GRAND ROUNDS CLINICI DEL MERCOLEDÌ
con il Policlinico San Matteo

Sistema Socio Sanitario
Regione Lombardia

Fondazione IRCCS Policlinico San Matteo

ATS Pavia

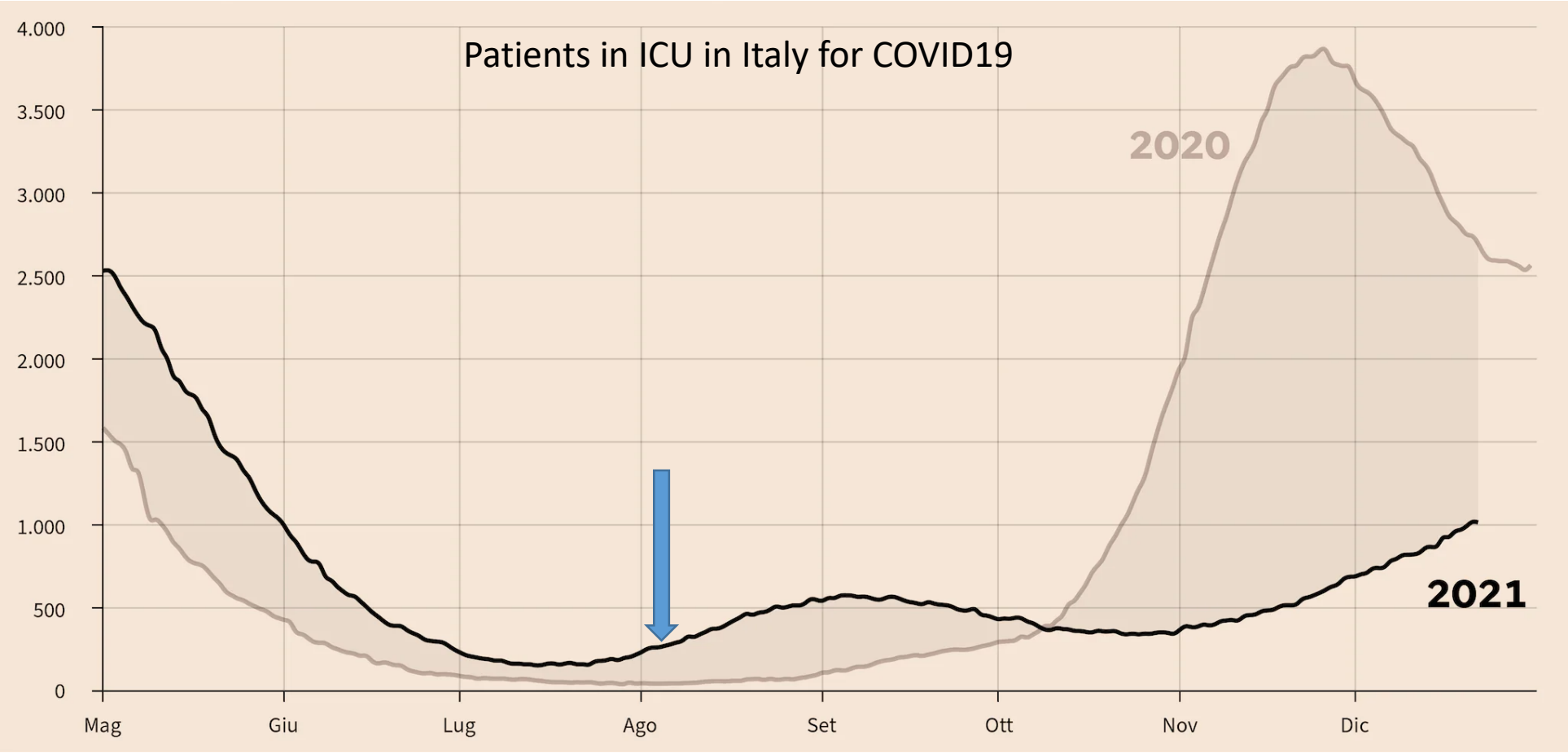
Aula Magna "C. Golgi"
& WEBINAR

28/09/2022

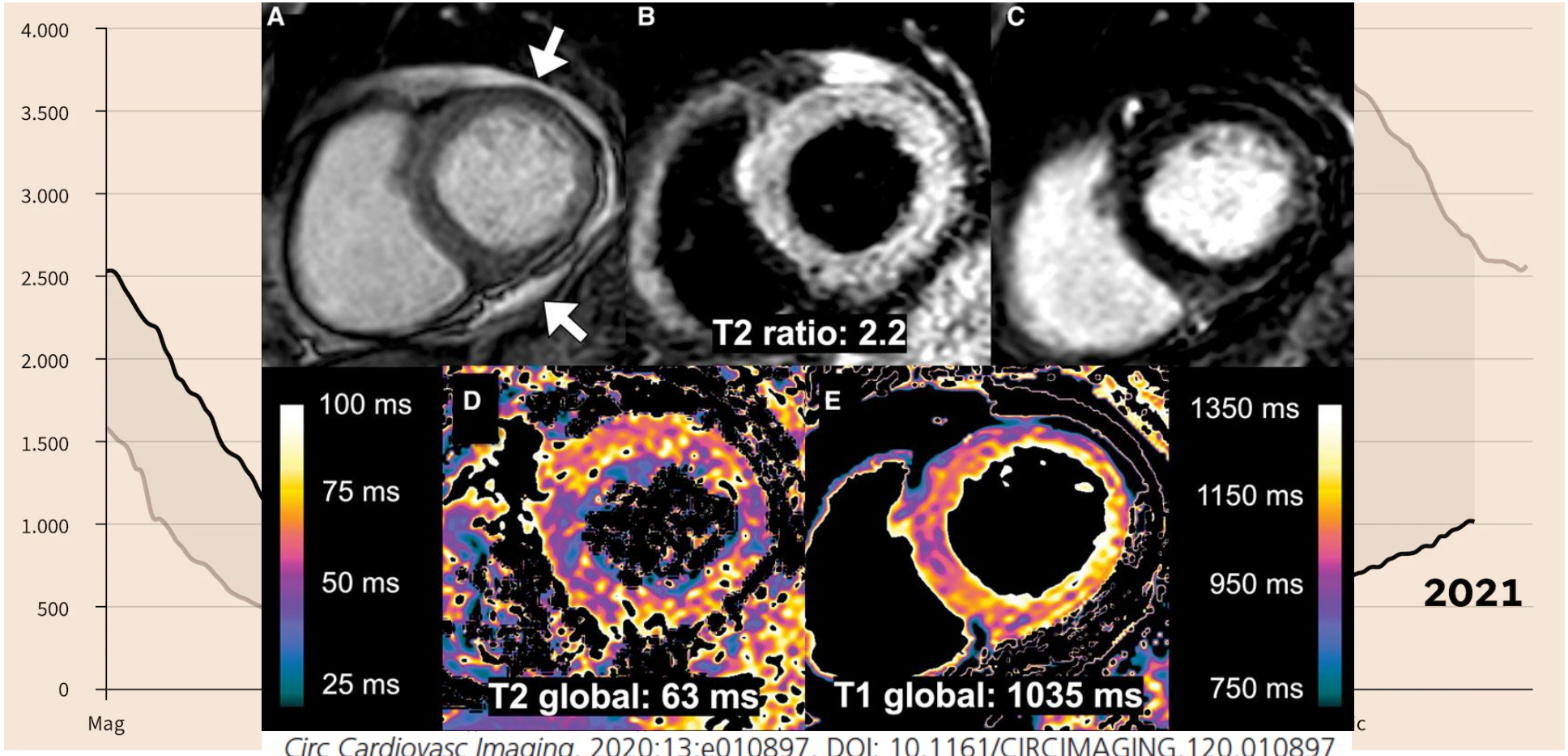
Rossana Totaro e Mirko Belliato

An unusual case of cardiogenic shock

On summer of 2021….



On sumn **COVID 19 and Myocarditis**



Circ Cardiovasc Imaging. 2020;13:e010897. DOI: 10.1161/CIRCIMAGING.120.010897

We received a call from the CICU of a spoke hospital…

A 41-year-old woman without significant past medical history and no previous cardiovascular disease, presented after 3 days of gastroenteritis and fever treated at home with rifampicin, without any benefits.

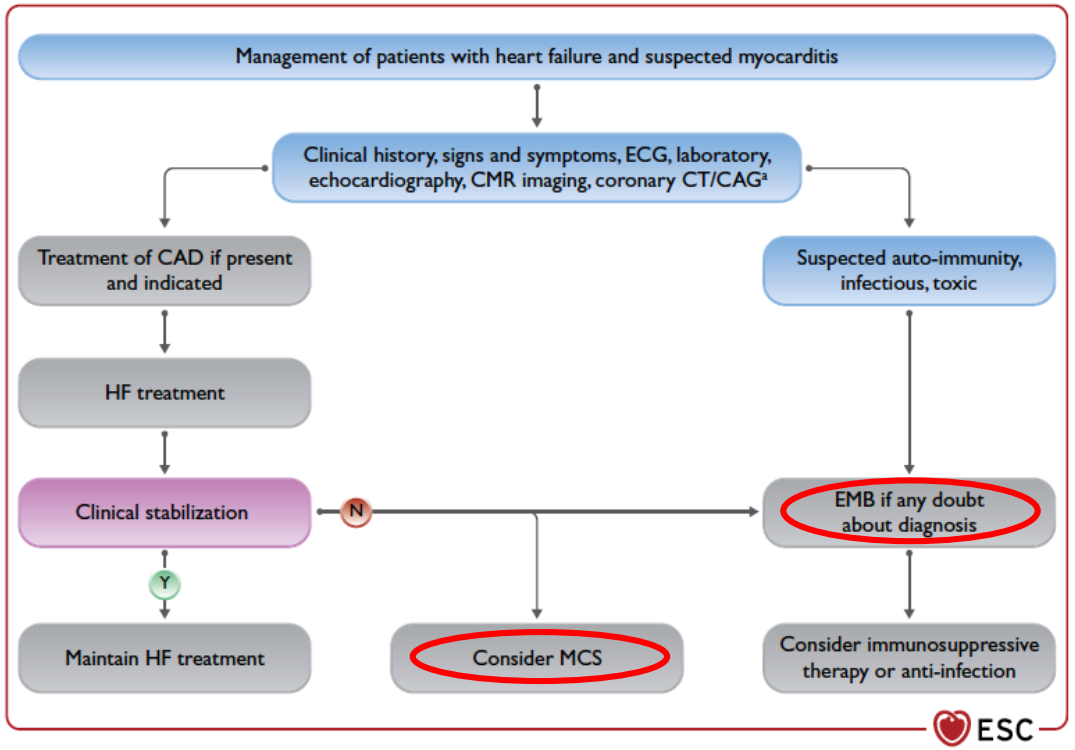
TTE revealed severely impaired LV systolic function and circumferential pericardial effusion.
Presumptive diagnosis: acute myo-pericarditis.

Past medical history:
- Allergic asthma
- …..nothing else

Covid test was negative

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)



European Heart Journal (2021) 42, 3599 3726

Rete regionale per la gestione del trattamento ECMO in pazienti in shock cardiogeno o arresto cardiaco refrattario

LIVELLO	CARATTERISTICHE
1	Struttura sanitaria con Terapia Intensiva Cardiologica
2	Struttura sanitaria in grado di gestire il trattamento ECMO con accesso a terapie short term
3	Strutture di riferimento regionale in grado di gestire il trattamento ECMO con accesso a terapie long term e/o trapianto (in sede o in rete) e di attivare un ECMO team mobile (24/24 e 7/7)

I centri di 3 livello devono rispettare le seguenti caratteristiche strutturali/organizzative:

- Disponibilità ECMO team mobile per incannulamento/trasporto 24/24 e 7/7 (anche tramite reperibilità)
- Disponibilità ricovero in ambiente intensivo 24/24
- Servizio di Emodinamica h24 e 7/7
- Disponibilità di un cardiologo ed un ecocardiografista h24 e 7/7
- Divisione di Cardiochirurgia
- Divisione di Chirurgia vascolare
- Possibilità di upgrading a supporto circolatorio meccanico long term e/o trapianto cardiaco
- Team multidisciplinare per impianto e gestione LVAD in classe INTERMACS 1 (MCS team)

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Table 32 **Endomyocardial biopsy in patients with suspected myocarditis**

Indication (see also section 4.3). Progressive or persistent severe cardiac dysfunction and/or life-threatening ventricular arrhythmias and/or Mobitz type 2 second-degree or higher AV block with lack of short-term (<1-2 weeks) expected response to usual medical treatment. The aim is to identify aetiology and to indicate specific treatment (e.g. giant cell myocarditis, eosinophilic myocarditis, cardiac sarcoidosis, systemic inflammatory disorders).[97,98,917,918,958]
Number and sites of the samples A minimum of 5 but possibly at least 7 samples, 3 for pathology, 2 for infections (DNA, PCR) and 2 for RNA viruses/viral replication. Left and/or right ventricle. CMR or PET guided sampling may be considered.[919]

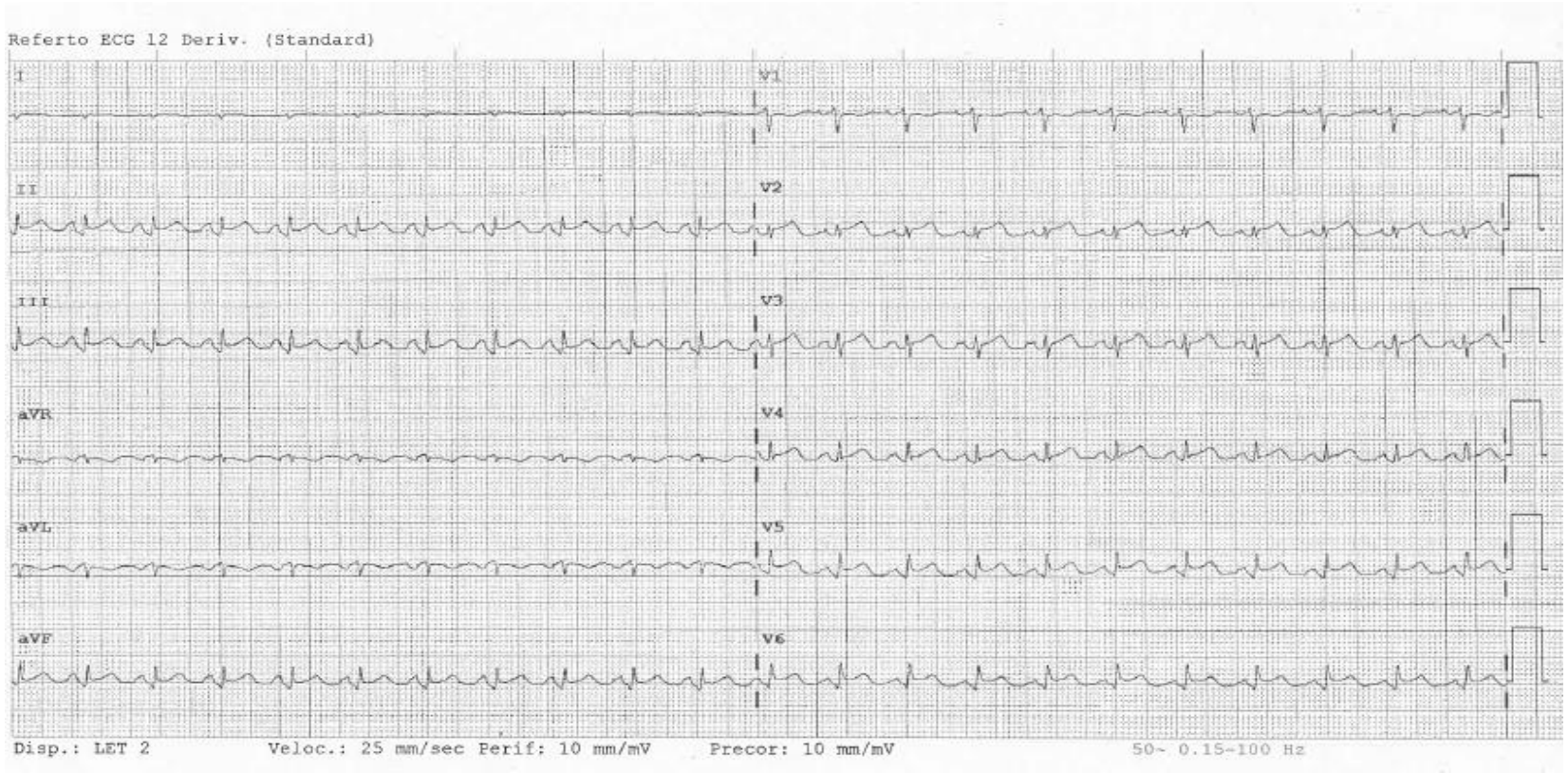
Table 31 **Diagnostic workup in suspected acute myocarditis**

