

Myocardite : comment évaluer le risque rythmique ?

Pr Charles Guenancia

Cardiologie

CHU Dijon

Liens d'intérêt

- Bourses de Recherche : MicroPort CRM
- Consultant : Abbott, Medtronic, BMS-Pfizer
- Honoraires : Boston, Medtronic, Astra-Zeneca, BMS-Pfizer

Définition

Symptoms

- Variable clinical presentation
- Dyspnea, palpitations, or chest pain, however viral symptoms may overshadow cardiac manifestations
- May present with arrhythmias resulting in palpitations, syncope, or sudden cardiac death.

Lab work

- ECG-non-specific, sinus tachycardia most common
- CXR: often normal, +/- cardiomegaly, pulmonary congestion
- Cardiac enzyme: may or may not be elevated
- Viral titers: may suggest viral infection, but does not confirm the etiology of cardiac disease
- Echo: non-specific, may mimic AMI, reduced EF, wall motion abnormalities, global hypokinesis, pericardial effusion

When to suspect myocarditis

- Remote history of viral illness with new cardiovascular problems that are not attributable to CAD or other causes, i.e. dysrhythmias, wall motion abnormalities, reduced LV EF.
- Tachycardia out of proportion to fever
- Young patients with low risk for CAD
- Unexplained heart failure +/- dysrhythmias

Diagnosis

- CMR: the presence of at least 2 of the Lake Louise criteria, early enhancement (hyperemia), edema and LGE in a nonischemic pattern
- EMB: gold standard, Dallas criteria used to standardize diagnosis. May help in identifying inflammatory cell infiltrate or myocyte damage

Mort subite et myocardite

Table 1. Clinical characteristics and circumstances of cardiac arrest in autopsied cases of sudden cardiac death (SCD) caused by myocarditis and other causes in persons aged 1–35 years and 36–49 years in Denmark during 2000–2006 and 2007–2009, respectively.

Clinical characteristics and circumstances of cardiac arrest	SCD caused by myocarditis (n = 42)	SCD from other causes (n = 711)	P-value ^a
Median age, years (IQR)	31 (22–36)	34 (27–43)	0.027
Females	28 (22–36)	34 (26–43)	0.105
Males	33 (27–36)	34 (27–43)	0.110
Females, n (%)	15 (31)	212 (30)	0.804
Medicolegal external examination ^b , n (%)	40 (95)	606 (87)	0.150
Witnessed deaths ^c , n (%)	23 (56)	261 (39)	0.032
Previous medical history ^d , n (%)			
Psychiatric disease	8 (19)	142 (20)	0.884
Neurological disorder	4 (10)	73 (10)	0.877
Infectious disease	3 (7)	19 (3)	0.095
Cardiovascular disease	2 (5)	84 (12)	0.163
Ischemic heart disease	1 (2)	22 (3)	0.794
Heart failure	0 (0)	39 (5)	0.119
Cardiac dysrhythmia	0 (0)	32 (5)	0.160
Liver disease	2 (5)	17 (2)	0.341
Autoimmune disease	2 (5)	31 (4)	0.902
Diabetes mellitus	1 (2)	39 (5)	0.383
Cerebrovascular disease	0 (0)	21 (3)	0.259
Place of cardiac arrest, n (%)			
Home	25 (60)	459 (65)	0.575
Public place	11 (26)	164 (23)	
Hospital/ambulance	6 (14)	65 (9)	
Other	0 (0)	20 (3)	
Not specified	0 (0)	3 (0.4)	
Activity prior to cardiac arrest, n (%)			
Awake and relaxed	20 (48)	361 (51)	0.532
Sleep	18 (43)	236 (33)	
Physical activity	2 (5)	74 (10)	
Not specified	2 (5)	40 (6)	

^aP-value for differences between SCD-myocarditis cases and cases with SCD from other causes.

^bData on whether a medicolegal external examination was performed were missing in 2% of all SCDs.

^cData on whether deaths were witnessed were missing in 5% of all SCDs.

^dTreatment at hospital up to 5 years before death.

IQR: interquartile range.

32/753 = 5,5 %

Incidence des arythmies ventriculaires

- **54/2523 (2.1%)** avec TV/FV dans les 90 premiers jours
 - 22% de mortalité
 - 43% DAI

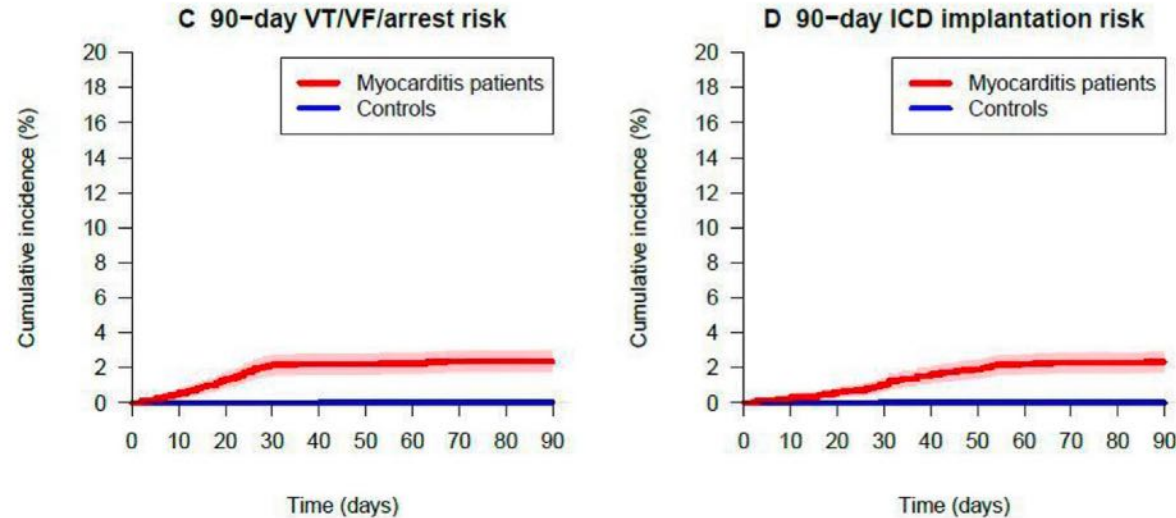


Figure 1 Crude 90-day outcomes of all-cause mortality, HF, ventricular arrhythmias and ICD implantation. HF, heart failure; ICD, implantable cardioverter-defibrillator; VF, ventricular fibrillation; VT, ventricular tachycardia.

