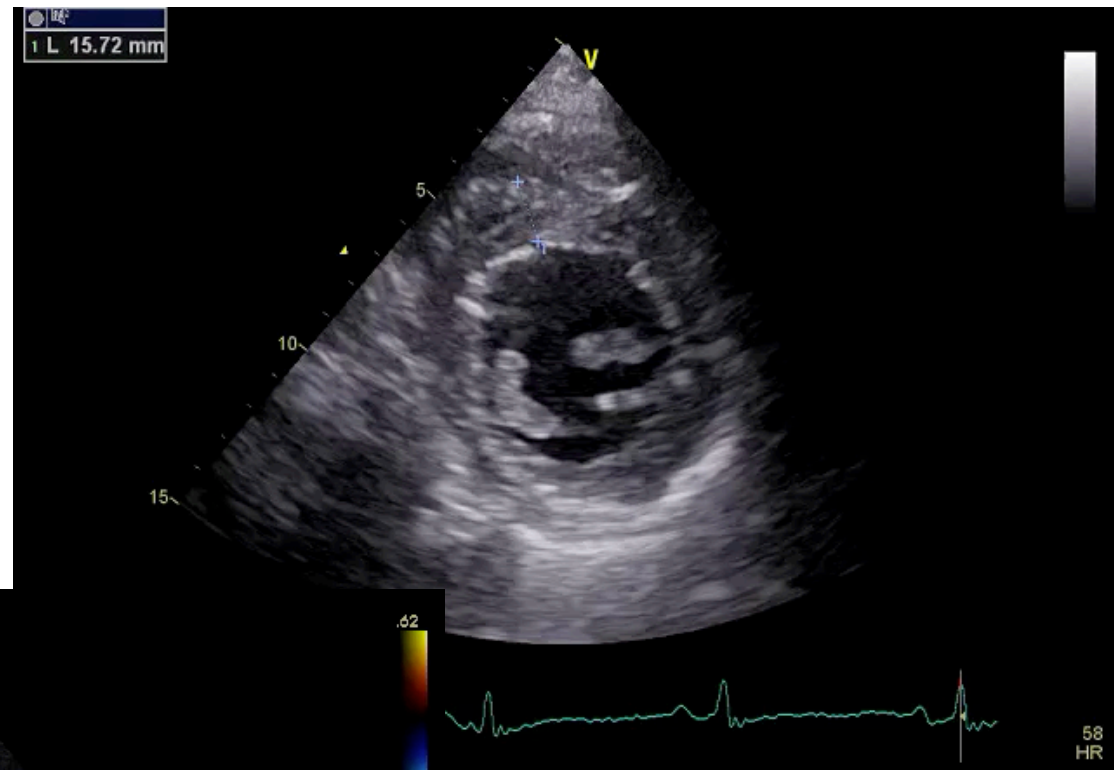
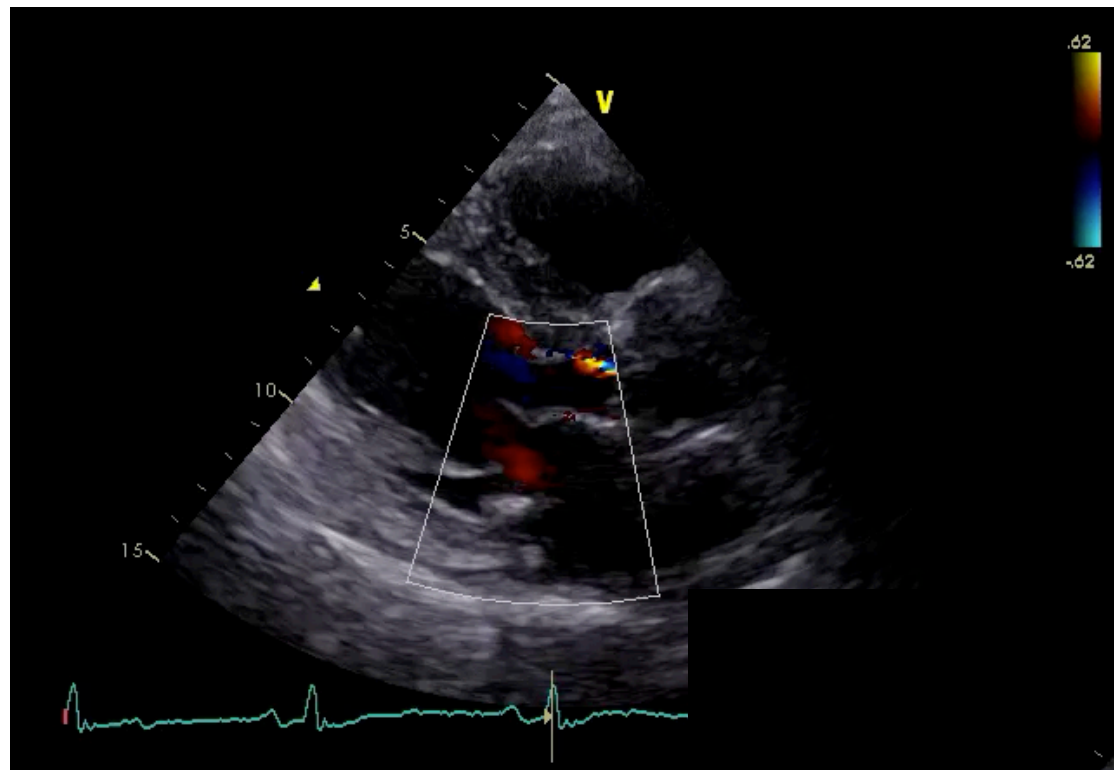
2021



