10° CONGRESSO NAZIONALE

CAMPUS Cuore

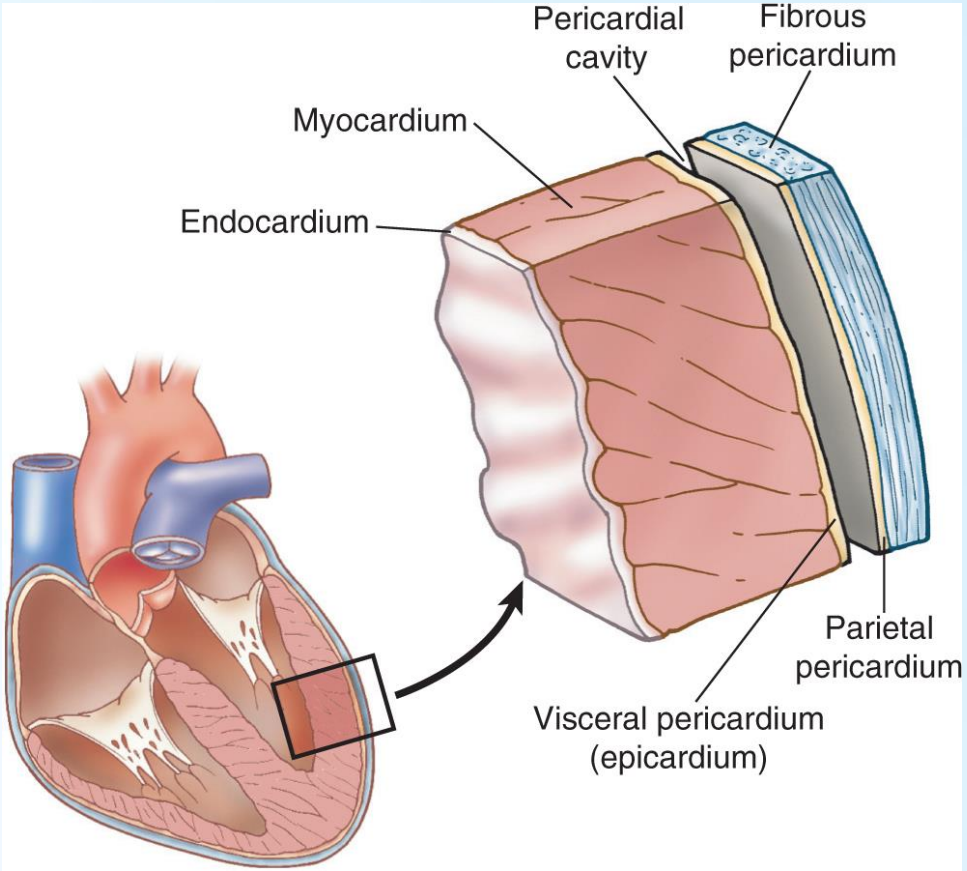
Quello che le Linee Guida Non Dicono

Napoli
Hotel Excelsior
14-15 aprile 2023

MIOPERICARDITI: LE EVIDENZE SCIENTIFICHE

Francesco Loffredo

Layers of the Heart



Pericarditis

- Pericardium surrounds the external surface of the heart and the roots of the great vessels.
- Two layers: outer tough fibrous pericardium; inner serous layer
- Serous pericardium has two layers:
  - The parietal layer lines the internal surface of the fibrous membrane.
  - It extends to the great vessels, where it then folds over on itself to form the inner visceral layer (epicardium).
- 10 to 50 mL of clear serous fluid lies between these layers and acts as a lubricant.
- The pericardium helps restrain the heart and isolate it from infections in the surrounding structures.
- Pericarditis is inflammation of the pericardium.

Acute pericarditis etiologies: Data from published clinical studies with unselected populations

	Western Europe (2007-2012)[1]	Africa (1995-2001)[2]
Idiopathic*	516 (55.0%)	32 (13.7%)
Specific etiology	417 (46.0%)	201 (86.3%)
▪ Neoplastic¶	85 (8.9%)	22 (9.4%)
▪ Tuberculosis¶	4 (<1.0%)	161 (69.5%)
▪ Autoimmune etiologies¶	25 (2.6%)Δ	12 (5.2%)
▪ Purulent¶	29 (3.0%)	5 (2.1%)

* Most idiopathic cases are likely viral.

¶ As a fraction of the entire sample.

Δ Autoimmune pericarditis can be caused by autoimmune disease or as a complication of myocardial infarction (MI) or cardiac surgery. In this table, we only report pericarditis caused by autoimmune disease, while the original paper (Gouriet et al) reports an additional 188 cases related to MI or cardiac surgery.

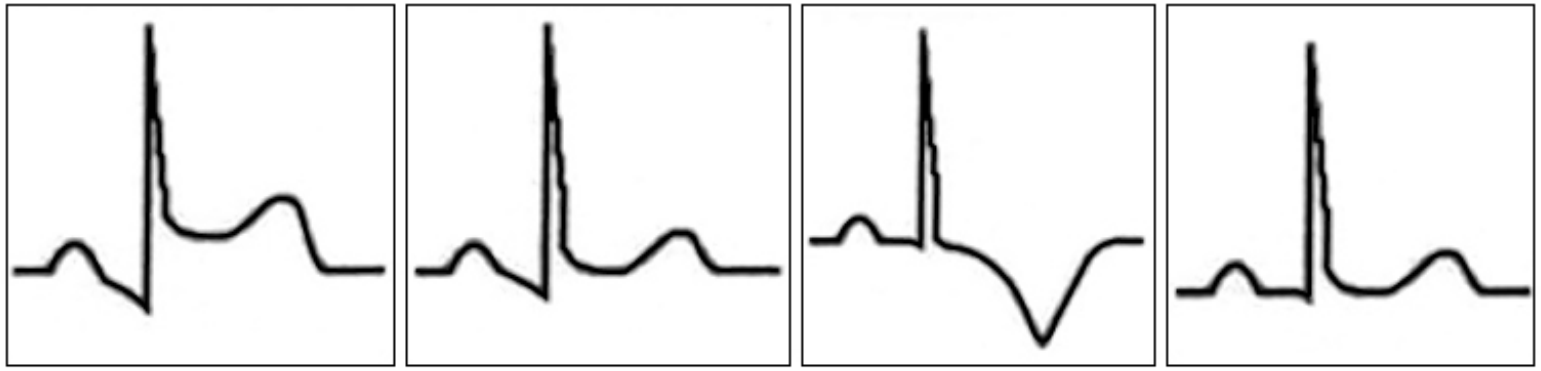
Data from:

1. *Gouriet F, Levy PY, Casalta JP, et al. Etiology of pericarditis in a prospective cohort of 1162 cases. Am J Med 2015; 128:784.*
2. *Reuter H, Burgess LJ, Louw VJ, et al. The management of tuberculous*

Diagnostic criteria for acute and recurrent pericarditis

Acute pericarditis (at least 2 criteria of 4):
Typical pleuritic chest pain
Pericardial friction rub
Suggestive ECG changes (typically widespread ST segment elevation, PR depression)
New or worsening pericardial effusion

Classical four stages of ECG evolution in acute pericarditis



Stage I | Stage II | Stage III | Stage IV

Stage I: diffuse ST elevation with PR depression

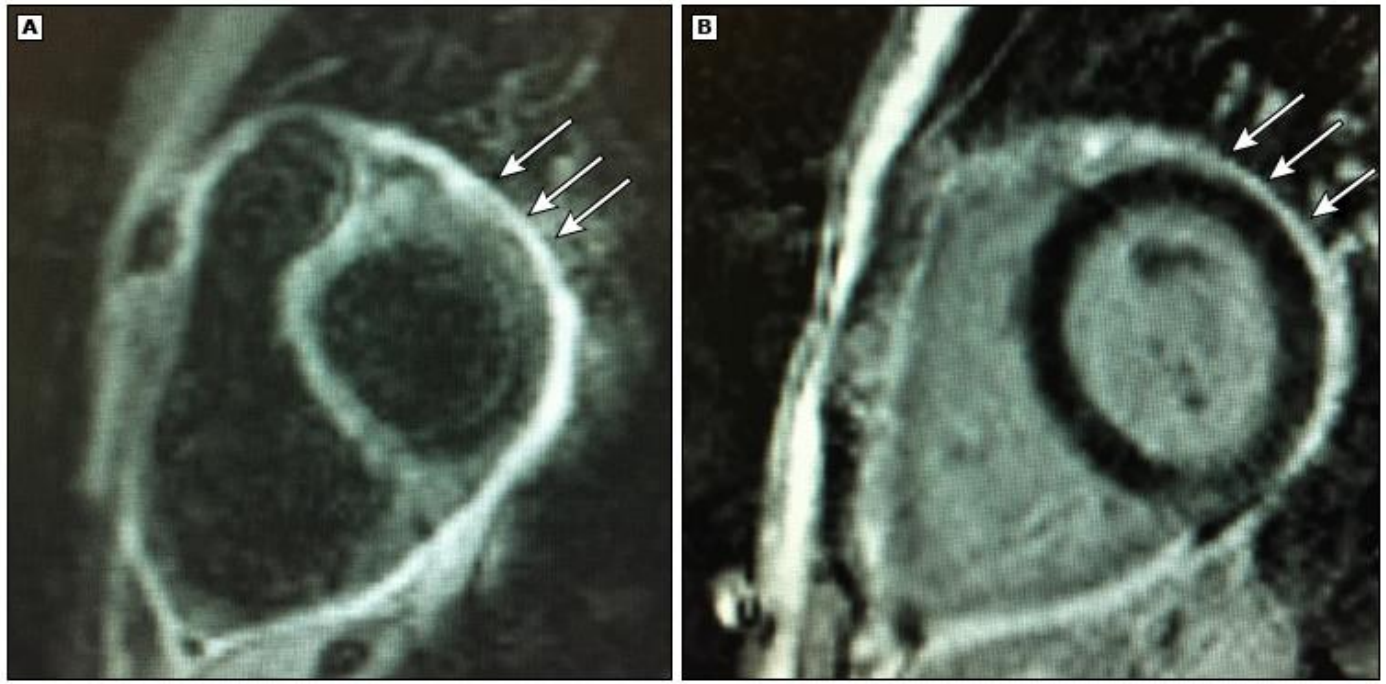
Stage II: normalization of ST and PR segments

Stage III: diffuse deep T-wave inversions

Stage IV: normalization of the ECG

ECG: electrocardiogram.

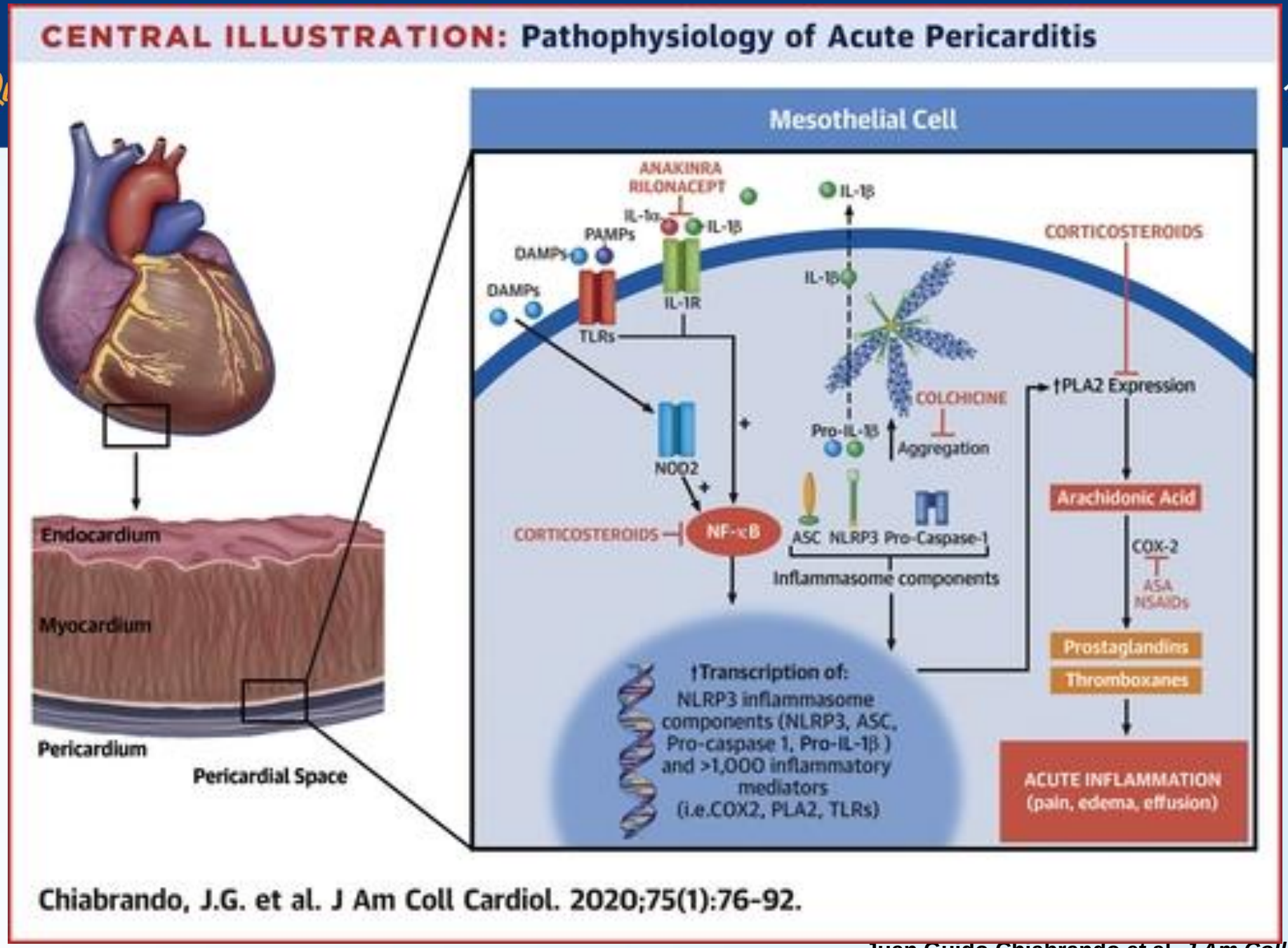
Pericardial edema and LGE by CMR



(A) Pericardial edema.

(B) Pericardial LGE.

LGE: late gadolinium enhancement; CMR: cardiac magnetic resonance.



Juan Guido Chiabrando et al. *J Am Coll Cardiol* 2020; 75:76-92.