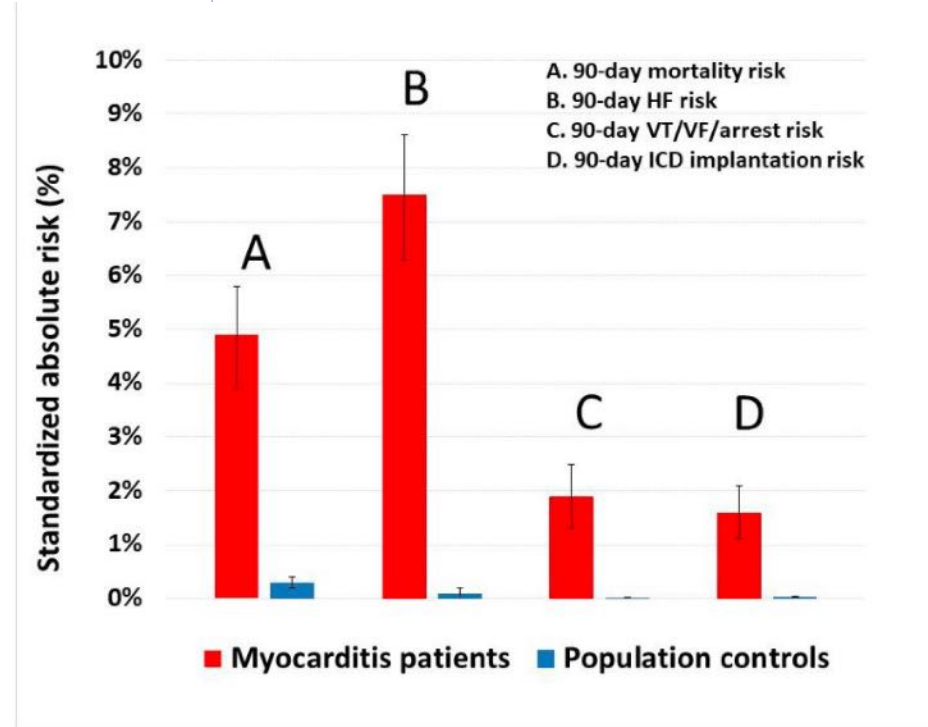
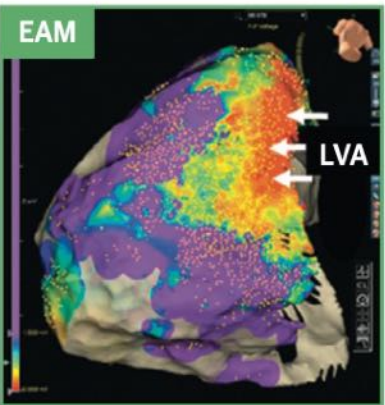
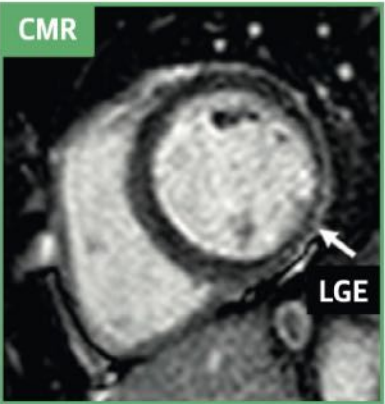


Figure 2 Standardised 90-day absolute risks of all-cause mortality, HF, ventricular arrhythmias and ICD implantation.

Kragholm et al. Open Heart 2021;8:e001806.