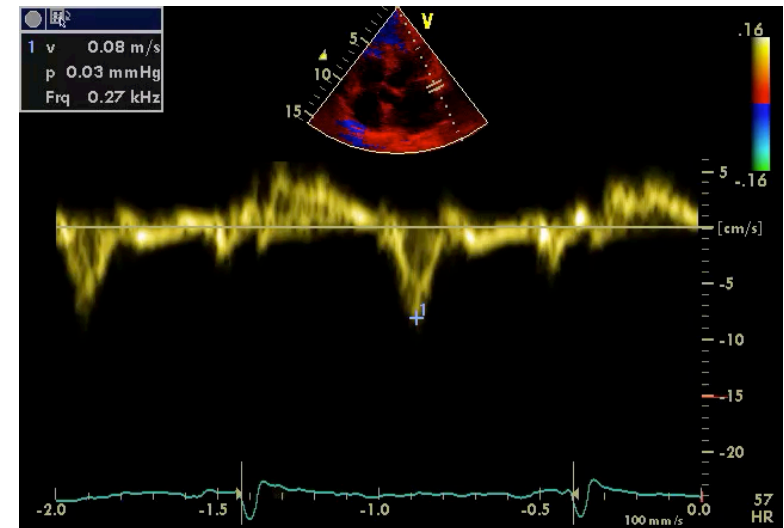
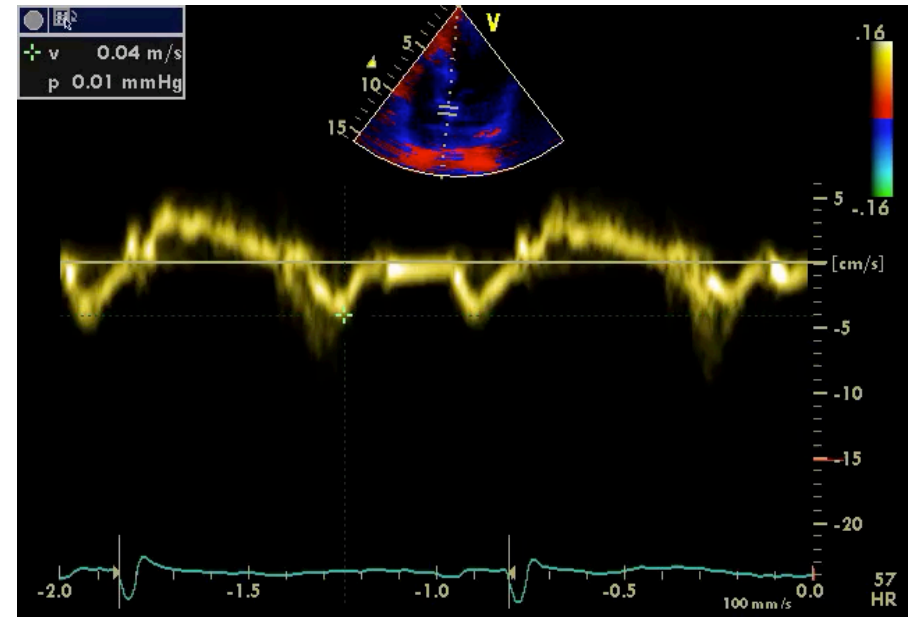
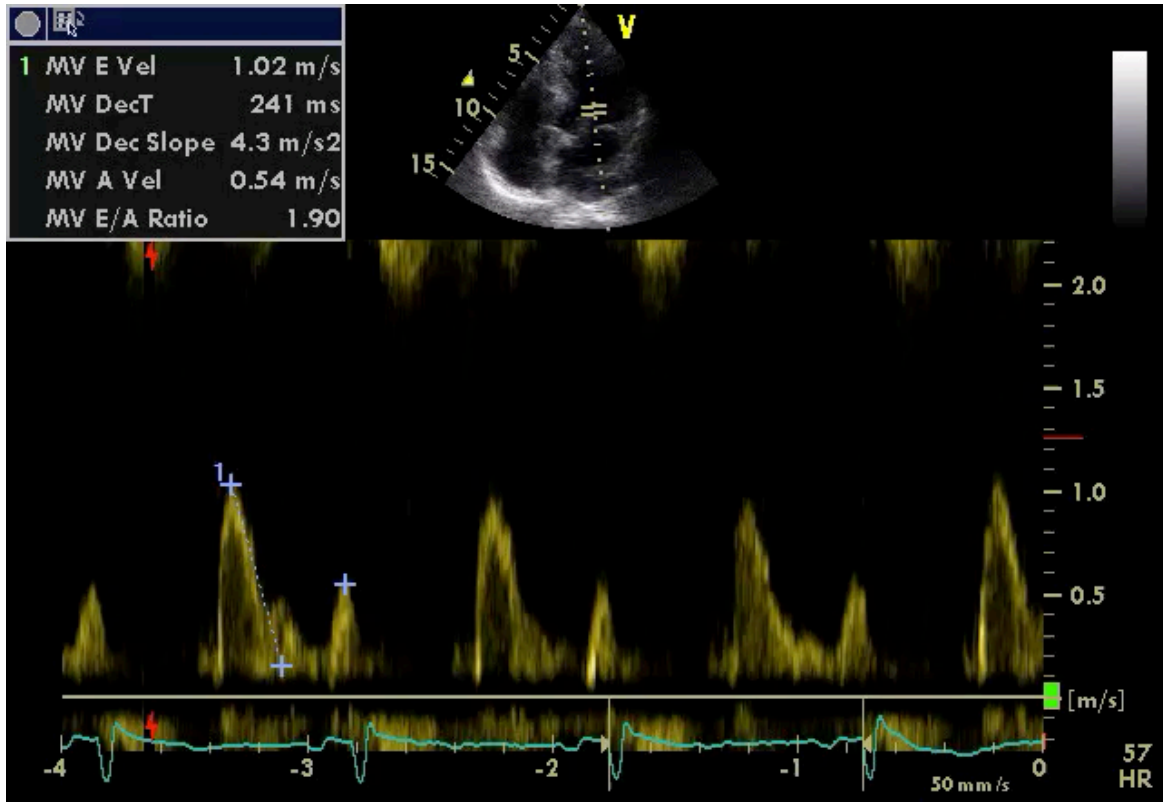
2024

2019





2025





Follow-up nefrologico

2023: 1,18 mg/dl, urea 50 g/l, eGFR Bis 1 43 ml/min, eGFR Bis 2 46 ml/min, Non disionie, emocromo nei limiti. All'esame delle urine proteinuria delle 24h 180 mg/24 h, albuminuria 111,8 mg

eGFR Bis 1 a giugno 2022 46 ml/min, eGFR Bis 2 49 ml/min

GFR a settembre 2021 52,5 ml/min

GFR a dicembre 2020 51,1 ml/min

GFR a novembre 2019 52ml/min

Take home messages

- Anticoagulation is mandatory in patients with Fabry Disease and Afib
- Microvascular dysfunction and Ischemia with non obstructive CAD is frequent in FD
- A Multidisciplinary team is necessary to take care of FD patients