Definition of suspected acute myocarditis			
Clinical presentation + ≥1 mandatory diagnostic test being positive (by preference CMR) in the absence of significant coronary artery, valvular or congenital heart disease, or other causes.			
		Sensitivity	**Specificity**
Clinical presentation			
Acute/new onset chest pain, dyspnoea, signs of left and/or right HF, and/or unexplained arrhythmias or aborted sudden death.		Low	Low
Mandatory diagnostic tests			
ECG	New and dynamic ST-T abnormalities, including pseudo-infarct ST segment elevation, atrial or ventricular arrhythmias, AV blocks, QRS abnormalities.	High	Low
Laboratory tests	Elevated troponins with dynamic changes consistent with myocardial necrosis. Standard tests including white blood cells count to exclude eosinophilia.[919,954]	Intermediate	Low
Echocardiography	New structural or function abnormalities, regional wall motion abnormalities or global ventricular dysfunction without ventricular dilatation or with, generally mild, dilatation, increased wall thickness due to myocardial oedema, pericardial effusion, intracardiac thrombi, not explained by other conditions (e.g., CAD, ACS or valvular heart disease).	High	Low
CMR	Oedema, inflammation and fibrosis detection, quantification and localization through T1 and T2 mapping, extracellular volume assessment and LGE (see *Table 33*).[955,956]	High	Intermediate
Additional diagnostic tests			
Coronary angiography or CTCA	Excludes significant CAD or ACS in clinically suspected myocarditis.	High	High
Endomyocardial biopsy	For diagnosis and indication to specific treatment (see *Table 32*).	Intermediate	High

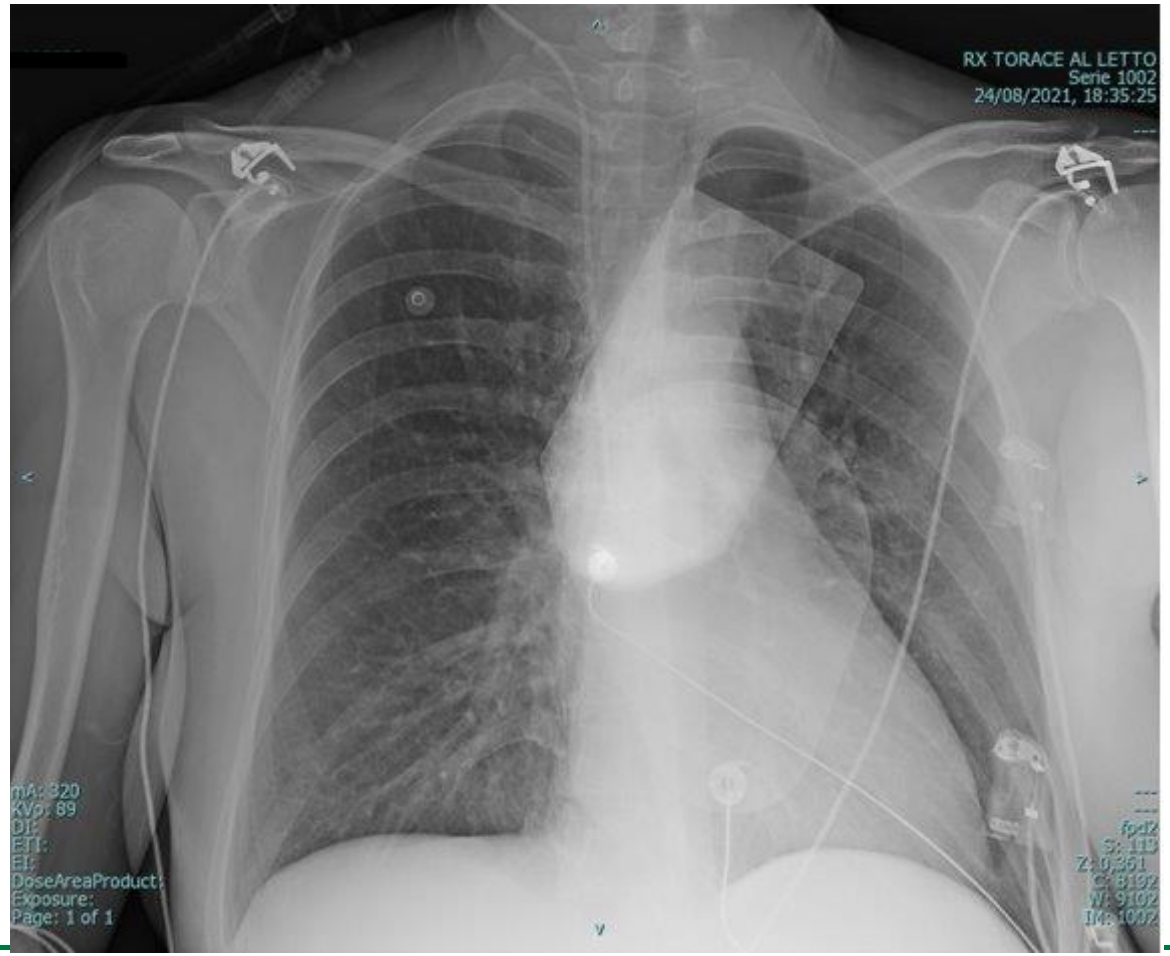
European Heart Journal (2021) 42, 3599 3726

Clinical course in CICU:

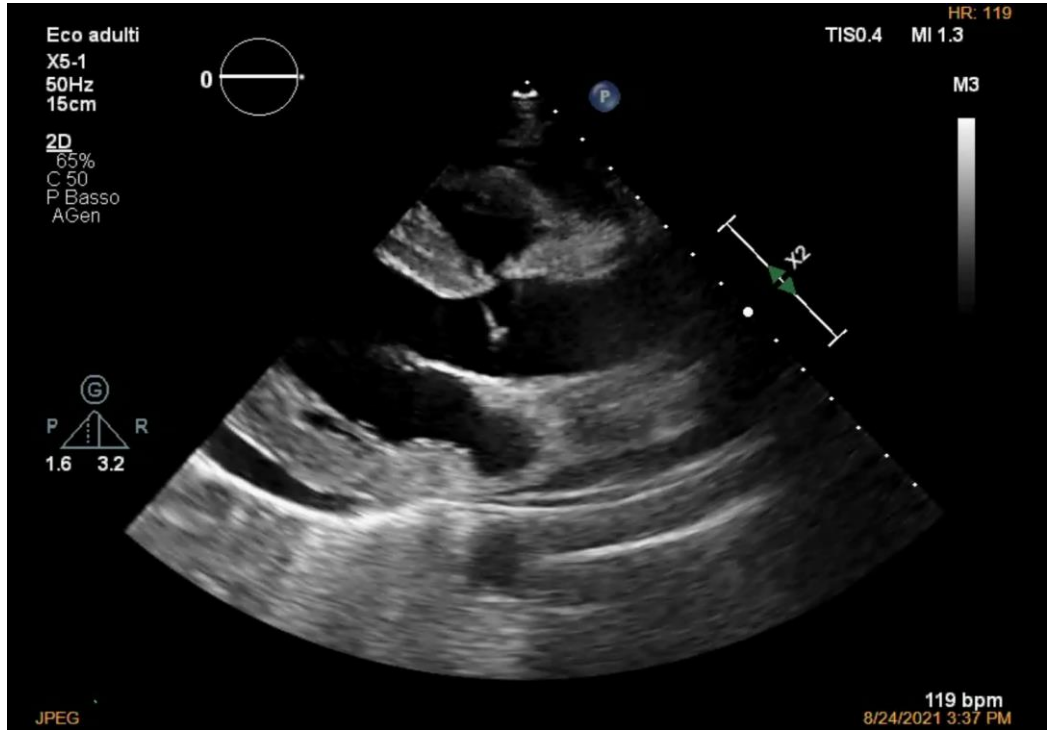
BP: 110/80 mmHg, HR: 115 bpm, SO2 98% on room air. Afebrile.
Physical examination: pale and cool extremities, gallop rhythm, jugular venous distension, pulsus paradoxus .

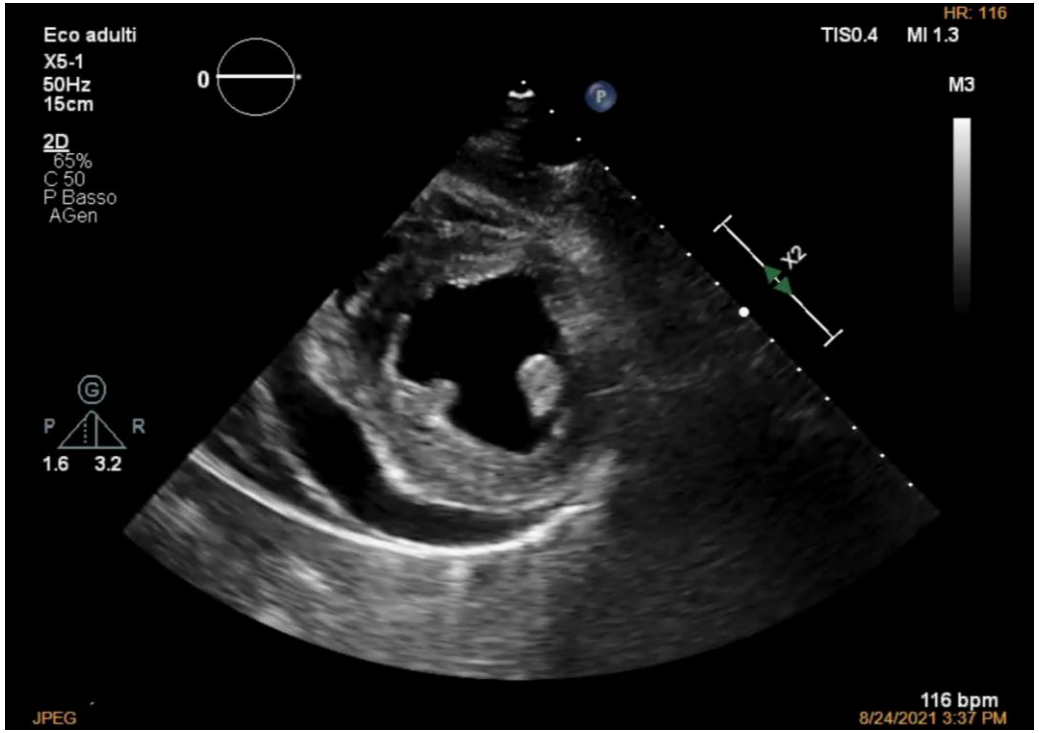


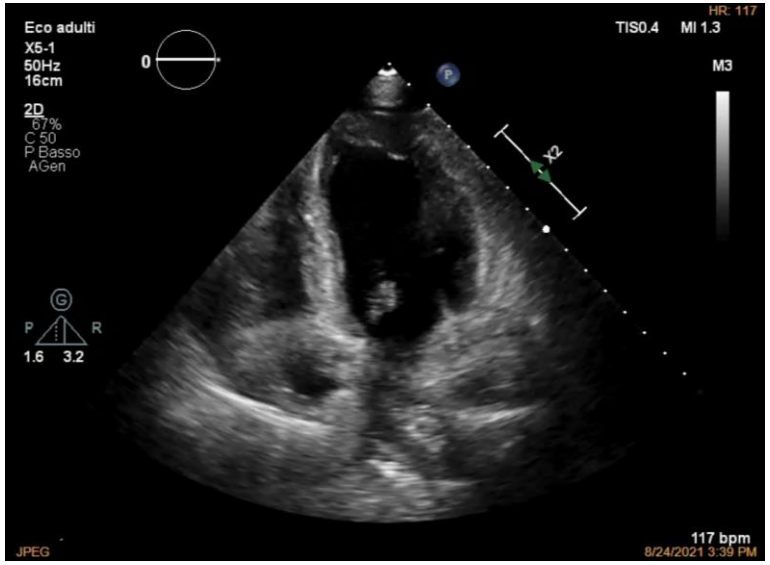
Clinical course in CICU:

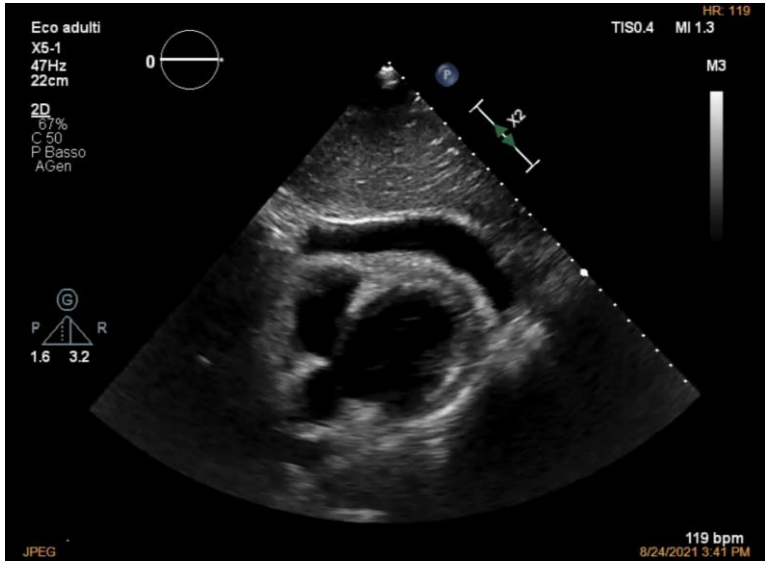


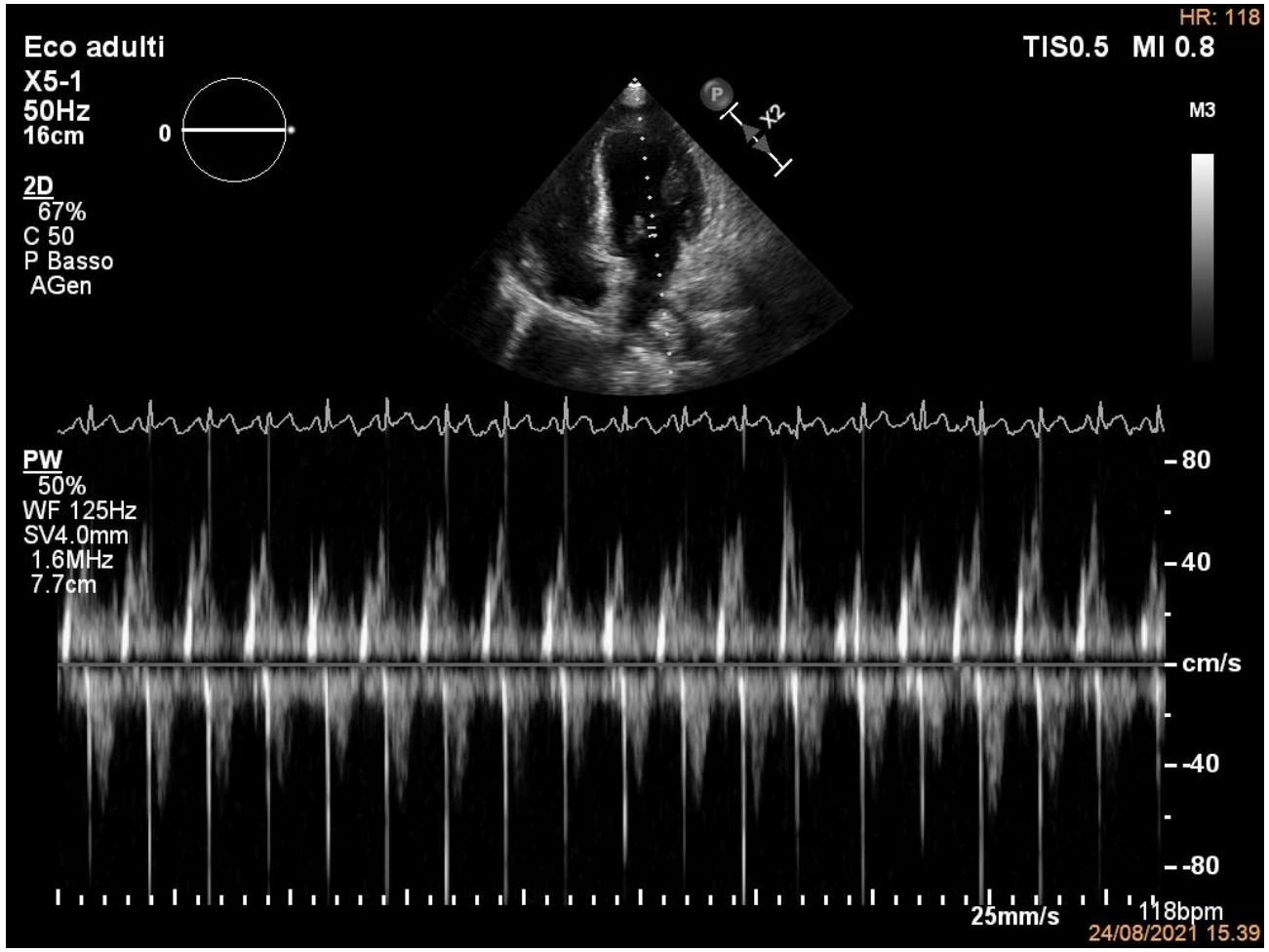
Echo findings:






