Early Endomyocardial Biopsy for all Myocarditis… CON

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  - Getinge
  - Fresenius Medical Care
  - Baxter
  - 3M
- ✓ RCTs funded by grants from the French Ministry of Health

Histology : Dallas Criteria

- **3 histological grades** *(Aretz, Hum Pathol, 87)*
  - ❖ Active myocarditis :
    - *Cellular infiltrate +, myocyte necrosis +*
  - ❖ Bordeline Myocarditis :
    - *Cellular infiltrate +, myocyte necrosis –*
  - ❖ Negative biopsy :
    - *Cellular infiltrate -, myocyte necrosis –*

- **Distribution and diffusion of the cellular infiltrate**
  - ❖ Focal, confluent or diffuse
  - ❖ Mild, moderate, severe

Insensitivity of Right Ventricular Endomyocardial Biopsy in the Diagnosis of Myocarditis

LAWRENCE H. CHOW, MD, STANLEY J. RADIO, MD, THOMAS D. SEARS, MD, FACC, BRUCE M. McMANUS, MD, PhD, FACC

Omaha, Nebraska

The clinical suspicion of myocarditis relies strongly on endomyocardial biopsy for confirmation, yet the sensitivity of the procedure in this setting has not been clearly defined. Biopsy sensitivity was determined in 14 hearts with histologically proved myocarditis studied ex vivo, including 12 autopsy hearts and 2 native hearts explanted at cardiac transplantation. With use of the Stanford and Cordis bioptomes, endoymocardial biopsy was performed near the apex on the right side of the ventricular septum (four to five samples/bioptome per patient) and repeated in the nonapical portion of the septum from the moderator band to the subpulmonary infundibulum (additional three to five samples/bioptome per patient).

In a casewise assessment, 43% to 57% of the endomyocardial samples were diagnostic for myocarditis, as calculated separately for each bioptome in each region of sampling (apical/nonapical). Both apical and nonapical sensitivity improved to 64% when the findings of the two bioptomes were combined (eight to nine samples/patient in each region). By collectively analyzing all available samples for each patient, 11 (79%) of 14 cases could be diagnosed, but this required a mean of 17.2 samples/patient, a number clinically unrealistic. The exclusion of four cases of fungal myocarditis from analysis did not significantly alter the results. In transmural ventricular sections, none of four patients with sudden death had inflammatory disease confined to the conduction system.

In conclusion, despite six to eight negative biopsy samples/patient with suspected myocarditis, repeat biopsy may still be warranted.

(J Am Coll Cardiol 1989;14:915–20)

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- 14 heart ex vivo proven myocarditis
- Sensitivity of EMB is low (43-57%) when evaluated with standard hematoxylin-eosin staining
- Since sampling sites do not always correspond to the distribution of inflammation

cal portion of the septum from the moderator band to the subpulmonary infundibulum (additional three to five samples/bioptome per patient).

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In conclusion, despite six to eight negative biopsy samples/patient with suspected myocarditis, repeat biopsy may still be warranted.

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AHA SCIENTIFIC STATEMENT

Recognition and Initial Management of Fulminant Myocarditis

A Scientific Statement From the American Heart Association

Endorsed by the Heart Failure Society of America and the Myocarditis Foundation.

Circulation. 2020;141:e69–e92. DOI: 10.1161/CIR.0000000000000745

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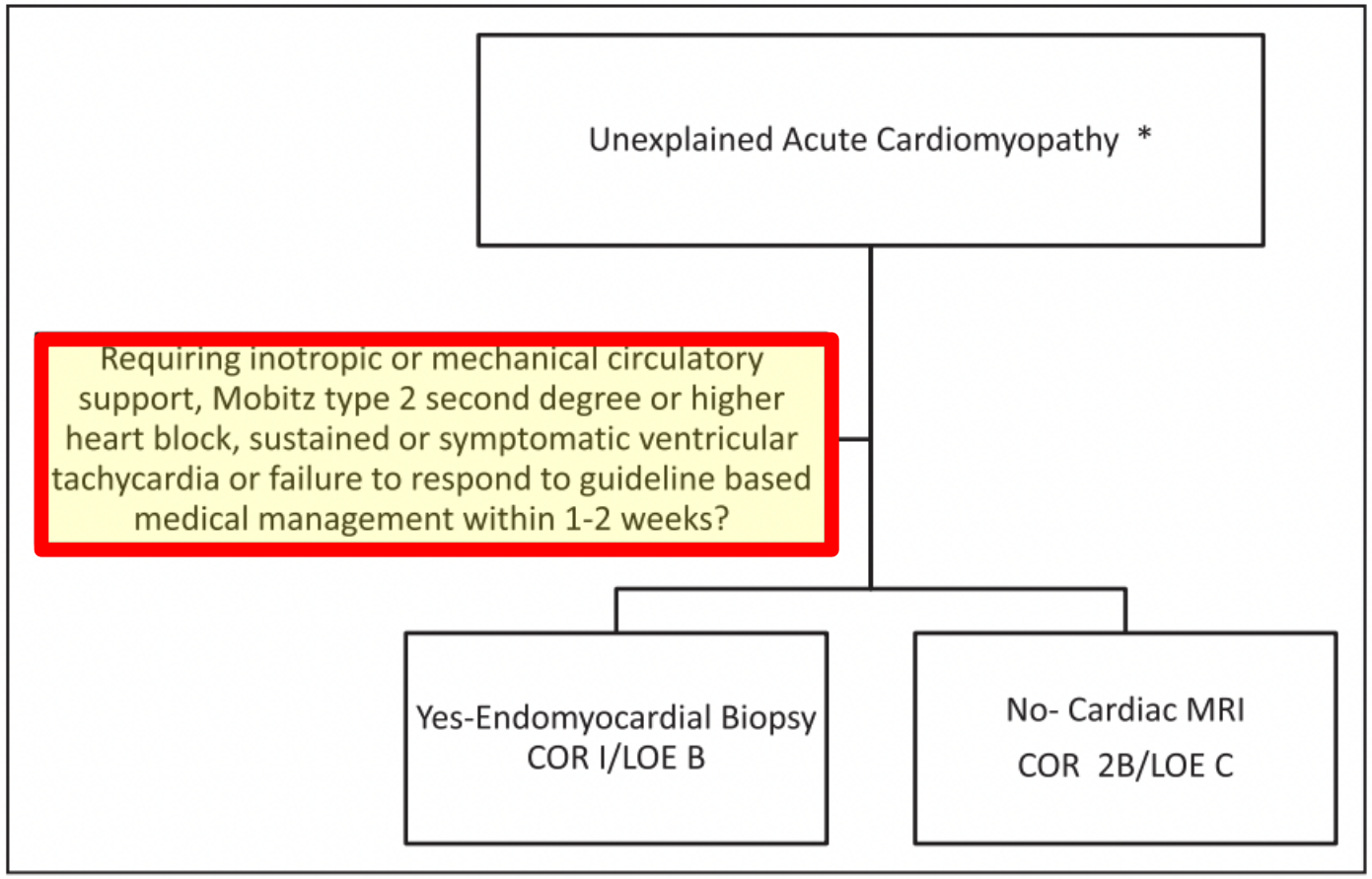

Figure 3. Indications for endomyocardial biopsy (EMB).
Guideline-based algorithm for whether EMB is indicated. COR indicates Class of Recommendation; LOE, Level of Evidence; and MRI, magnetic resonance imaging. *Usually a dilated cardiomyopathy. Fulminant myocarditis may have normal end-diastolic diameter with mildly thickened walls. Exclude ischemic, hemodynamic (valvular, hypertensive), metabolic, and toxic causes of cardiomyopathy as indicated clinically. Reprinted from Bozkurt et al.[3] Copyright © 2016, American Heart Association, Inc.