Drug therapy in acute and recurrent pericarditis for adult patients

Drug	Antiinflammatory dose	Duration of initial or maintenance dose*	Tapering regimen¶
First-line therapy for most patients:Δ			
Aspirin◇	650 to 1000 mg orally 3 times daily	1 to 2 weeks	Decrease dose by about 250 mg per week
or			
Ibuprofen◇	600 to 800 mg orally 3 times daily§	1 to 2 weeks	Decrease dose by 200 mg per week
or			
Indomethacin◇	25 to 50 mg orally 3 times daily	1 to 2 weeks	Decrease dose by 25 mg per week
plus			
Colchicine¥‡	0.5 to 0.6 mg orally 2 times daily	3 months (acute) 6 months or more (recurrent)	Usually not tapered
Second-line therapy (for refractory cases or patients with a contraindication to NSAID therapy):			
Prednisone	0.2 to 0.5 mg/kg daily	2 to 4 weeks (acute or recurrent†)	Gradual tapering over 2 to 3 months; refer to UpToDate topic review of treatment of acute pericarditis, section on glucocorticoids
plus			
Colchicine¥‡	0.5 to 0.6 mg orally 2 times daily	3 months or more (acute) 6 months or more (recurrent) Colchicine is generally continued for 4 weeks or more after discontinuation of glucocorticoid	Usually not tapered
Third-line therapy: Second-line therapy plus aspirin dosed as for first-line therapy			
Fourth-line therapy: One of the following agents (or pericardiectomy)			
Rilonacept	Loading dose of 320 mg delivered as 2 SC doses of 160 mg on the same day at 2 different sites	160 mg SC weekly for several months	Slow taper over 3 months or more
Anakinra	1 to 2 mg/kg daily (maximum dose 100 mg daily)	Several months	Slow taper over 3 months or more
Azathioprine	1 mg/kg daily increasing to 2 to 3 mg/kg daily (maximum dose 150 mg daily)	Several months	Not tapered
IVIG	400 to 500 mg/kg IV daily	5 days (may repeat after 1 month)	Not tapered

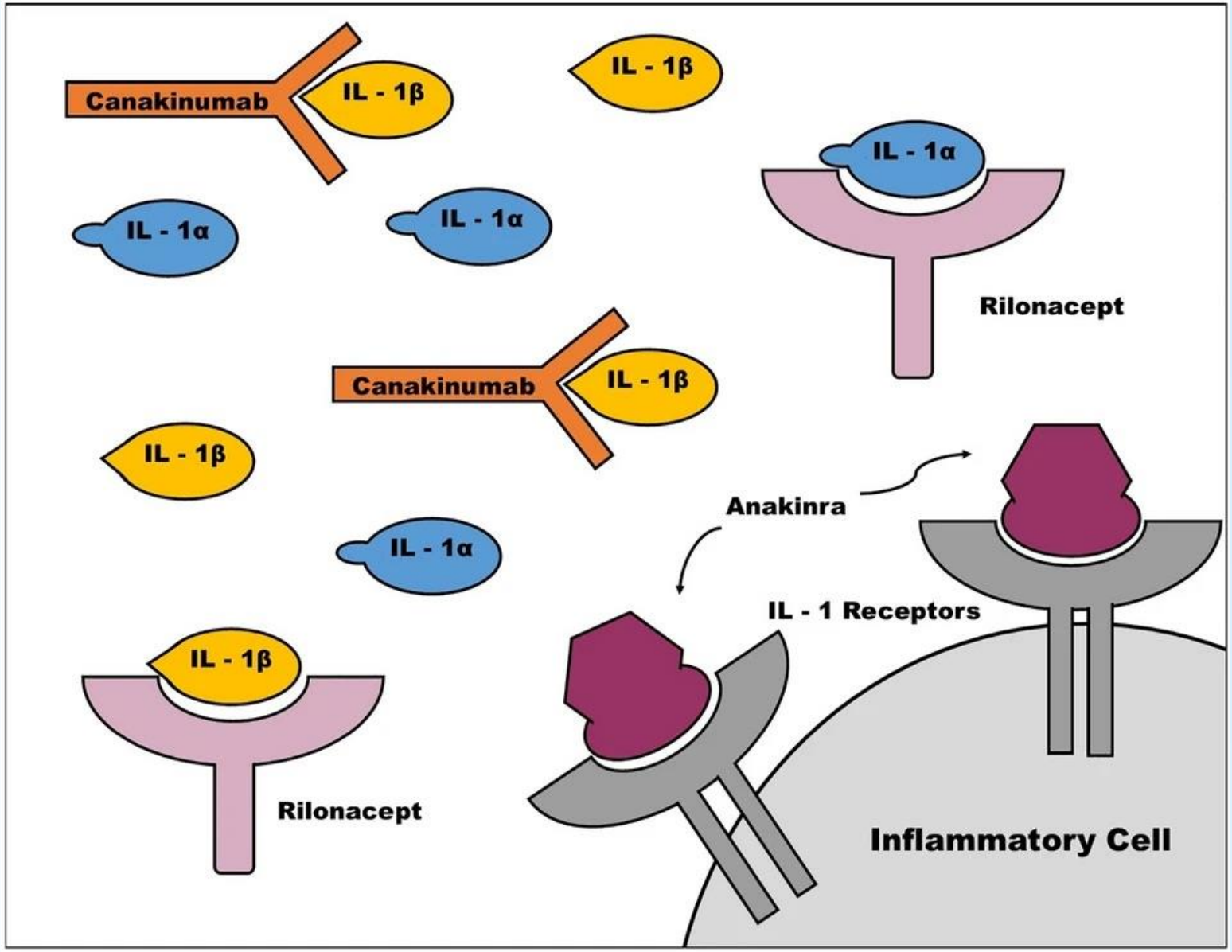
NSAID: nonsteroidal antiinflammatory drug; SC: subcutaneous injection; IVIG: intravenous immunoglobulin; IV: intravenous; CRP: C-reactive

Table 1 Mechanism of action, half-life, dosing, and common adverse effects for the IL-1 antagonists

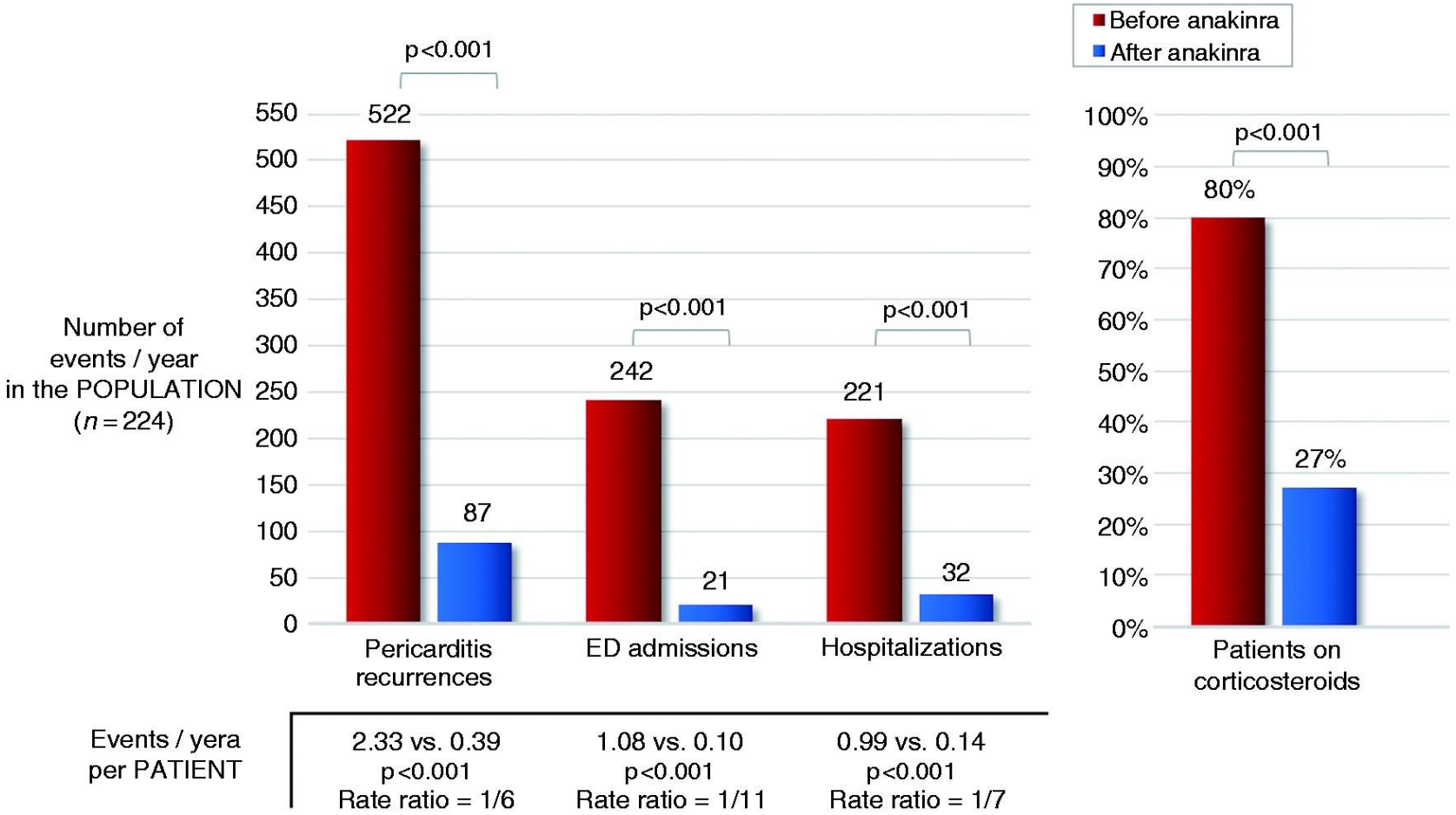
From: Interleukin-1 Antagonists for the Treatment of Recurrent Pericarditis

Drug	Mechanism of action	Half-life	Dosage	Common adverse effects
Anakinra	Interleukin-1 receptor antagonist	2.6 hours [33]	100 mg daily (or 1 mg/kg/day) [33, 72]	Injection-site reactions [59, 60, 71] Increased skin and respiratory infections [44, 51, 58,59,60] Transaminitis [51] Leukopenia [58, 60]
Canakinumab	Human IgGκ monoclonal antibody to IL-1β	26.1 days [36]	2–5 mg/kg/month [83, 84]	Increased skin and respiratory infections [46, 67, 68] Transaminitis [46, 53, 66, 67] Increased cholesterol and triglycerides [66]
Rilonacept	Circulating IL-1 receptor trap	7 days [39]	320 mg loading dose followed by 160 mg weekly [76]	Injection-site reactions [48, 49, 55, 64] Increased skin and respiratory infections [48, 49, 55] Transaminitis [48, 49, 55, 70] Leukopenia [48, 55] Increased cholesterol and triglycerides [49]

IG immunoglobulin, *IL* interleukin



Recurrences, emergency department admissions, hospital admissions before and after anakinra

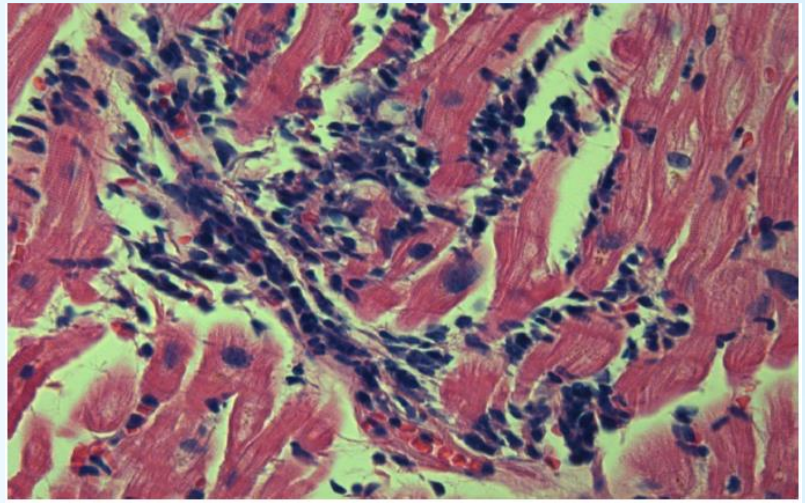


Eur. J. Prev. Cardiol., Volume 27, Issue 9, 1 June 2020, Pages 956–964, https://doi.org/10.1177/2047487319879534

LA MIOCARDITE

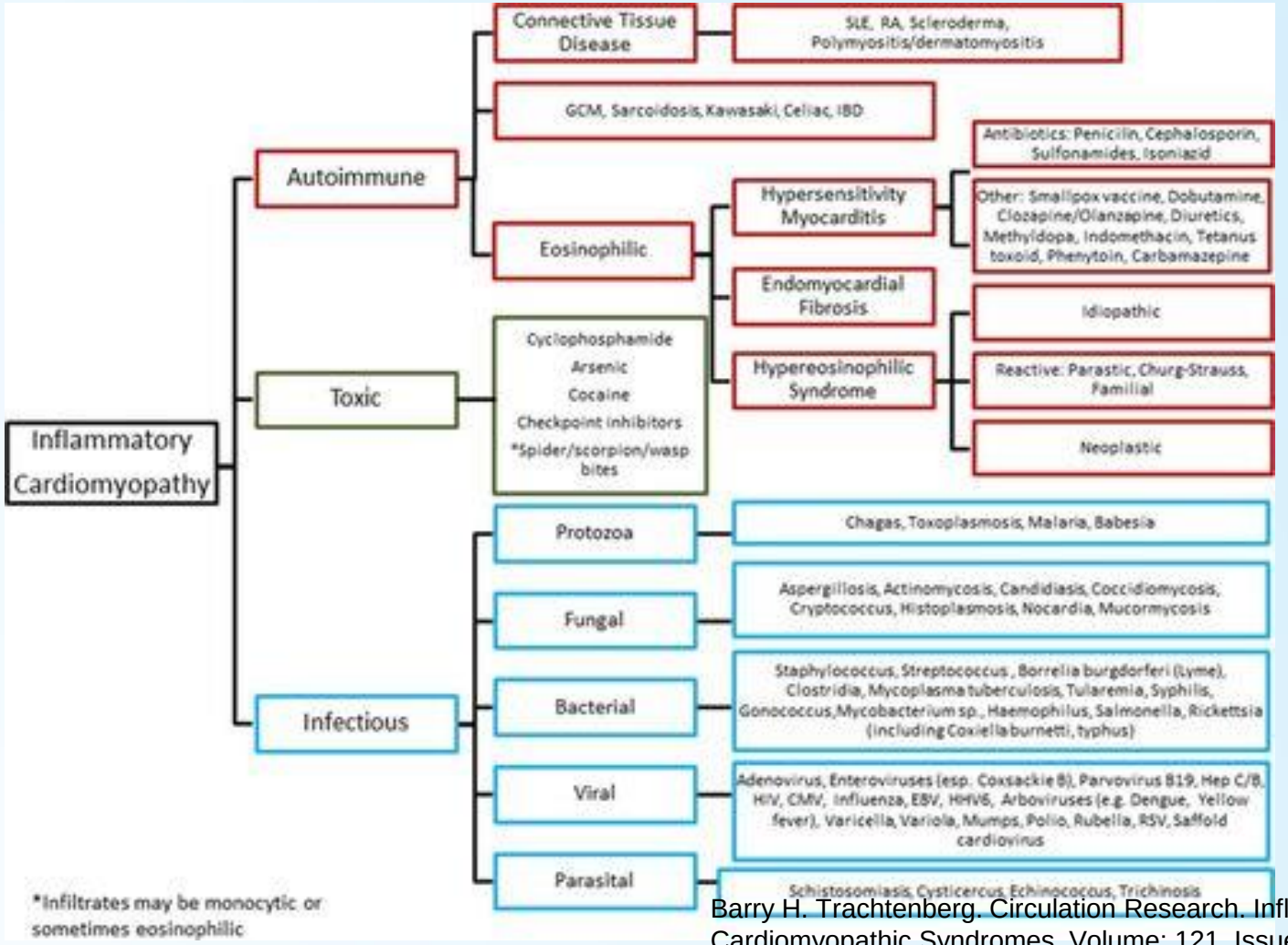
World Health Organization

danno infiammatorio del miocardio secondario a diversi possibili agenti endogeni o esogeni