Eco adulti
X5-1
50Hz
16cm
2D
67%
C 50
P Basso
AGen
HR: 117
TIS0.4 MI 1.3
M3
1.6 3.2
117 bpm
8/24/2021 3:39 PM
JPEG


Eco adulti
X5-1
47Hz
22cm
2D
67%
C 50
P Basso
AGen
HR: 119
TIS0.4 MI 1.3
M3
1.6 3.2
119 bpm
8/24/2021 3:41 PM
JPEG


Eco adulti
X5-1
50Hz
16cm
2D
67%
C 50
P Basso
AGen
HR: 118
TIS0.5 MI 0.8
M3
PW
50%
WF 125Hz
SV4.0mm
1.6MHz
7.7cm
80
40
cm/s
-40
-80
25mm/s
118bpm
24/08/2021 15.39

[redacted]

Gas ematici [redacted]

B-pH	7,506	*		[7,350 - 7,450]
B-Pressione parziale di ossigeno (pO2)	98,8		mmHg	[83,0 - 108,0]
B-Pressione parziale di anidride carbonica (pCO2)	24,9	*	mmHg	[32,0 - 45,0]

Gas ematici corretti con la temperatura [redacted]

B-pH (T°C)	7,521		
B-Pressione parziale ossigeno (pO2, T °C)	93,5	mmHg	
B-Press. parziale anidride carbonica (pCO2, T °C)	23,7	mmHg	

Ossimetria [redacted]

B-Emoglobina (Hb)	15,0		g/dL	[11,7 - 17,4]
B-Ematocrito (Hct)	45,9		%	[37,0 - 51,0]
B-Saturazione dell'ossigeno (sO2)	97,7		%	[95,0 - 99,0]
B-Ossiemoglobina (fO2Hb)	96,2		%	[94,0 - 98,0]
B-Carbossiemoglobina (fCOHb)	0,5		%	[0,5 - 1,5]
B-Metaemoglobina (fMetHb)	1,0		%	[0,0 - 1,5]
B-Deossiemoglobina (fHHb)	2,3		%	[0,0 - 5,0]

Elettroliti [redacted]

B-Ioni Sodio (Na+)	136,0		mmol/L	[135,0 - 153,0]
B-Ioni potassio (K+)	4,1		mmol/L	[3,5 - 5,3]
B-Ioni calcio (Ca++)	1,09	*	mmol/L	[1,15 - 1,29]
B-Ioni cloro (Cl-)	106,0		mmol/L	[94,0 - 110,0]

Stato di ossigenazione [redacted]

B-Concentrazione totale di ossigeno (O2),c	9,1		mmol/l	[7,1 - 9,9]
B-pO2 e saturazione di Hb al 50 % (p50),c	23,1	*	mmHg	[24,0 - 28,0]
B-Gradiente di O2 (A-a),c	21,5		mmHg	[15,0 - 37,0]
Rapporto pO2/FIO2,c	470,0			[>400]

Stato metabolico [redacted]

B-Glucosio	168,0	*	mg/dL	[70,0 - 105,0]
B-Lattato	2,1	*	mmol/L	[0,6 - 1,7]

Stato acido base [redacted]

B-Bicarbonati (HCO3-),c	19,5	*	mmol/L	[21,0 - 28,0]
B-Eccesso di base standard (SBE),c	-3.1	*	mmol/L	[-2,0 - 2,0]
B-Gap anionico,c	14,2		mmol/L	[10,0 - 20,0]
B-Osmolarità (mOsm),c	281,0		mmol/Kg	[275,0 - 295,0]

Note cliniche

Temperatura (T °C)	36,0		°C	
Frazione inspirata di O2 (FiO2)	21		%	

[redacted]

Gas ematici [redacted]

B-pH	7,417			[7,320 - 7,420]
B-Pressione parziale di ossigeno (pO2)	31,8		mmHg	[24,0 - 40,0]
B-Pressione parziale di anidride carbonica (pCO2)	34,1	*	mmHg	[41,0 - 51,0]

Gas ematici corretti con la temperatura [redacted]

B-pH (T°C)	7,432
B-Pressione parziale ossigeno (pO2, T °C)	29,700
B-Press. parziale anidride carbonica (pCO2, T °C)	32,500

Ossimetria [redacted]

B-Emoglobina (Hb)	14,1		g/dL	[11,7 - 17,4]
B-Ematocrito (Hct)	43,2		%	[35,0 - 45,0]
B-Saturazione dell'ossigeno (sO2)	51,5		%	[40,0 - 70,0]
B-Ossiemoglobina (fO2Hb)	50,7		%	[40,0 - 70,0]
B-Carbossiemoglobina (fCOHb)	0,5		%	[0,5 - 1,5]
B-Metaemoglobina (fMetHb)	1,1		%	[0,0 - 1,5]
B-Deossiemoglobina (fHHb)	47,7		%	[25,0 - 55,0]

Elettroliti [redacted]

B-Ioni Sodio (Na+)	138,0		mmol/L	[135,0 - 153,0]
B-Ioni potassio (K+)	3,7		mmol/L	[3,5 - 5,3]
B-Ioni calcio (Ca++)	1,03	*	mmol/L	[1,15 - 1,29]
B-Ioni cloro (Cl-)	108,0		mmol/L	[94,0 - 110,0]

Stato di ossigenazione [redacted]

B-Concentrazione totale di ossigeno (O2),c	4,5	mmol/L	
B-pO2 e saturazione di Hb al 50 % (p50),c	31,1	mmHg	

Stato metabolico [redacted]

B-Glucosio	148,0	*	mg/dL	[70,0 - 105,0]
B-Lattato	2,2		mmol/L	[0,6 - 2,4]

Stato acido base [redacted]

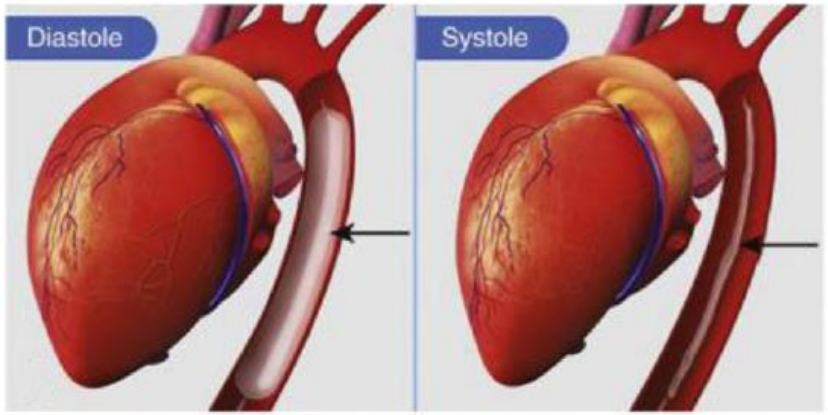
B-Bicarbonati (HCO3-),c	21,6	*	mmol/L	[22,0 - 29,0]
B-Eccesso di base standard (SBE),c	-2.3		mmol/L	
B-Gap anionico,c	12,0		mmol/L	[10,0 - 20,0]
B-Osmolarità (mOsm),c	284,5		mmol/Kg	[275,0 - 295,0]

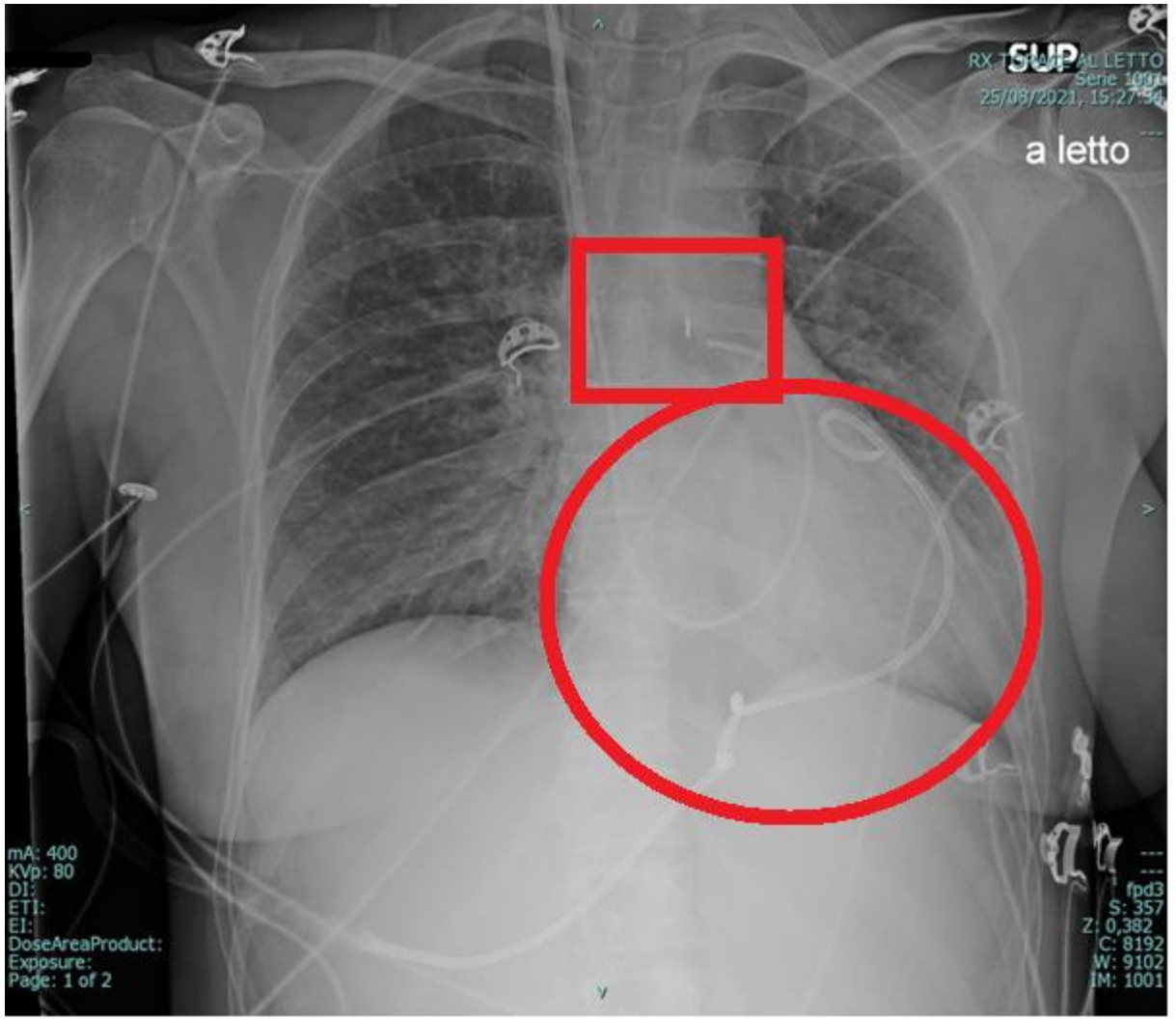
Note cliniche

Temperatura (T °C)	36,000
Frazione inspirata di O2 (FiO2)	21,000

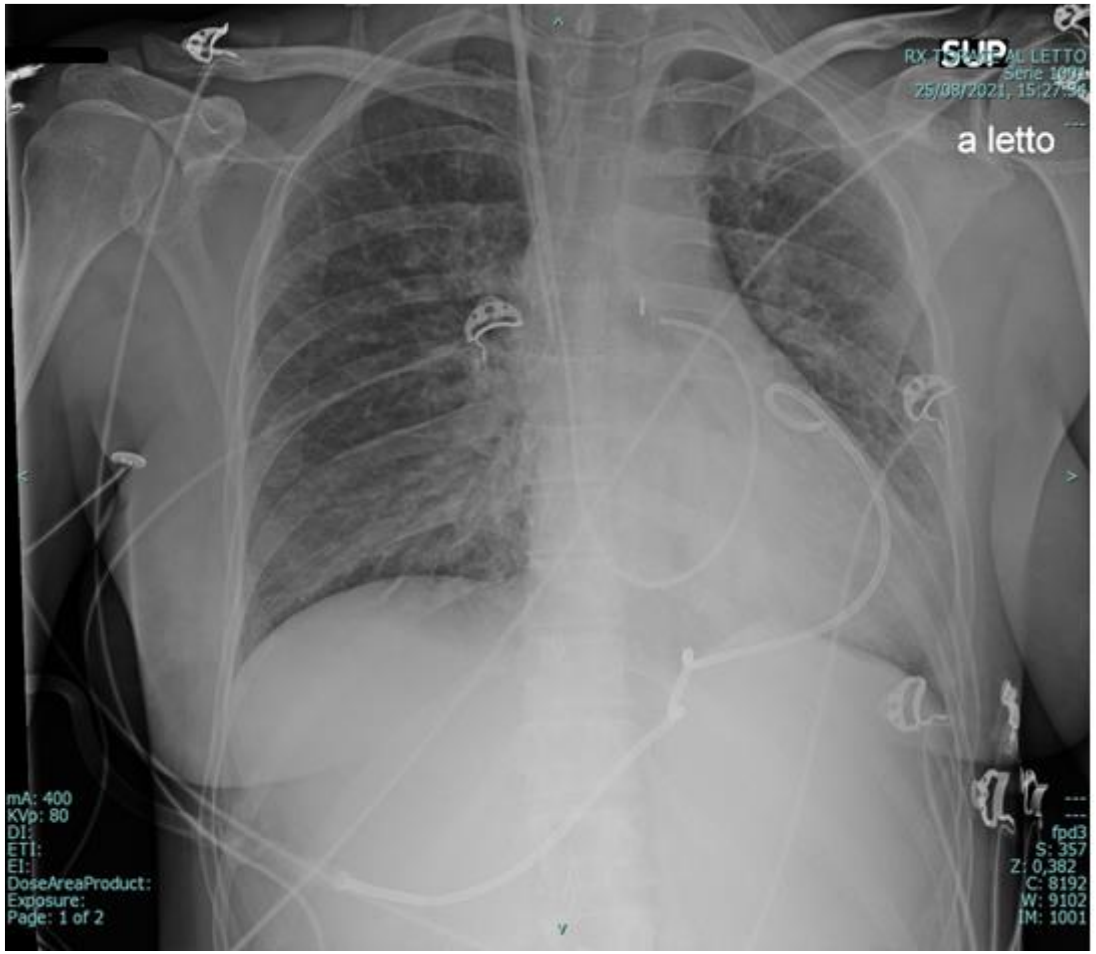
Patients was then transferred in Cardiopulmonary Intensive Care Unit and pericardiocentesis was performed, draining 600 cc of citrine effusion.

To improve hemodynamics, intra-aortic balloon pump (IABP) was placed via femoral access.





Given high clinical suspicion of acute fulminant myocarditis, endomyocardial biopsy with right heart catheterization were performed.



CI 1.7l/min/m2

PAPm 18 mmHg

PVC 10 mmHg

PAOP 15 mmHg

SvO2 50%

Despite the mechanical (IABP) and pharmacological support (dobutamine 3 gamma/kg/min), arterial blood gas showed a further increase in serum lactate concentration so dobutamine was replaced with epinephrine 0.05 gamma/kg/min in addition to sodium nitroprusside.