Il fenotipo ipertrofico – MALATTIA DI ANDERSON-FABRY

Casi clinici interattivi

Guida Gianluigi, MD, FHFA

Cardiologia Universitaria

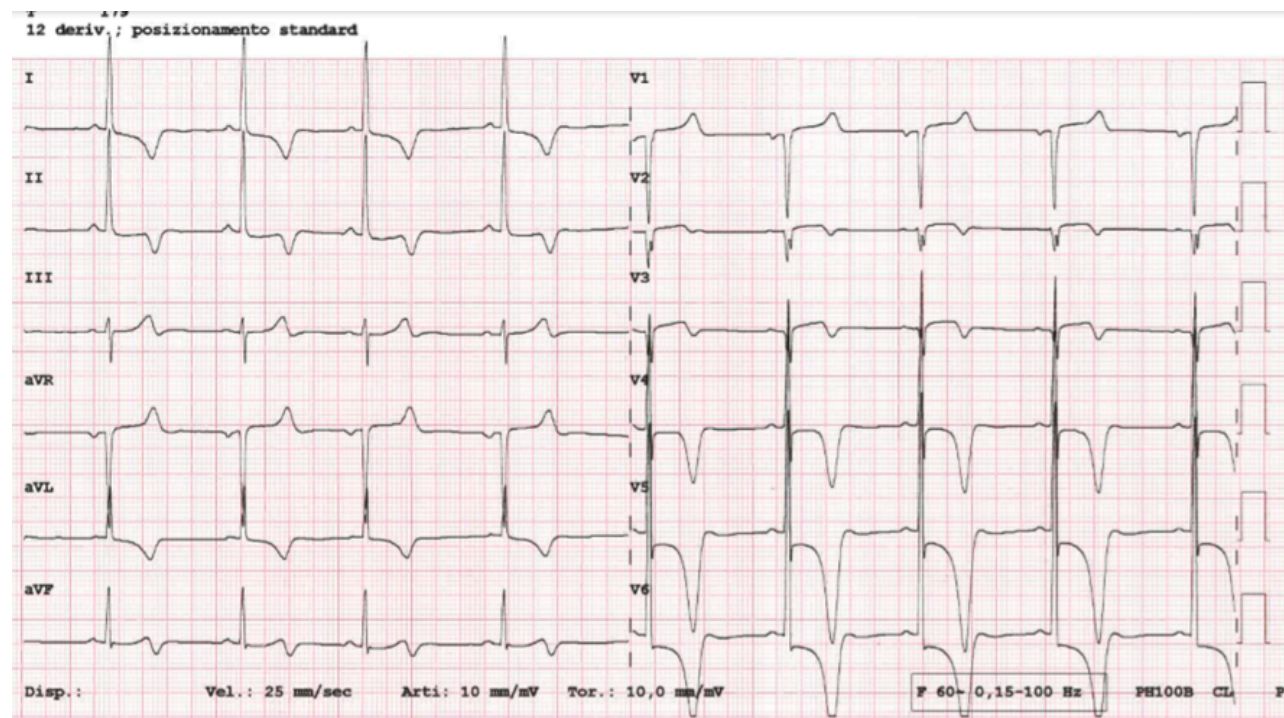


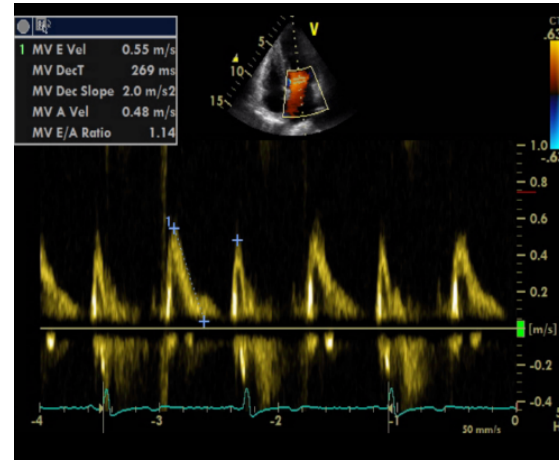
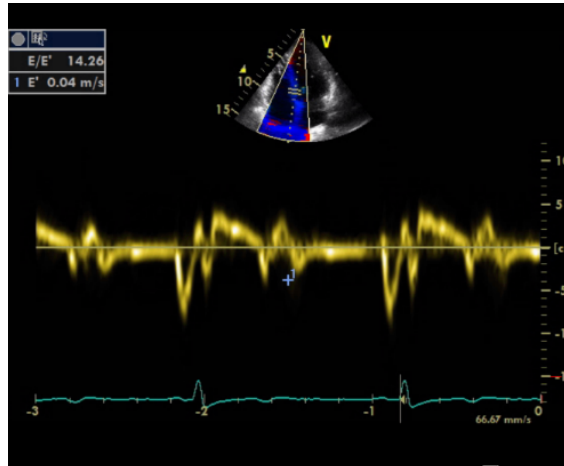
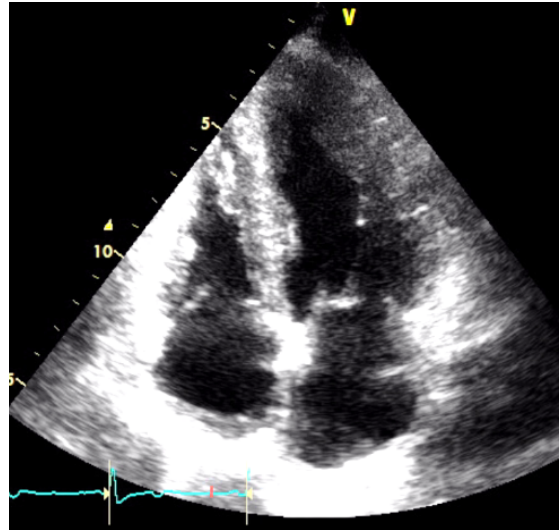
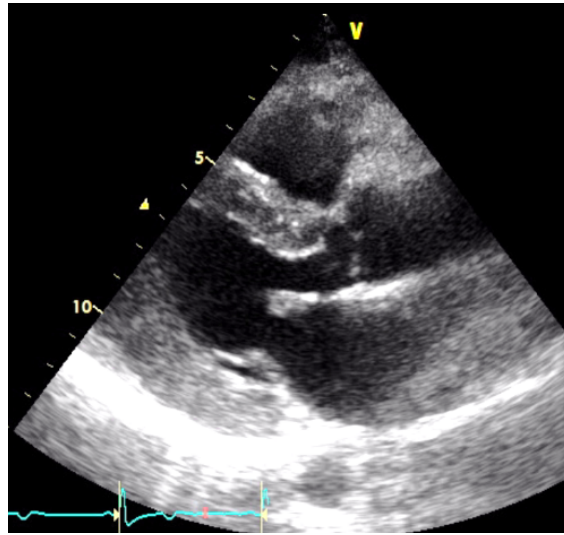
**I.R.C.C.S. Policlinico
San Donato**

Gruppo San Donato

Clinical Case

- ✓ Female, 54 y.o
- ✓ Previous quadrantectomy+radio+chemotherapy for breast carcinoma
- ✓ Family history of heart disease (mother and brother)
- ✓ Arterial hypertension
- ✓ Two episodes of dizziness and asthenia





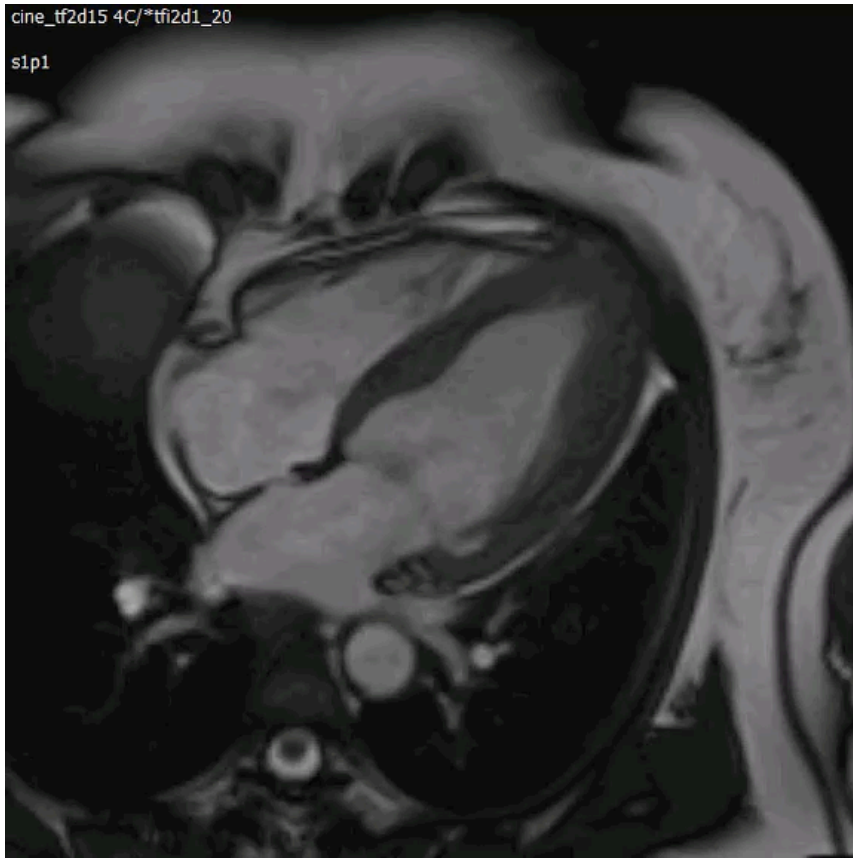
Which is the diagnosis?