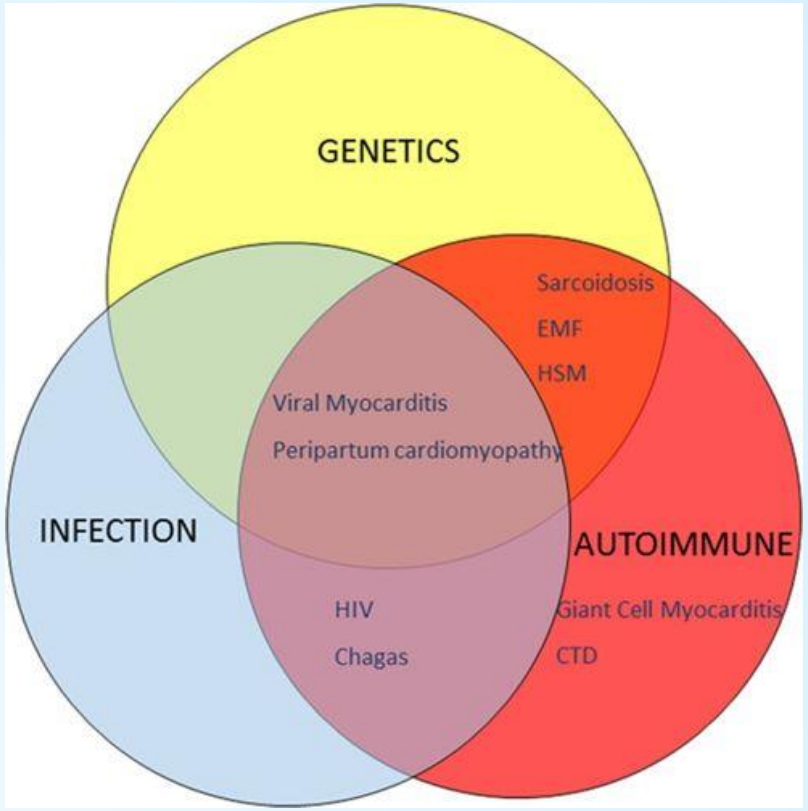


Epidemiologia

- Nel Global Burden of Disease report del 2019, il tasso di miocardite era 6.1 per 100,000 negli uomini e 4.4 per 100,000 nelle donne tra 35 e 39 anni.
- La mortalità in questo braccio di età era riportata a 0.2 per 100,000 negli uomini rispetto a 0.1 per 100,000 nelle donne.



Barry H. Trachtenberg. Circulation Research. Inflammatory Cardiomyopathic Syndromes, Volume: 121, Issue: 7, Pages: 803-818, DOI: (10.1161/CIRCRESAHA.117.310221)



Barry H. Trachtenberg. Circulation Research. Inflammatory Cardiomyopathic Syndromes, Volume: 121, Issue: 7, Pages: 803-818, DOI: (10.1161/CIRCRESAHA.117.310221)

LA MIOCARDITE

danno infiammatorio del miocardio secondario a diversi possibili agenti endogeni o esogeni

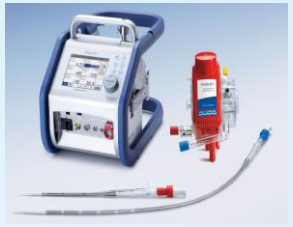
ATTIVA	CRONICA	CARDIOMIOPATIA INFIAMMATORIA CRONICA
Istologia: INFILTRATO INFIAMMATORIO CON O SENZA FIBROSI	PERSISTENTE INFIAMMAZIONE>1 MESE Istologia: fibrosi SENZA necrosi o anormalità dei miociti	INFIAMMAZIONE + CMD O CM IPOCINETICA NON DILATATA Istologia: fibrosi CON necrosi o anormalità dei miociti

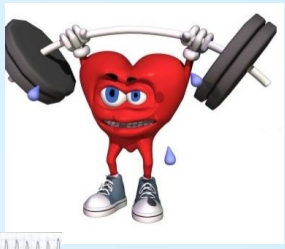
Management of Acute Myocarditis and Chronic Inflammatory Cardiomyopathy
An Expert Consensus Document
Enrico Ammirati, Maria Frigerio

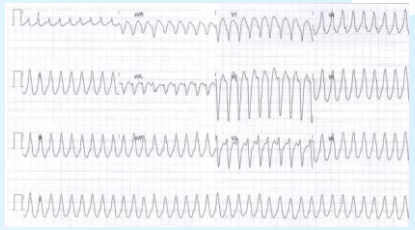
ESORDIO COMPLICATO DA:

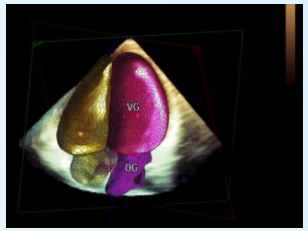
- QUADRO FULMINANTE
- ARITMIE VENTRICOLARI SOSTENUTE
- DISFUNZIONE VENTRICOLARE SINISTRA

ESORDIO NON COMPLICATO









Diagnosi

Definitiva si basa sui risultati della BEM (criteri istologici di Dallas, sens 10-35%), integrati con ricerca PCR genoma virale e analisi immunoistochimica.

Inflammatory infiltrate of the myocardium with necrosis and/or degeneration of adjacent myocytes not typical of the ischemic damage associated with coronary artery disease

Table 3 Indications for endomyocardial biopsy

Clinical presentation
• Suspected fulminant myocarditis or acute myocarditis with acute HF, LV dysfunction and/or rhythm disorders. • Suspected myocarditis in haemodynamically stable patients.

LA MIOCARDITE

danno infiammatorio del miocardio secondario a diversi possibili agenti endogeni o esogeni

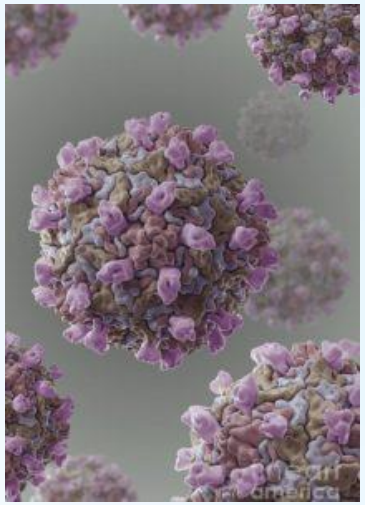
LINFOCITARIA	A CELLULE GIGANTI/SARCOIDOSI	EOSINOFILA
Istologia: infiltrato infiammatorio con linfociti (da Virus o ICI)	Istologia: granuloma/attivazione macrofagica	Istologia: infiltrato eosinofilo (eosinofilia periferica non sempre presente)

Management of Acute Myocarditis and Chronic Inflammatory Cardiomyopathy
An Expert Consensus Document
Enrico Ammirati, Maria Frigerio

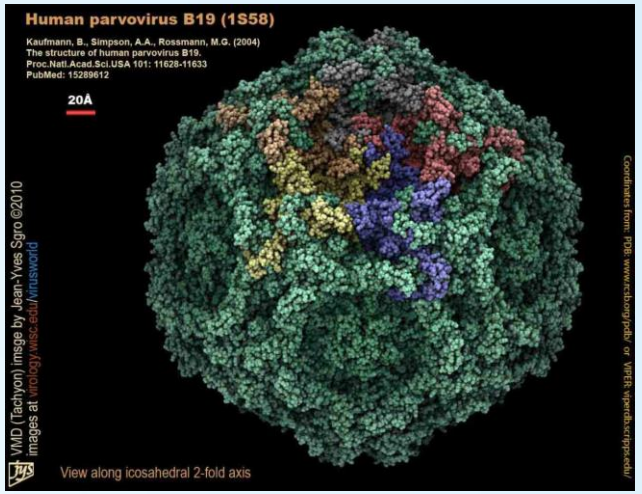
Lake Louise criteria 2010 and updated 2018

Disease	Method	Finding	Sensitivity	Specificity
Myocarditis[85–87]				
Early phase (<14 days from symptom onset)	CMR	**T1 weighted imaging**: early gadolinium enhancement is suggestive of hyperaemia and capillary leak. LGE is suggestive of cell necrosis and fibrosis. **T2 weighted imaging**: presence of myocardial oedema (typically subepicardial)	67%	91%
Late phase (>14 days after symptom onset)	CMR	**T2 weighted imaging**: imaging modality with the greatest diagnostic accuracy	71%	72%

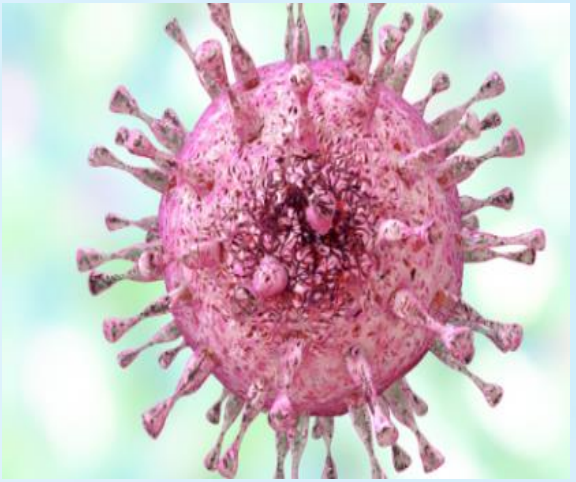
LA MIOCARDITE ACUTA VIRALE



enterovirus

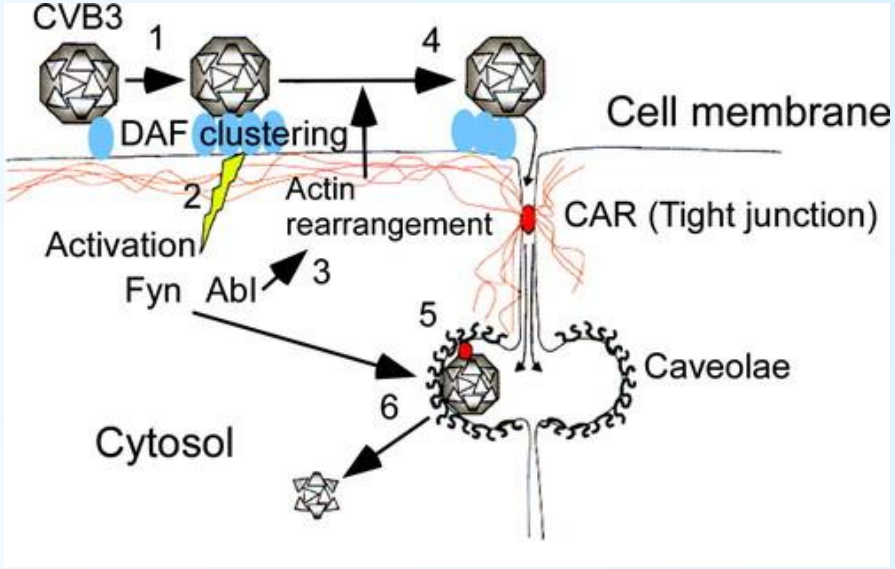


PV B19



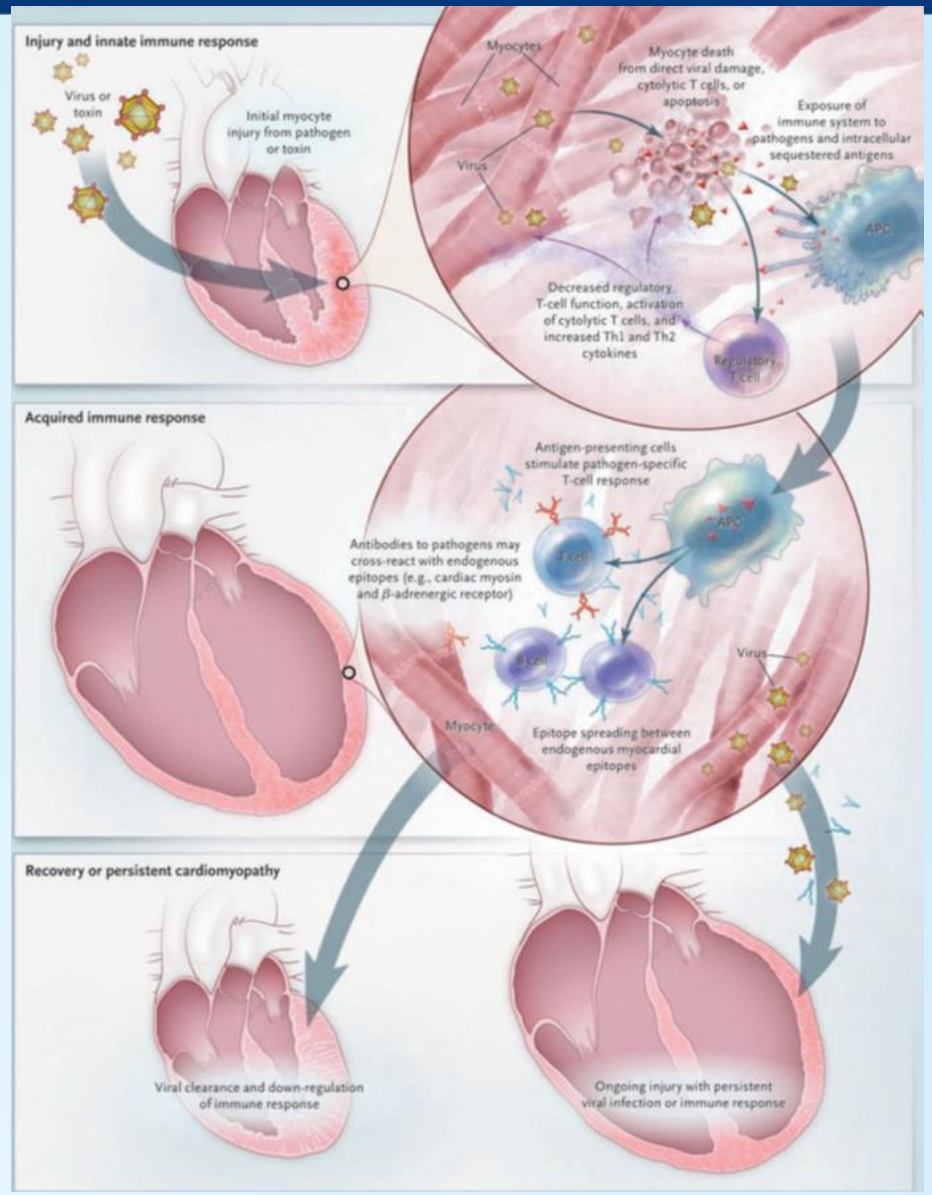
HHV6

Le attuali conoscenze sulla patogenesi della miocardite virale derivano principalmente da modelli murini di miocardite da enterovirus (cocksakie B) e da colture cellulari isolate, i cui principi sono stati poi generalizzati per altri tipi di miocardite



Virus-mediated myocarditis

Virus-triggered myocarditis (Es:Coronavirus)



Toshitaka Yajima. Circulation. Viral Myocarditis, Volume: 119, Issue: 19, Pages: 2615-2624, DOI: (10.1161/CIRCULATIONAHA.108.766022)

Cooper LT jr., Myocarditis. N Engl J Med. 2009; 360:1526

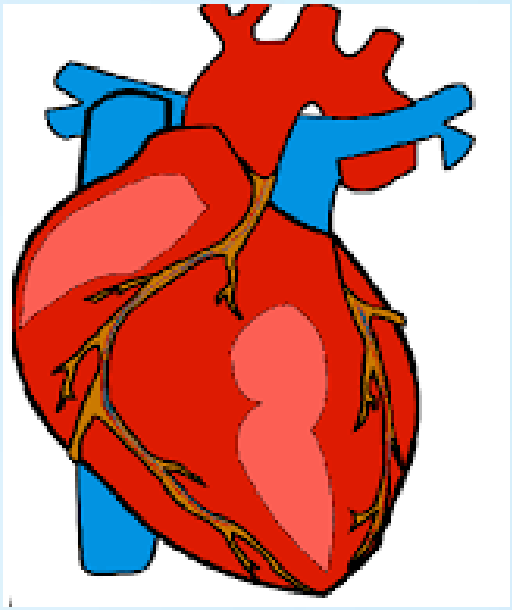
Anche se vi sono evidenze di questo meccanismo nel modello sperimentale murino, nell'uomo la dimostrazione di un danno diretto da coxsackievirus è estremamente limitata e non è dimostrato il danno diretto di altri virus

L'attuale esperienza clinica sembra indicare che i casi di miocardite da coxsackie nell'adulto siano molto rari

Esistono ancora controversie per quanto riguarda i meccanismi che determinano la transizione dal trigger iniziale alla infiammazione del miocardio e dal danno miocardico acuto alla disfunzione cronica.