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)

With the special contribution of the Heart Failure Association (HFA) of the ESC

ESC European Society of Cardiology

European Heart Journal (2021) **42**, 3599–3726
doi:10.1093/eurheartj/ehab368

EMB		
EMB should be considered in patients with rapidly progressive HF despite standard therapy when there is a probability of a specific diagnosis, which can be confirmed only in myocardial samples.[97,98]	IIa	C

JAMA | Review

Diagnosis and Treatment of Acute Myocarditis
A Review

Enrico Ammirati, MD, PhD; Javid J. Moslehi, MD

JAMA April 4, 2023 Volume 329, Number 13

Table 2. Diagnostic Assessment in Adult Patients With Suspected Acute Myocarditis

Diagnostic assessment	Description
Vital signs and associated clinical signs	Assess hemodynamic status: blood pressure, heart rate, oxygen saturation, temperature, and other findings that can suggest etiology (eg, cutaneous rash, diplopia[a]).
Medical history	Check for recent respiratory infections, systemic inflammatory conditions, previous myocarditis, allergies, asthma, travels, illicit drugs, drugs including clozapine and anticancer therapies, vaccine, food (eg, raw meat consumption[b]), and family history of myocarditis, cardiomyopathy, and sudden cardiac death.
Electrocardiogram (ECG)	Approximately 62%-96% of people have an abnormal ECG. ST-segment elevation mimicking acute myocardial infarction occurs in approximately 58% of people with myocarditis.[13] QRS width >120 ms, second- or third-degree atrioventricular block, and ventricular arrhythmias are associated with high-risk.
Laboratory tests	Increase in troponin, creatine kinase (CK), CK-MB, C-reactive protein, differential white blood count (eg, eosinophils), hepatic and kidney function tests, arterial blood gas analysis (in patients with acute heart failure), autoimmunity screening if an autoimmune cause is suspected.
Serology	In patients with possible infectious cause, consider antibodies for HIV and *Borrelia* species.
Nasopharyngeal swab	Polymerase chain reaction to rule out SARS-CoV-2 or other respiratory viruses, such as H1N1 influenza, in patients with recent or ongoing respiratory symptoms.
Echocardiogram	Left ventricular ejection fraction is normal in about 75% of patients. Typical findings that can suggest acute myocarditis: (1) nondilated or mildly dilated left ventricle; (2) presence of increased wall thickness; (3) abnormal echogenicity; (4) generally mild segmental hypokinesia (especially in the inferior/inferolateral walls), but severe forms can present severe diffuse hypokinesia; (5) diastolic dysfunction; (6) pericardial effusion; and (7) impaired global longitudinal strain.
Coronary angiography/ computed tomography angiography	May be used if it is necessary to exclude coronary abnormalities or spontaneous coronary artery dissections or coronary artery disease in patients with cardiovascular risk factors or elderly patients.

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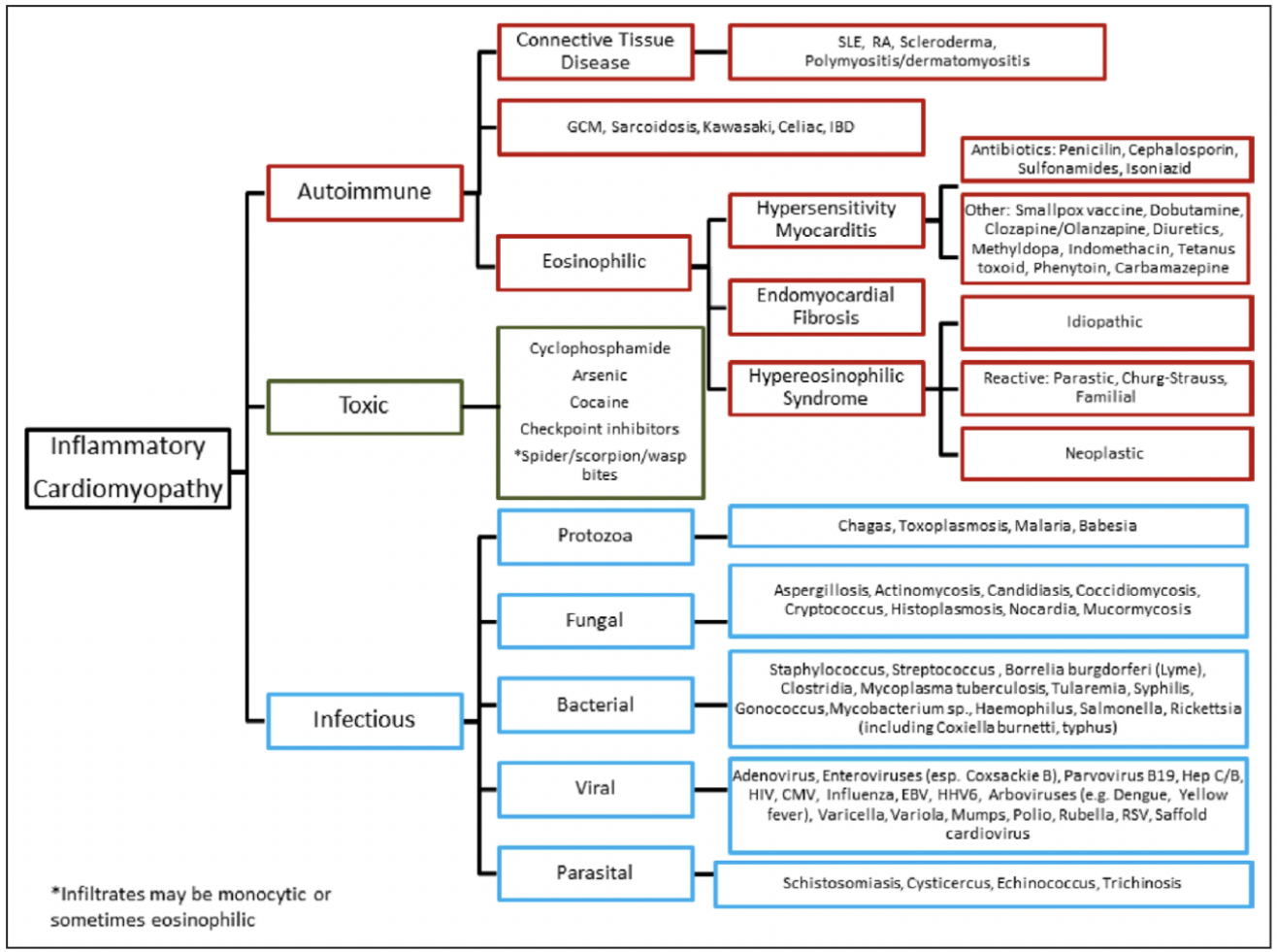

Figure 5. Causes of lymphocytic myocarditis.