Apical HCM



Cardiac Magnetic Resonance findings

cineSSFP, TIRM (T2-weighted), LGE



- Normal LV and RV volumes
- LVEF 79%
- Maximum LV wall thickness 13 mm (antero-basal septum)
- Apical hypertrophy (11-12 m, **7.7 mm/mq**, lateral apex)
- Apical/base ratio: 0.92
- LM mass index 103 g/m² (n.v. 44-77 g/m²)
- No LGE

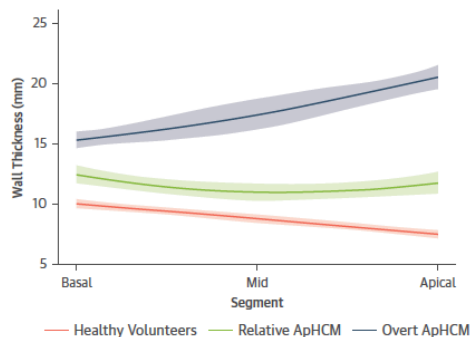


ORIGINAL RESEARCH

Improved Diagnostic Criteria for Apical Hypertrophic Cardiomyopathy

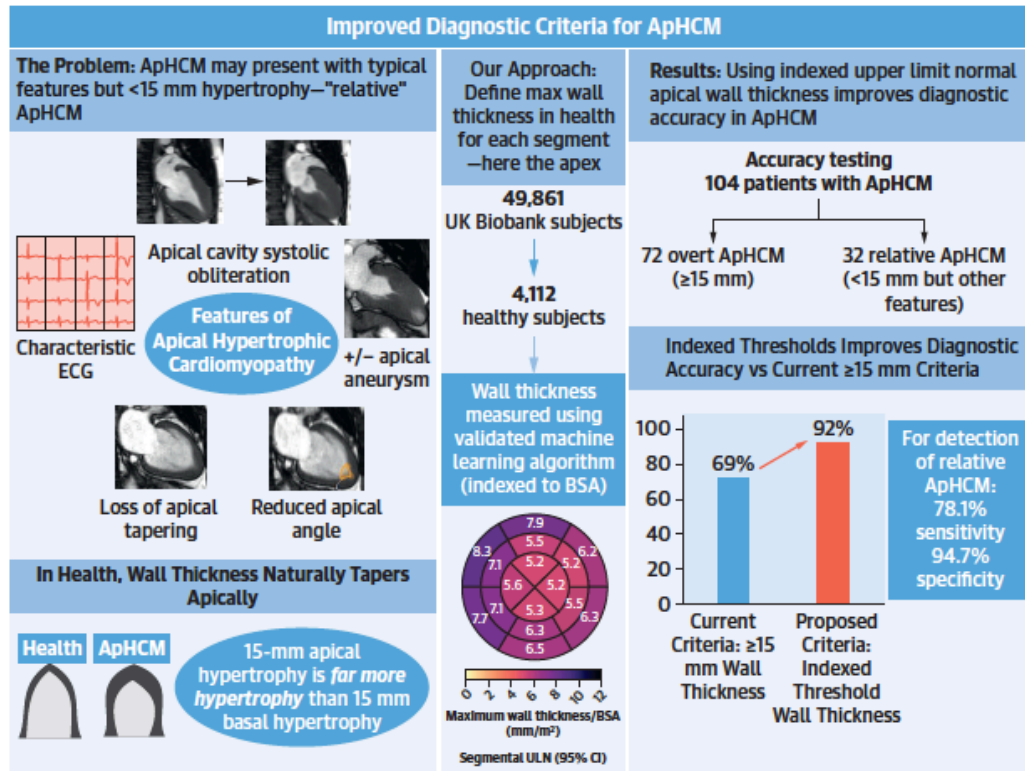
Rebecca K. Hughes, MBBS,^{a,b,*} Hunain Shiwani, BMBS,^{a,b,*} Stefania Rosmini, MD, PhD,^{b,c} João B. Augusto, MD,^{a,b,d} Liam Burke, BSc,^e Yue Jiang, BSc,^e Iain Pierce, PhD,^b George Joy, MBBS,^{a,b} Silvia Castelletti, MD,^f Michele Orini, PhD,^a Peter Kellman, PhD,^g Hui Xue, PhD,^g Luis R. Lopes, MD, PhD,^{a,b} Saidi Mohiddin, MBChB, MD,^{b,h} Thomas Treibel, MD, PhD,^{a,b} Charlotte Manisty, MA, MBBS, PhD,^{a,b} Gabriella Captur, MD, PhD, MSc,^{a,e,i} Rhodri Davies, MBBS, PhD,^{a,b,e,j} James C. Moon, MD, MBBS^{a,b,j}

FIGURE 3 Plots Demonstrating Variation in Maximum Wall Thickness From Base to Apex for 3 Cohorts



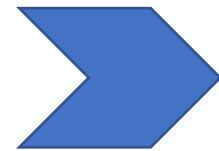
Healthy volunteer controls (apex:base ratio = 0.77), overt apical hypertrophic cardiomyopathy (ApHCM) (apex:base ratio = 1.31), and relative ApHCM (apex:base ratio between health and overt disease at 1). Abbreviation as in Figure 1.

CENTRAL ILLUSTRATION Using New Indexed Apical Wall Thickness Thresholds Improves the Diagnostic Accuracy of ApHCM



Hughes RK, et al. J Am Coll Cardiol Img. 2024;17(5):501-512.

ApHCM = apical hypertrophic cardiomyopathy; BSA = body surface area; ECG = electrocardiogram; ULN = upper limit of normal.



August 2016: dizziness, ECG negative
T-waves



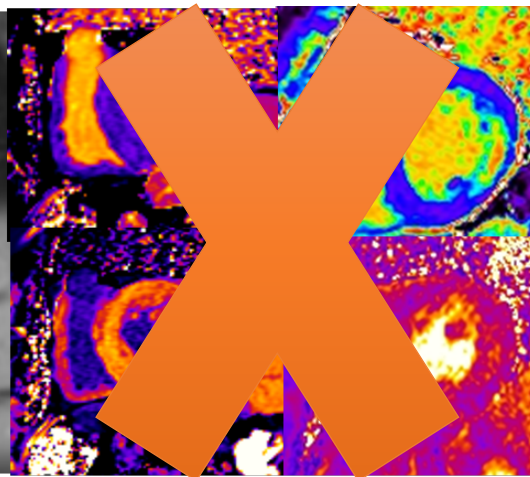
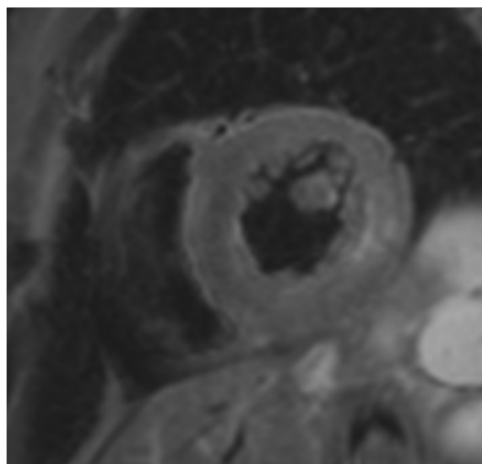
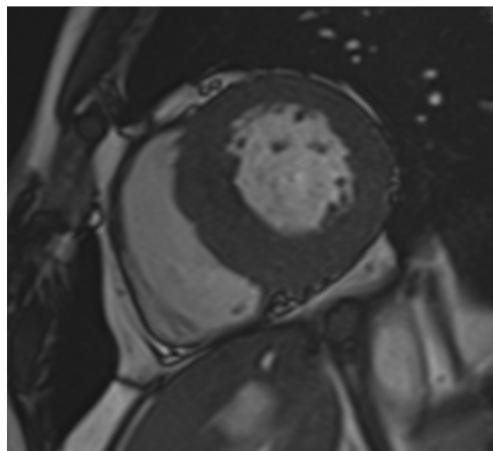
September 2016: echo and CMR
diagnosis of apical HCM
No genetic test performed