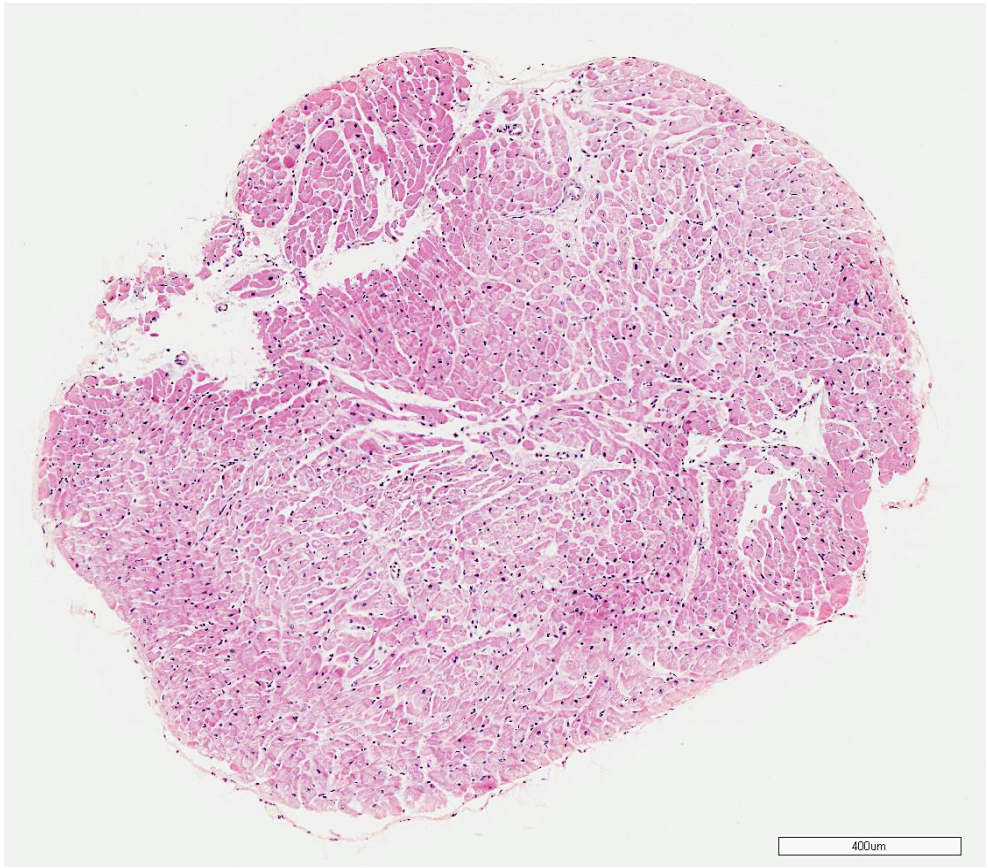
S-Amilasi	48,0		mU/ml	[25,0 - 125,0]
S-Bilirubina Totale	0,55		mg/dl	[0,2 - 1,1]
S-Fosfatasi Alcalina	59,0		Ul/L	[46,0 - 170,0]
S-Gamma-GT	41,0		mU/ml	[11,0 - 53,0]
S-Colinesterasi	5735,0		mU/ml	[5300,0 - 12900,0]
S-ALT	35,0	*	mU/ml	[11,0 - 34,0]
S-AST	100,0	*	mU/ml	[11,0 - 39,0]
S-Proteine Totali	6,1	*	g/dl	[6,6 - 8,7]
S-Sodio	136,9		mEq/l	[135 - 153]
S-Potassio	3,89		mEq/l	[3,50 - 5,30]
S-Cloruro	102,0		mEq/l	[94,0 - 110,0]
S-Calcio	8,10	*	mg/dl	[8,60 - 10,30]
S-Magnesio	1,50	*	mg/dl	[1,70 - 2,55]
S-Urea	41,0		mg/dl	[10,0 - 50,0]
S-Creatinina (Modificato)	0,92		mg/dl	[0,55 - 1,02]
eGFR (Filtrato Glomerulare Stimato)	77		mL/min/1,73m(2)	

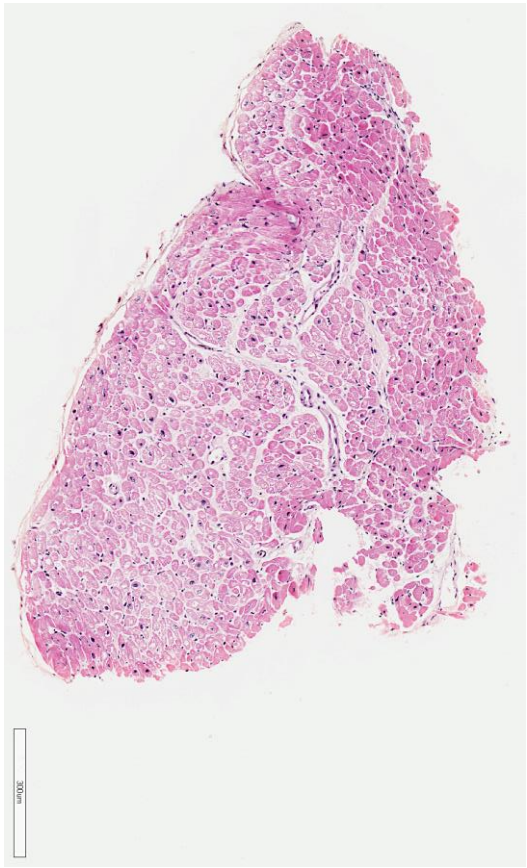
La stima delle eGFR è valida per soggetti di razza caucasica di età superiore a 18 anni. Non è raccomandata per donne in gravidanza, soggetti defedati e/o affetti da patologie multiple (Ann Int Med 2009 150:604-12).

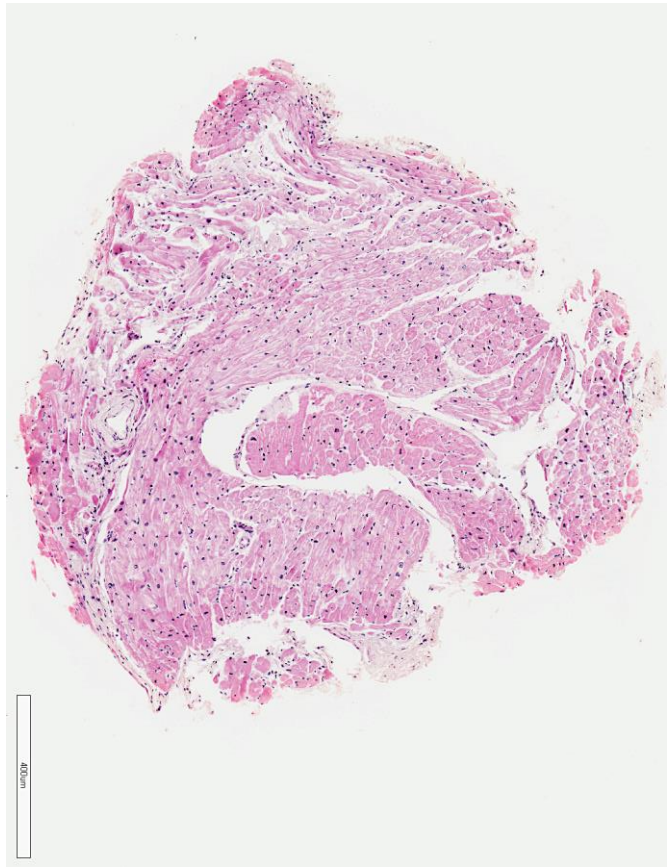
S-Proteina C Reattiva	0,95	*	mg/dl	[<0,5]

hsTNI peak 19100 ng/l (URL 47 ng/l)

EMB 5549-T-22 (First EMB)







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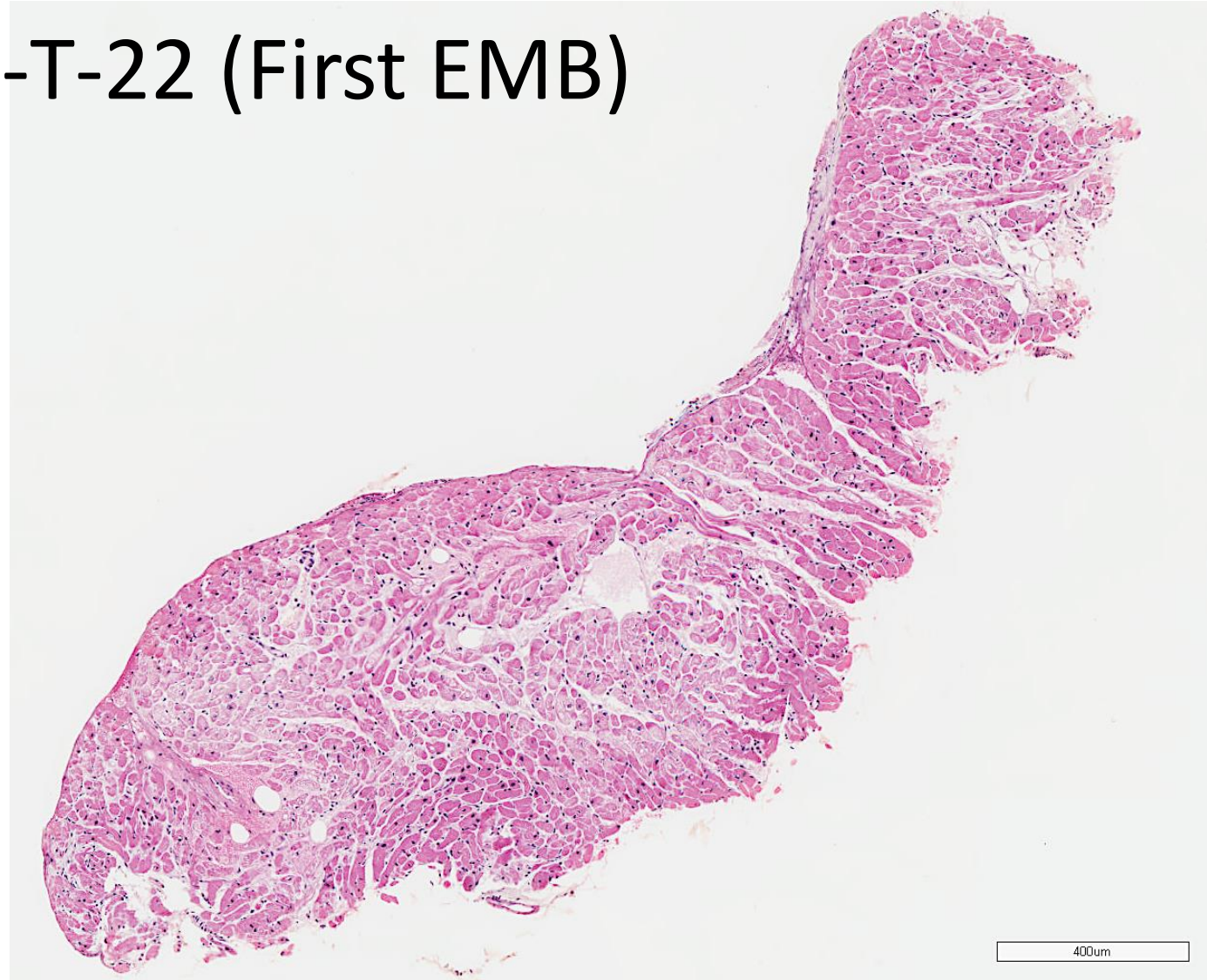

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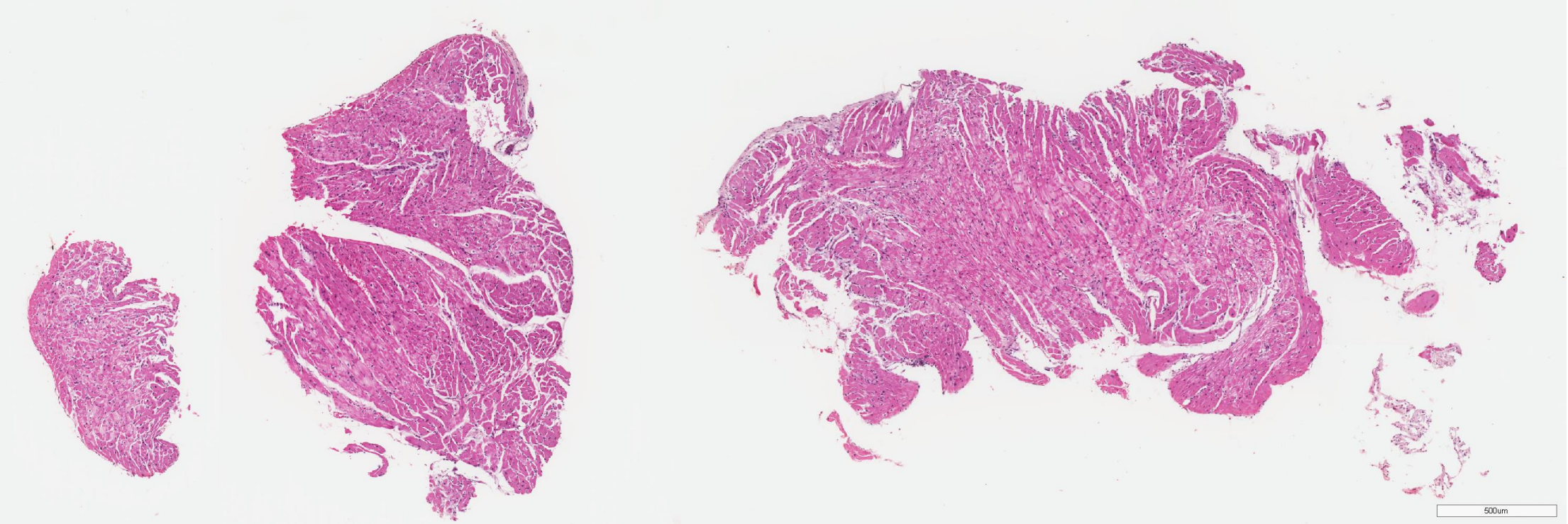