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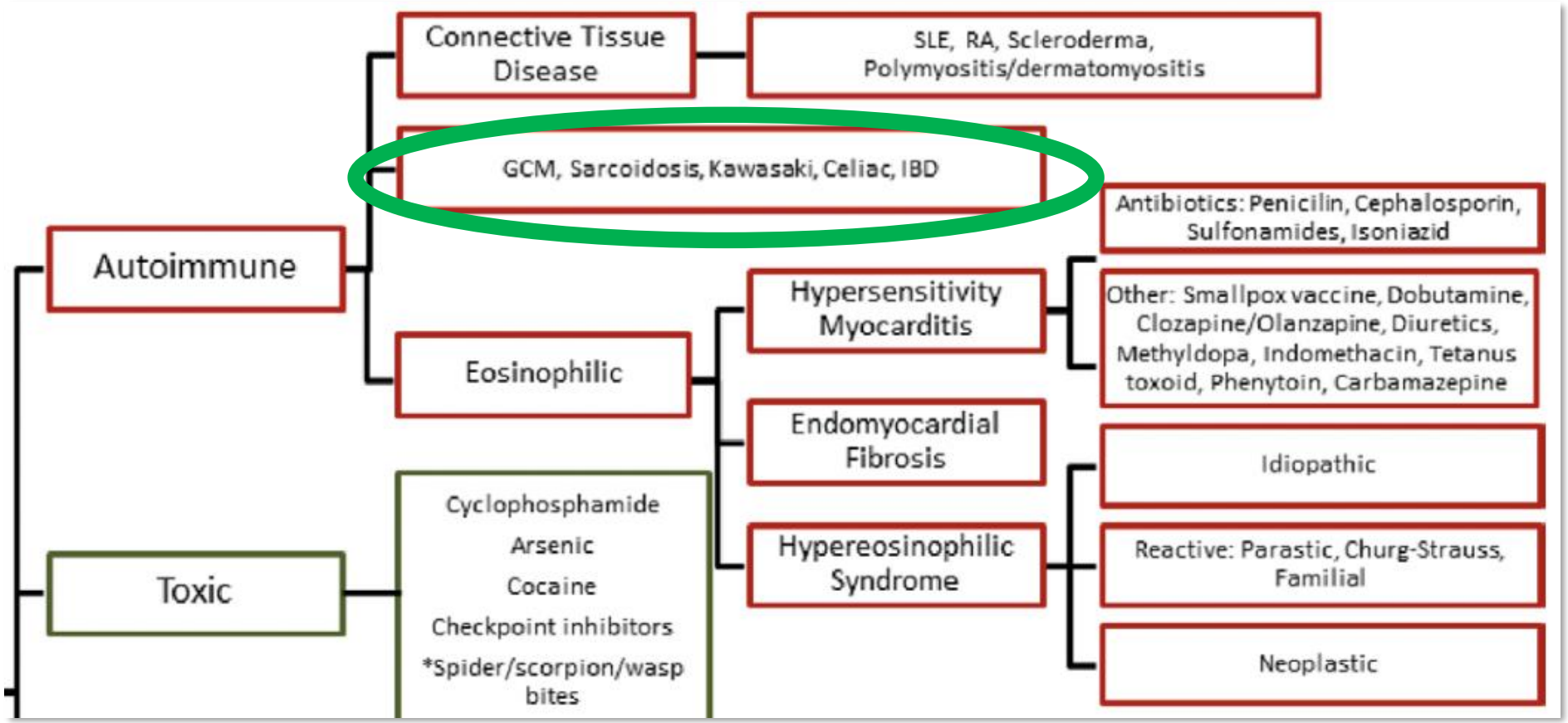

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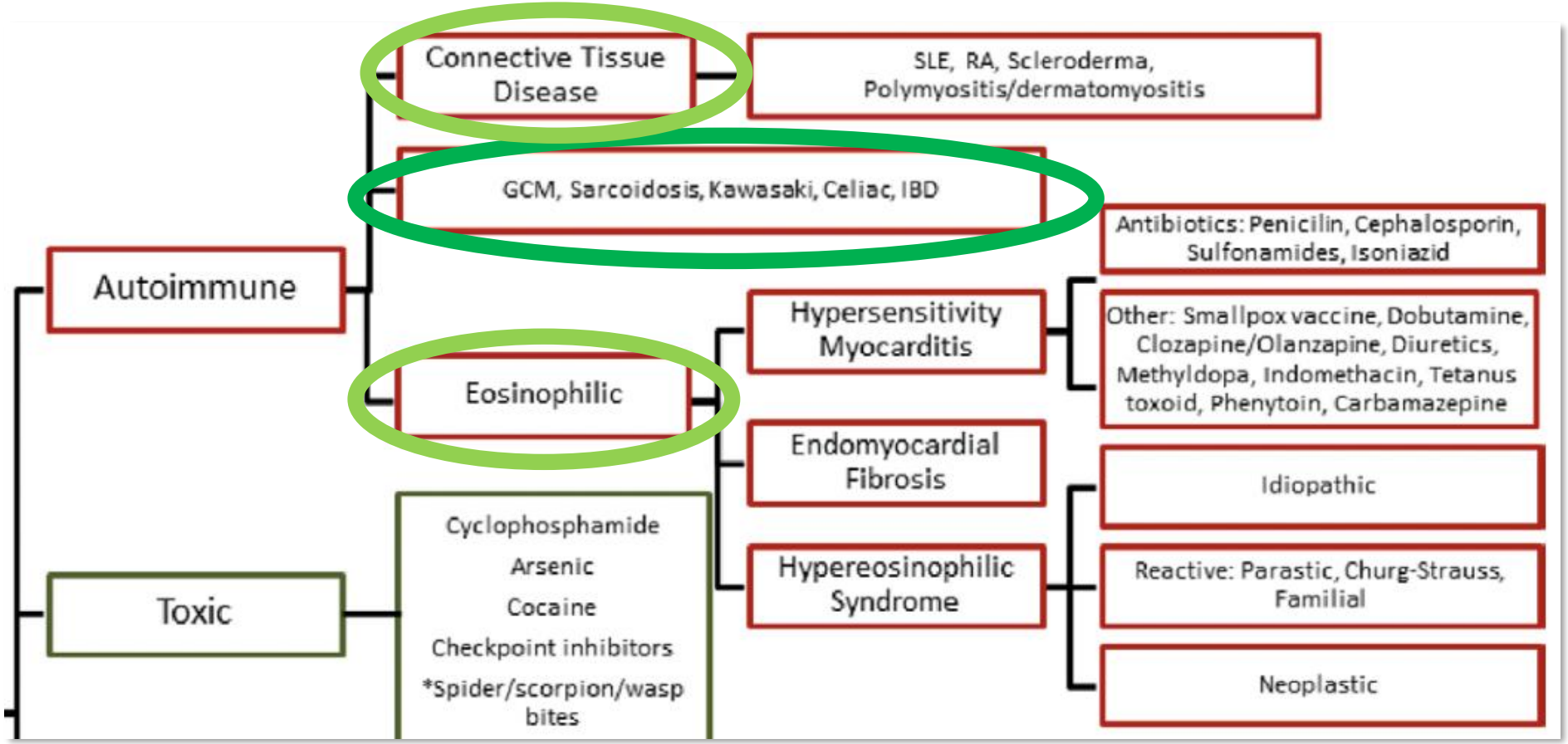

Real-life data in fulminant myocarditis…

Venoarterial Extracorporeal Membrane Oxygenation for Acute Fulminant Myocarditis in Adult Patients: A 5-Year Multi-Institutional Experience

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(Ann Thorac Surg 2016;101:919–26)

Table 1. Patient Characteristics Before ECMO (n = 57)

Characteristic	Value
M/F	20/37 (35.1/64.9)
Age, years	37.6 ± 11.8
Patient status	
Shock	38 (66.7)
Cardiac arrest	12 (21.0)
Hemodynamic instablility	7 (12.3)
ECMO access	
Femoro-femoral	47 (82.4)
Femoro-femoral + central	2 (3.5)
Central	6 (10.5)
Femoral-subclavian	1 (1.7)
LV apex-subclavian	1 (1.7)
SBP, mm Hg	61.8 ± 30.4
Arterial size, French	18.8 ± 3.86
Venous size, French	23.8 ± 6.38
Distal perfusion of cannulated femoral artery	
No	21 (36.9)
Yes	36 (63.1)
IABP	
No	20 (35.2)
Yes	37 (64.8)
LV vent	
No	43 (75.4)
Yes	14 (24.6)
LV distension	
No	41 (71.9)
Yes	16 (28.1)
Blood values at ECMO start	
pH	7.2 ± 0.1
PaO_2, mm Hg	68.8 ± 47.5
Lactate, mmol/L	12.0 ± 4.6
Bilirubin, mg/dL	6.0 ± 6.2
Myocardial biopsy	
No	42 (73.7)
Yes	15 (26.3)

Heart Failure Association of the ESC, Heart Failure Society of America and Japanese Heart Failure Society Position statement on endomyocardial biopsy