December 2018: follow-up CMR



Cardiac MRI protocol for hypertrophic phenotype



bSSFP

Volumes
EF
Mass
Morphology
CMR-FT



TISSUE CHARACTERIZATION

Contrast media at 0.10–0.15 mmol/kg – blood sample for hematocrit

T2w

Edema
Inflammation

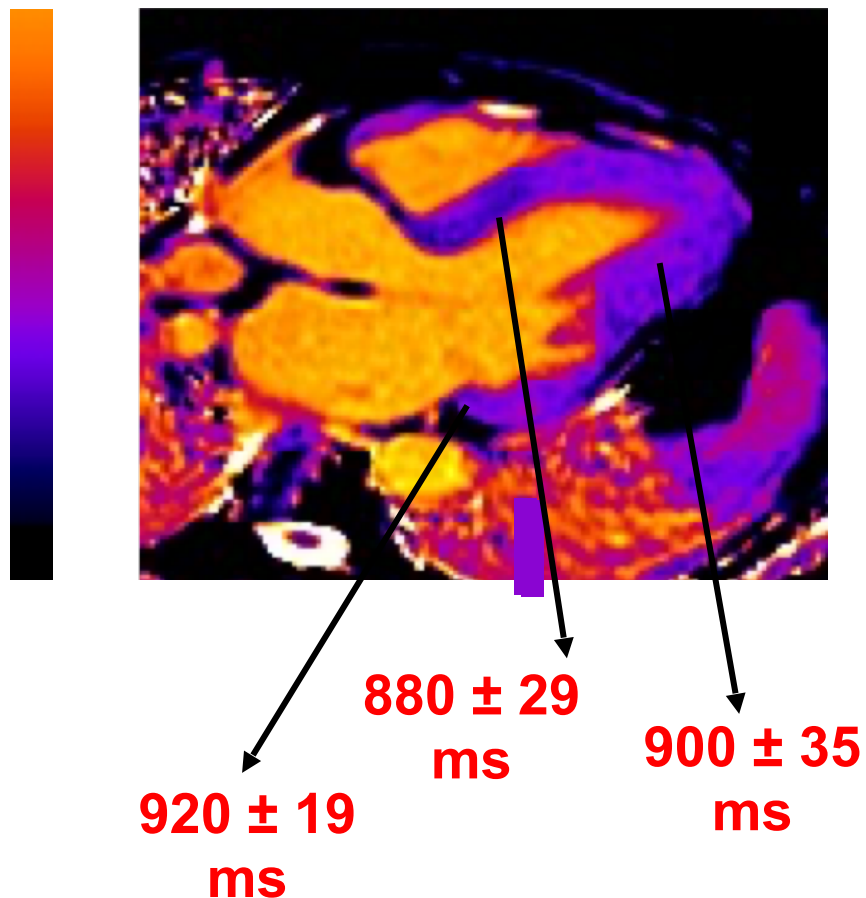
Mapping

Reduction of T1 ->
myocardial storage
Pseudonormalisation of
T1 in LGE areas

LGE

Myocardial fibrosis/oedema





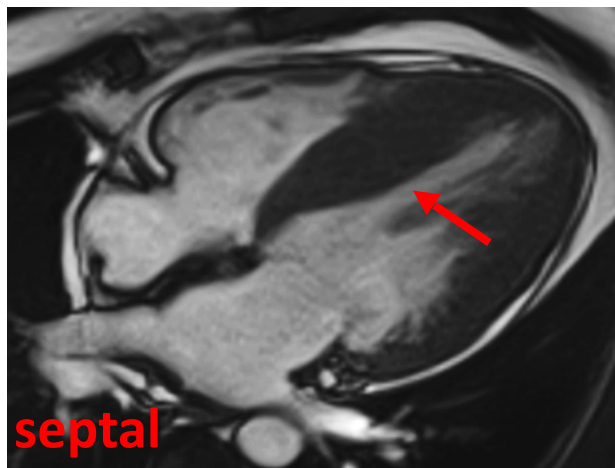
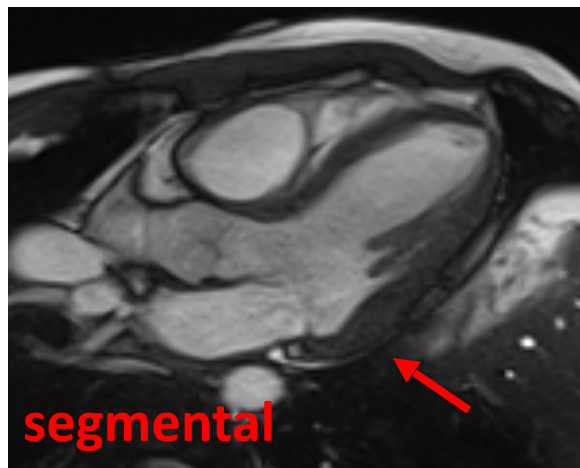
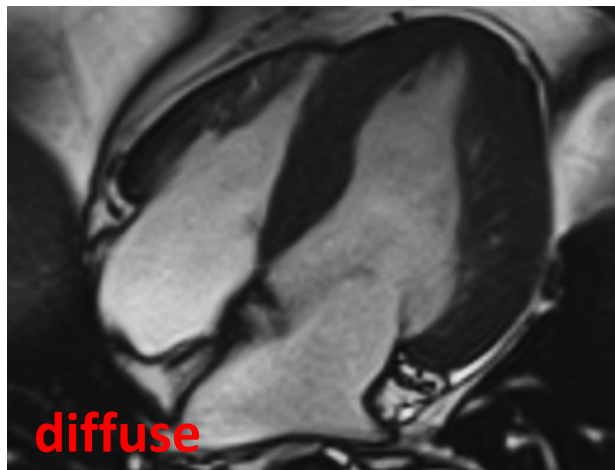
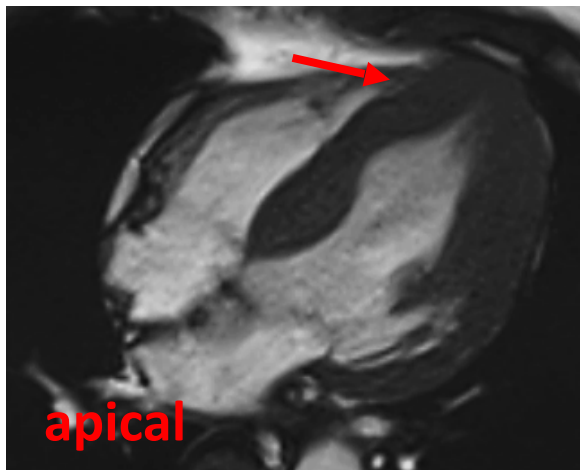
T1 map (MOLLI) normal value: 1009±21 ms

Mutation of GLA gene Exon 5 c.644 A>G
p.N215S *
Cardiac variant of Fabry disease

Alpha-galactosidase A activity **1.1 nmol/h/ml**
(normal value >3 nmol/h/ml)