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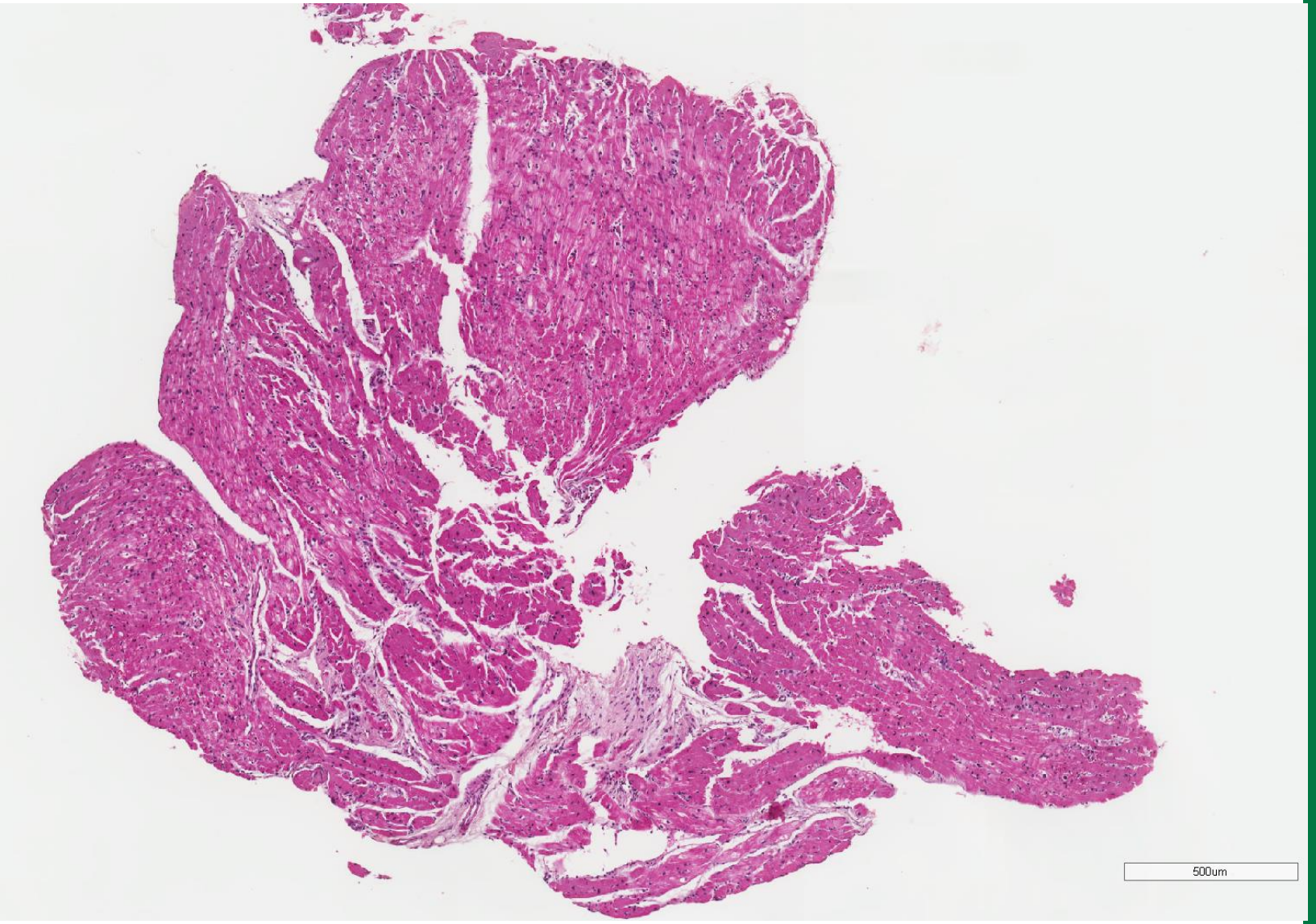
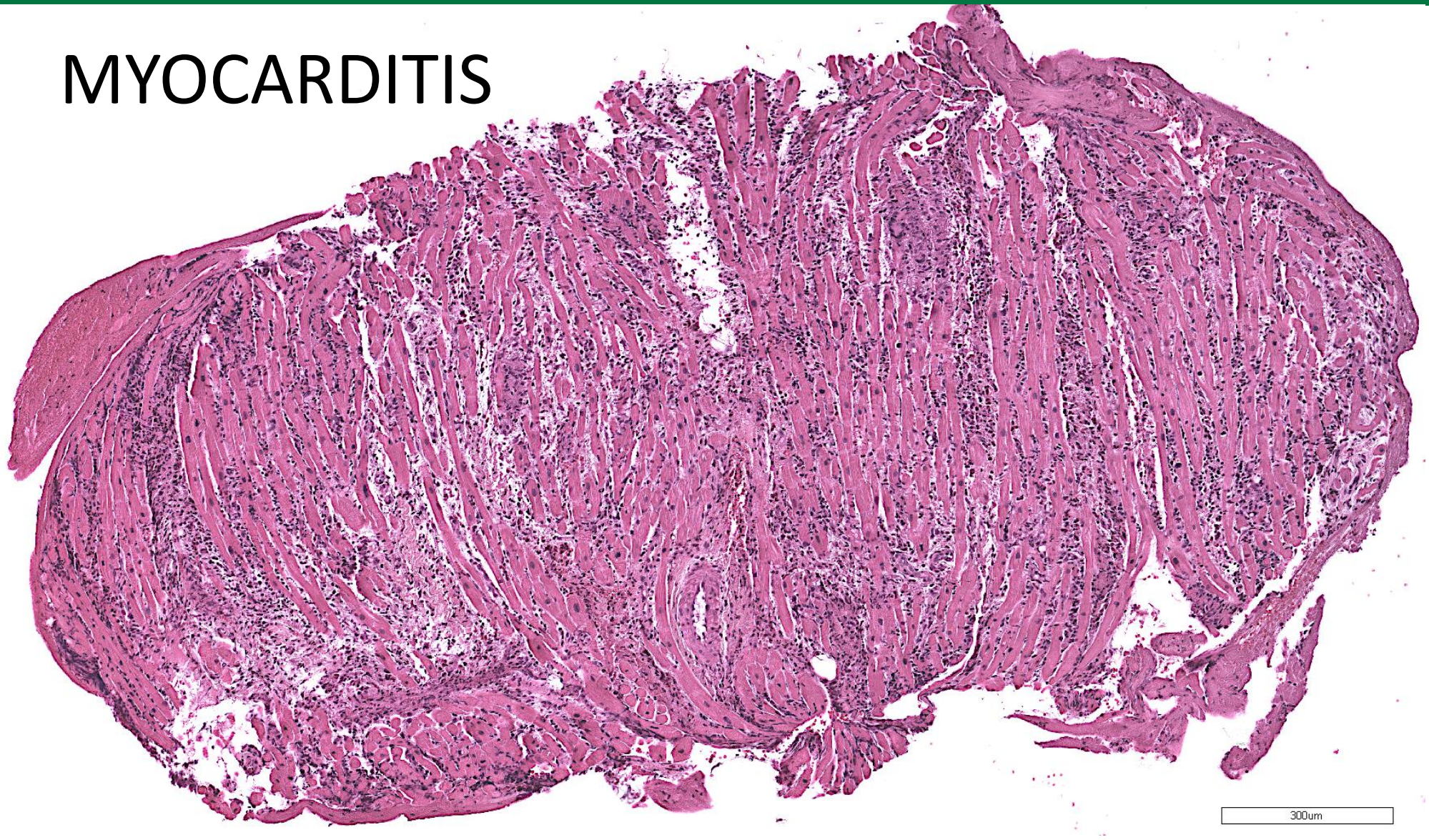
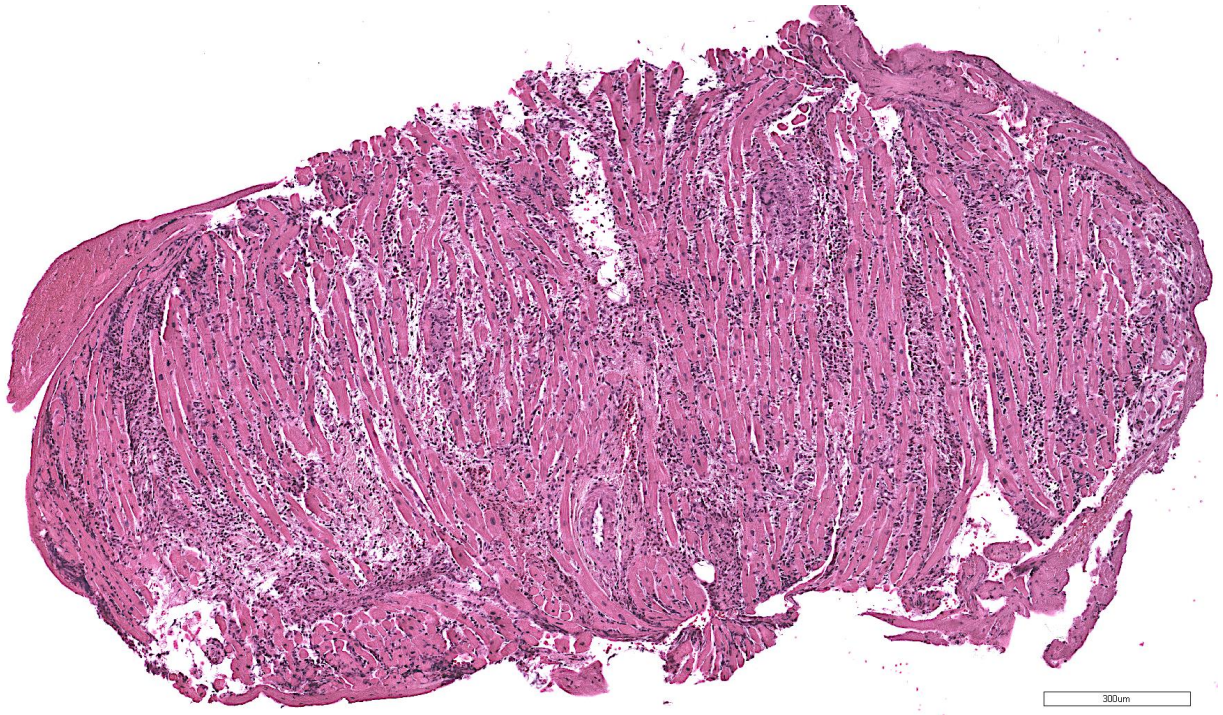


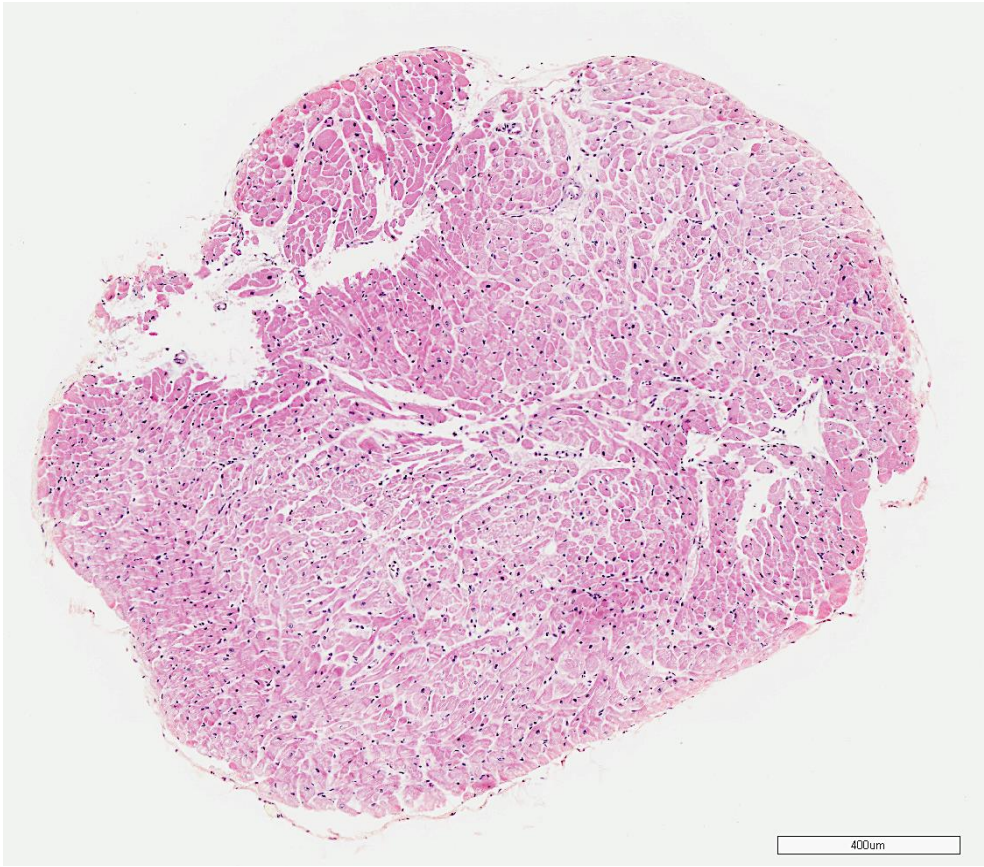
MYOCARDITIS



MYOCARDITIS



First EMB



Endomyocardial biopsy results

Studio al microscopio ottico

Miociti senza significative immagini di ipertrofia. Focali immagini di miofibrillolisi. Non immagini riferibili a necrosi coagulativa. Bande di contrattura legate alla procedura bioptica.

Interstizio senza significativa fibrosi. Edema interstiziale e stravasi emorragici vs. procedurali. Rari e sparsi infiltrati infiammatori linfocitari, sparsi macrofagi non configuranti miocardite acuta linfocitaria. Non eosinofili, non cellule giganti. Non depositi di amiloide.

Piccoli vasi intramurali senza immagini di microtrombi o vasculite.

Endocardio lievemente ispessito per fibrosi. In un campione trombosi endocardica murale recente.

In sintesi:

- esclusa miocardite acuta linfocitaria, eosinofila e giagantocellulare;
- esclusa necrosi coagulativa;
- escluse malattie da accumulo intramiocitarie,
- esclusa amiloidosi cardiaca;
- non visibili microtrombi dei piccoli vasi intramurali;

Si segnalano: edema interstiziale e piccola trombosi murale endocardica (un campione).

Endomyocardial biopsy (EBM) was negative for myocarditis according to the Dallas criteria and immunohistochemistry, but showed interstitial edema.

Both EBM and blood sample were negative for viral RNA/DNA.

European Heart Journal (2013) 34, 2636–2648
doi:10.1093/eurheartj/eht210

ESC REPORT

Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases

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Table 4 Diagnostic criteria for clinically suspected myocarditis

Clinical presentations[a]
Acute chest pain, pericarditic, or pseudo-ischaemic
New-onset (days up to 3 months) or worsening of: dyspnoea at rest or exercise, and/or fatigue, with or without left and/or right heart failure signs
Subacute/chronic (>3 months) or worsening of: dyspnoea at rest or exercise, and/or fatigue, with or without left and/or right heart failure signs
Palpitation, and/or unexplained arrhythmia symptoms and/or syncope, and/or aborted sudden cardiac death
Unexplained cardiogenic shock
Diagnostic criteria
I. ECG/Holter/stress test features
Newly abnormal 12 lead ECG and/or Holter and/or stress testing, any of the following: I to III degree atrioventricular block, or bundle branch block, ST/T wave change (ST elevation or non ST elevation, T wave inversion), sinus arrest, ventricular tachycardia or fibrillation and asystole, atrial fibrillation, reduced R wave height, intraventricular conduction delay (widened QRS complex), abnormal Q waves, low voltage, frequent premature beats, supraventricular tachycardia
II. Myocardiocytolysis markers
Elevated TnT/TnI
III. Functional and structural abnormalities on cardiac imaging (echo/angio/CMR)
New, otherwise unexplained LV and/or RV structure and function abnormality (including incidental finding in apparently asymptomatic subjects): regional wall motion or global systolic or diastolic function abnormality, with or without ventricular dilatation, with or without increased wall thickness, with or without pericardial effusion, with or without endocavitary thrombi
IV. Tissue characterization by CMR
Oedema and/or LGE of classical myocarditic pattern (see text)

Clinically suspected myocarditis if ≥1 clinical presentation and ≥1 diagnostic criteria from different categories, in the absence of: (1) angiographically detectable coronary artery disease (coronary stenosis ≥ 50%); (2) known pre-existing cardiovascular disease or extra-cardiac causes that could explain the syndrome (e.g. valve disease, congenital heart disease, hyperthyroidism, etc.) (see text). Suspicion is higher with higher number of fulfilled criteria.
[a]If the patient is asymptomatic ≥2 diagnostic criteria should be met.

EBM potential limitations: myocarditis is usually a focal process, adequate sampling of the myocardium not always feasible in urgent conditions.

Considering an acute myocarditis, the most likely clinical diagnosis, we decided at day 2 to initiate high-dose steroids as immunosuppressive (intravenous methylprednisolone 1 g daily for 3 days).
Given the positive result on the ANA test, intravenous immunoglobulins were administered for 4 days.