Petar M. Seferović[1]*, Hiroyuki Tsutsui[2], Dennis M. McNamara[3], Arsen D. Ristić[4,5], Cristina Basso[6], Biykem Bozkurt[7], Leslie T. Cooper Jr[8], Gerasimos Filippatos[9], Tomomi Ide[2], Takayuki Inomata[10], Karin Klingel[11], Aleš Linhart[12], Alexander R. Lyon[13], Mandeep R. Mehra[14], Marija Polovina[4,5], Ivan Milinković[4,5], Kazufumi Nakamura[15], Stefan D. Anker[16], Ivana Veljić[4], Tomohito Ohtani[17], Takahiro Okumura[18], Thomas Thum[19,20], Carsten Tschöpe[21], Giuseppe Rosano[22], Andrew J.S. Coats[23,24], and Randall C. Starling[25]

ESC European Society of Cardiology

European Journal of Heart Failure (2021) **23**, 854–871
doi:10.1002/ejhf.2190

Table 4 Contraindications for endomyocardial biopsy

Absolute contraindications

- Intracardiac thrombus
- Ventricular aneurysm
- Severe tricuspid, pulmonary or aortic stenosis
- Aortic and tricuspid mechanical prosthesis

Relative contraindications

- Active bleeding
- Infection and fever
- Infective endocarditis
- Pregnancy
- Recent cerebrovascular accident/TIA (<1 month)
- Uncontrolled hypertension
- Thin ventricular wall (for the biopsy of the myocardium)
- Coagulopathy
- Contrast media hypersensitivity[a]
- Uncooperative patient

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Table 1 Major and minor complications of endomyocardial biopsy

Major complications	Minor complications
Death (0–0.07%)	Chest pain (transient) (0–1.8%)
Cardiac perforation/haemopericardium/tamponade (0–6.9%)	Deep vein thrombosis (0.23–3.8%)
Pneumothorax/air embolism (0–0.8%)	Puncture site haematoma/nerve palsy (0–0.64%)
Thromboembolism (0–0.32%)	Hypotension/vaso-vagal syncope (0–4.3%)
Valvular trauma (0.02–1.1%)	Arterial trauma/vascular damage/fistulae (0.32–2.8%)
Severe arrhythmias/atrioventricular block (0–11%)	

Safety of Endomyocardial Biopsy in New-Onset Acute Heart Failure Requiring Veno-Arterial Extracorporeal Membrane Oxygenation

Robert M.A. van der Boon, MD, PhD; Wijnand K. den Dekker, MD, PhD; Christiaan L. Meuwese, MD, PhD; Roberto Lorusso, MD, PhD; Jan H. von der Thüsen, MD, PhD; Alina C. Constantinescu, MD, PhD; Olivier C. Manintveld, MD, PhD; Thijs S.R. Delnoij, MD, PhD; Joris. J. van der Heijden, MD; Nicolas M.D.A. van Mieghem, MD, PhD; Corstiaan A. den Uil, MD, PhD

Circ Heart Fail. 2021;

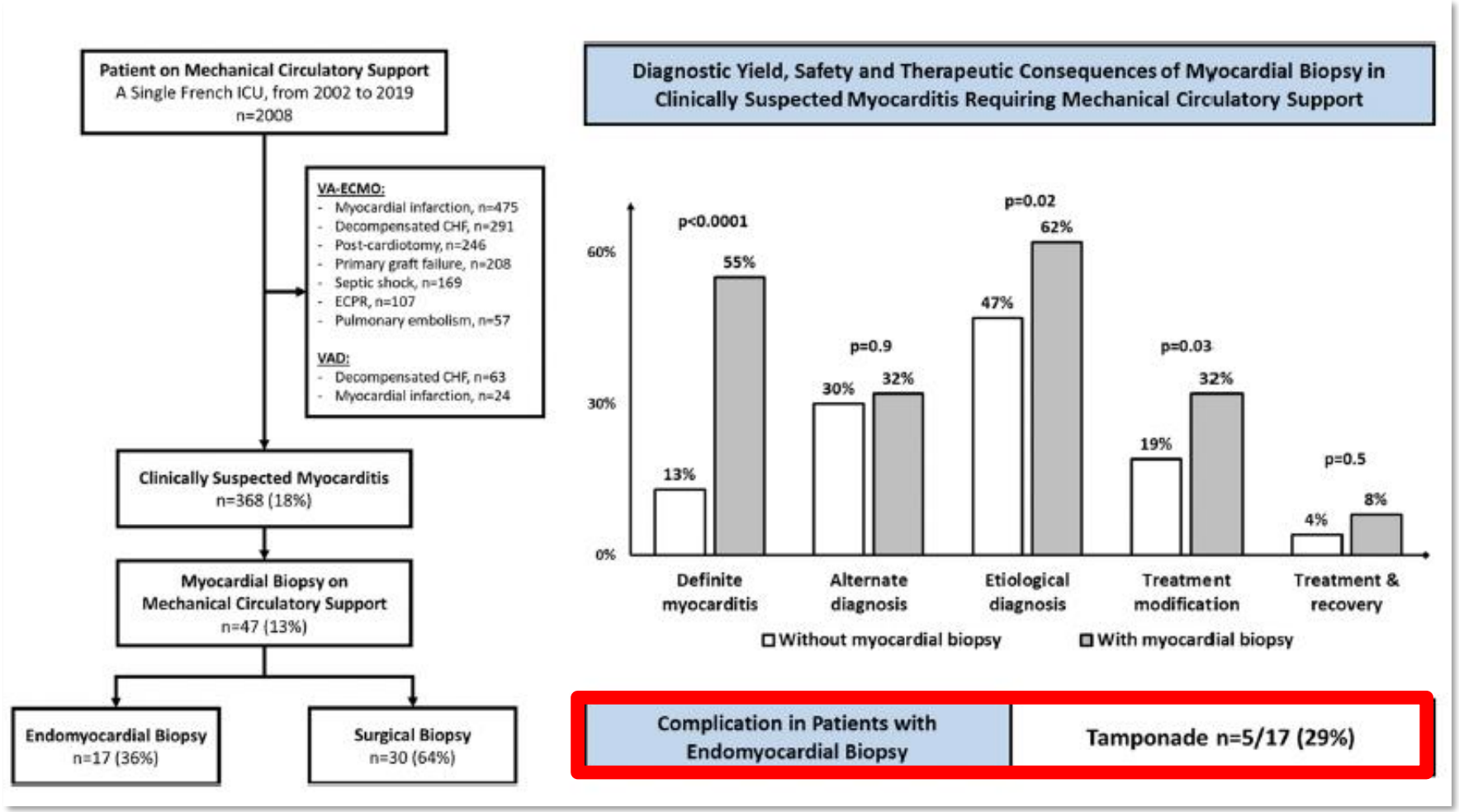
Table 2. Safety and Histopathologic Outcomes According to Timing of Biopsy

	Overall (n=230)	EMB-ECMO (n=23)	Acute EMB (n=125)	Elective EMB (n=82)	*P* value
All complications	37 (16.1)	8 (34.8)	18 (14.4)	11 (13.4)	0.04
Major complications	19 (8.3)	6 (26.1)	10 (8.0)	3 (3.7)	0.003
Death	0	0	0	0	
Sustained ventricular tachycardia or need of cardiopulmonary resuscitation	8 (3.5)	3 (13.0)	4 (3.2)	1 (1.2)	0.02
Cardiac tamponade	10 (4.3)	3 (13.0)	5 (4.0)	2 (2.4)	0.08
Stroke	0	0	0	0	
Pneumothorax	2 (0.9)	0	2 (1.6)	0	0.42
Minor complications	21 (9.1)	2 (8.7)	10 (8.0)	9 (11.0)	0.77
Atrioventricular block or need for (temporary) pacemaker	5 (2.2)	1 (4.3)	3 (2.4)	1 (1.2)	0.64
Pericardial effusion	11 (4.8)	1 (4.3)	4 (3.2)	6 (7.3)	0.40
Hypotensive episode	4 (1.7)	0	2 (1.6)	2 (2.4)	0.72
Nonsustained ventricular tachycardia	1 (0.4)	0	1 (0.8)	0	0.65