LysoGb3 **5,58 nMol/L**
(normal value 0,08-1,13 nMol/L)



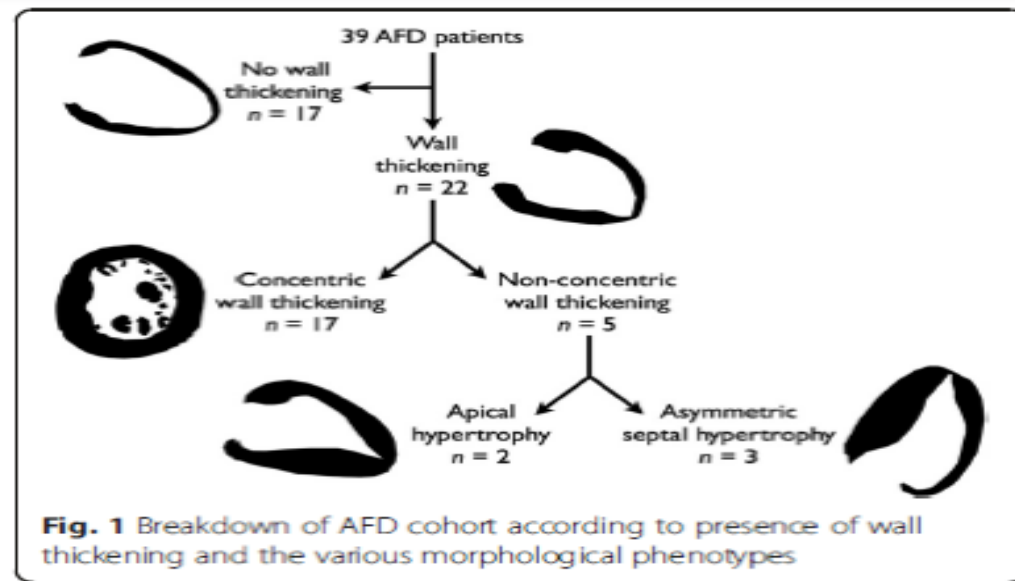


RESEARCH

Open Access

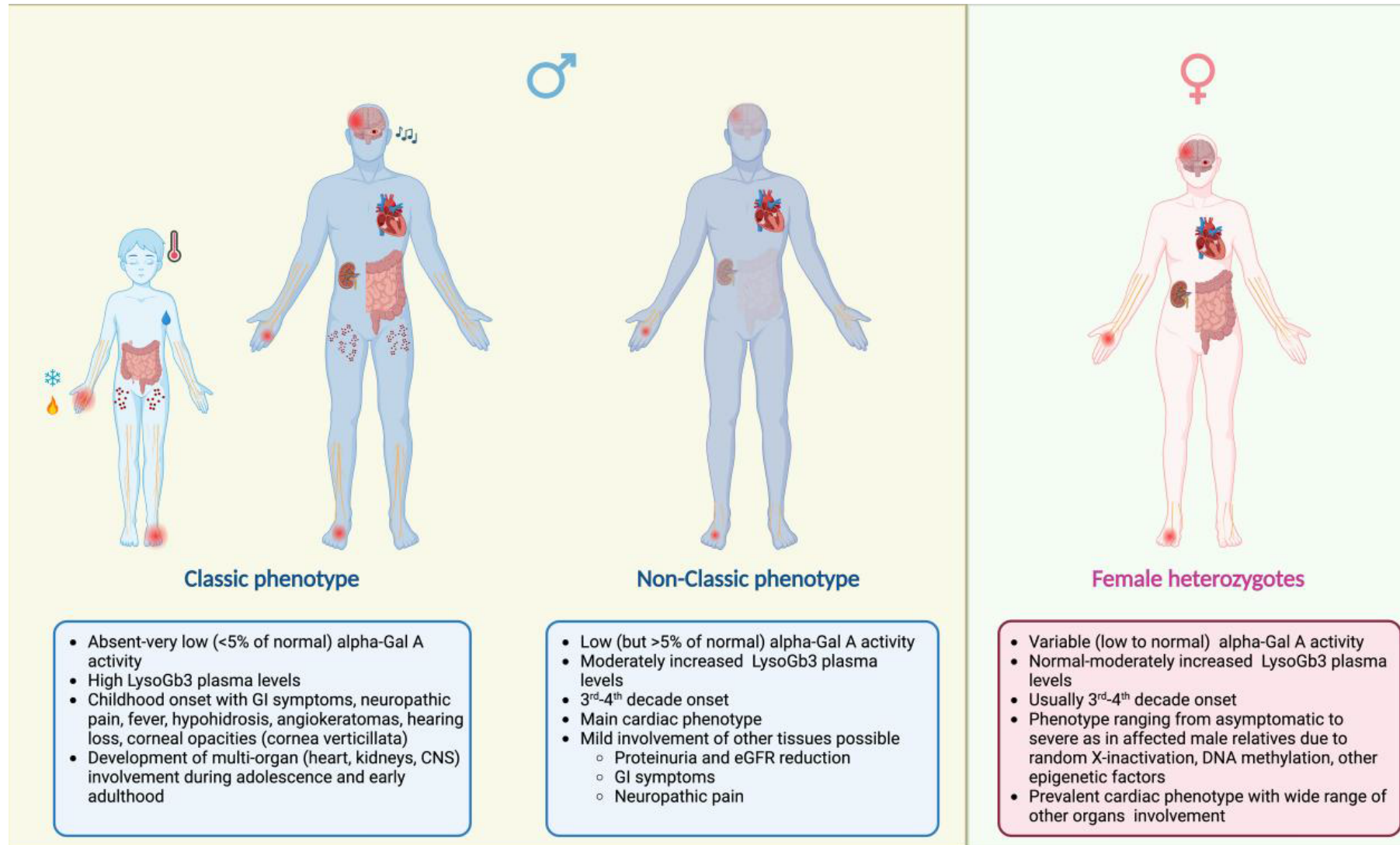


Cardiovascular magnetic resonance demonstration of the spectrum of morphological phenotypes and patterns of myocardial scarring in Anderson-Fabry disease



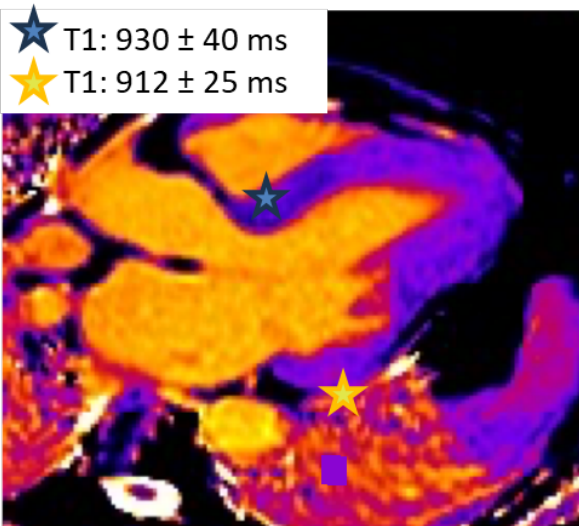
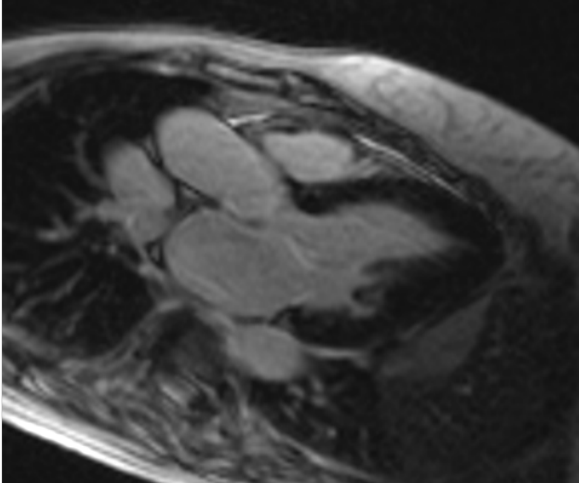
Deva et al, JCMR 2016