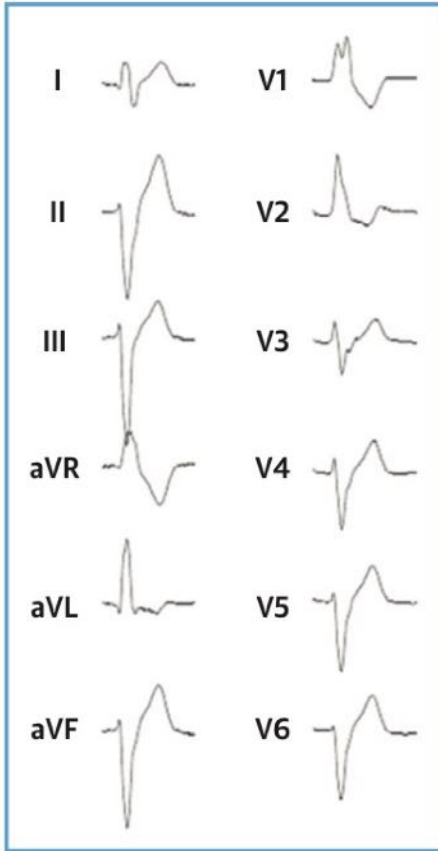
Arythmies ventriculaires et myocardites

Substrate Localization



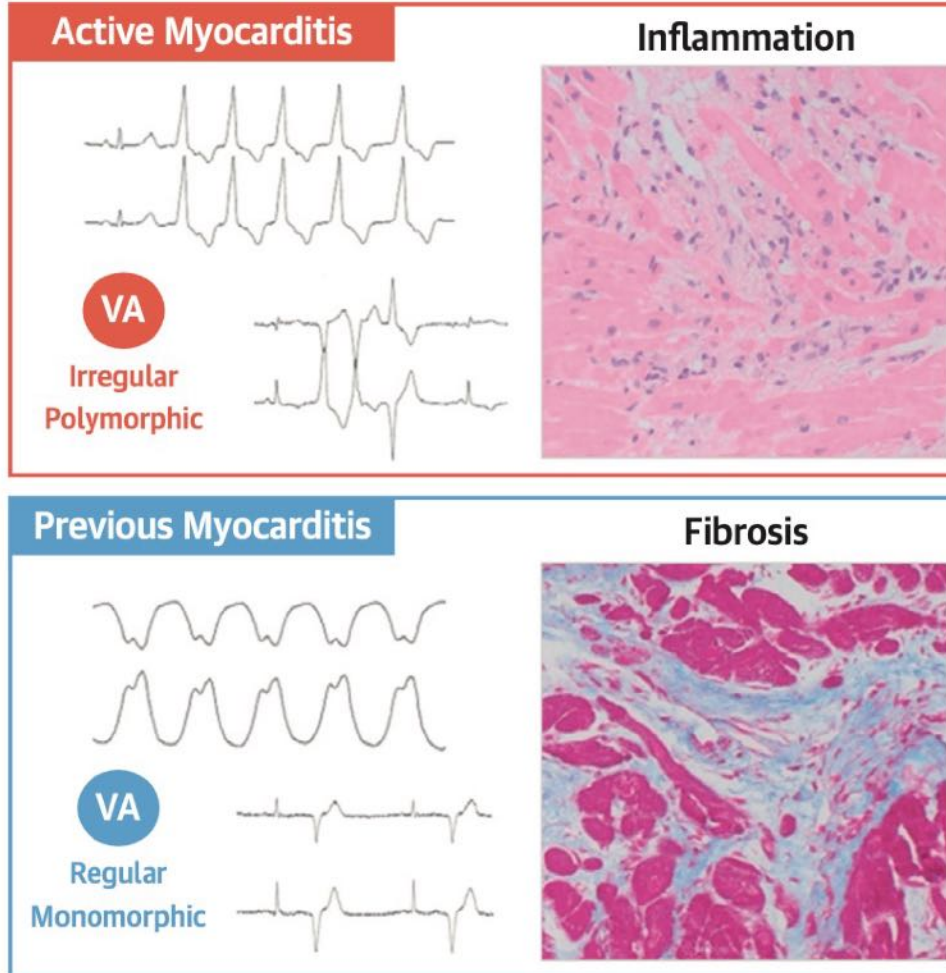
Inferoposterior LV wall
Subepicardial - Midwall

Dominant Morphology



RBBB Superior axis

Relationship with Myocardial Inflammation



Admission pour TV/FV et myocardite (n=189)

➔ 66%

➔ 34%

Cohorte française MYOCARD-ICD

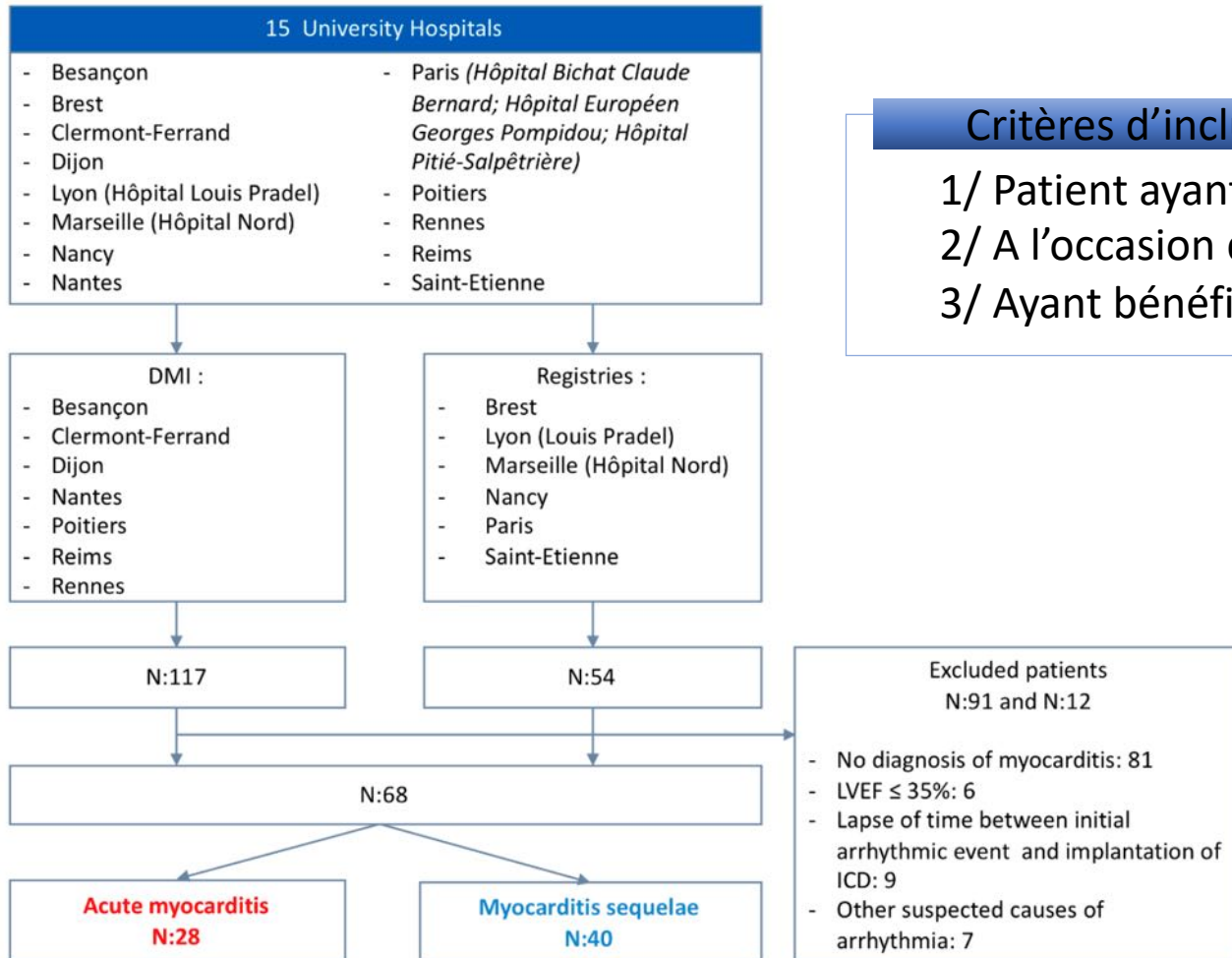


Figure 1. Study population.