Diagnostic yield, safety and therapeutic consequences of myocardial biopsy in clinically suspected fulminant myocarditis unweanable from mechanical circulatory support

Yann Marquet[1], Guillaume Hékimian[1], Guillaume Lebreton[2,3], Mathieu Kerneis[2,4], Philippe Rouvier[5], Pierre Bay[6], Alexis Mathian[7], Nicolas Bréchot[1], Juliette Chommeloux[1], Matthieu Petit[1], Melchior Gautier[1], Lucie Lefevre[1], Ouriel Saura[1], David Levy[1], Paul Quentric[7,8], Quentin Moyon[1,7], Sofia Ortuno[1], Matthieu Schmidt[1,2], Pascal Leprince[2,3], Charles-Edouard Luyt[1,2], Alain Combes[1,2] and Marc Pineton de Chambrun[1,2,7,8]*

Marquet *et al. Annals of Intensive Care* (2023) 13:78



Does EMB change patient's outcomes ?

Differences in Prognosis and Cardiac Function According to Required Percutaneous Mechanical Circulatory Support and Histological Findings in Patients With Fulminant Myocarditis: Insights From the CHANGE PUMP 2 Study

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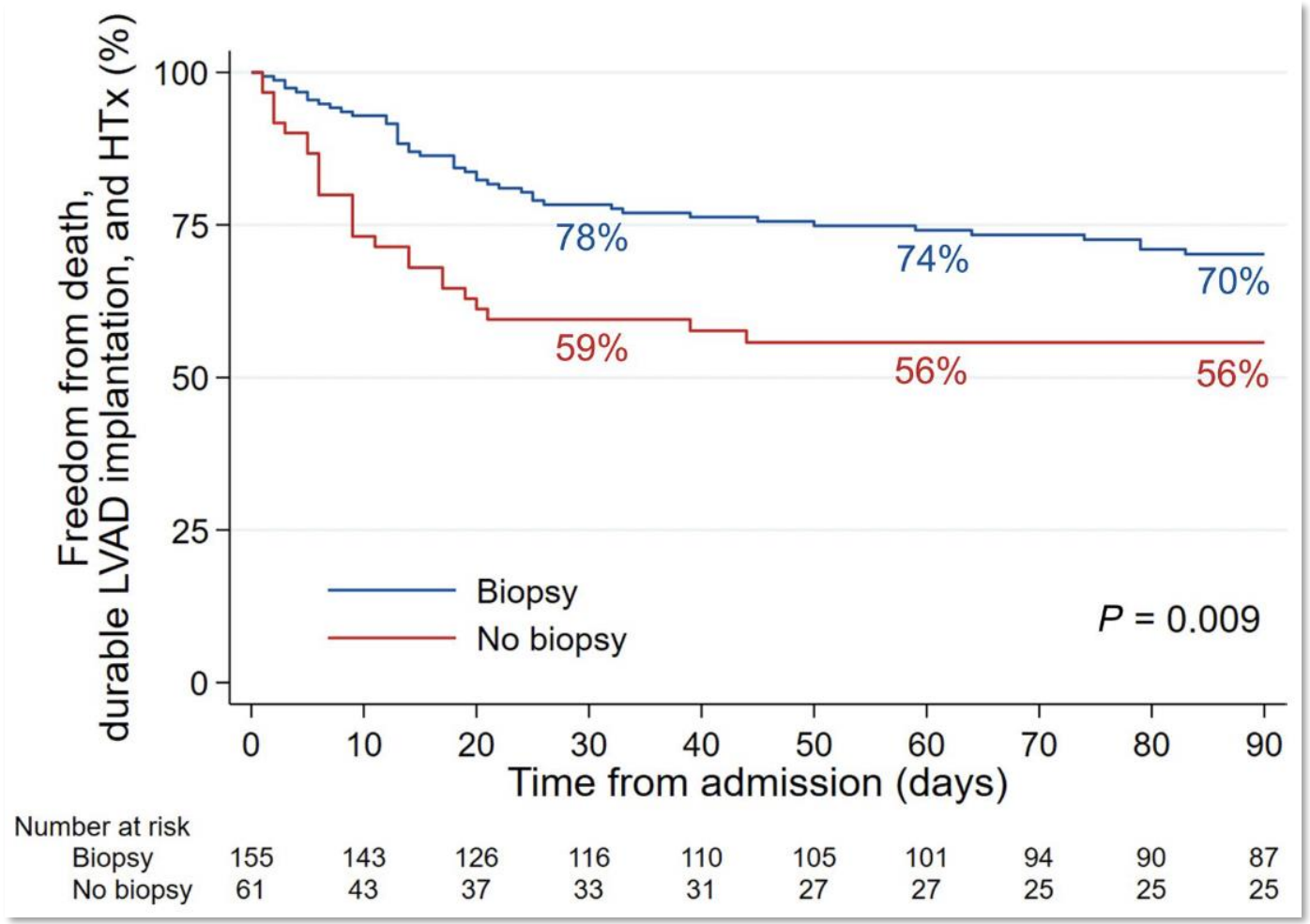
J Am Heart Assoc. 2022;11:e023719.



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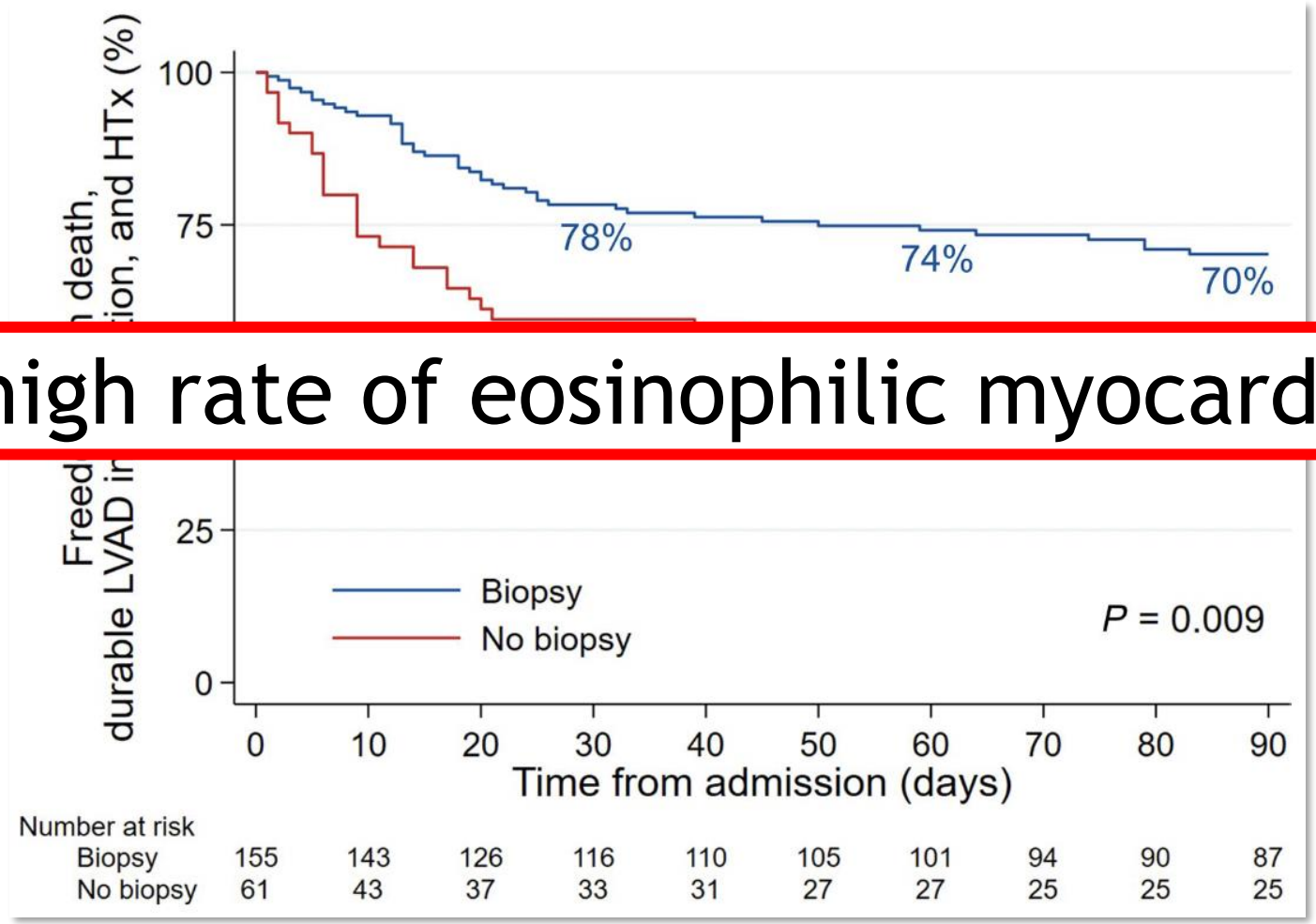