Autoimmune antibodies & friends

		ENDOCRINOLOGIA	
S-Ab-Anti-Tireoglobulina su Siero	S-Ab-Anti-Tireoglobulina	<20.0	[<40]
S-FT4 su Siero	S-FT4	12.96	[8,00 - 19,00]
S-Procalcitonina su Siero	P-Procalcitonina	0.08	[0,00 - 0,50]
S-TSH (III generazione) su Siero	S-TSH	**4.016***	[0,400 - 4,000]
		PROTEINE	
S-Complemento Fattore C4 su Siero	Complemento Fattore C4	24.8	[10,0 - 40,0]
S-Fattore Reumatoide su Siero	Fattore Reumatoide	<10	[<20]
S-Titolo antistreptolisinico su Siero	S-Titolo antistreptolisinico	**545.0***	[< 400,0]ValoriA
		AUTOIMMUNITA'	
S-Ab anti Ena Screen su Siero	S-Ab Anti Ena Screening	Negativo	Negativo
S-Ab anti ds-DNA su Siero	S-Ab Anti-Dsdna-Eia	**11.0***	<10 Negativo
	S-Ab Anti-Dsdna-Ifi	Negativo	Negativo < 1:10

S-Ab anti ds-DNA IFI su Siero			
S-Ab anti Cardiolipina IgM su Siero	Anticorpi Anti Cardiolipina IgM	2.1	<10 Negativo10-40Debolepositivo>40Positivo
S-Ab anti Cardiolipina IgG su Siero	Anticorpi Anti Cardiolipina IgG	1.8	<10 Negativo10-40Debolepositivo>40Positivo
S-Ab anti mitocondri (IFI) su Siero	S-Ama (Ab Antimitocondrio)	Negativo	Negativo < 1:40
S-Ab anti NUCLEO IFI (HEp-2) su Siero	Ana Pattern1	Positivo Nucleolare Omogeneo (AC-8)* 1:640	
	Nota	* ICAP International Consensus	
Ab-anti Citoplasma Granulociti Neutrofili su Siero	C-ANCA IFI	Negativo	Negativo <1:20
	P-ANCA IFI	Negativo	Negativo <1:20
S-Peptide Ciclico Citrullinato su Siero	S-Anti Ccp	0.3	<7 Negativo7-10Dubbio>10Positivo
S-Ab anti Muscolo liscio (IFI) su Siero	S-Asma	Negativo	Negativo < 1:40
S-Ab anti B2glicoproteina IgM su Siero	Anticorpi Anti beta 2 Glicoproteina IgM	0.6	<7 Negativo7-10Debolepositivo>10Positivo
S-Ab anti B2glicoproteina IgG su Siero	Anticorpi Anti beta 2 Glicoproteina IgG	0.6	<7 Negativo7-10Debolepositivo>10Positivo
S-Ab antimitocondri (M2) su Siero	S-Ab anti mitocondri (M2)	Negativo	Negativo

Virus & friends:

Adenovirus DNA su tampone nasale	1	Adenovirus-DNA (PCR)	NON RILEVABILE
	1	Unita di misura	copie/ml
	1	Range di riferimento	(< 45 non rilevabile, >= 45 positivo)
Virus Parainfluenzale 2 RNA su tampone nasale	1	Virus Parainfluenzale tipo 2-RNA	NON RILEVABILE
	1	Virus Parainfluenzale tipo 2-RNA	(< 45 non rilevabile, >= 45 positivo)
	1	Virus Parainfluenzale tipo 2-RNA	copie/ml

Virus Respiratori

Virus Parainfluenzale RNA tipo 1/3 su tampone nasale	1	Virus Parainfluenzale RNA tipo 1/3	NON RILEVABILE
	1	Unita di misura	copie/ml
	1	Range di riferimento	(< 45 non rilevabile, >= 45 positivo)
Virus Parainfluenzale 4 RNA su tampone nasale	1	Virus Parainfluenzale tipo 4-RNA	NON RILEVABILE
	1	Parainfluenza 4 RNA Non refertabile	copie/ml
	1	Parainfluenza 4 RNA Non refertabile	(< 45 non rilevabile, >= 45 positivo)
Metapneumovirus RNA su tampone nasale	1	Metapneumovirus-RNA	NON RILEVABILE
	1	Unita di misura	copie/ml
	1	Range di riferimento	(< 45 non rilevabile, >= 45 positivo)

Coronavirus RNA OC43/HKU1 su tampone nasale	1	Coronavirus RNA OC43/HKU1	NON RILEVABILE
	1	Unita di misura	copie/ml
	1	Range di riferimento	(< 45 non rilevabile, >= 45 positivo)
Coronavirus RNA 229E/NL63 su tampone nasale	1	Coronavirus RNA 229E/NL63	NON RILEVABILE
	1	Range di riferimento	(< 45 non rilevabile, >= 45 positivo)
	1	Unita di misura	copie/ml
Rhinovirus - Enterovirus RNA su tampone nasale	1	Rhinovirus - Enterovirus RNA	NON RILEVABILE
	1	Unita di misura	copie/ml
	1	Range di riferimento	(< 45 non rilevabile, >= 45 positivo)
Virus Respiratorio Sinciziale RNA su tampone nasale	1	RSV RNA	NON RILEVABILE
	1	Unita di misura	copie/ml
	1	Range di riferimento	(< 45 non rilevabile, >= 45 positivo)

STILL NOTHING

Virus & friends:

Analisi	T.Prel	Esito	Risultato
Mycobacterium tuberculosis - Ricerca DNA su Liquido pericardico	1	Mycobacterium tuberculosis - Ibridazione diretta	Negativa
Colturale per Aerobi su Liquido pericardico		Esito coltura :	Negativa
Brodocoltura per Aerobi su Liquido pericardico		Esito coltura :	Negativa
Colturale per Anaerobi su Liquido pericardico		Esito coltura :	Negativa
		Esito coltura :	Negativa
Colturale per micobatteri su Liquido pericardico		Esito colorazione Ziehl Neelsen:	Assenza di bacilli alcool-acido resistenti
		Esito coltura :	Negativa

S-Alfafetoproteina su Siero	S-Alfa fetoproteina	< 1.3	[<12] IU/ml
S-Ca125 su Siero	S-Ca125	**35.3***	[<35] IU/ml
S-Ca19.9 su Siero	S-Ca19.9	**39.2***	[<37] IU/ml
S-CEA su Siero	S-CEA	< 1.0	Non fumatori: <2,5Fumatori:<5 ng/ml
	Nota	Si informa che a partire dal 12/04/2019 la modalit? di calibrazione della misura del CEA e i valori di riferimento sono stati modificati.PereventualichiarimentiilLaboratorio?adisposizione.	
ENDOCRINOLOGIA			
S-Procalcitonina su Siero	P-Procalcitonina	0.08	[0,00 - 0,50] ng/ml

STILL NOTHING

Virus & friends:

Analisi	T.Prel	Esito	Risultato	Normalit	
Colturale per Aerobi su Tampone nasale dx		Esito coltura :	Assenza di flora patogena		
Colturale per miceti su Tampone nasale dx		Esito ricerca miceti:	Negativa		
Anticorpi totali anti Treponema pallidum su Siero		Anticorpi totali anti Treponema Pallidum	<0.1	(<= 0.9 Negativo, 0.9 - 1.1 Dubbio*, > 1.1 Positivo)	
		Sierologie Batteriologia			
Brucella IgG su Siero		Brucella IgG	0.02	(<0.9 Negativo; 0.9-1.1 Dubbio; >1.1 Positivo)	
Brucella IgM su Siero		Brucella IgM	0.08	(<0.9 Negativo; 0.9-1.1 Dubbio; >1.1 Positivo)	
Widal su Siero		Paratifo A	Negativa	(positiva >= 1/80)	
		Paratifo B	Negativa	(positiva >= 1/80)	
		Tifo O	Negativa	(positiva >= 1/80)	
		Tifo H	Negativa	(positiva >= 1/80)	

Analisi	T.Prel	Esito	Risultato	Normalit	Fla
		Sierologie Batteriologia			
Chlamydia pneumoniae IgG su Siero		Chlamydia pneumoniae IgG	0.44	(<0.9 Negativo; 0.9-1.1 Dubbio; >1.1 Positivo)	
Chlamydia pneumoniae IgA su Siero		Chlamydia pneumoniae IgA	0.25	(<0.9 Negativo; 0.9-1.1 Dubbio; >1.1 Positivo)	
Mycoplasma pneumoniae IgG su Siero		Mycoplasma pneumoniae IgG	1.58	(<10 negativo, >=10 positivo)	
Mycoplasma pneumoniae IgM su Siero		Mycoplasma pneumoniae IgM	3.40	(<10 negativo; >=10 positivo)	

STILL NOTHING

Virus and mycobacteria on pericardial effusion:

Analisi	T.Prel	Esito	Risultato
Citomegalovirus DNA su liquido pericardico	1	CMV DNA Multimateriale	NON RILEVABILE
	1	Unita di misura	copie/ml
	1	Range di riferimento	(< 45 non rilevabile, >= 45 positivo)
Virus Epstein Barr DNA su liquido pericardico	1	Virus Epstein-Barr DNA (PCR)	NON RILEVABILE
	1	Unita di misura	copie/ml
	1	Range di riferimento	(< 20 non rilevabile, >= 20 positivo)
Parvovirus B19 DNA su liquido pericardico	1	Parvovirus B19-DNA (PCR)	NON RILEVABILE
	1	Unita di misura	copie/ml
	1	Range di riferimento	(< 20 non rilevabile, >= 20 positivo)
Adenovirus DNA su liquido pericardico	1	Adenovirus-DNA (PCR)	NON RILEVABILE
	1	Unita di misura	copie/ml
	1	Range di riferimento	(< 20 non rilevabile, >= 20 positivo)
Enterovirus RNA su liquido pericardico	2	Entero RNA Calcolato	NON RILEVABILE
	2	Unita di misura	copie/ml
	2	Range di riferimento	(< 20 non rilevabile, >= 20 positivo)

Analisi	T.Prel	Esito	Risultato
Mycobacterium tuberculosis - Ricerca DNA su Liquido pericardico	1	Mycobacterium tuberculosis - Ibridazione diretta	Negativa
Colturale per Aerobi su Liquido pericardico		Esito coltura :	Negativa
Brodocoltura per Aerobi su Liquido pericardico		Esito coltura :	Negativa
Colturale per Anaerobi su Liquido pericardico		Esito coltura :	Negativa
		Esito coltura :	Negativa
Colturale per micobatteri su Liquido pericardico		Esito colorazione Ziehl Neelsen:	Assenza di bacilli alcool-acido resistenti
		Esito coltura :	Negativa

Virus & friends:

Analisi	T.Prel	Esito	Risultato	Normalit🔲
Citomegalovirus anticorpi IgG su siero	1	Citomegalovirus IgG (CLIA)	149.00	(<12 negativo, >14 positivo)
Citomegalovirus anticorpi IgM su siero	1	Citomegalovirus IgM (CLIA)	<18	(>22 positivo)
Virus Epstein-Barr anticorpi VCA IgG su siero	1	Virus di Epstein-Barr VCA IgG (ELISA)	230	(<20 negativo)
Virus Epstein-Barr anticorpi VCA IgM su siero	1	Virus di Epstein-Barr VCA IgM (ELISA)	<20	(<20 negativo; >40 positivo)
Virus Epstein-Barr anticorpi EBNA IgG su siero	1	Virus di Epstein-Barr EBNA IgG (ELISA)	86	(<5 negativo; >20 positivo)
Parvovirus B19 anticorpi IgG su siero	1	Parvovirus B19 IgG (CLIA)	<0.9	(<0.9 negativo; >1.1 positivo)
Parvovirus B19 anticorpi IgM su siero	1	Parvovirus B19 IgM (CLIA)	<0.9	(<0.9 negativo; >1.1 positivo)
HIV 1-2 test di conferma su siero		HIV 1-2 Western blot	NEGATIVO	
		gp 41	-	
		p 24	-	
		gp 160	-	
		p 31	-	
		gp 140	-	
		gp 36 (HIV 2)	-	
HIV 1-2 anticorpi e HIV1 antigene p24 su siero		HIV1-2 anticorpi e HIV1 antigene p24	DUBBIO	

Virus Epatite B antigene HBsAg su siero	HBsAg	NEGATIVO
Virus Epatite B anticorpi anti-HBsAg su siero	HBsAb	836.7
Virus Epatite C anticorpi (Test di screening) su siero	HCV anticorpi (ELISA)	NEGATIVO

HIV-1 serology results uncertain so HIV RNA count was requested.

Clinical course:

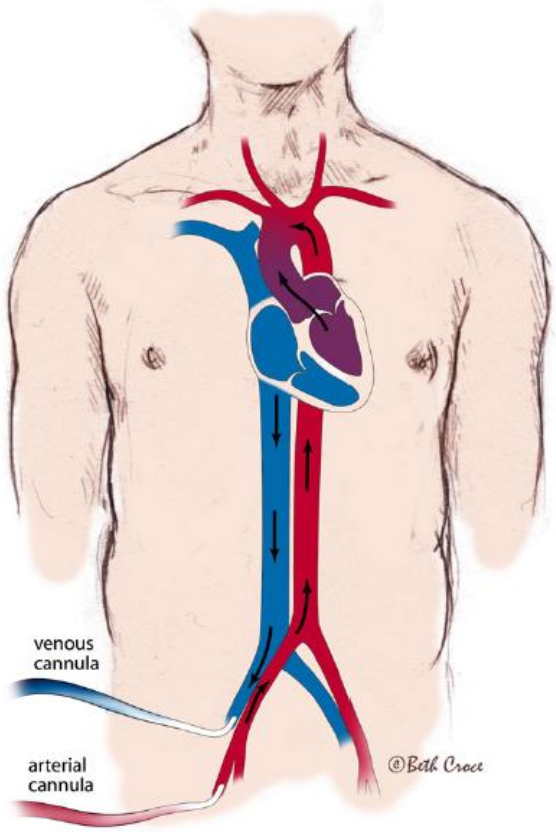
On the third day the patient's critical conditions got worse, with low urine output, increase in serum lactate concentration and ScVO2 below 50%.

A repeat TTE showed severe worsening biventricular dysfunction with 10% LV ejection fraction and significant mitral valve regurgitation.

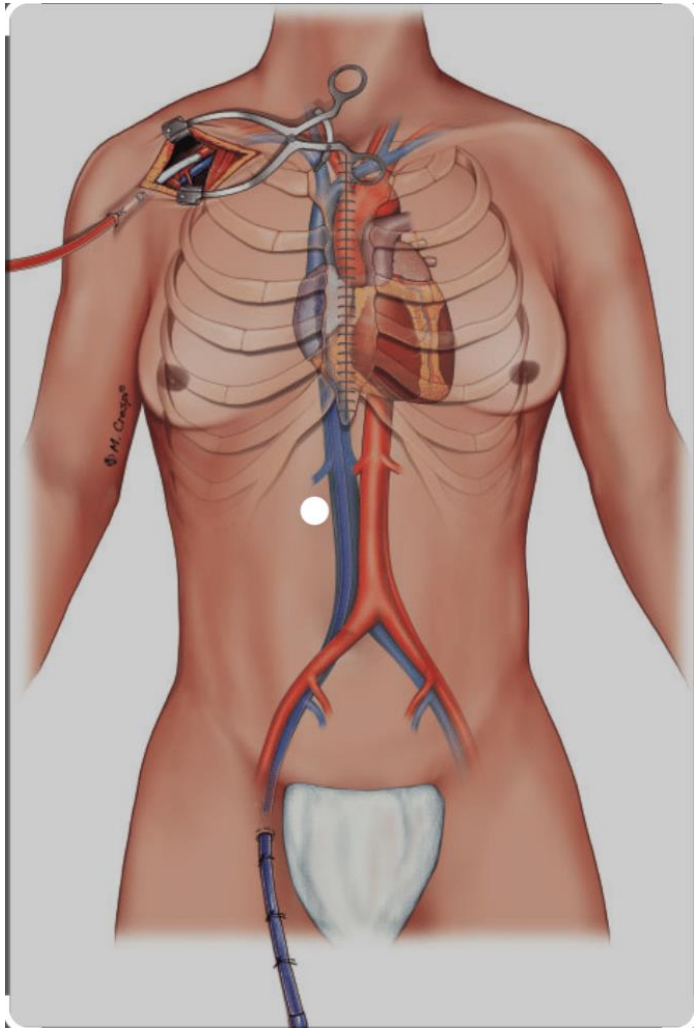
Cardiac index resulted severely depressed (CI 1.5 l/kg/min^2) with a slight increase of mean pulmonary capillary wedge pressure and significant increase in mean right atrial pressure.

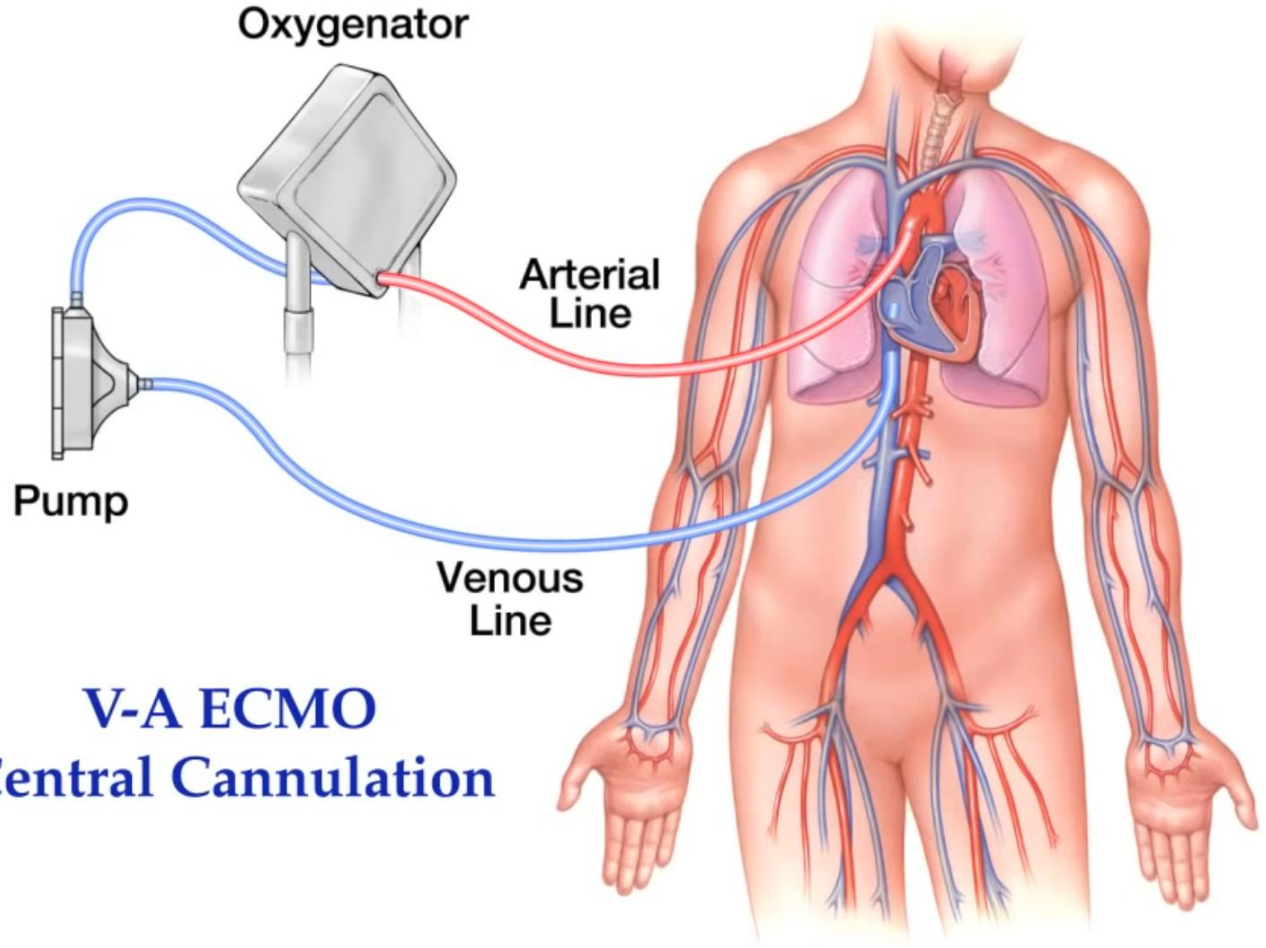
Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) support was then necessary.