Critères d'inclusion

- 1/ Patient ayant présenté une TV ou un FV
- 2/ A l'occasion d'une myocardite aiguë ou sur une séquelle de myocardite
- 3/ Ayant bénéficié après cet épisode de l'implantation d'un DAI

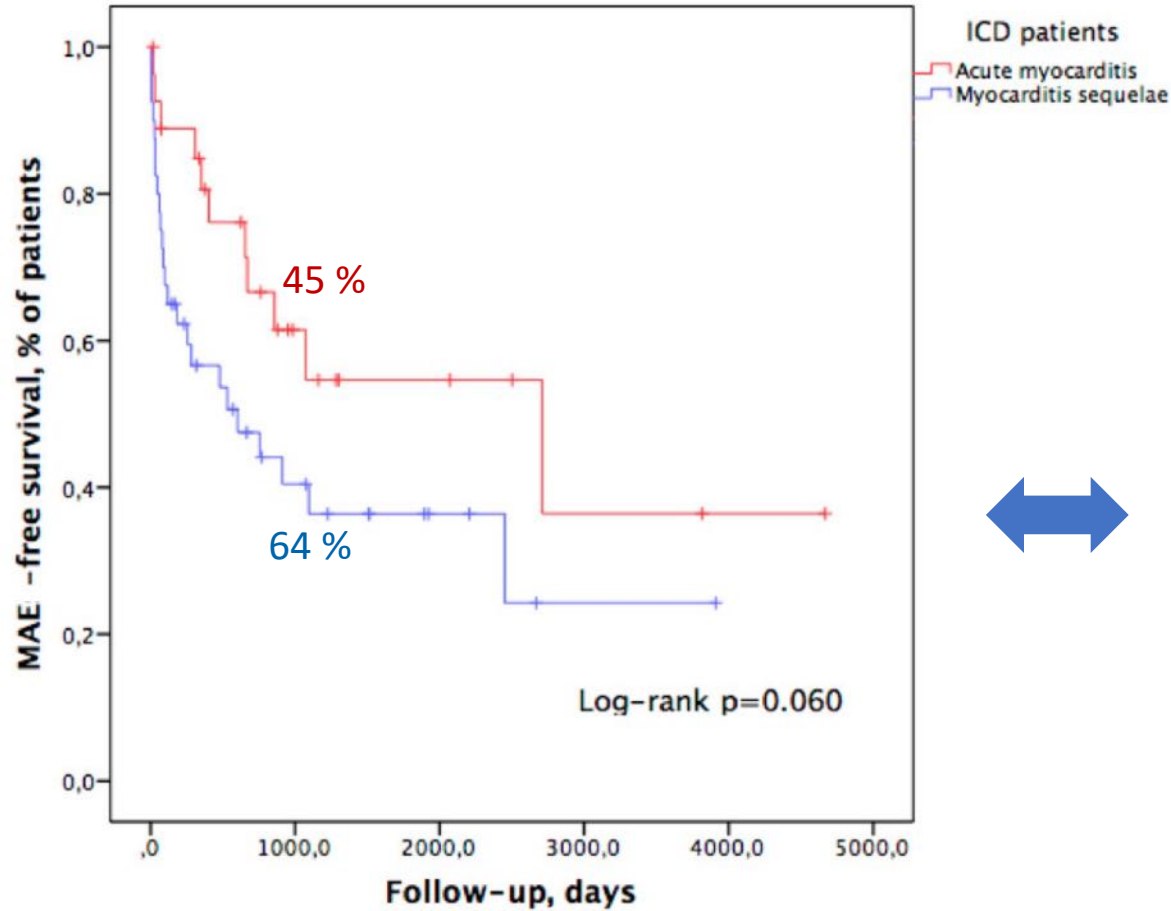


Article

High Risk of Sustained Ventricular Arrhythmia Recurrence After Acute Myocarditis

Laurent Rosier ^{1,†}, Amir Zouaghi ^{2,†}, Valentin Barré ³, Raphaël Martins ³, Vincent Probst ⁴, Eloi Marijon ⁵, Nicolas Sadoul ⁶, Samuel Chauveau ⁷, Antoine Da Costa ⁸, Marc Badoz ⁹, Michael Peyrol ¹⁰, Jérémie Barraud ¹⁰, Grégoire Massoullie ¹¹, Romain Eschalier ¹¹, Madeline Espinosa ¹², François Lesaffre ¹², Rodrigue Garcia ¹³, Bruno Degand ¹³, Antoine Noël ¹⁴, Jacques Mansourati ¹⁴, Fabrice Extramiana ¹⁵, Vincent Algalarrondo ¹⁵, Hervé Devilliers ¹⁶, Yves Cottin ^{1,17}, Estelle Gandjbakhch ^{2,†} and Charles Guenancia ^{1,17,*†‡§}

Suivi rythmique



Number at risk

	0	1000,0	2000,0	3000,0	4000,0
Acute myocarditis	28	8	4	2	1
Myocarditis sequelae	40	10	3	1	0

Rosier L et al. J. Clin. Med. 2020, 9, 848

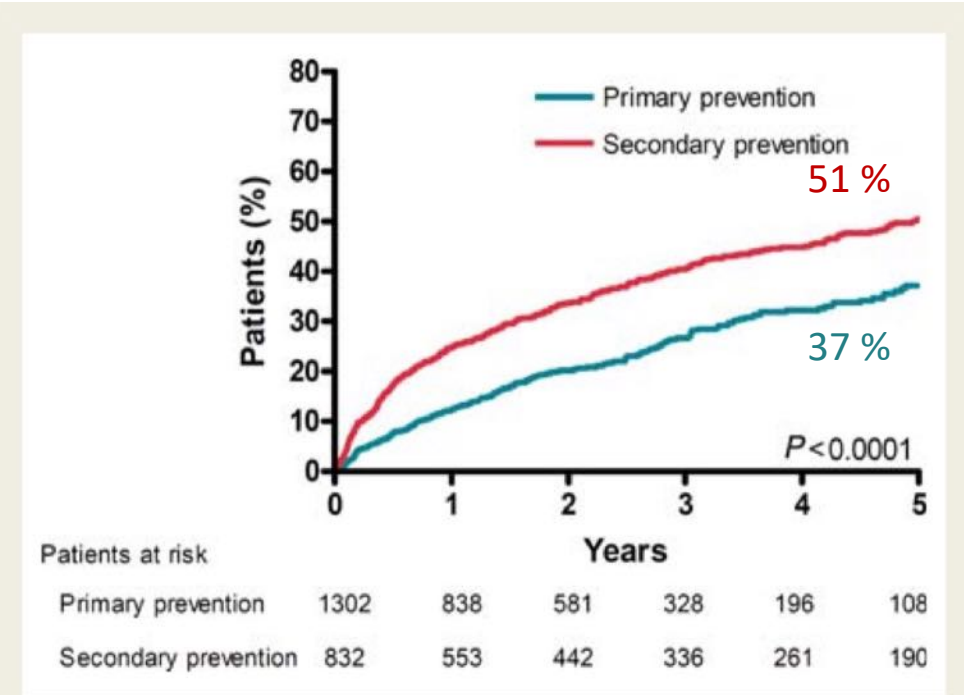


Figure 2 Appropriate therapy. Kaplan–Meier curves of appropriate therapy for primary and secondary prevention implantable cardioverter defibrillator recipients.