Very high rate of eosinophilic myocarditis (22%)

Fulminant myocarditis proven by early biopsy and outcomes

Florent Huang [1,2], Enrico Ammirati[3], Maharajah Ponnaiah [4], Santiago Montero [5], Victor Raimbault[2], Darryl Abrams[6], Guillaume Lebreton [7], Vincent Pellegrino[8], Joshua Ihle[8], Maurizio Bottiroli[3], Romain Persichini[9], Marisa Isabel Barrionuevo-Sánchez[10], Albert Ariza-Solé[10], Pauline Yeung Ng[11], Simon Wai Ching Sin[12], Raj Ayer[13], Hergen Buscher[13], Slimane Belaid[14], Clément Delmas[14], Rita Ferreira[15], Roberto Roncon Albuquerque Jr[15], Teresa López-Sobrino[16], Jeroen J. H. Bunge[17], Christoph Fisser[18], Guillaume Franchineau[19], Jamie McCanny[20], Shinichiro Ohshimo[21], Alessandro Sionis [22], Francisco José Hernández-Pérez[23], Eduardo Barge-Caballero[24], Martin Balik[25], Henrique Muglia[26], Sunghoon Park[27], Dirk W. Donker[28,29], Beatriz Porral[30], Nadia Aïssaoui[31], Armand Mekontso Dessap[32], Virginia Burgos[33], Mathieu Lesouhaitier[34]*, Justin Fried[35], Jae-Seung Jung[36], Sandra Rosillo[37], Vincent Scherrer[38], Saad Nseir[39], Hadrien Winszewski[40], Pablo Jorge-Pérez[41], Antoine Kimmoun[42], Rodrigo Diaz[43], Alain Combes[2,44], Matthieu Schmidt [2,44], and for the FULLMOON Study Group†

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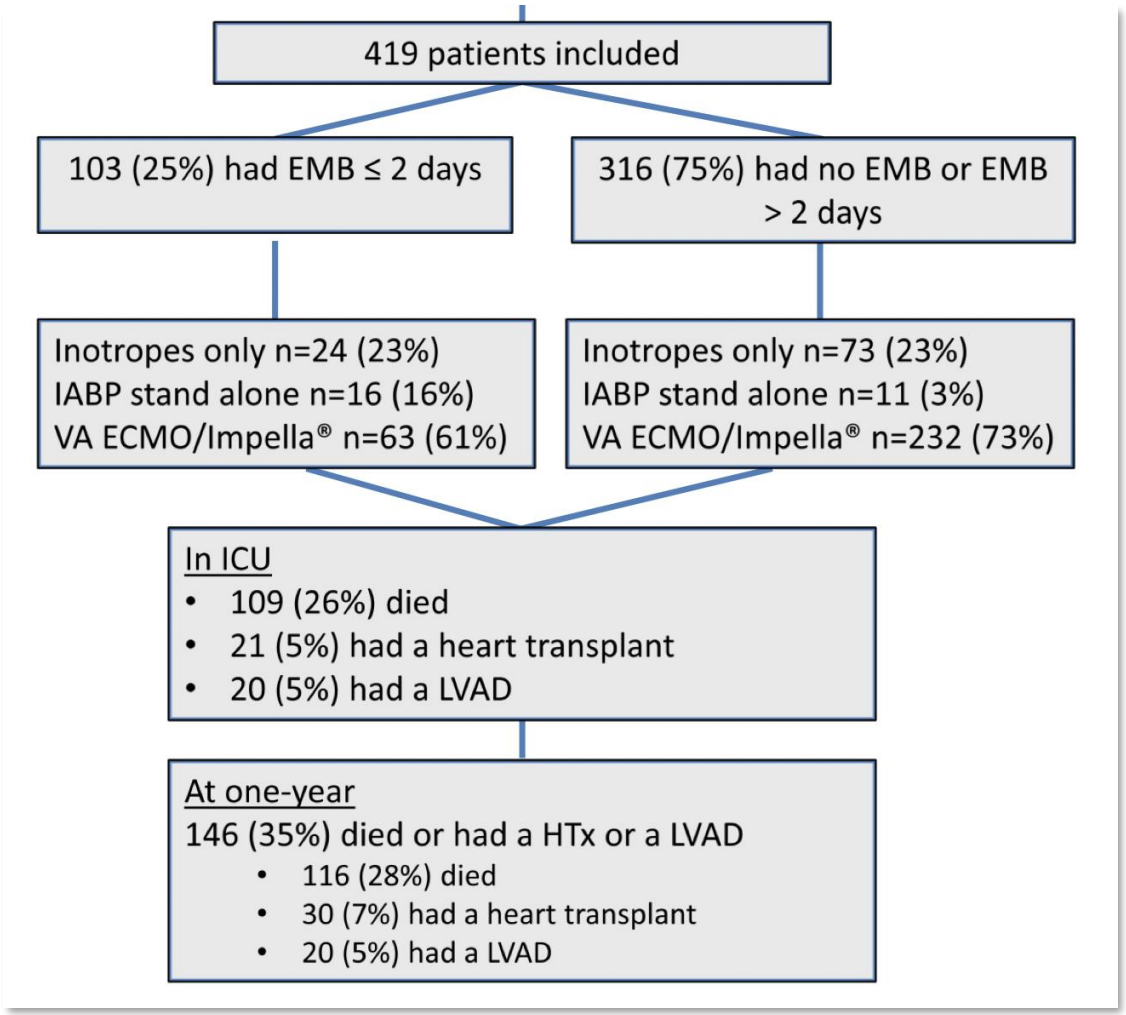