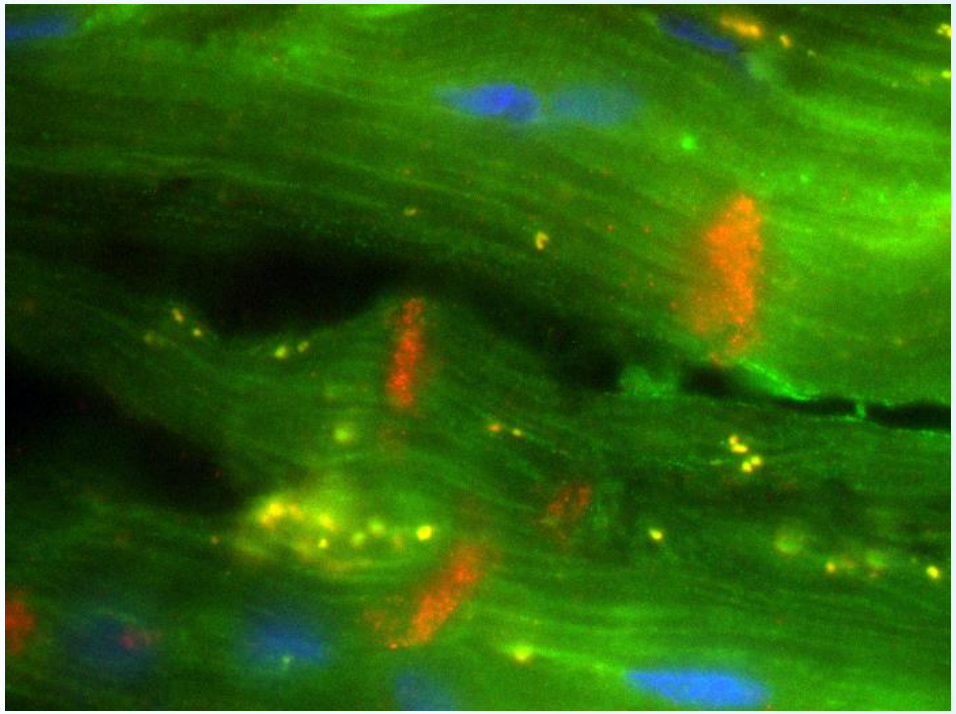
Management of Acute Myocarditis and Chronic Inflammatory Cardiomyopathy
An Expert Consensus Document
Enrico Ammirati, Maria Frigerio

Desmoplakin Cardiomyopathy & inflammation

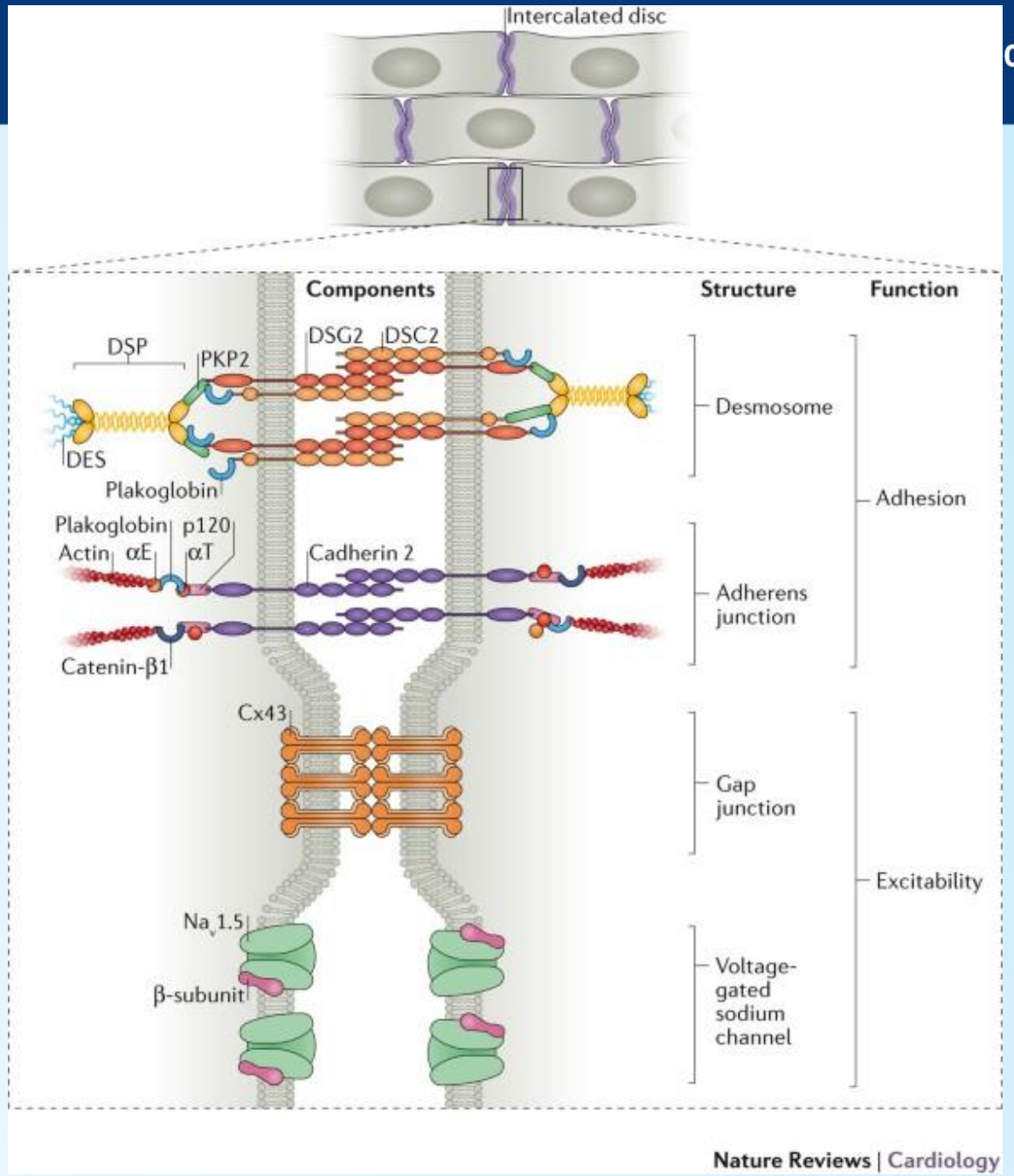


DSP e Desmosoma… by-stander??

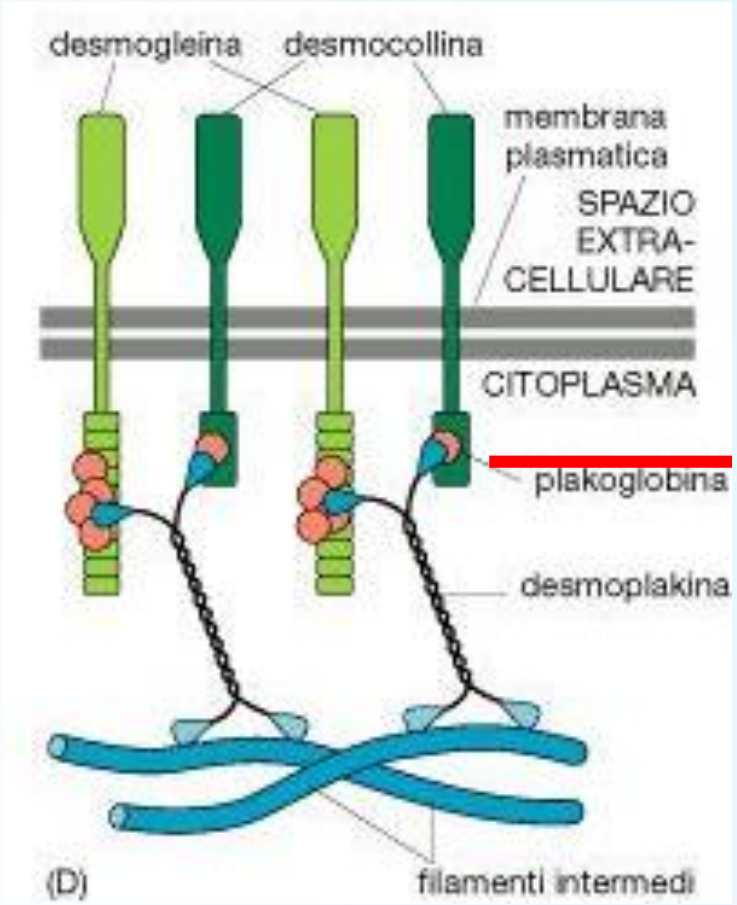
Plakoglobin, RED



Desmoplakin (DSP) is a structural protein that links the cardiac desmosome to intermediate filaments and is critical for normal force transmission in the myocardium



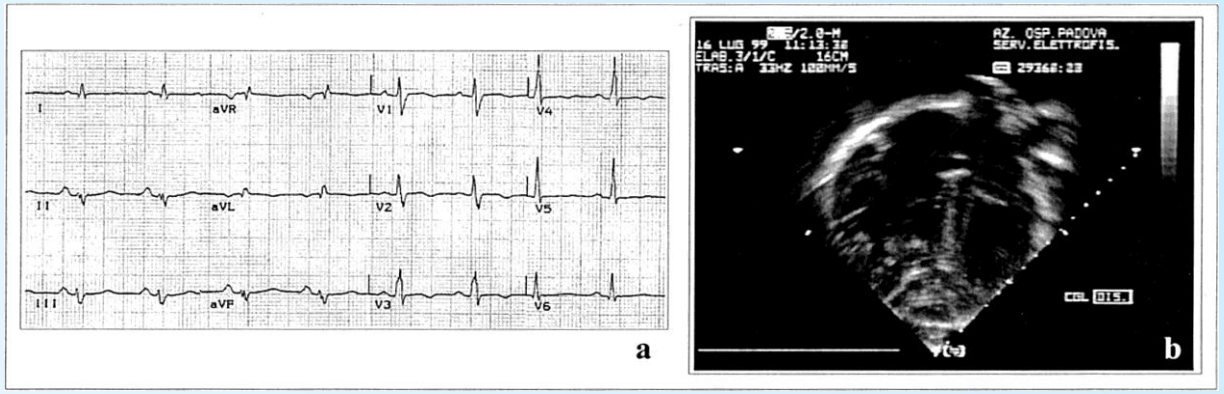
Desmoplakin (DSP) is a structural protein that links the cardiac desmosome to intermediate filaments and is critical for normal force transmission in the myocardium



REPORT | VOLUME 71, ISSUE 5, P1200-1206, NOVEMBER 01, 2002

Mutation in Human Desmoplakin Domain Binding to Plakoglobin Causes a Dominant Form of Arrhythmogenic Right Ventricular Cardiomyopathy

Alessandra Rampazzo * • Andrea Nava • Sandro Malacrida * • ... Gaetano Thiene • Jeffrey A. Towbin • Gian A. Danieli • Show all authors • Show footnotes



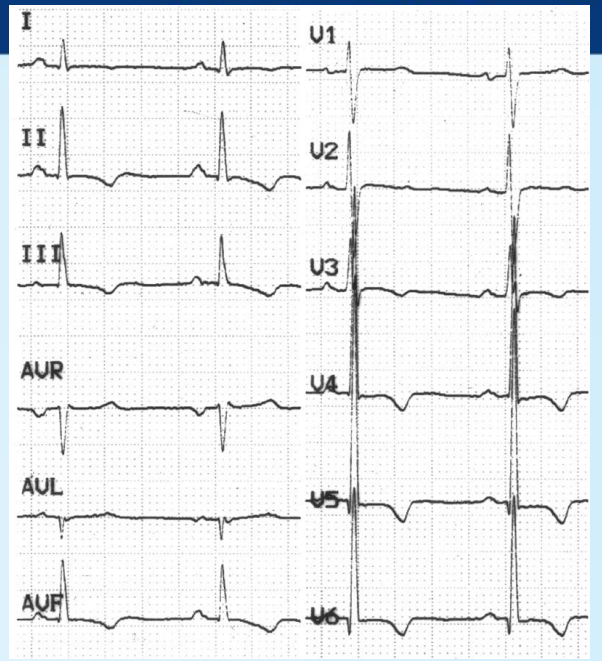
Mutations in the DSP gene encoding desmoplakin were first identified in an autosomal recessive form of ARVC, with a high predisposition toward ventricular arrhythmias

Circulation
Volume 112, Issue 5, 2 August 2005, Pages 636-642
https://doi.org/10.1161/CIRCULATIONAHA.104.532234

ARRHYTHMIA/ELECTROPHYSIOLOGY

Novel Mutation in Desmoplakin Causes Arrhythmogenic Left Ventricular Cardiomyopathy

Mark Norman, BSc, MBBS, MRCP, Michael Simpson, BSc, Jens Mogensen, MD, PhD, Anthony Shaw, PhD, Sîan Hughes, MBBS, PhD, MRCPath, Petros Syrris, PhD, Srijita Sen-Chowdhry, MA, MBBS, MRCP, Edward Rowland, MD, FRCP, Andrew Crosby, PhD, and William J. McKenna, MD, DSc, FRCP

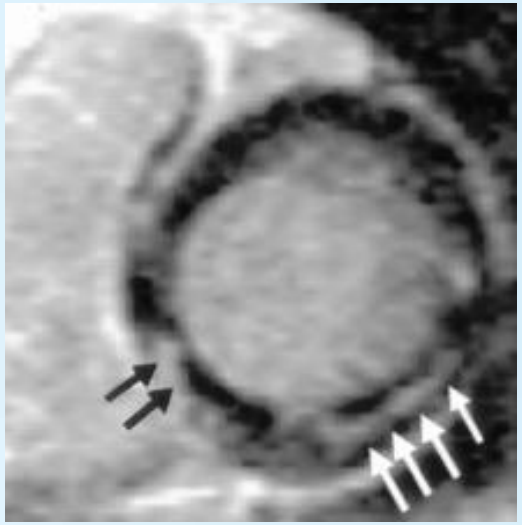


Circulation: Genomic and Precision Medicine
Volume 11, Issue 12, December 2018
https://doi.org/10.1161/CIRCGEN.118.002373

CLINICAL LETTER

Desmoplakin Variant-Associated Arrhythmogenic Cardiomyopathy Presenting as Acute Myocarditis

Kaitlyn Reichl, BS, Sarah E. Kreykes, MS, CGC, Cindy M. Martin, MD, and Chetan Shenoy,



Circulation
Volume 141, Issue 23, 9 June 2020;, Pages 1872-1884
https://doi.org/10.1161/CIRCULATIONAHA.119.044934

American Heart Association.