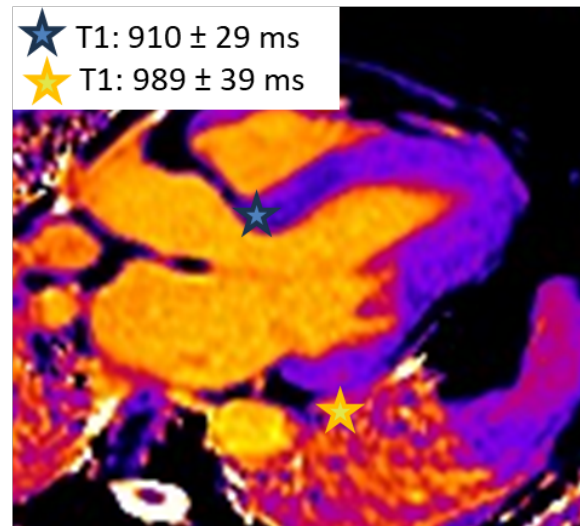
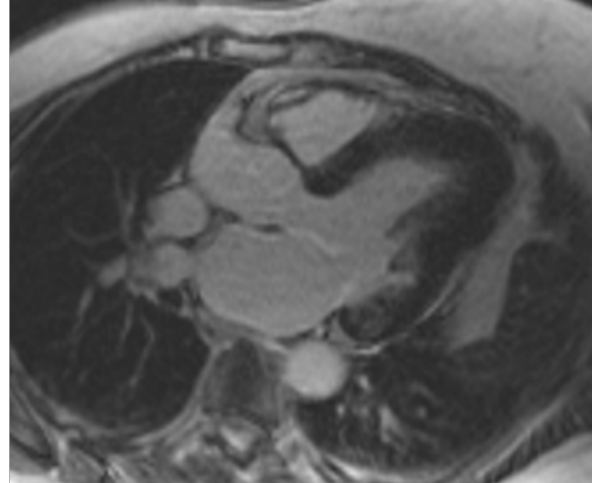


Pieroni et al, EHJ 2024

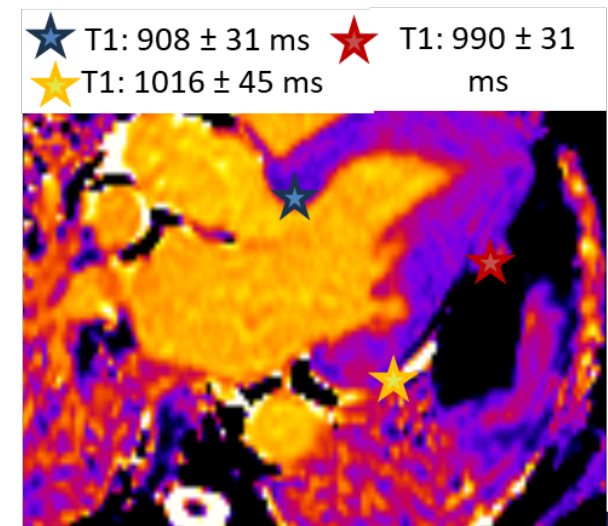
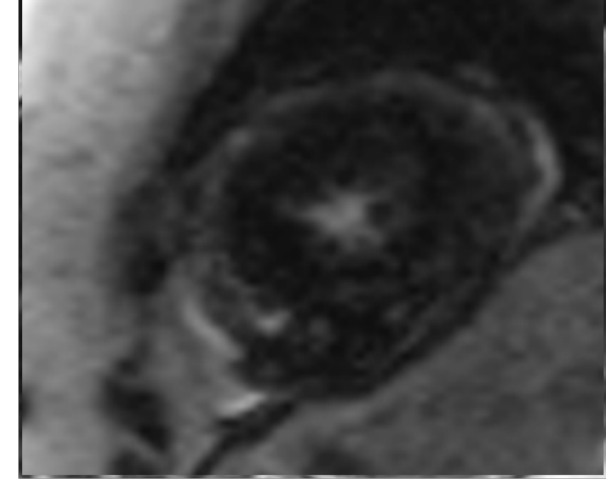
2018



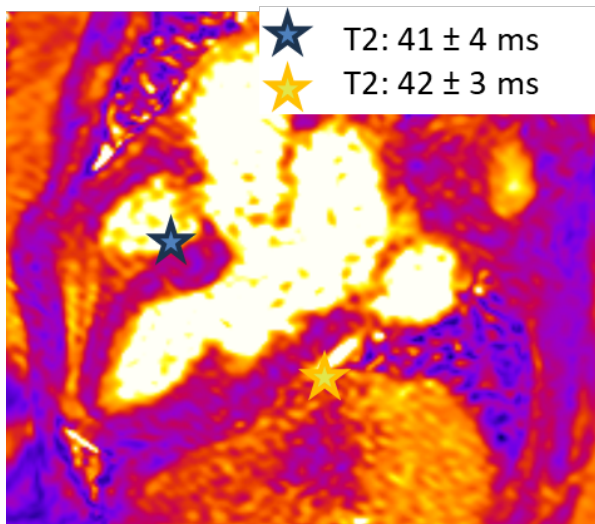
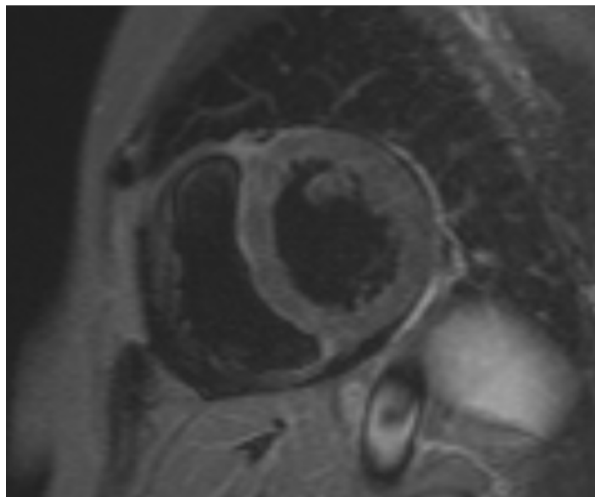
2020