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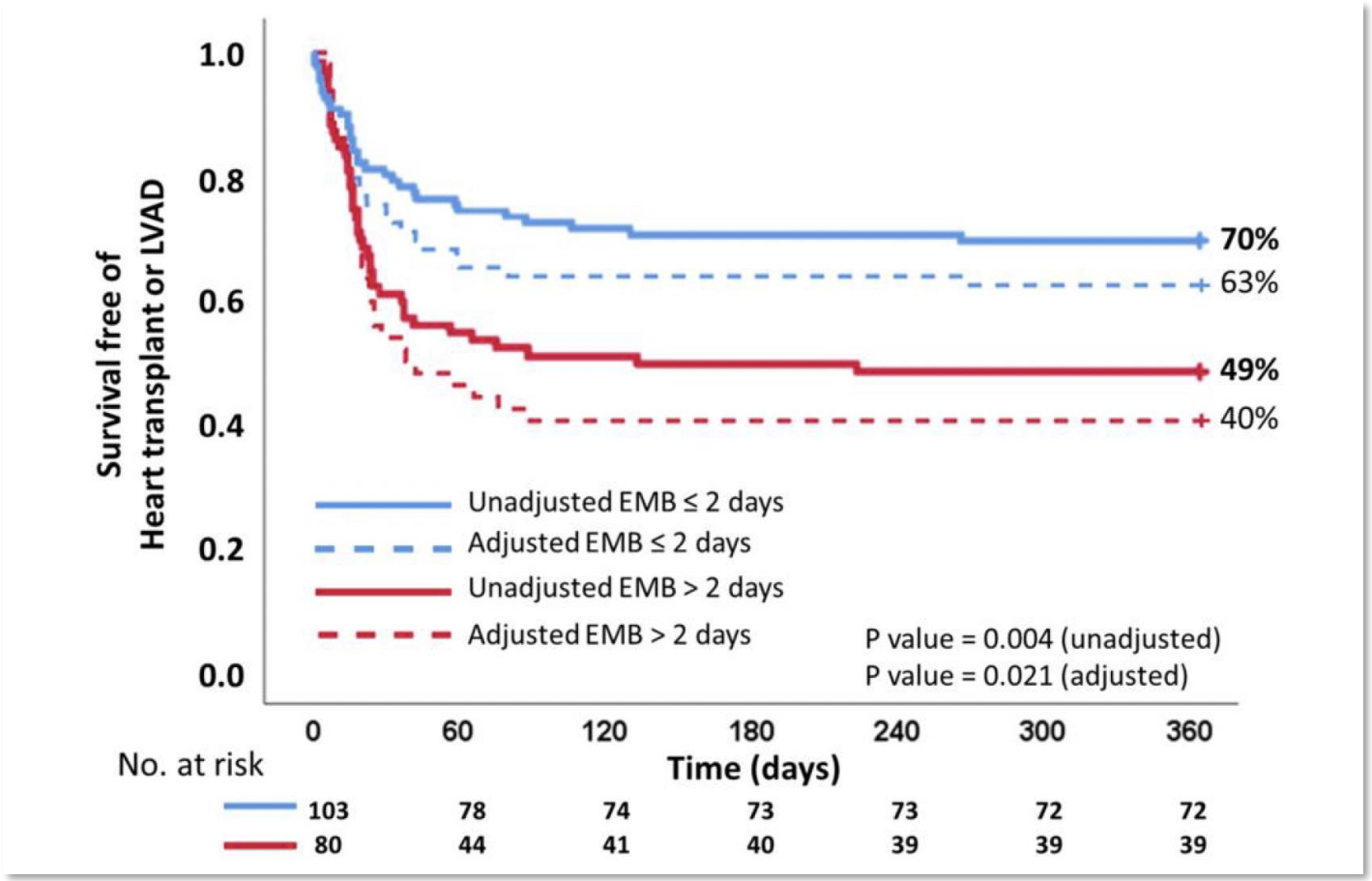

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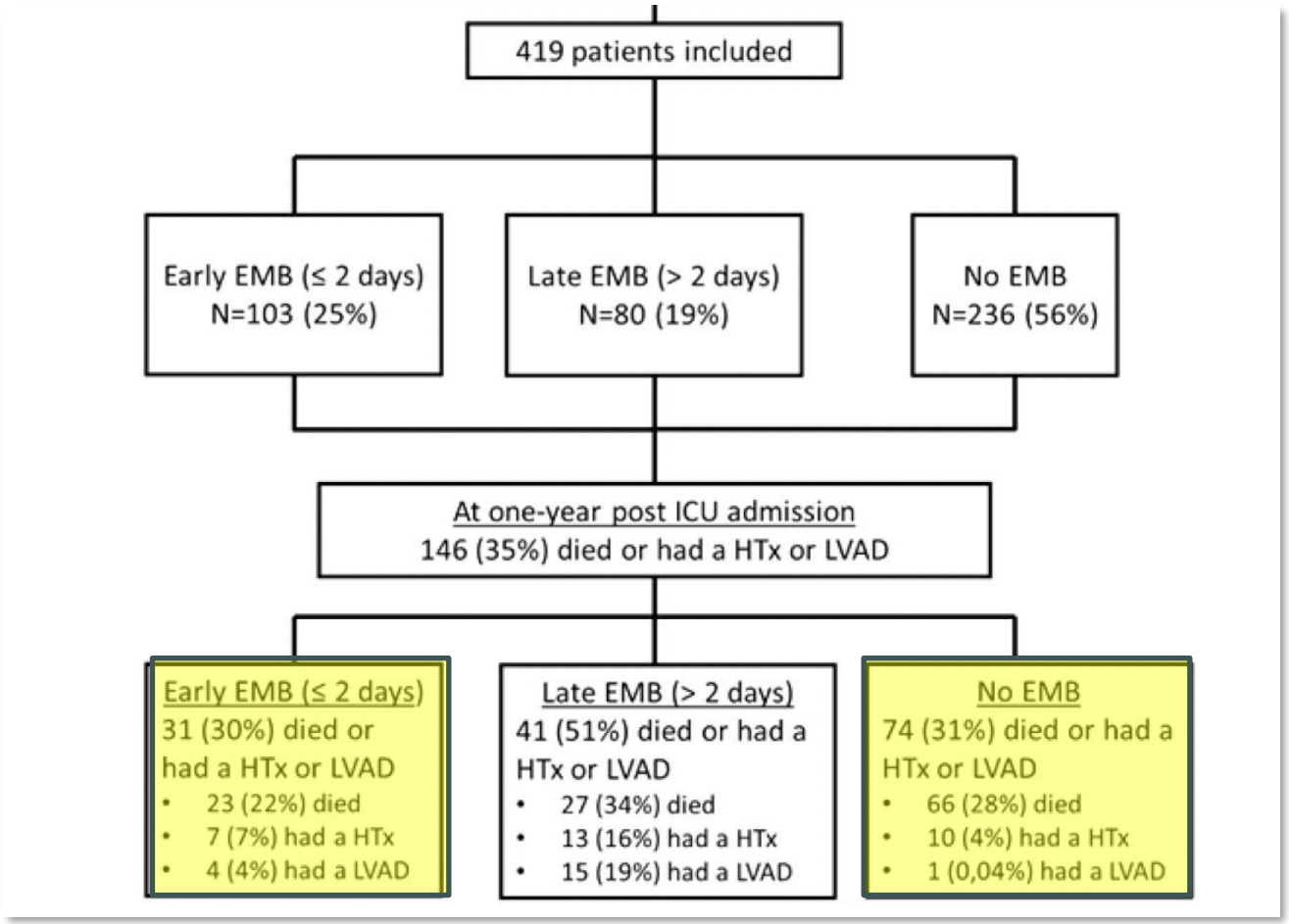

Diagnostic yield, safety and therapeutic consequences of myocardial biopsy in clinically suspected fulminant myocarditis unweanable from mechanical circulatory support