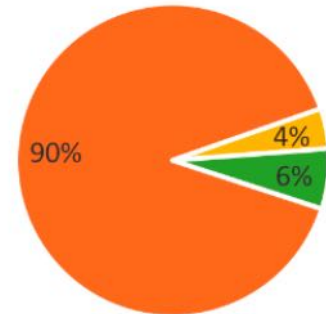
van Welsenes GH et al. Long-term follow-up of primary and secondary prevention implantable cardioverter defibrillator patients. Europace 2011;13(3):389-94

Type d'évènements rythmiques au suivi

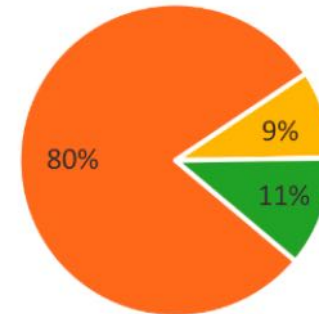
Acute myocarditis, 143 MAE

p=0.137

Myocarditis sequelae, 90 MAE



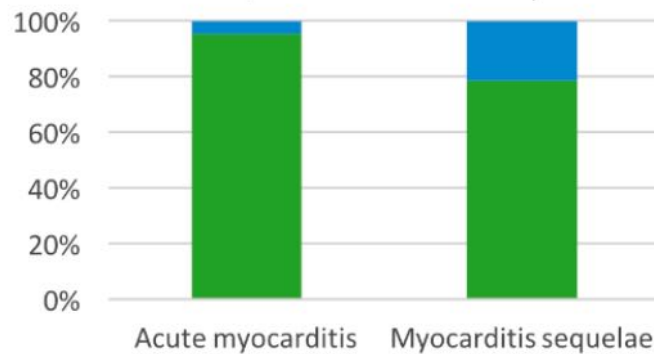
■ VT ■ VF ■ Electrical storm



■ VT ■ VF ■ Electrical storm

Ventricular tachycardia

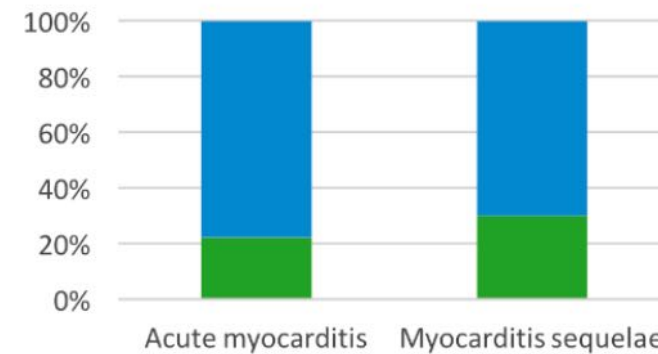
p=0.004



■ ATP ■ Shock

Electrical storm

p=1.000

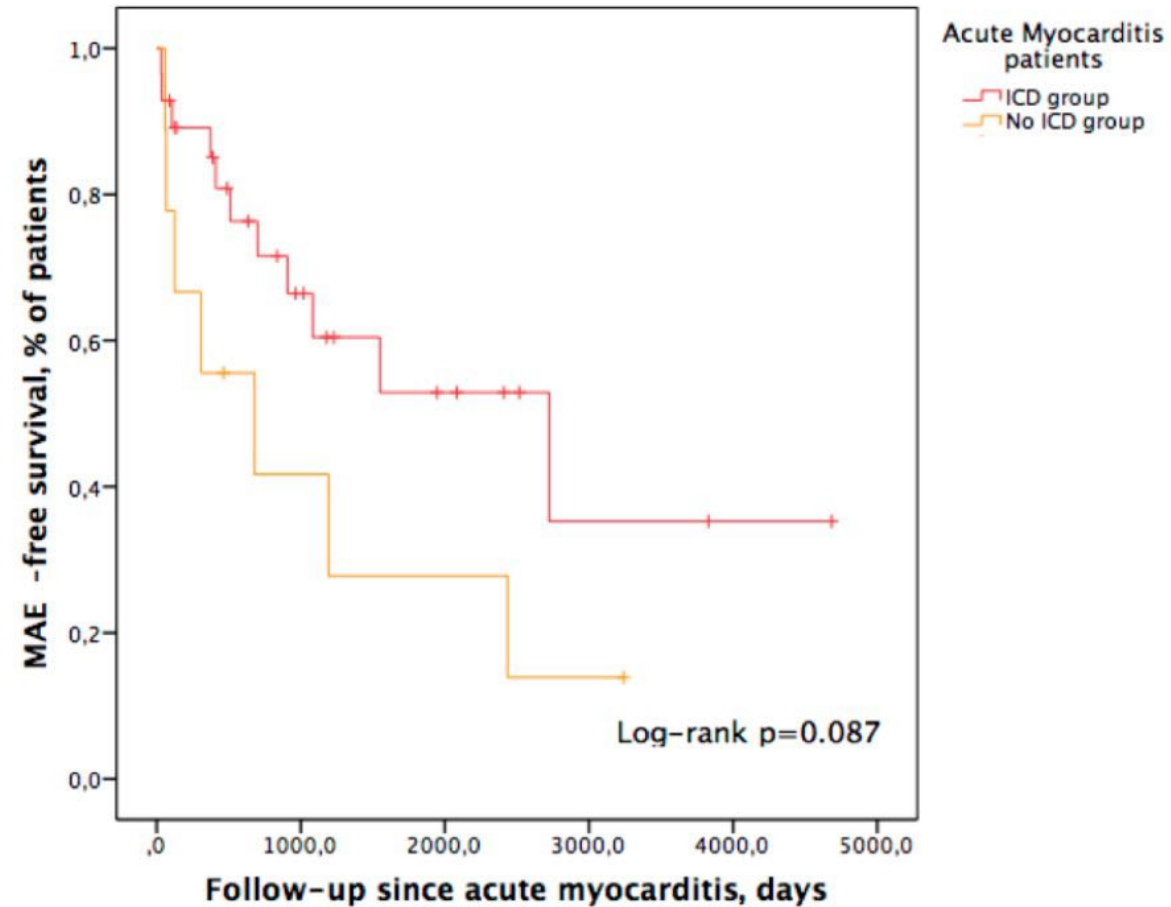


■ ATP ■ Shock

Rosier L et al. J. Clin. Med. 2020, 9, 848



Biais de sélection (d'implantation) ?