The patients was awake, and a Femoro-Femoral VA ECMO started.

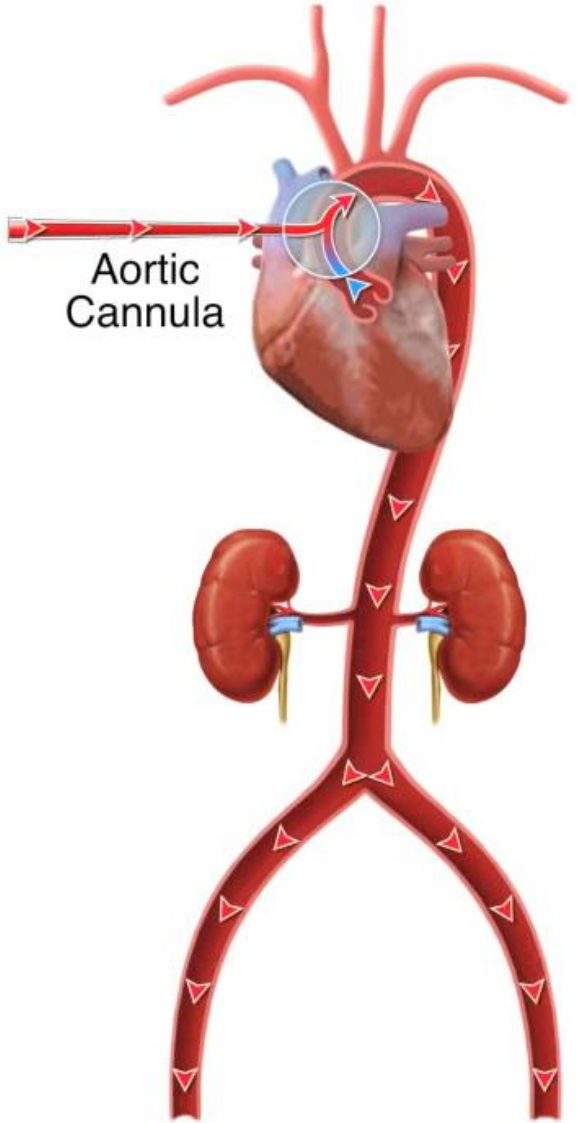


The patients was sedated and intubated, and the Femoro-Femoral VA ECMO was converted in a Axillar-Femoral VA ECMO.





V-A ECMO
Central Cannulation



Patient management during ECMO:

- The patient was extubated at the end of the procedure;
- She remains awake in spontaneous breathing;
- She keep a good mobilization at the bed and a FKT therapy was instituted;
- The normal per OS feeding was kept.

The day after the HIV viral load performed at day +1 was available…

2records estratti

Analisi	T.Prel	Esito	Risultato	Normalit🞐	Flag	Un.misura
Virus HIV-1 RNA quantitativo su plasma	1	HIV1 RNA analisi quantitativa (bDNA)	299138	(<50 non rilevabile, >=50 positivo)		copie/ml
		Nota	Si prega di inviare un campione di sangue senza anticoagulante e un campione di sangue con anticoagulante (EDTA) per controllo			

The day after the HIV viral load performed at day +1 was available…

2records estratti

Analisi	T.Prel	Esito	Risultato	Normalit	Flag	Un.misura
Virus HIV-1 RNA quantitativo su plasma	1	HIV1 RNA analisi quantitativa (bDNA)	299138	(<50 non rilevabile, >=50 positivo)		copie/ml
		Nota	Si prega di inviare un campione di sangue senza anticoagulante e un campione di sangue con anticoagulante (EDTA) per controllo			

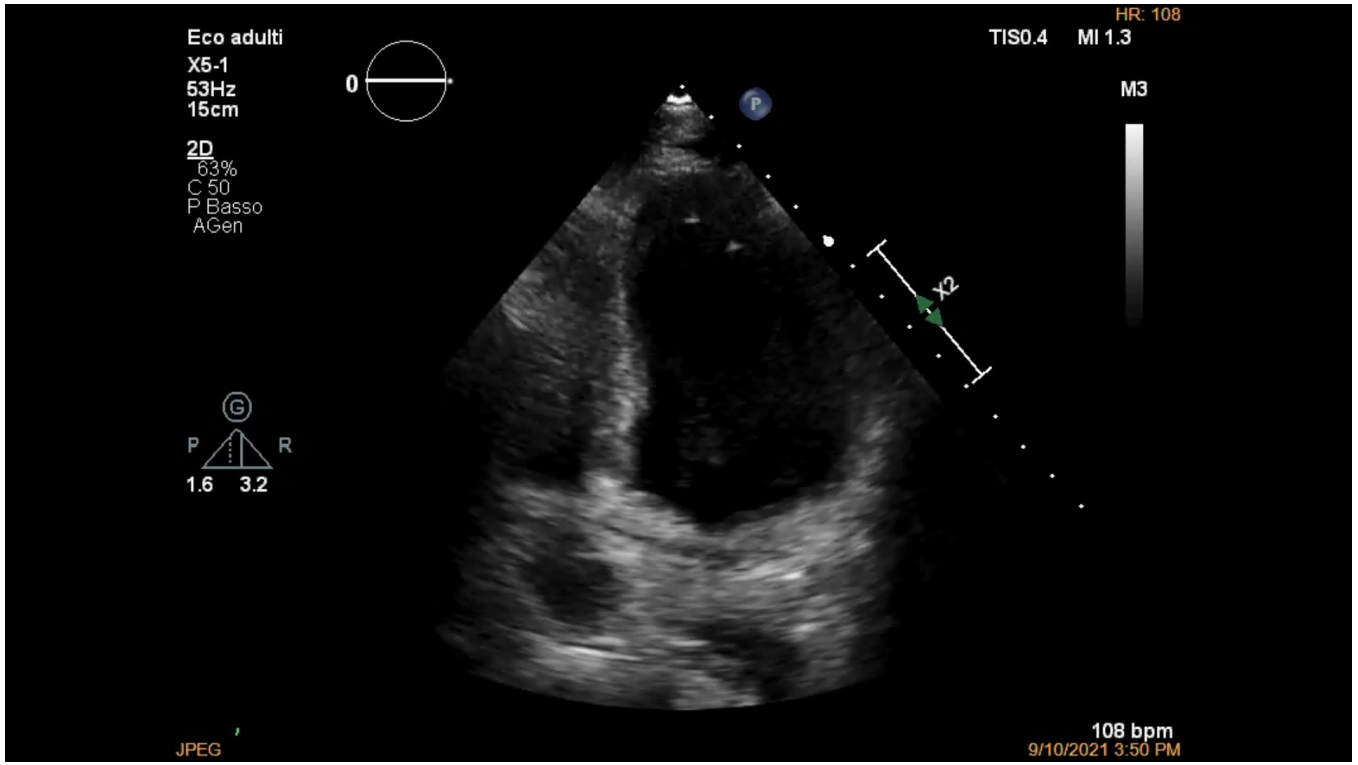
HIV specific therapy was then started, and steroids therapy was stopped

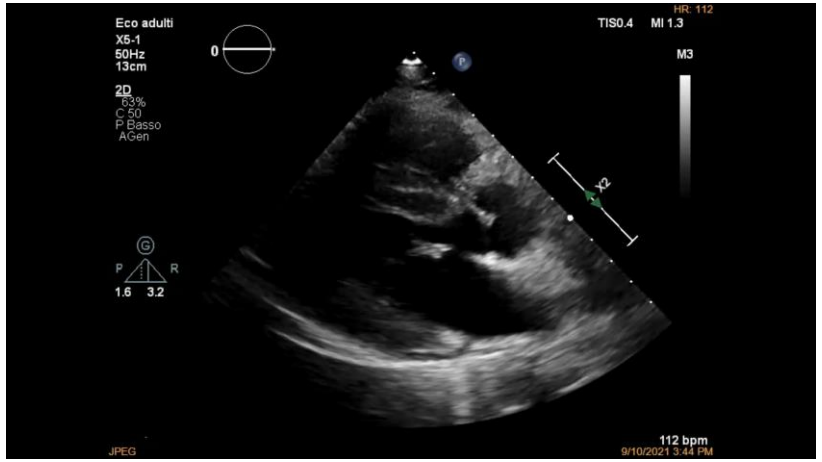
Analisi	T.Prel	Esito	Risultato	Normalit	Flag	Un.misura
HIV 1-2 anticorpi e HIV1 antigene p24 su siero		HIV1-2 anticorpi e HIV1 antigene p24	DUBBIO			
		Nota	Risultato invariato rispetto al campione precedente del 24-08-2021			
Virus HIV-1 RNA quantitativo su plasma	1	HIV1 RNA analisi quantitativa (bDNA)	84174	(<50 non rilevabile, >=50 positivo)		copie/ml

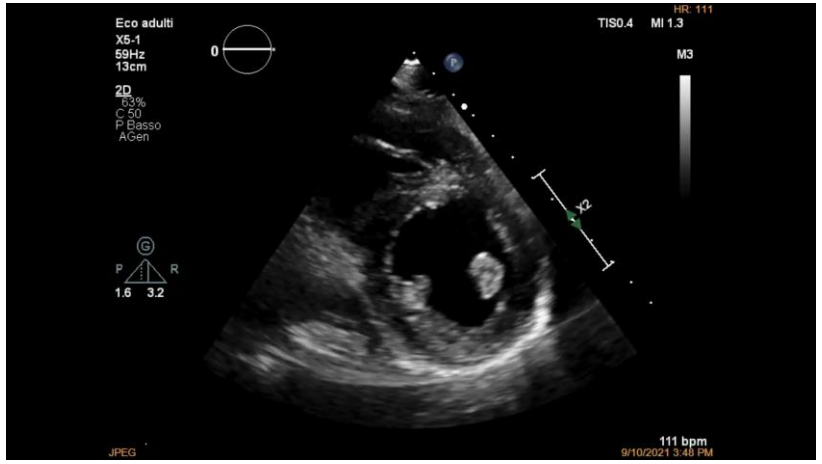
Day + 5

Clinical course:

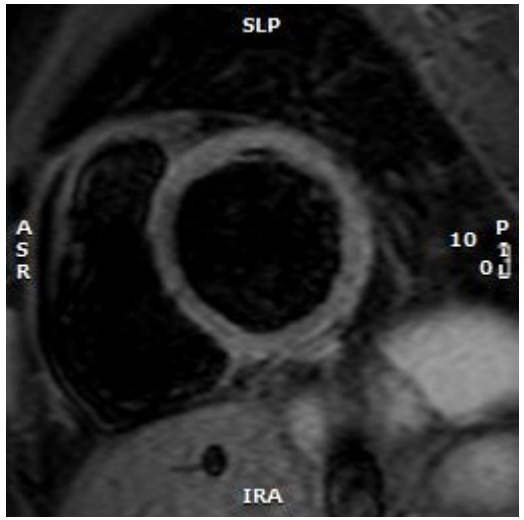
- Improvement of cardiac function was gradually observed
- Day 10: an infusion of levosimendan was performed for 24 hrs (2y/Kg/min)
- Day 11: VA ECMO support was removed
- Day 13: IABP was removed
- The patient was discharged to the CICU at day 14 with a 65% LVEF, absence of significant mitral regurgitation and TAPSE of 19 mm.

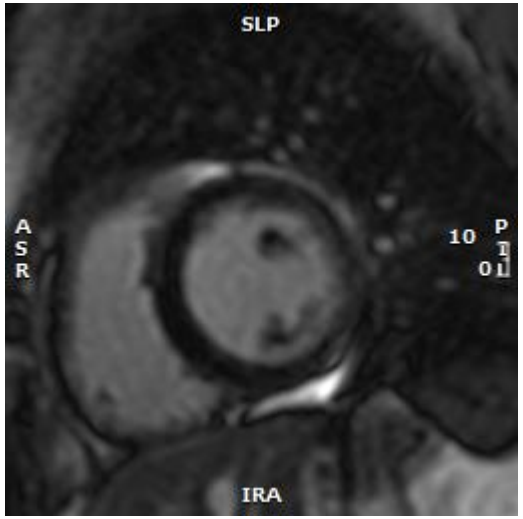

Eco adulti
X5-1
53Hz
15cm
2D
63%
C 50
P Basso
AGen
HR: 108
TIS0.4 MI 1.3
M3
0
X2
P
G
P R
1.6 3.2
JPEG
108 bpm
9/10/2021 3:50 PM

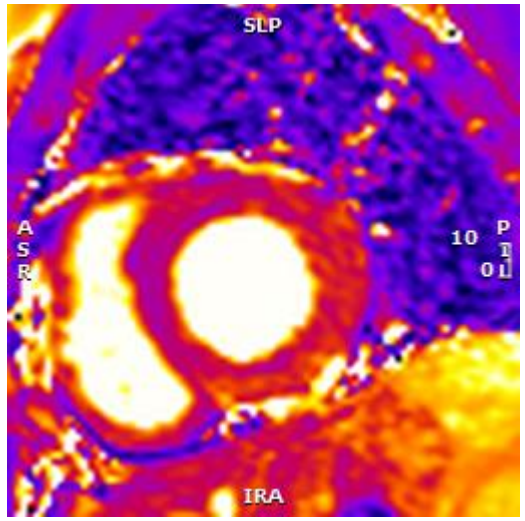

Eco adulti
X5-1
50Hz
13cm
2D
63%
C 50
P Basso
AGen
HR: 112
TIS0.4 MI 1.3
M3
0
X2
P
G
P R
1.6 3.2
JPEG
112 bpm
9/10/2021 3:44 PM


Eco adulti
X5-1
59Hz
13cm
2D
63%
C 50
P Basso
AGen
HR: 111
TIS0.4 MI 1.3
M3
0
X2
P
G
P R
1.6 3.2
JPEG
111 bpm
9/10/2021 3:48 PM

Cardiac MRI after 30 days







Nelle sequenze TIRM T2 si apprezza **iperintensità del segnale miocardico in corrispondenza delle pareti basali e delle pareti anteriore e settale nel tratto medio**. Nei limiti della presenza di evidenti artefatti da movimento, la valutazione del mapping T1 nativo, effettuata solo sul **setto interventricolare** medio, evidenzia **valori nettamente aumentati fino a circa 1180 msec.** Anche il tempo T2 è stato valutato prevalentemente sul setto interventricolare, compreso tra 54 e 57 msec lievemente aumentato; per quanto valutabile visivamente e nei limiti degli artefatti da movimento, esso sembrerebbe essere maggiormente aumentato in corrispondenza della parete inferiore e delle pareti laterali fino a circa 63 msec. Nelle sequenze acquisite tardivamente dopo somministrazione di mdc **si apprezza late enhancement subepicardico in corrispondenza della parete infero-laterale medio-basale, focale della giunzione posteriore media e sembra apprezzarsi subottimale annullamento del segnale miocardico in corrispondenza delle pareti**

ESC European Society of Cardiology
European Heart Journal (2021) 42, 3599–3726
doi:10.1093/eurheartj/ehab368

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

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%

Table 33 Cardiac magnetic resonance in patients with suspected myocarditis[955,956]

Indication
Indicated at baseline, in all patients with clinical history + ECG, elevated troponin or echocardiographic abnormalities, and significant CAD excluded or unlikely.
Advised at follow-up in patients with persistent dysfunction at echocardiography, arrhythmias or ECG abnormalities.[a]
Main findings
At baseline: T1-weighted (inflammation, injury) and T2-weighted (oedema) sequences, extracellular volume and LGE within 2 weeks after symptom onset.[956,960]
At follow up: LGE to evaluate the degree of scarring, T1 and T2 to identify persistent inflammation.[a]
Diagnostic significance
At least one T2-based criterion (global or regional increase of myocardial T2 relaxation time or an increased signal intensity in T2-weighted images), with at least one T1-based criterion (increased myocardial T1, extracellular volume, or LGE) in the acute phase.
Only one (i.e., T2-based or T1-based) marker may still support a diagnosis of acute myocardial inflammation in an appropriate clinical scenario, albeit with less specificity in the acute phase.
A negative T1/T2 scan does not exclude a still ongoing inflammatory process in the chronic phase.[a]

Is acute heart failure due to HIV a reliable and probable diagnosis?