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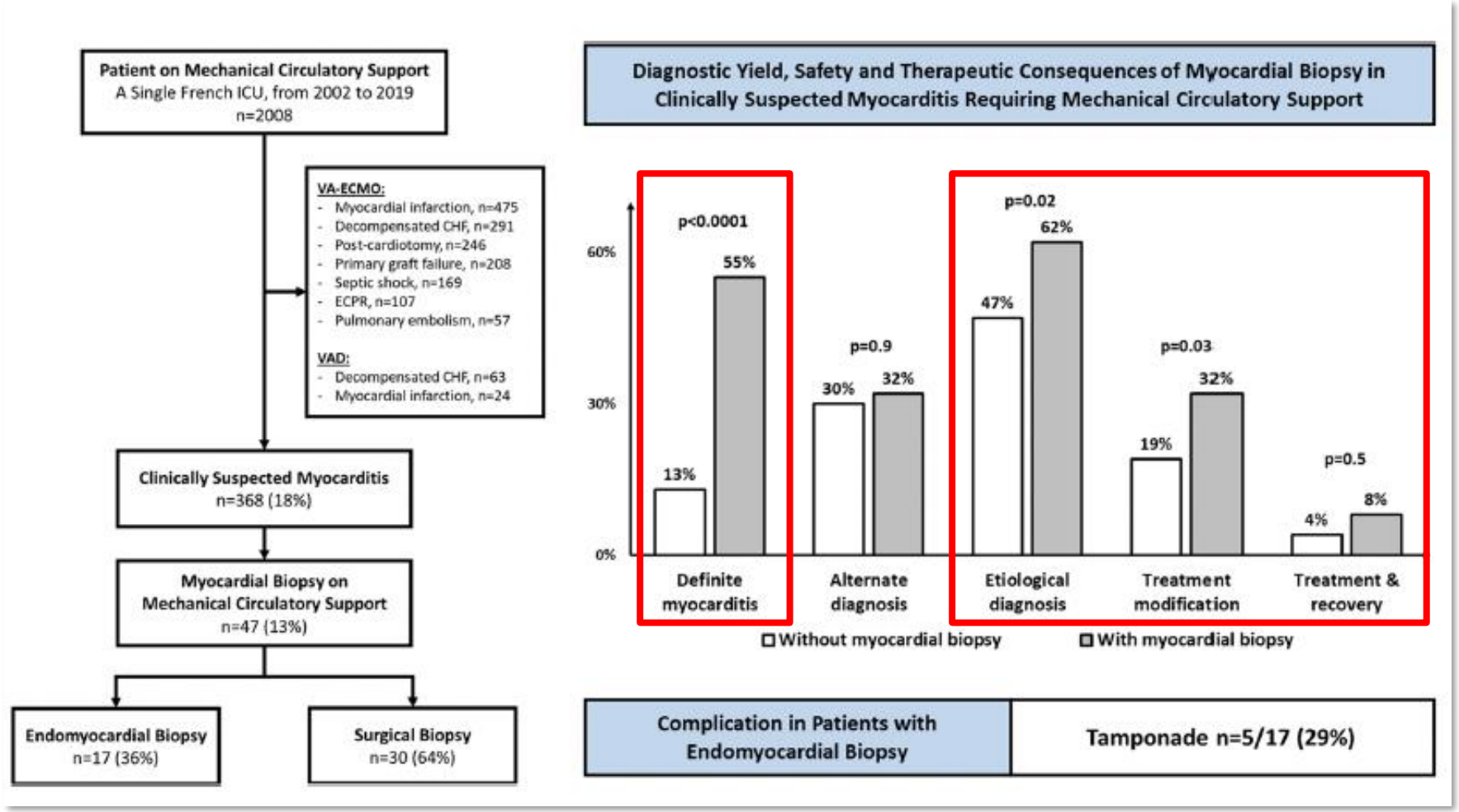

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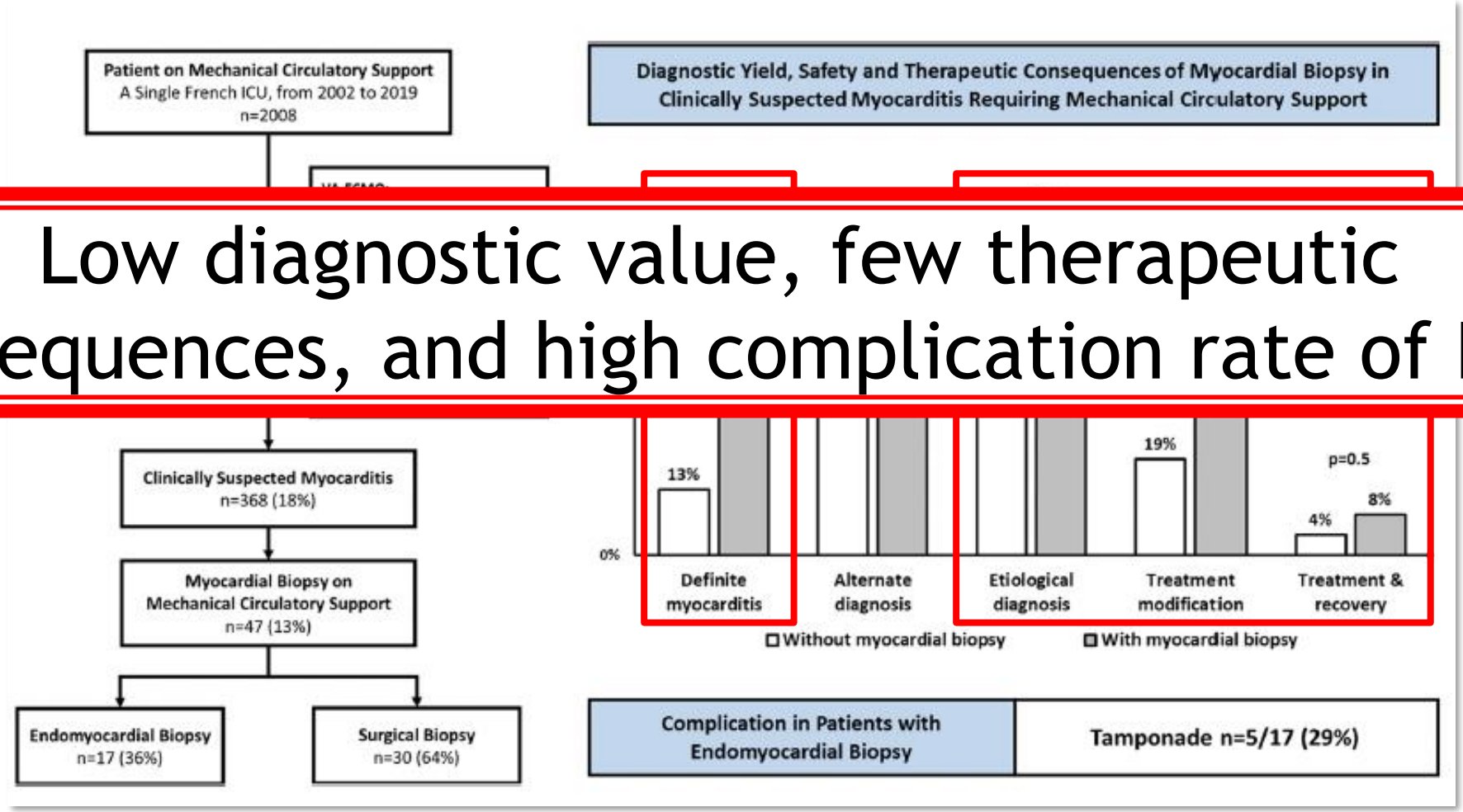

Low diagnostic value, few therapeutic consequences, and high complication rate of EMB

Conclusion

- Most of the non-ischemic acute left ventricular dysfunctions have no specifc treatment
- To date, no viral treatment has been shown effective in treating viruses-induced FM.

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- To date, no viral treatment has been shown effective in treating viruses-induced FM.
- Elevated blood eosinophil count is frequently sufficient to start a promptly efficient corticosteroid treatment
- Systemic autoimmune diseases with cardiac involvement are usually diagnosed and treated without EMB
- No evidence of immunosuppressant efficacy in non-viral, non-autoimmune disease-associated lymphocytic myocarditis.
- Giant-cell myocarditis is very rare. Effectiveness of a specifc treatment has been seriously challenged in patients on t-MCS…

Conclusion

- **Endomyocardial biopsy**
  - Remains largely underperformed in real-life series
    - *Sensitivity remains low…*
  - Need to better define indication?

- **When to perform?**
  - Unusual clinical presentation
  - **Suspected etiology that may need specific treatment**
  - CMRI guided if possible
  - Should be early in these situations…

- Difficulties to transpose results reported in myocarditis without t-MCS