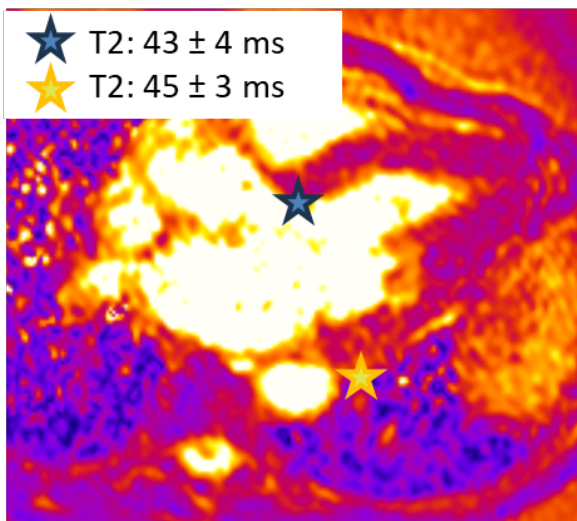
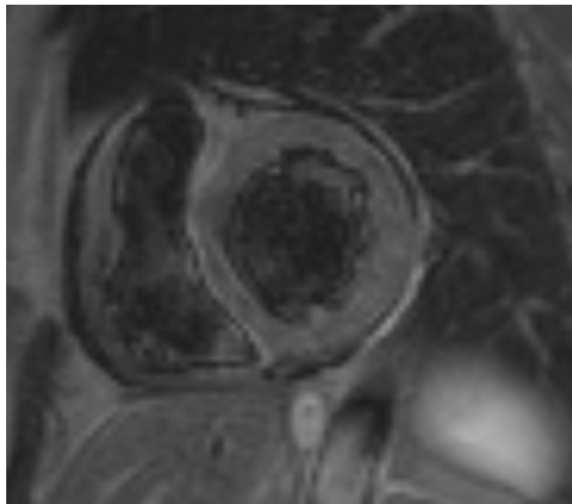
2022



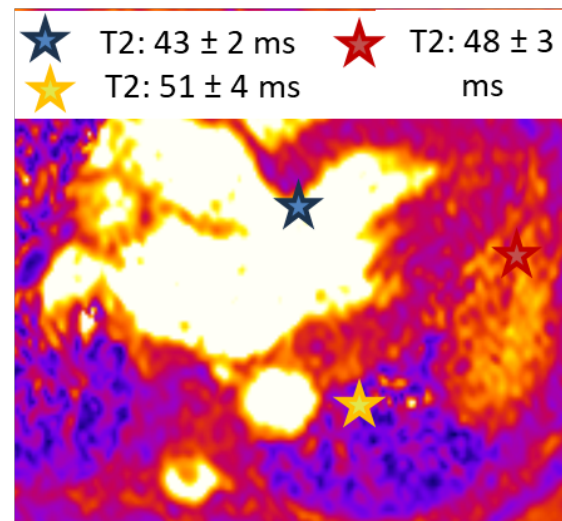
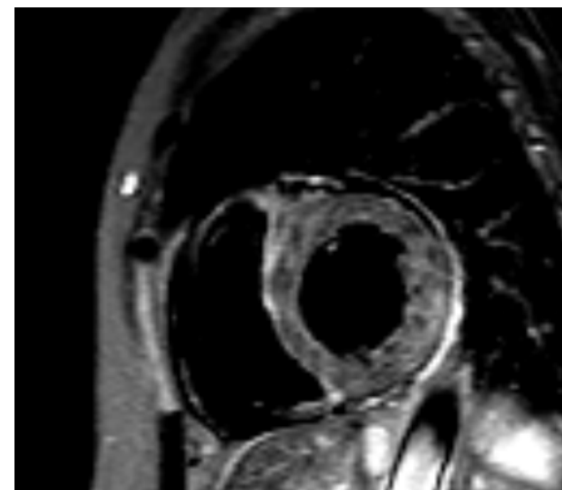
2018

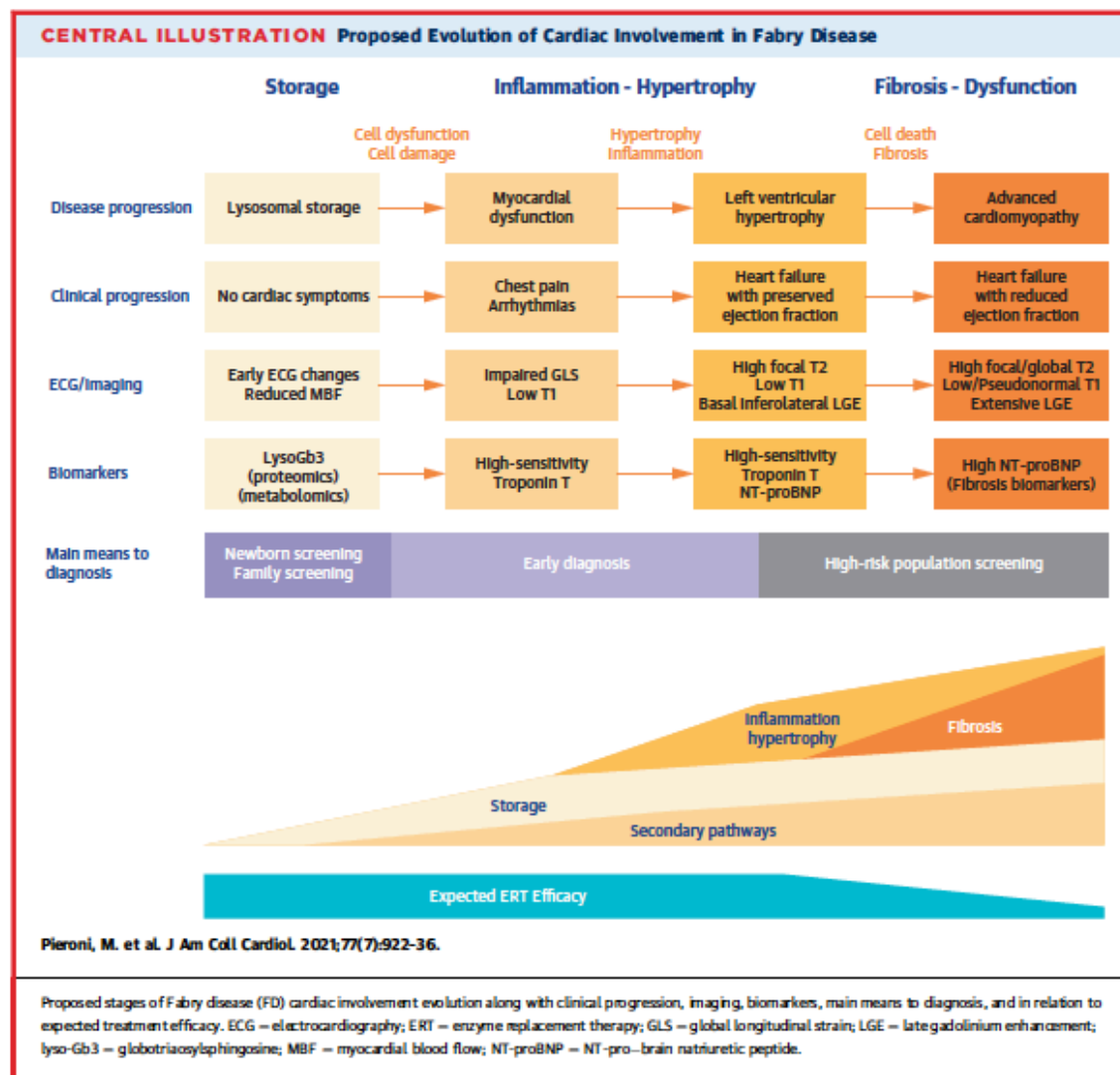


2020



2022





Take-home messages

- **CMR protocol for hypertrophic phenotype requires mapping sequences**
- T1 mapping is essential for the differential diagnosis of hypertrophic phenotypes (athlete's heart, amyloidosis, hypertrophic cardiomyopathy, Fabry disease).
- In Fabry disease, native T1 is useful for non-invasive early detection of myocardial storage.