Contemporary Reviews in Cardiovascular Medicine

Heart Failure in Patients With Human Immunodeficiency Virus Infection

Epidemiology, Pathophysiology, Treatment, and Future Research

Joshua Remick, MD; Vasiliki Georgiopoulou, MD; Catherine Marti, MD, MSc; Igho Ofotokun, MD, MSc; Andreas Kalogeropoulos, MD, PhD; William Lewis, MD; Javed Butler, MD, MPH

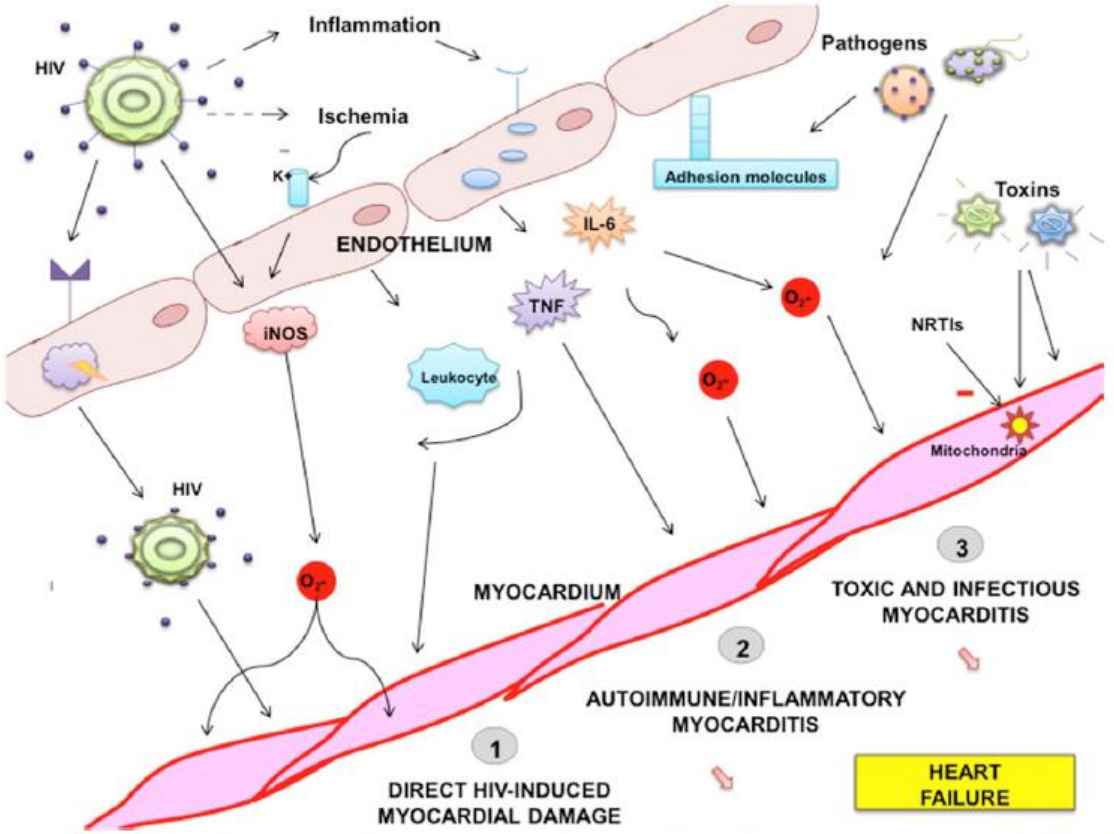


Figure. Pathophysiology of human immunodeficiency virus (HIV)–associated heart failure. HIV causes damaged myocardium directly and also indirectly through inflammation and increased susceptibility to infections, toxins, and, eventually, ischemia. The endothelium serves as a reservoir of HIV and also acts to elaborate cytokines, such as tumor necrosis factor (TNF) and interleukin-6 (IL-6), and free radicals in response to increased inflammation. Other causes of myocardial dysfunction among HIV-infected individuals include mitochondrial damage resulting from HIV therapy such as nucleoside reverse transcriptase inhibitors (NRTIs) and other toxins. iNOS indicates inducible nitric oxide synthase.

Circulation. 2014;129:1781-1789

Case report

INTERNATIONAL JOURNAL OF STD & AIDS

International Journal of STD & AIDS
2017, Vol. 28(2) 199–201

DOI: 10.1177/0956462416654852
journals.sagepub.com/home/std
SAGE

Acute onset myopericarditis as unusual presentation of primary HIV infection

Giacomo Vandi[1], Leonardo Calza[1], Nicolò Girometti[1], Roberto Manfredi[1], Giuseppina Musumeci[2], Isabella Bon[2] and Maria Carla Re[2]

The histopathologic studies of the biopsy specimen revealed a mild fibrosis of the myocardial right ventricular tissue, and inflammatory findings compatible with an active myocarditis. The real-time PCR analysis on bioptic sample excluded the presence of EBV, HSV-1/2, HHV8, CMV, PARVO B19, Enterovirus, and Adenovirus.

Only HHV6 DNA was reactive (<10 copies/µg DNA) and HIV-DNA (69 copies/µg). An immunofluorescence staining was performed to highlight the HIV p24 protein and a positive signal was detected in myocardial tissue. Considering the low avidity level of the anti-HIV IgG antibodies (0.5 AI) and the positivity of HIV-DNA in the endomyocardial tissue, we believe that the clinical manifestation presented by our patient in the absence of other causative agents can be referred to the recent primary HIV infection.

Case reports

Fulminant myocarditis during HIV seroconversion: recovery with temporary left ventricular mechanical assistance

Antonio Brucato, Tiziano Colombo*, Edgardo Bonacina**, Carloandrea Orcese***, Luca Vago§, Fabrizio Oliva*, Giada Distefano*, Maria Frigerio*, Roberto Paino*, Michela Violin§§, Salvatore Agati*, Ettore Vitali*

CD34, myeloperoxidase). Histological examination showed severe interstitial edema and numerous capillary hemorrhages, with extensive cardiomyocyte damage, consisting of diffuse areas of contraction band necrosis. Rare intravascular thrombi were also present. An interstitial inflammatory infiltrate was present, consisting of macrophages, lymphocytes and neutrophil granulocytes (Fig. 1) and was associated with prominent perivascular nuclear basophilic debris. Immunochemical investigation showed relatively sparse lymphocytes with an absolute prevalence of CD3-positive lymphocytes (T lymphocytes) (Fig. 2). Additional immunohistological investigations with antisera for Toxoplasma and *Cytomegalovirus*, and *in situ* hybridization for Epstein-Barr virus (Eber 1, Eber 2 probes) were all negative.

Immunohistochemical evaluation for the presence of HIV antigens was performed using a monoclonal antibody directed against the p24 viral protein (Dako, Milan, Italy)[1]; the polymerase chain reaction (PCR) for HIV *pol* and *gag* genes were performed as previously described[2]; they were both negative.

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Ital Heart J 2004; 5 (3): 228-231

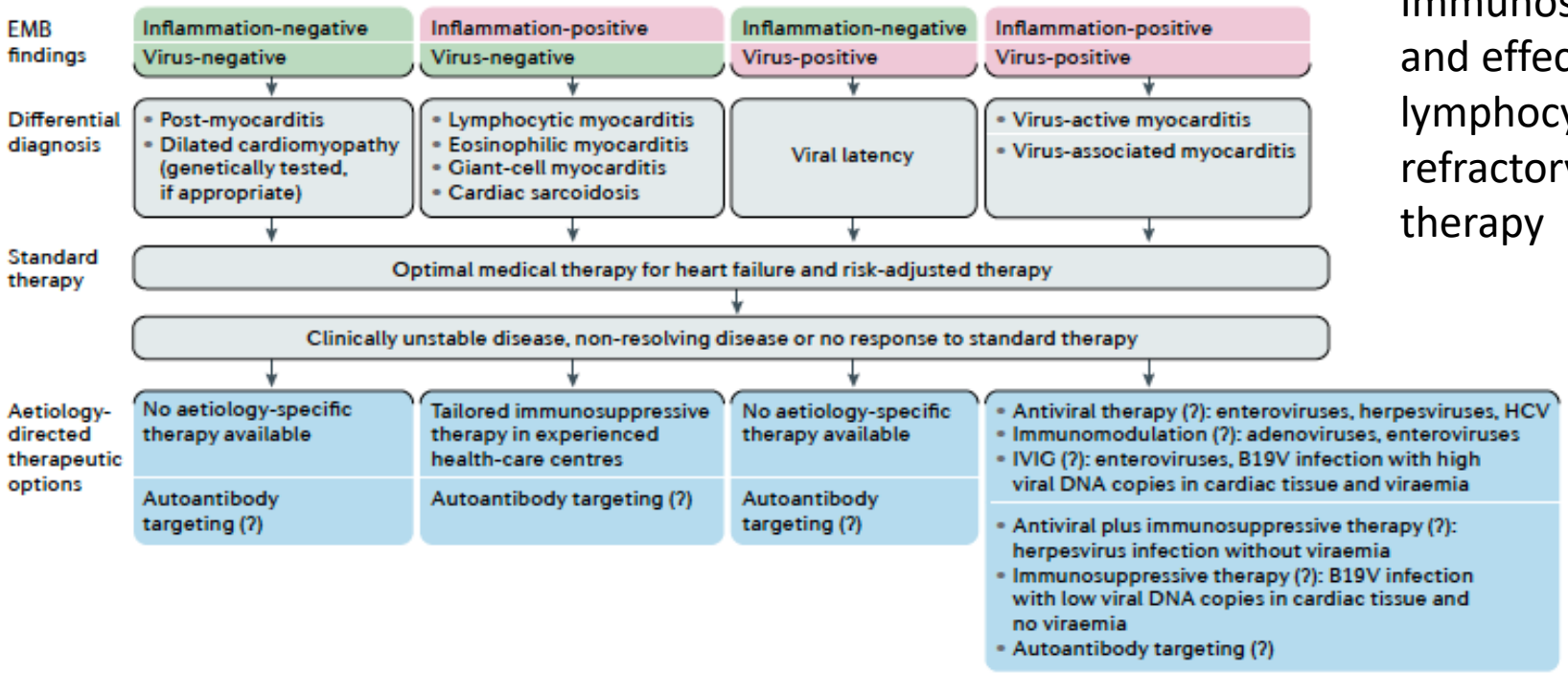
Take Home Messages and Talking Points

- Myocarditis and acute inflammatory cardiomyopathy represent an important diagnostic and therapeutic challenge for physicians.
- Our patient's clinical history support the clinical suspect of acute myocarditis even if EMB was negative.
- Although EMB is considered the gold standard for the diagnosis of myocarditis, there are some potential limitations. First of all, myocarditis is usually a focal process and accurate diagnosis depends primarily on adequate sampling of the myocardium, not always feasible in urgent conditions.
- In these cases, non-invasive imaging techniques such as cardiac magnetic resonance (CMR) imaging can be useful to support the clinical diagnostic suspicion of myocarditis.

Knowledge gaps and future directions

Myocarditis and inflammatory cardiomyopathy: current evidence and future directions

Carsten Tschöpe[1,2,3]✉, Enrico Ammirati[4], Biykem Bozkurt[5,6], Alida L. P. Caforio[7], Leslie T. Cooper[8], Stephan B. Felix[9,10], Joshua M. Hare[11], Bettina Heidecker[12], Stephane Heymans[13,14], Norbert Hübner[2,15,16], Sebastian Kelle[2,3,17], Karin Klingel[18], Henrike Maatz[15], Abdul S. Parwani[3], Frank Spillmann[3], Randall C. Starling[19], Hiroyuki Tsutsui[20], Petar Seferovic[21] and Sophie Van Linthout[1,2]



Immunosuppressive therapy is mandatory for specific forms of virus-negative autoimmune myocarditis, such as eosinophilic myocarditis, giant- cell myocarditis and cardiac sarcoidosis.

Immunosuppressive therapy is also safe and effective in clinically unstable lymphocytic virus-negative myocarditis refractory to standard heart failure therapy

Nat Rev Cardiol **18**, 169–193 (2021).

Lymphocytic and/or eosinophilic inflammatory infiltrates are seen in most EMB from fulminant myocarditis patients (about 85%)

The rationale for IV steroids in the acute setting to reduce myocardial inflammation favouring recovery appears strong

No trial has tested this hypothesis in the very acute phase of AM

No specific medications in acute phase are recommended beyond supportive therapy with inotropes and t-MCS

MYTHS – MYocarditis THerapy with Steroids

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI · IRCCS

Valutazione della sicurezza e dell'efficacia della

Terapia con METILPREDNISOLONE 1 g

in 250 di mL di soluzione fisiologica

(3 somministrazioni per 3 giorni) vs. soluzione fisiologica 250 mL

per il trattamento di pazienti con

miocardite acuta complicata/fulminante

Trial clinico farmacologico di fase III, in singolo cieco,
no-profit (IIT), multicentrico, internazionale,
randomizzato e controllato con valutazione in cieco degli endpoint.

INCLUSION CRITERIA

- **SUSPECTED ACUTE MYOCARDITIS COMPLICATED BY ACUTE HEART FAILURE OR CARDIOGENIC SHOCK and LV SYSTOLIC DYSFUNCTION**
- Age 18-69;
- NT-proBNP ≥ 1600 pg/mL or BNP ≥ 400 pg/mL;
- **LVEF < 41% and LV-EDD < 56 mm (parasternal long-axis view) on echocardiogram;**
- Increased troponin (3x URL) at the time of screening (any troponin assays are accepted);
- Clinical onset of cardiac symptoms within 3 weeks from randomization;
- Excluded coronary artery disease by coronary angiogram in subjects ≥ 46 years of age, in case myocarditis is not histologically proven;
- Randomization within 72 hours from hospital admission;
- EMB is not considered necessary before randomization, even though highly recommended to define the specific histology of myocarditis.

EXCLUSION CRITERIA

- **Known autoimmune disease or other conditions that can benefit from immunosuppression**;
- **Already on oral/IV corticosteroid therapy or other immunosuppressive therapies** (colchicine or NSAID excluded);
- Known chronic cardiac disease (i.e. previous cardiomyopathy);
- Ongoing administration of ICI (Immune Checkpoint Inhibitors);
- **Cardiac arrest before randomization**;
- Pregnancy (known pregnancy or POSITIVE human chorionic gonadotropin test measures for women of 18-50 years of age);
- Any other significant disease or disorder which expected life expectancy <12 months, in the opinion of the Investigator
- Involved in another clinical trial
- **t-MCS instituted more than 48 hours before randomization**;
- **Judged too sick to initiate t-MCS**;
- Evidence of active bacterial or fungal infectious disease. In case of only suspected active bacterial or fungal infectious disease, the suggested test, if available, procalcitonin (cut off of >10 ng/mL)
- Known chronic infective disease, such as HIV infection or tuberculosis;
- Eosinophil count >7% of the leukocytes
- Echocardiographic presence of images suggestive for other cardiac disease
- Contraindication to corticosteroids, including allergies to this medication and its excipients.

MYTHS - MYocarditis THerapy With Steroids (MYTHS)

ClinicalTrials.gov Identifier: [redacted]

Recruitment Status : Recruiting
First Posted : December 9, 2021
Last Update Posted : June 24, 2022

See Contacts and Locations

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Niguarda Hospital

Collaborators:
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Regione Lombardia

GRAZIE