ORIGINAL RESEARCH ARTICLE

Desmoplakin Cardiomyopathy, a Fibrotic and Inflammatory Form of Cardiomyopathy Distinct From Typical Dilated or Arrhythmogenic Right Ventricular Cardiomyopathy

Eric D. Smith, MD, Neal K. Lakdawala, MD, Nikolaos Papoutsidakis, MD, PhD, Gregory Aubert, MD, PhD, Andrea Mazzanti, MD, Anthony C. McCanta, MD, Prachi P. Agarwal, MBBS, Patricia Arscott, MS, Lisa M. Dellefave-Castillo, MS, Esther E. Vorovich, MD, Kavitha Nutakki, MBBS, Lisa D. Wilsbacher, MD, PhD, Silvia G. Priori, MD, PhD, Daniel L. Jacoby, MD, Elizabeth M. McNally, MD, PhD, and Adam S. Helms, MD, MS

AIM OF THE STUDY: to determine the key clinical phenotypes and diagnostic features that distinguish DSP cardiomyopathy from typical DCM or ARVC

The largest series of DSP mutation carriers reported to date

STUDY POPULATION:

- 107 patients with pathogenic *DSP* mutations
  98% truncating
- 81 patients with pathogenic *PKP2 (Plakofilina)* mutations as a comparison cohort
  100% truncating

- 40% probands
- 60% genotype-positive family members

Clinical data including:

- ECG
- Echo
- CMR
- 18FDG-PET
- Rhythm monitoring

Clinical Presentation of DSP Cardiomyopathy Is Distinct From PKP2 Cardiomyopathy

1

LV/RV dysfunction

Clinical features

ECG

LGE pattern

	DSP, n=107	*PKP2*, n=81	*P* Value
Female	69%	51%	0.01
Age at evaluation, y	36±16	39±20	0.24
Proband	41%	42%	1.0
Normal ventricular function	36% (37/103)	60% (47/79)	0.002
RV predominant	14% (14/103)	40% (32/79)	<0.001
LV predominant	51% (52/103)	0% (0/79)	<0.001
Palmoplantar keratoderma or curly hair	55% (54/98)	2% (1/46)	<0.001
Moderate/intense exercise	53% (42/80)	NA	NA
Truncating mutation	98%	100%	0.51
TFC definite ARVC	34% (35/103)	49% (39/79)	0.036
TFC borderline ARVC	28% (29/103)	14% (11/79)	
TFC possible ARVC	38% (39/103)	37% (29/79)	
Episodic chest pain	21%	4%	0.001
Troponin elevation	15%	0%	<0.001
T wave inversions V1–V2	15% (15/101)	13% (10/76)	0.83
T wave inversions V1–V3	8% (8/101)	50% (38/76)	<0.001
T wave inversions V4–V6	21% (20/96)	22% (17/76)	0.85
Left bundle-branch block	1% (1/96)	0% (0/76)	1.0
Right bundle-branch block	2% (2/96)	1% (1/76)	1.0
Frequent PVCs (>500/24 h)	56% (32/57)	61% (23/38)	0.83
LV LGE	40% (23/57)	10% (5/51)	<0.001
LVEF, %	46±14, n=103	59±8, n=79	<0.001
VT outcome	28%	30%	0.87

Norman et al. Circulation. 2020;141:1872–1884

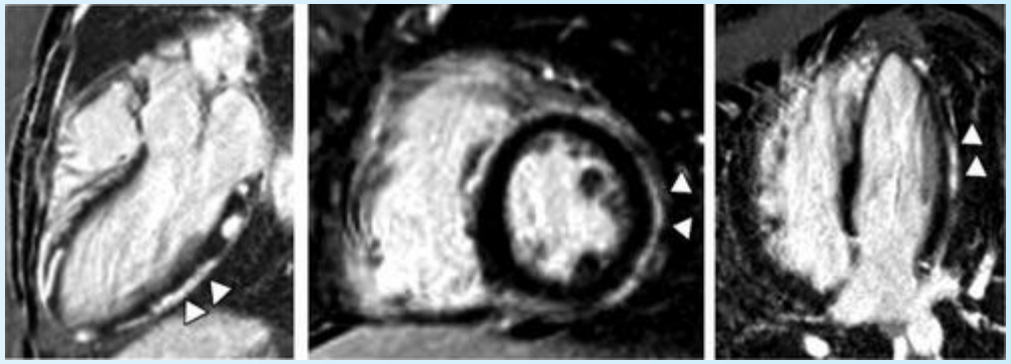
Left Dominant Arrhythmogenic Cardiomyopathy With Fibrosis Is the Primary Manifestation of *DSP* Cardiomyopathy

Patients with predominant RV Cardiomyopathy usually show concomitant LV involvement

	Normal Ventricular Function (N=37)	Predominant RV Involvement (N=14)	Predominant LV Involvement (N=52)	*P* Value
Female	76%	57%	60%	0.48
Age at evaluation, y	32±14	46±16	35±16	0.02
Truncating mutation	95%	100%	100%	0.14
Palmoplantar keratoderma or curly hair	50% (18/36)	54%	61% (27/44)	0.63
Proband	10%	64%	54%	<0.001
Moderate/intense exercise	61% (14/23)	46% (5/11)	49% (22/45)	0.63
LV enlargement	6% (2/35) *P*<0.001	29% *P*=0.48	60% (30/50) *P*<0.001	<0.001
LV systolic dysfunction	0% *P*≤0.001	50% *P*=1.0	86% *P*≤0.001	<0.001
LVEF, %	68±5	50±10	37±13	<0.001
RV systolic dysfunction	0% *P*≤0.001	79% *P*≤0.001	31% *P*=0.09	<0.001
RV focal WMA	0% (0/19) *P*=0.021	64% (7/11) *P*<0.001	8% (2/26) *P*=0.11	<0.001
ECG T wave inversions (V1–V2)	15% (5/34)	7% (1/14)	18% (9/50)	0.60
ECG T wave inversions (V1–V3)	3% (1/34)	7% (1/14)	12% (6/50)	0.34
ECG T wave inversions (V4–V6)	3% (1/32) *P*≤0.001	14% (2/14) *P*=0.09	36% (17/47) *P*=0.005	0.006
Frequent PVCs (>500/24 h)	29% (6/21) *P*=0.001	71% (5/7) *P*=0.37	72% (21/29) *P*=0.012	0.006
Episodic chest pain	14%	14%	29%	0.18
Acute myocardial injury*	8%	14%	21%	0.24
LV LGE	0% (0/19) *P*<0.001	27% (3/11) *P*=0.31	74% (20/27) *P*<0.001	<0.001
RV EDV, mL (MRI)	128±31 (n=18)	181±44 (n=10)	153±48 (n=22)	0.009
LV EDV, mL (MRI)	134±33 (n=18)	170±40 (n=10)	172±54 (n=24)	0.02
ARVC task force diagnosis	0.001			
Possible	68% *P*≤0.001	22% *P*=0.17	21% *P*≤0.001	
Borderline	19% *P*=0.12	21% *P*=0.55	37% *P*=0.056	
Definite	13% *P*=0.001	57% *P*=0.049	42% *P*=0.071	
VT outcome	13.5% *P*=0.001	21% *P*=0.009	37% *P*=0.11	0.04

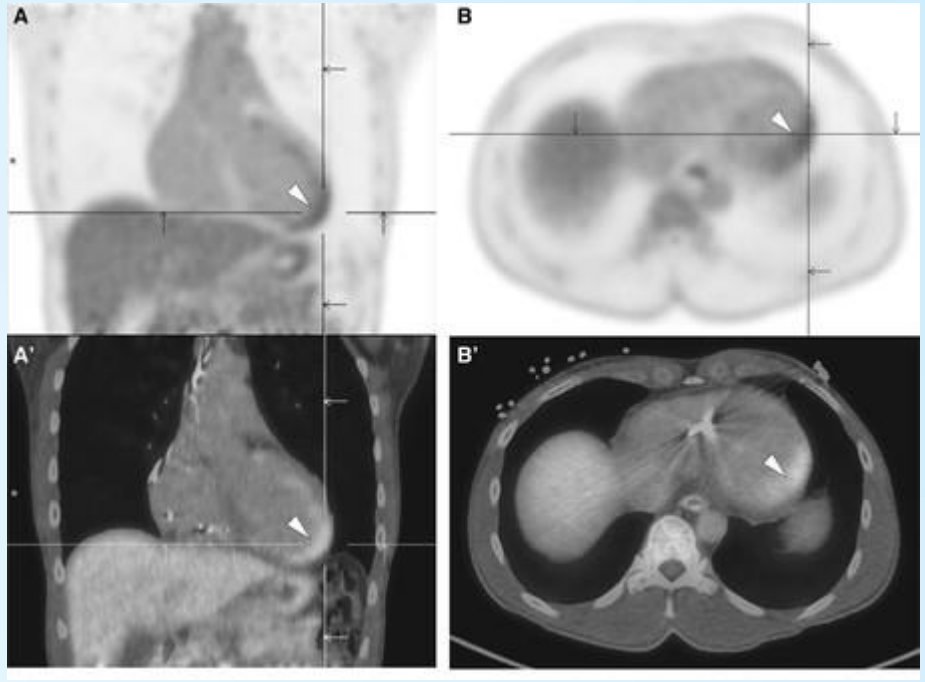
Norman et al. Circulation. 2020;141:1872–1884

Recurrent LV inflammation and fibrosis as primary disease mechanisms in DSP Cardiomyopathy



Acute myocardial injury was observed in 15% of patients with DSP without a significant difference among the 3 clinically defined groups

CMR demonstrating LGE in the LV in 90% of them, also in patients with normal ventricular systolic function
In 1 of these cases LV LGE was extensive

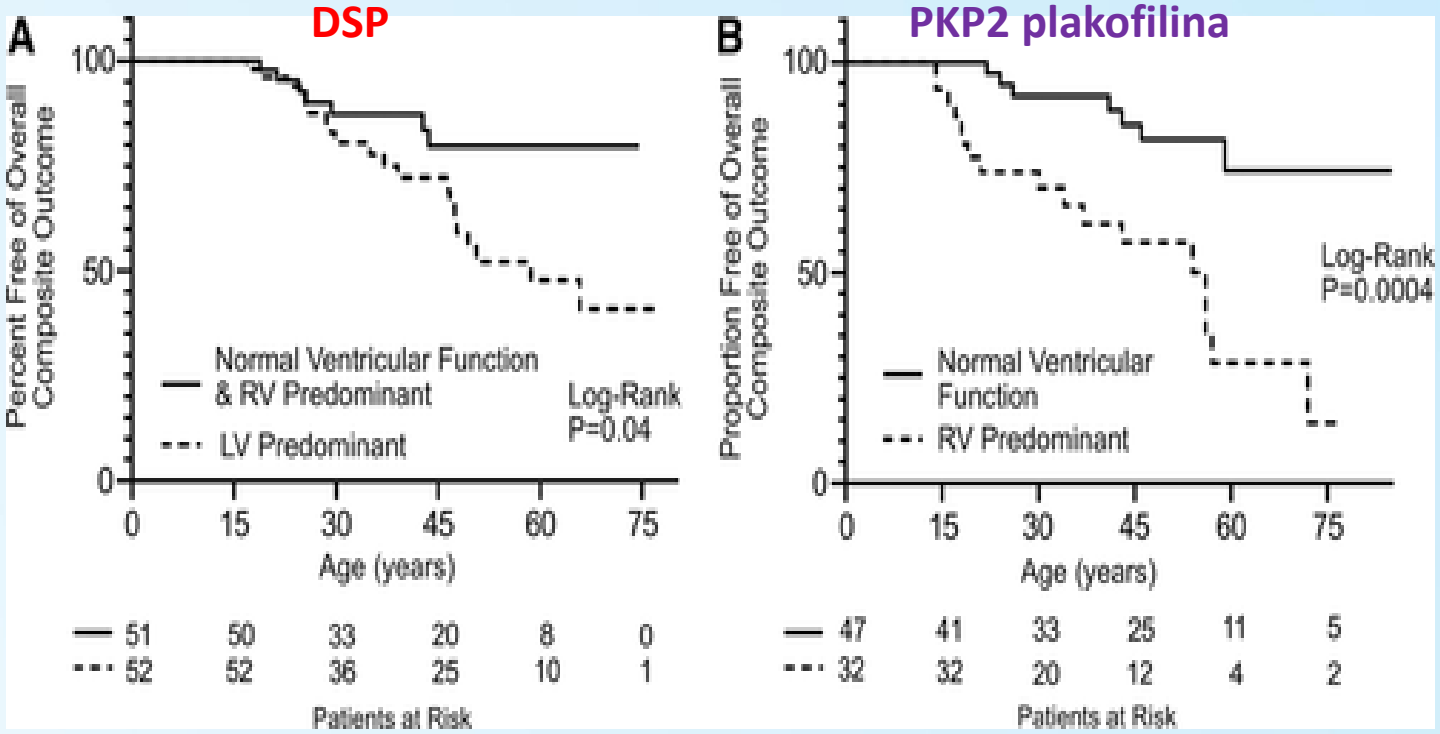


4 of the patients with troponin elevation also underwent cardiac 18FDG PET with evidence of **active inflammation** in the myocardium.

Norman et al. Circulation. 2020;141:1872–1884

Risk Stratification for Severe Ventricular Arrhythmias Requires a Genotype-Specific Approach for DSP Cardiomyopathy

	No Severe Arrhythmia	Severe Arrhythmia	*P* Value	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
DSP							
LVEF <55%	47% (36/76)	85% (23/27)	0.001	85%	53%	39%	91%
LVEF <35%	17% (13/76)	48% (13/27)	0.004	48%	83%	50%	85%
RV dysfunction	30% (23/76)	33% (9/27)	0.81				
LV LGE	34% (15/44)	50% (6/12)	0.35				
Frequent PVCs	51% (24/47)	80% (8/10)	0.16				
Moderate/intense exercise	58% (34/59)	38% (8/21)	0.137				
Acute myocardial injury episodes	21%	20%	0.93				
PKP2							
LVEF <55%	9% (5/55)	21% (5/24)	0.27				
LVEF <35%	4% (2/55)	0% (0/24)	0.57				
RV dysfunction	18% (10/55)	71% (17/24)	<0.001	71%	82%	63%	86%
LV LGE	6% (2/36)	20% (3/15)	0.14				
Frequent PVCs	48% (13/27)	91% (10/11)	0.03	91%	52%	43%	93%



*Composite outcome of SVT, SCD or appropriate ICD intervention

Risk stratification on the basis of variables studied in DCM or ARVC are inadequate DSP cardiomyopathy.