Number at risk

ICD group	28	8	4	2	1
No ICD group	9	3	2	1	0

Rosier L et al. J. Clin. Med. 2020, 9, 848

Cohorte italienne

Europe (5 + Italy)
 Paris, Hôpital La Pitié Salpêtrière
 Edgem, Antwerp University Hospital, Belgium
 Maastricht, Cardiovascular Research Institute Maastricht
 Ljubljana, University Medical Centre
 Manchester, University Hospital Of South Manchester

JAPAN (1)
 Sendai, Tohoku University Graduate School of Medicine

Italy (8)
 Trieste, Azienda Sanitaria Universitaria Integrata di Trieste
 Udine, Azienda Sanitaria Universitaria Integrata di Udine
 Bologna, S. Orsola-Malpighi Hospital
 Pisa, Gabriele Monasterio Foundation
 Torino, AQU Città della Salute e della Scienza di Torino
 Milano, De Gasperi Cardio Center, Niguarda Hospital
 Milano, Centro Cardiologico Monzino, IRCCS,
 Milano, Vita Salute University and San Raffaele Hospital

USA (2)
 Rochester, Division of Cardiovascular Diseases, Mayo Clinic
 San Diego, Division of Cardiology, University of California

Coordinating center: Trieste
 16 Centres (156 patients)

MAJOR ARRHYTHMIC EVENTS AFTER HOSPITAL DISCHARGE

- No major tachyarrhythmic events in the F-up (63%)
- Major tachyarrhythmic events in the F-up (37%)

Biopsy proven acute myocarditis
 N = 98

Diagnosis with only Cardiac Magnetic Resonance criteria (Lake Louise Criteria)
 N = 58

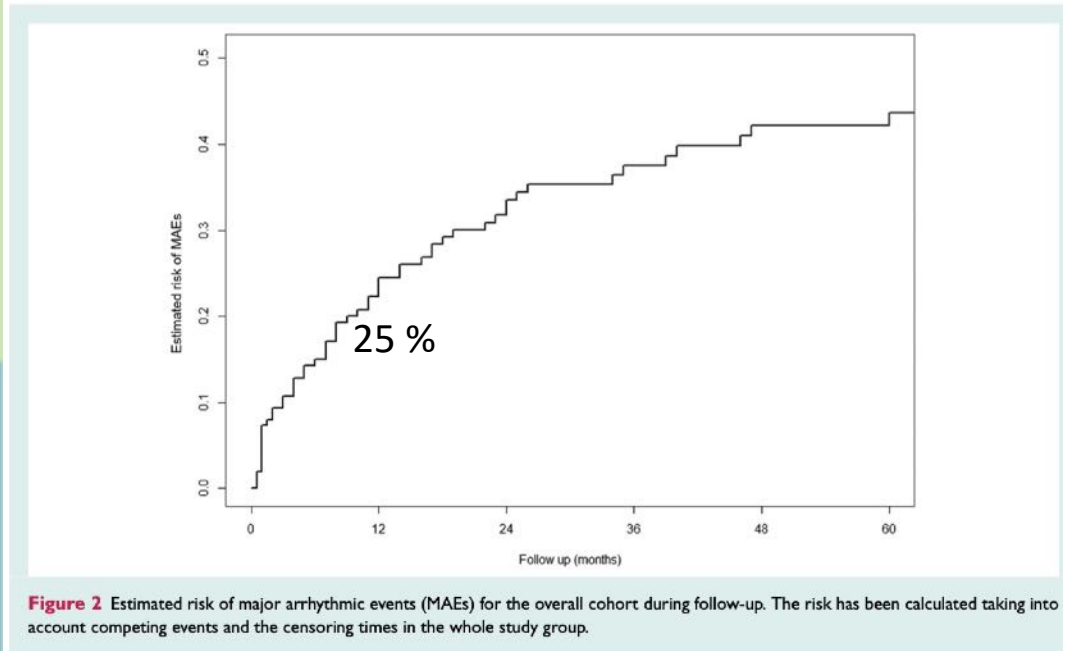
Points

Sustained VT: 1
 LGE involving ≥2 myocardial segments: 1
 Positive STIR: 0
 Total Points: 2

6-month event prob: 0.05
 1-year event prob: 0.1
 2-year event prob: 0.2

Patients with Acute Myocarditis with life-threatening ventricular tachyarrhythmias at presentation, alive at discharge and without occurrence of HTx or LVAD implantation during the index hospitalisation
 N = 156

19% and 45% in the acute group



	No. of patients with available data	All patients (n = 156)	MAEs at follow-up (n = 58, 37%)	No MAEs at follow-up (n = 98, 63%)	P-value
ICD implantation prior to discharge	156	93 (60)	47 (81)	46 (47)	<0.001

Gentile et al European Journal of Heart Failure (2021) 23, 2045–2054

Monocentrique Allemagne

51 patients avec TV/FV en phase aigue d'une myocardite implantés d'un DAI
→ 31 (61%) patients avec récurrence au suivi