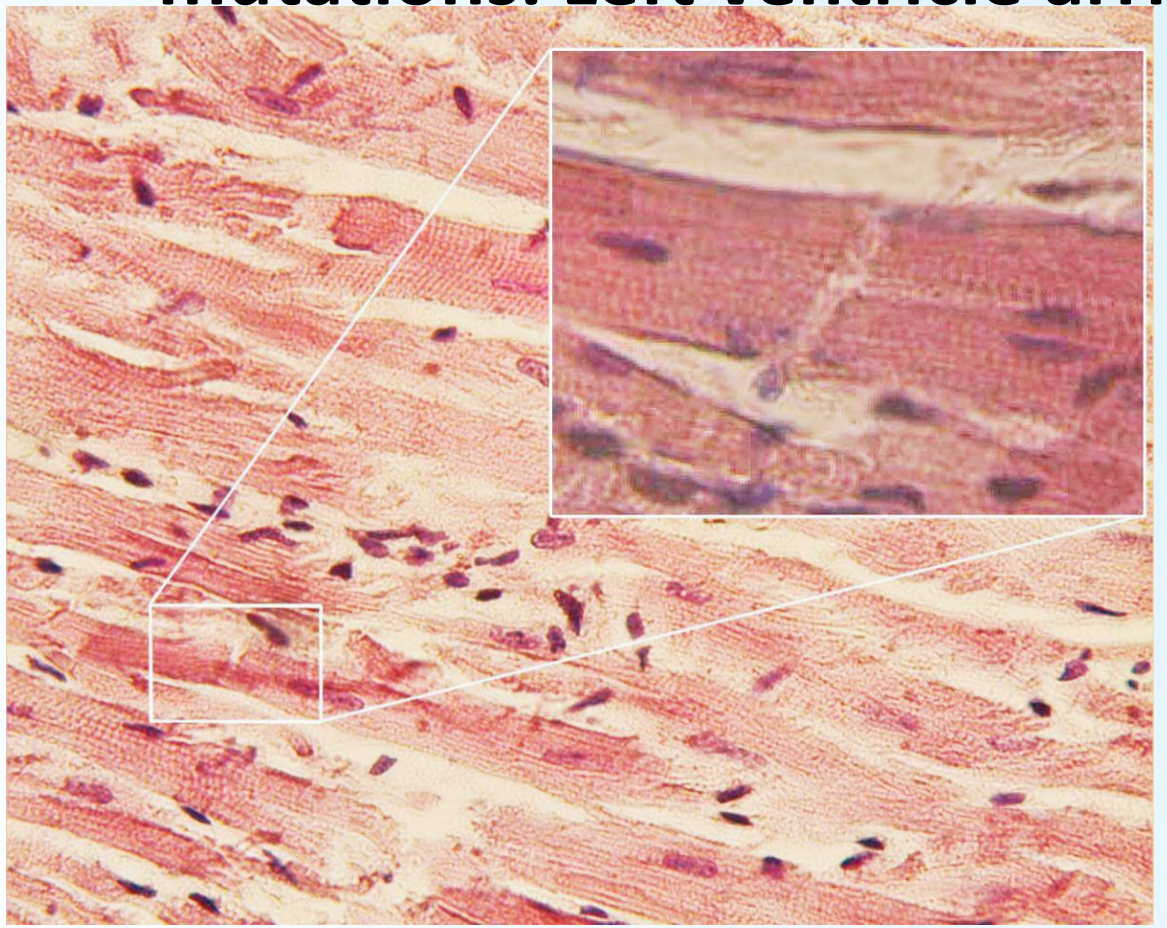
- Many events occurred in an ejection fraction range of 35% to 55%.
- Criteria predictive of events in ARVC, including RV systolic dysfunction, T wave inversions, and male sex had no basis at all for either clinical recognition or risk stratification in DSP cardiomyopathy.

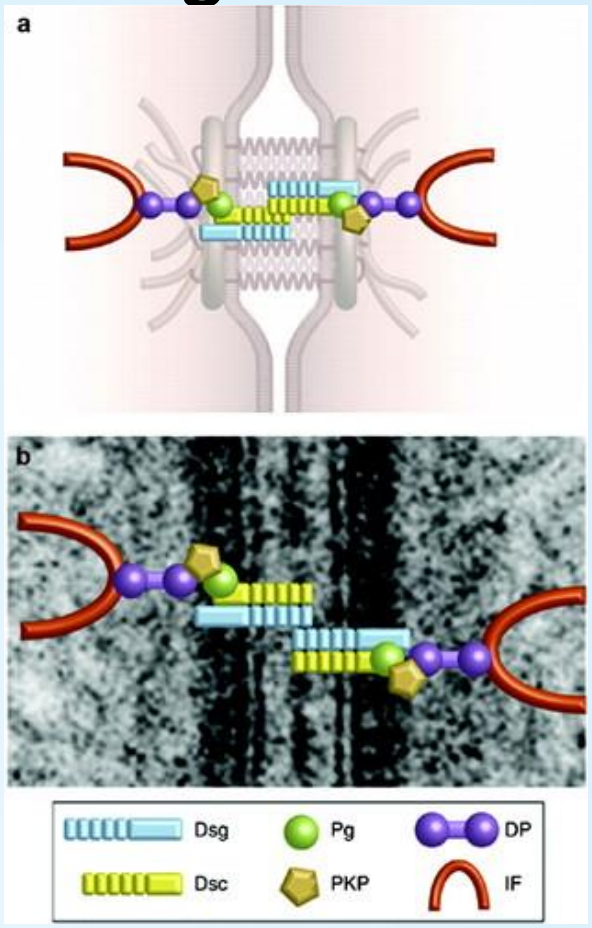
Norman et al. Circulation. 2020;141:1872–1884

Conclusions

- DSP cardiomyopathy is a **distinct form** of cardiomyopathy, marked by a high proclivity for **LV dysfunction and fibrosis and arrhythmias**, and associated with **intermittent myocardial inflammatory episodes** that appear clinically similar to myocarditis
- Diagnostic and risk stratification variables that perform well for PKP2-associated ARVC exhibit poor accuracy for diagnosis and risk assessment for DSP mutation carriers
- A **genotype-specific management** approach is essential for DSP cardiomyopathy

Recurrent inflammatory myocarditis associated with desmoplakin mutations. Left ventricle arrhythmogenic cardiomyopathy?





***1-Desmoplakin* Variant-Associated Arrhythmogenic Cardiomyopathy Presenting as Acute Myocarditis.** Kaitlyn Reichl et al. AHA-Circulation

The pathophysiology underlying inflammation in is not well understood. Sen-Chowdhry et al[1] postulated that *inflammatory myocarditis is part of the natural history of* ***Arrhythmogenic Cardiomyopathy, where it has a genetic rather than an infective basis. Disease progression is purported to occur through episodes of myocarditis, involving cardiomyocyte loss followed by repair and***

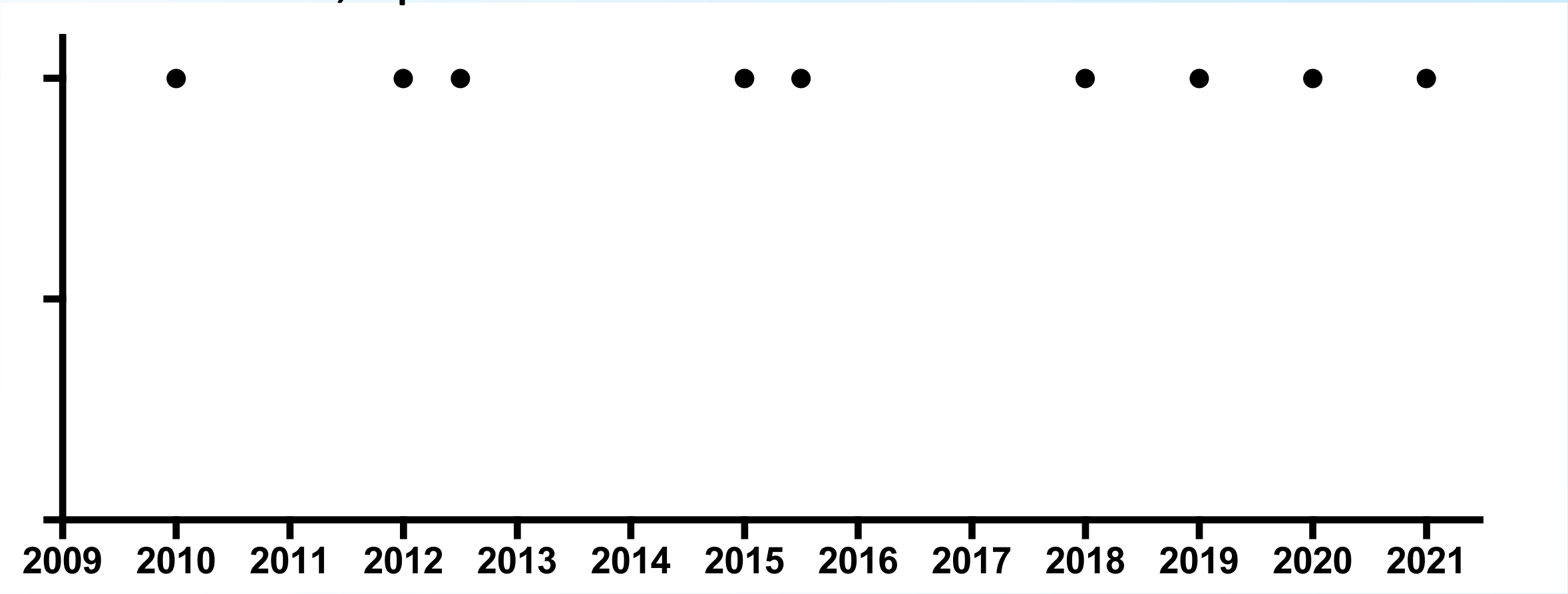
- Giovane donna di 24 anni, Nega fattori di rischio Cardiovascolare.
  Storia di *miocardite recidivante (I episodio 2010)*

- Giunge in PS per dolore toracico ed elevazione dei markers di miocardionecrosi. Indici di flogosi nella norma

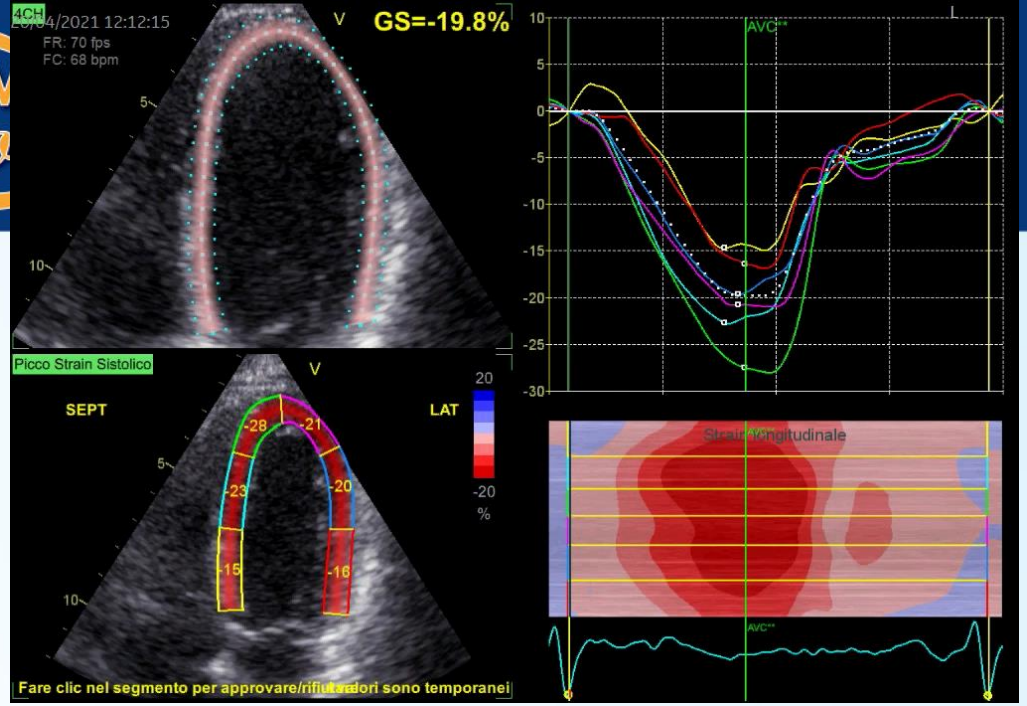
- **EO:** 115/70 mmHg, FC 80 bpm

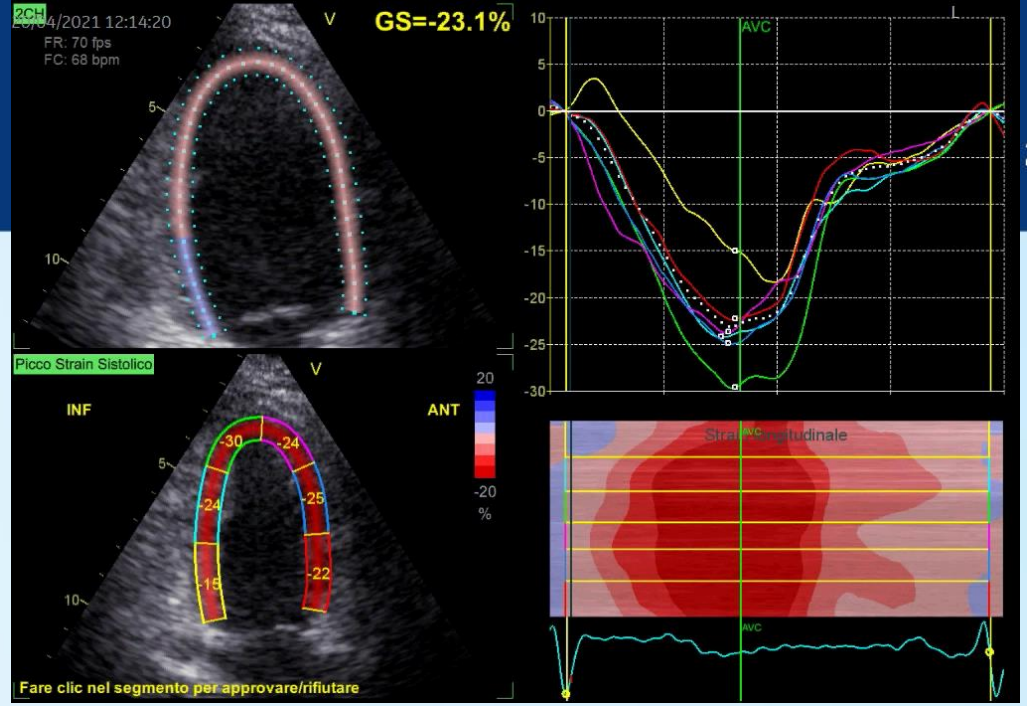
- **ECG:** Ritmo sinusale ad FC 80 bpm. *Bassi voltaggi diffusi.*
  Onde T negative in D3

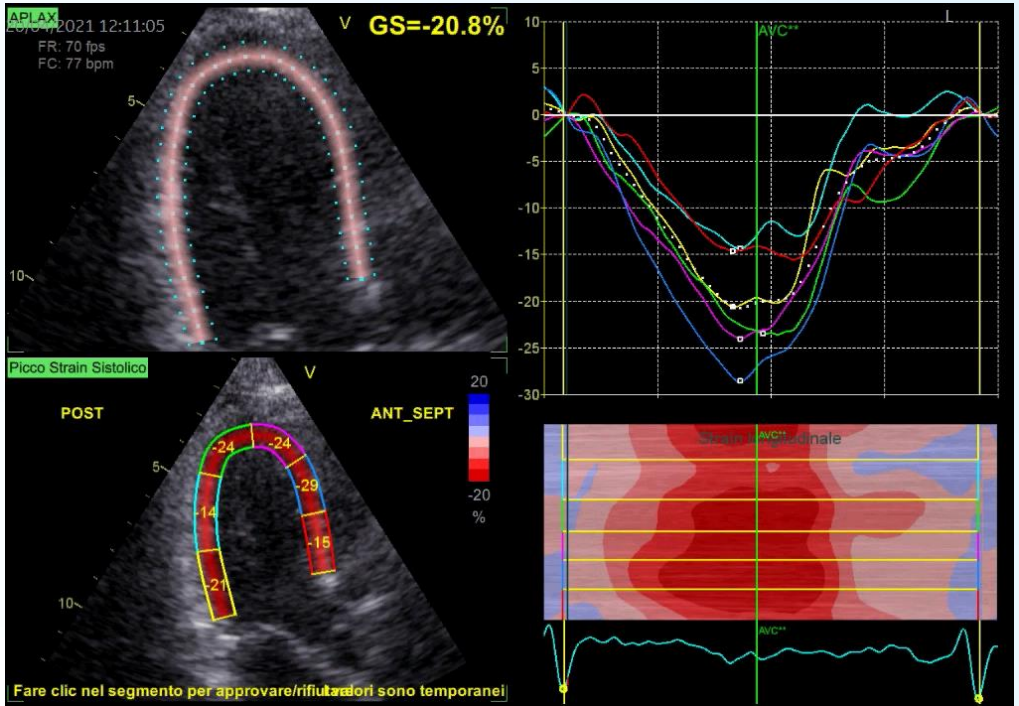
9 episodi miocarditici documentati, altri probabilmente asintomatici, spesso in concomitanza con stress emotivi

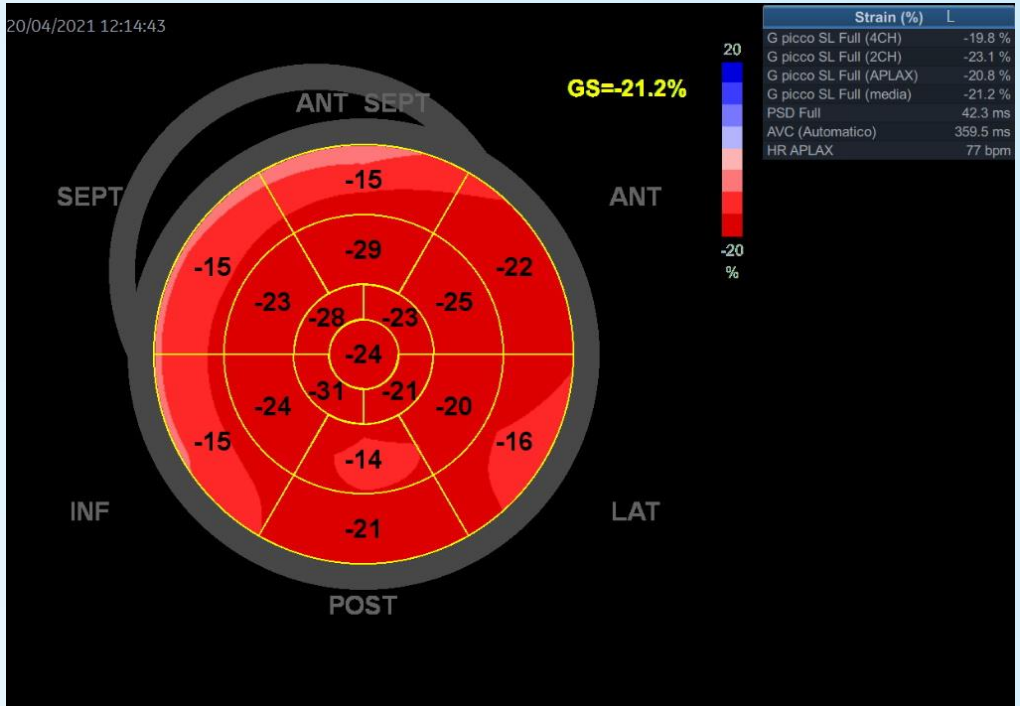


Ecocardiogramma: Ventricolo normali dimensioni. Cinesi globale e segmentaria conservate(FE 55%). Assenza di versamento pericardico.

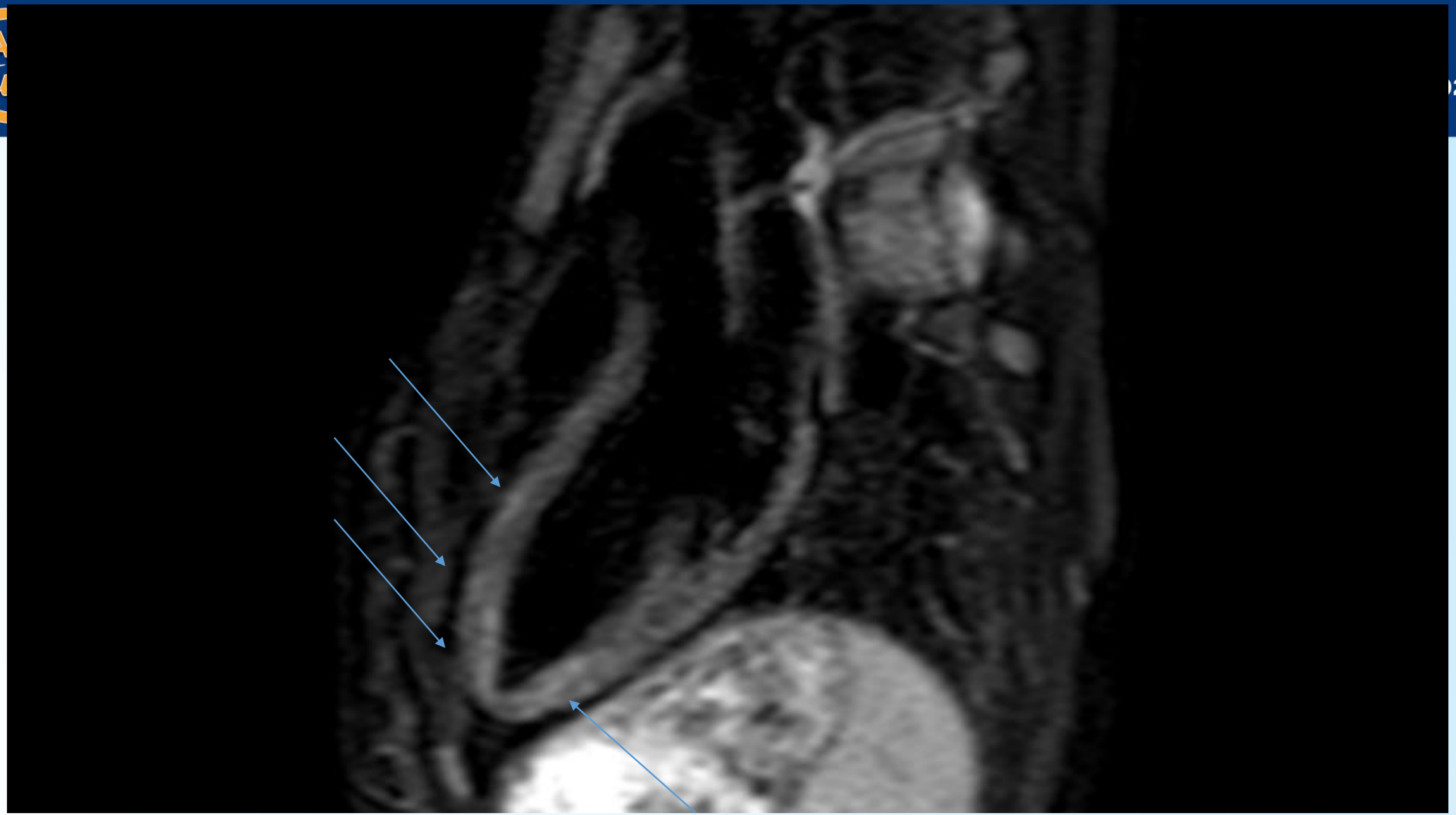

4CH
FR: 70 fps
FC: 68 bpm
GS=-19.8%
AVC**
Picco Strain Sistolico
SEPT
LAT
20
-20
%
-28
-21
-23
-20
-15
-16
Strain Longitudinale
Fare clic nel segmento per approvare/rifiutare


2CH
FR: 70 fps
FC: 68 bpm
GS=-23.1%
AVC
Picco Strain Sistolico
INF
ANT
20
-20
%
-30
-24
-24
-25
-15
-22
Strain Longitudinale
Fare clic nel segmento per approvare/rifiutare

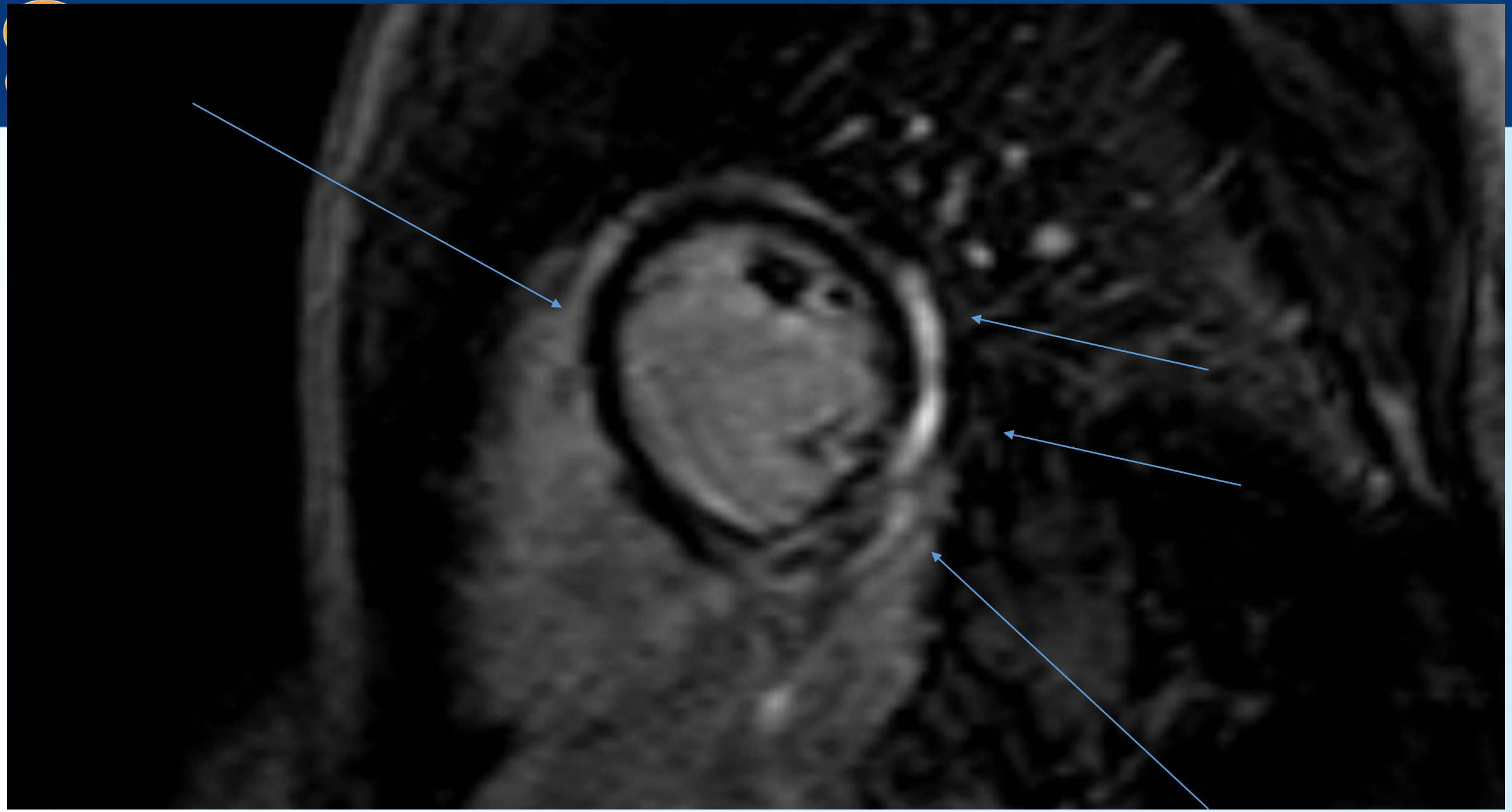

APLAX
FR: 70 fps
FC: 77 bpm
GS=-20.8%
AVC**
Picco Strain Sistolico
POST
ANT_SEPT
20
-20
%
-24
-24
-29
-14
-15
-21
Strain Longitudinale
Fare clic nel segmento per approvare/rifiutare


20/04/2021 12:14:43
GS=-21.2%
ANT_SEPT
SEPT
ANT
INF
LAT
POST
20
-20
%
-15
-29
-22
-15
-23
-28
-23
-25
-24
-31
-21
-24
-20
-15
-16
-14
-21
Strain (%) L
G picco SL Full (4CH) -19.8 %
G picco SL Full (2CH) -23.1 %
G picco SL Full (APLAX) -20.8 %
G picco SL Full (media) -21.2 %
PSD Full 42.3 ms
AVC (Automatico) 359.5 ms
HR APLAX 77 bpm

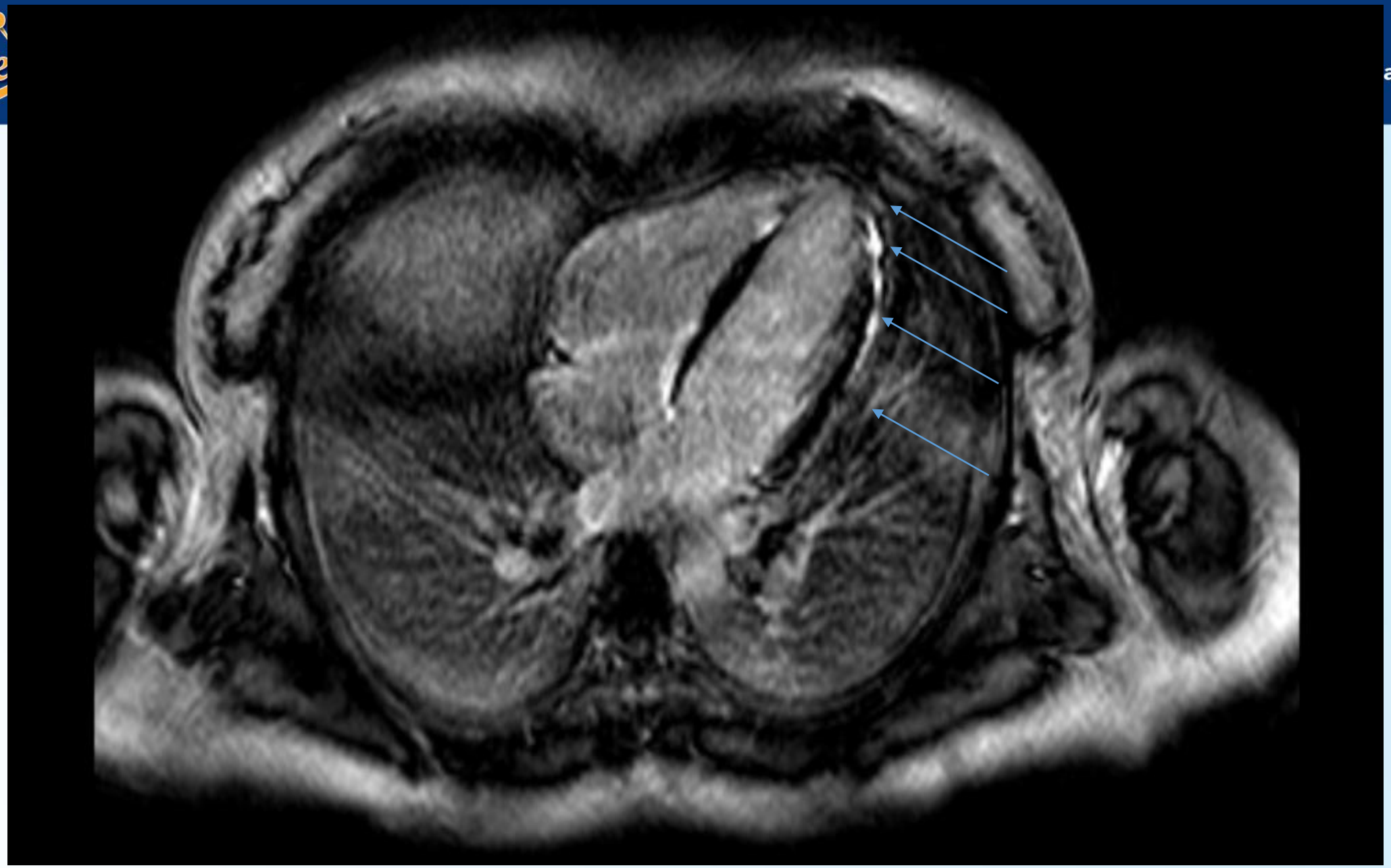
RMN cardiaca: Parziale riattivazione flogistica di aree estese di danno miocardico con *pattern non ischemico*, coinvolgenti in maniera diffusa il miocardio ventricolare sinistro.