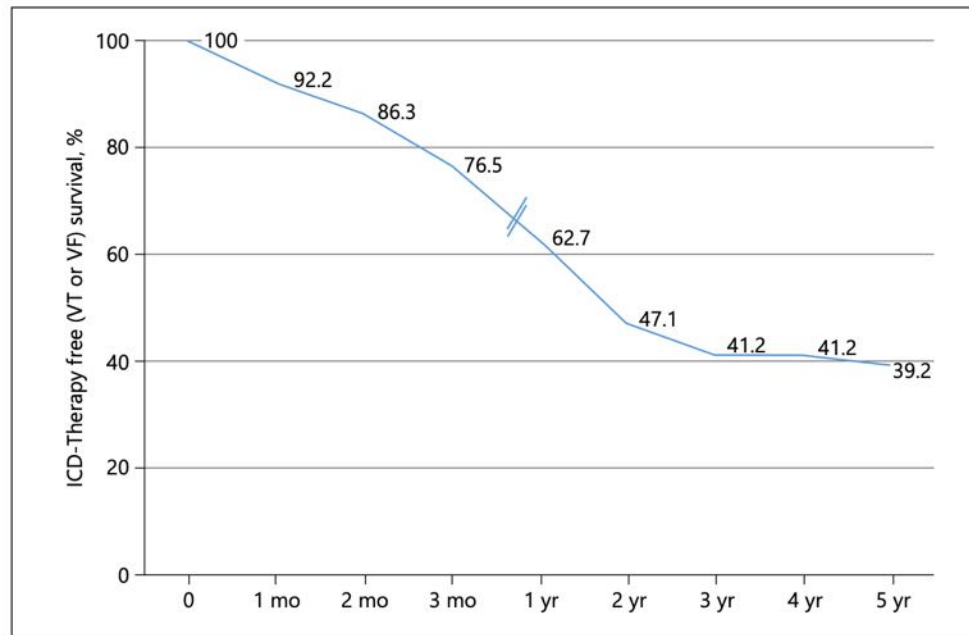


Fig. 5. Temporal distribution of recurrent tachycardias, documented for up to 5 years after the primary episode. The majority of tachycardias occurred in the first 36 months after the initial phase of myocarditis in this patient population. ICD, implantable cardioverter defibrillator; VF, ventricular fibrillation; VT, ventricular tachycardia.

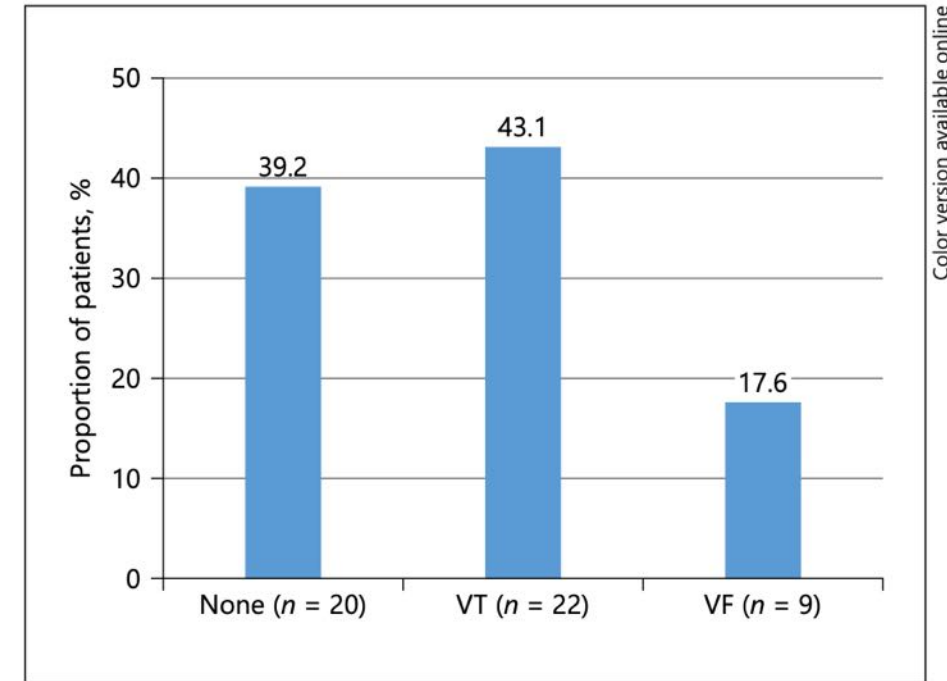


Fig. 4. Type of tachycardia: 61% of all patients (31 of 51) experienced recurring arrhythmias. Implanted ICDs documented mostly VT (43%; 20 patients) and to a less extent VF (18%; 11 patients). ICD, implantable cardioverter defibrillator; VF, ventricular fibrillation; VT, ventricular tachycardia.

Sasko et al Cardiology 2021;146:213–221

Guidelines ESC 2022

Treatment of arrhythmias in patients with inflammatory heart disease does not differ from generally accepted clinical principles. Symptomatic VAs may require AADs such as amiodarone and/or beta-blockers.^{791–793} Of note, in a retrospective observational study, patients with sustained VAs during the acute phase of myocarditis (LVEF $53 \pm 10\%$) had a high risk (45% at 3 years) of VT/VF recurrences during follow-up.⁷⁹⁴

794. Rosier L, Zouaghi A, Barré V, Martins R, Probst V, Marijon E, et al. High risk of sustained ventricular arrhythmia recurrence after acute myocarditis. *J Clin Med* 2020;**9**: E848.