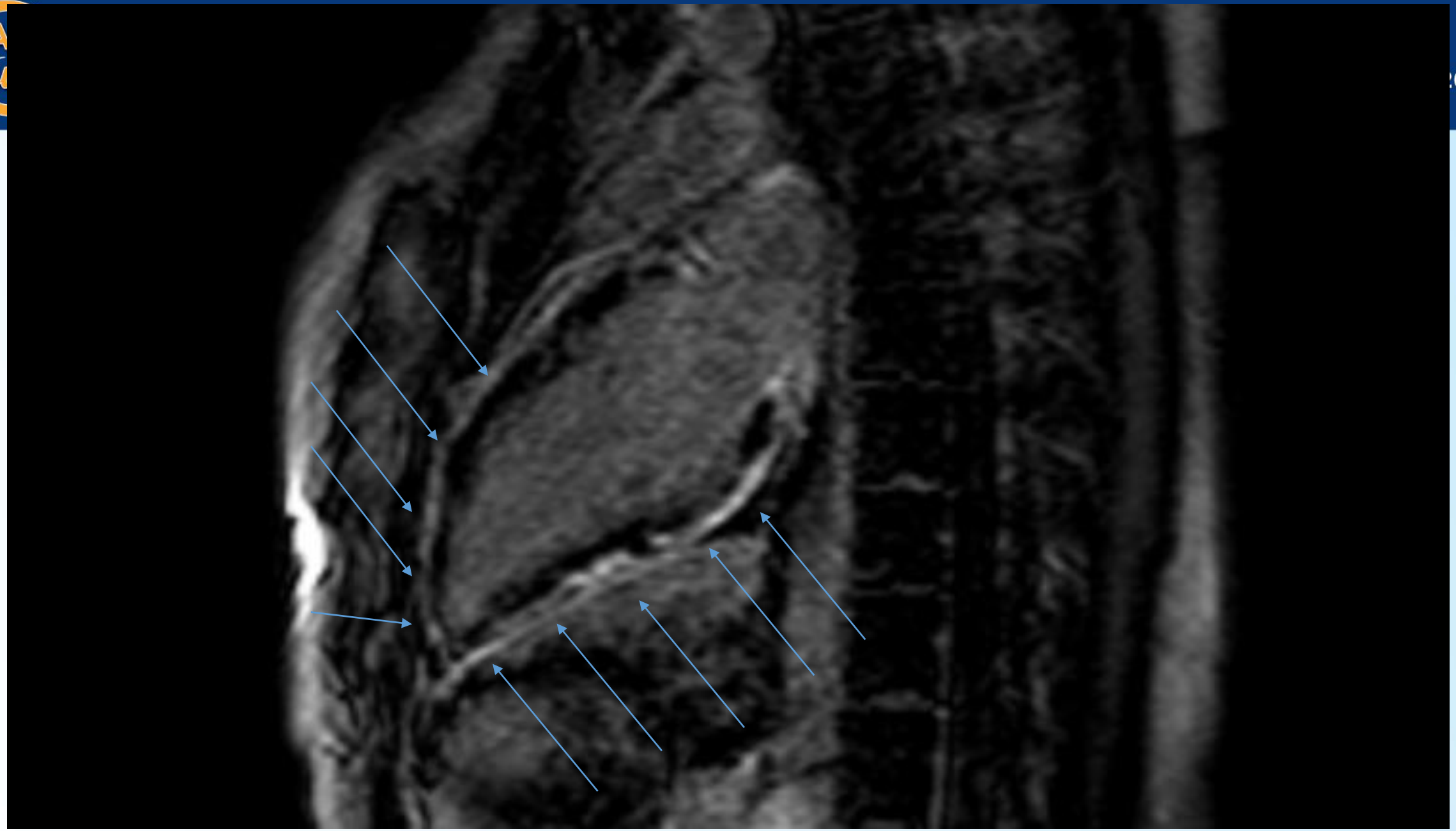
Sequenza T2 stir per edema in sezione LA iperintensità di segnale all’apice in toto



Sequenza Late gadolinium enancement per valutazione fibrosi: (ad anello epicardico del Vsx)



Sequenza Late gadolinium enancement per valutazione fibrosi



Biopsia endomiocardica setto del ventricolo destro

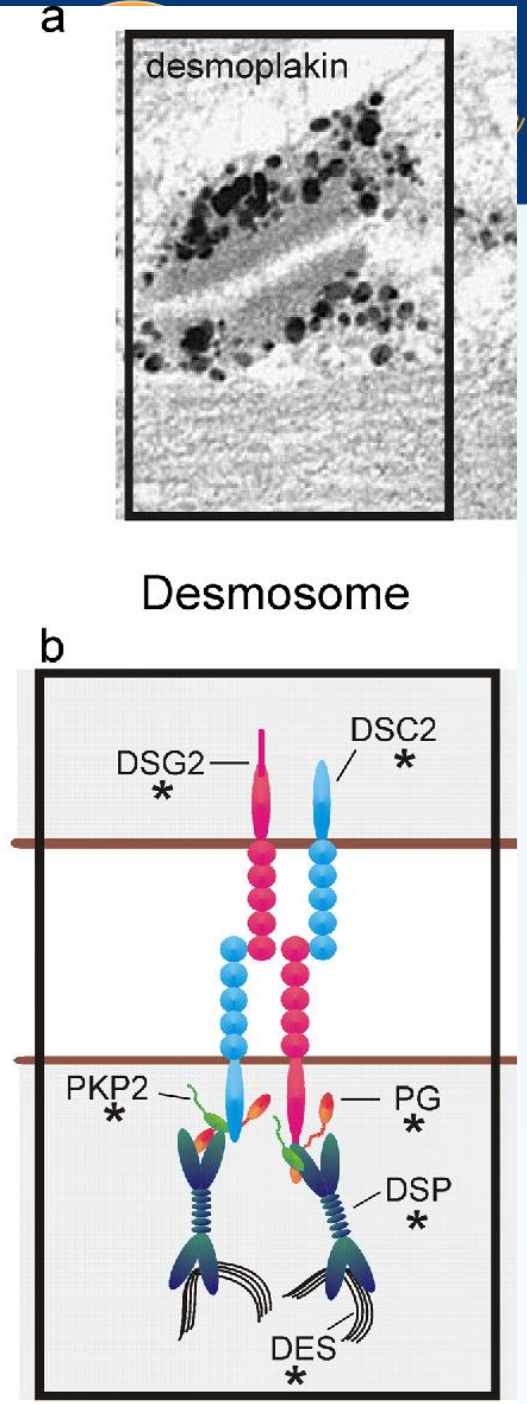
Reperti macroscopici
A) Biopsia endomiocardica .

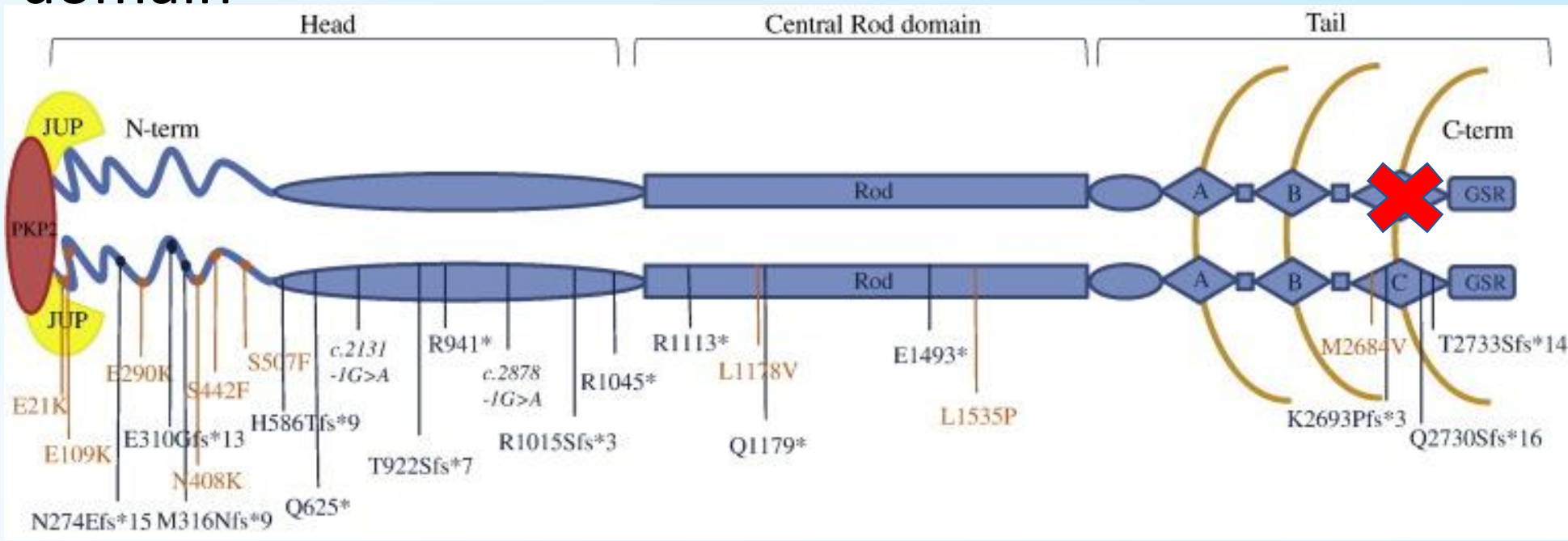
Reperti microscopici
Pervenuti 3 frammenti rappresentativi di endomiocardio con spiccato edema interstiziale, diffusi infiltrati linfomonocitari (CD 3+ >7/mm²) associati a necrosi dei cardiomiociti (diametro medio 15 µm, range 13-18 µm). Non evidenza di fibrosi sostitutiva, infiltrazione adiposa o patologia dei piccoli vasi.

Negativa la ricerca su biopsia di virus miocarditici

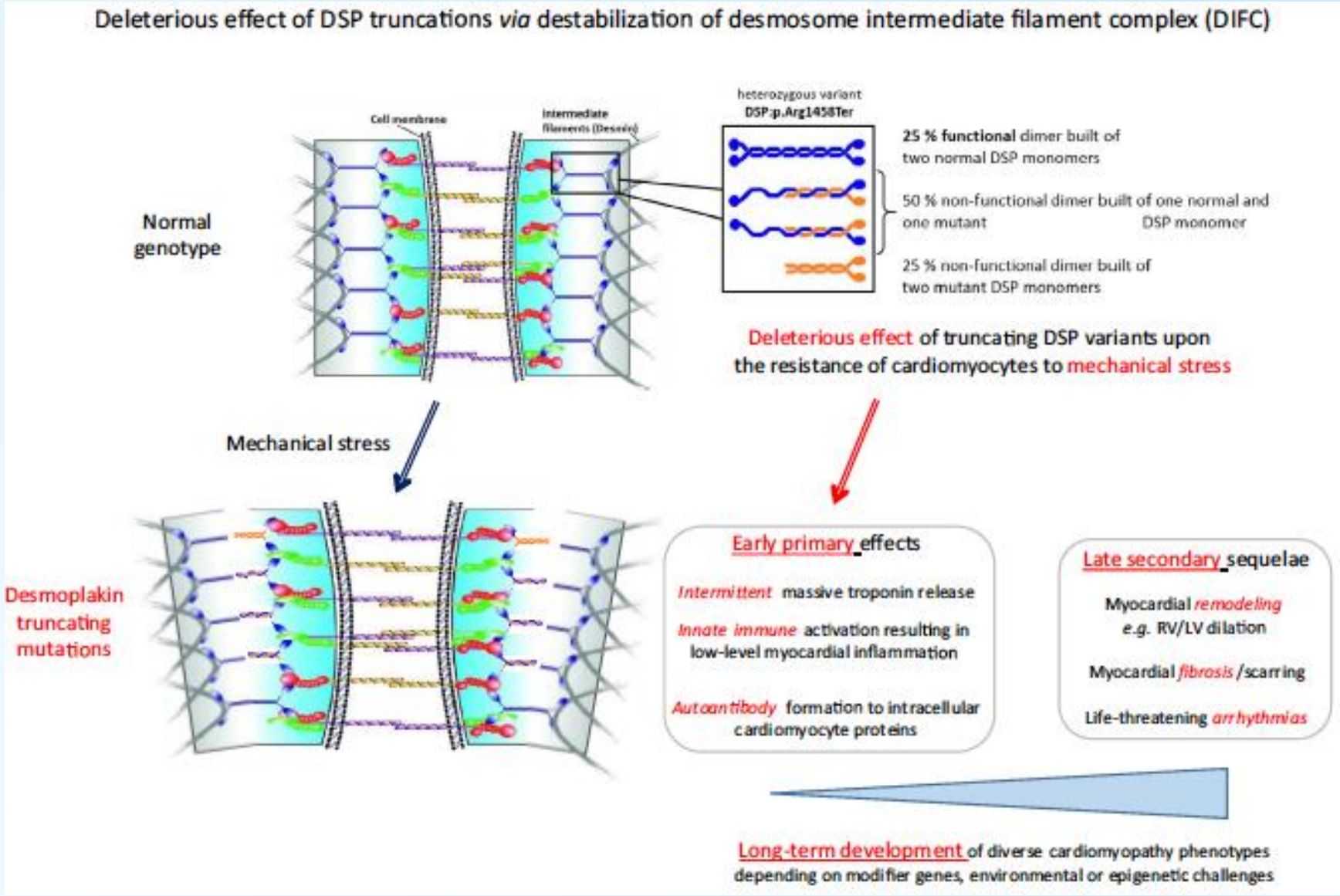
Identification of a frameshift mutation in the tail C domain

K2430Ifs*6





Mechanical failure hypothesis



J Am Heart Assoc. 2020;9:e015289