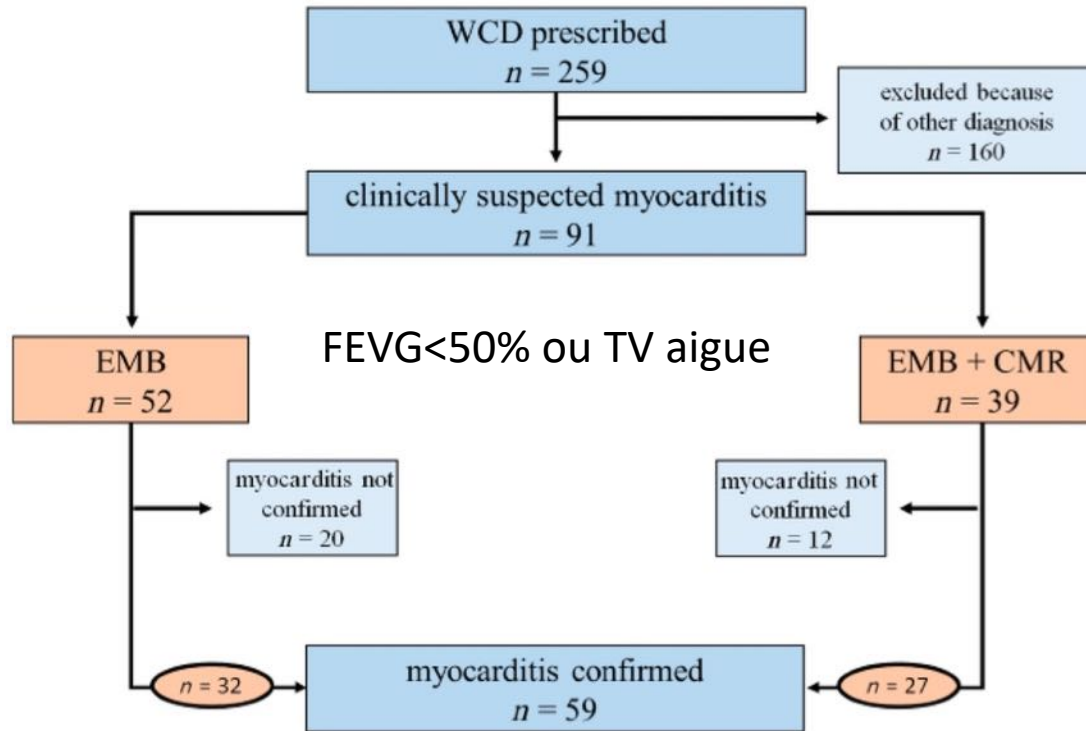
Secondary prevention of SCD and treatment of VA

In patients with haemodynamically not-tolerated SMVT occurring in the chronic phase of myocarditis, an ICD implantation is recommended. ^{794,805}	I	C
In patients with haemodynamically not-tolerated sustained VT or VF during the acute phase of myocarditis, ICD implantation before hospital discharge should be considered. ^{788,794,806}	IIa	C
AADs should be considered (preferably amiodarone and beta-blockers) in patients with symptomatic non-sustained or sustained VAs during the acute phase of myocarditis.	IIa	C
In post-myocarditis patients with recurrent, symptomatic VT, AAD treatment should be considered.	IIa	C
Catheter ablation, performed in specialized centres, should be considered in post-myocarditis patients with recurrent, symptomatic SMVT or ICD shocks for SMVT in whom AADs are ineffective, not tolerated, or not desired. ^{752,801,802}	IIa	C
In patients with haemodynamically tolerated SMVT occurring in the chronic phase of myocarditis, ICD implantation should be considered.	IIa	C

European Heart Journal (2022) 43, 3997–4126

Intérêt de la life vest ?

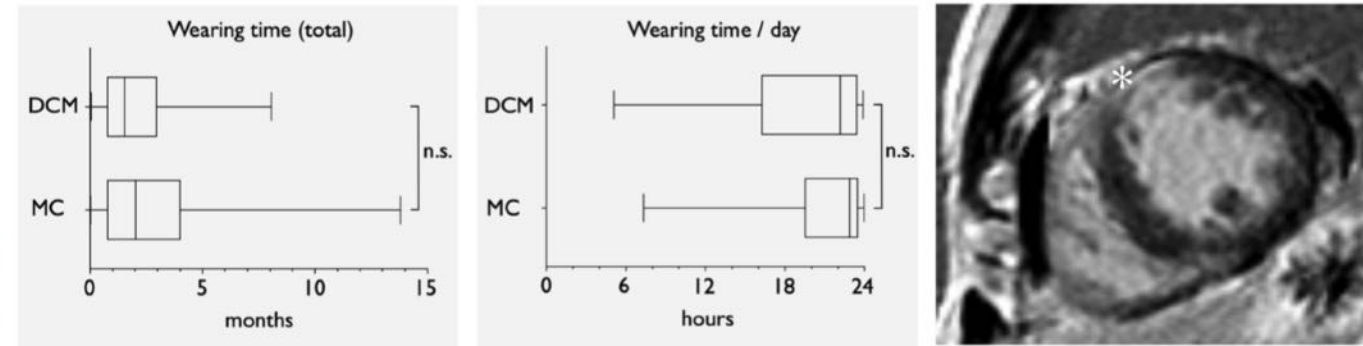
Tscholl et al. ESC Heart Failure 2021; 8: 2428–24



2/59 patients avec TV soutenue
3%

During the acute phase of myocarditis, ICD implantation should be deferred until resolution of the acute episode. Because myocarditis may heal completely, the indication for ICD implantation and its timing remain controversial even beyond the acute stage. Bridging the critical period to full recovery by a WCD vest in patients with myocarditis and VT or VF appears to be a promising therapeutic option.^{598,599}

Blaschke et al. ESC Heart Failure 2021; 8: 2591–2596



C

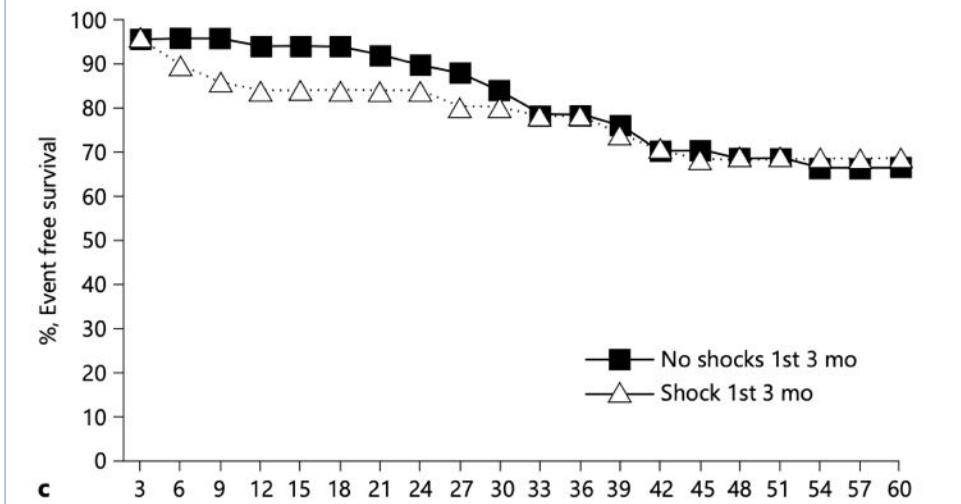
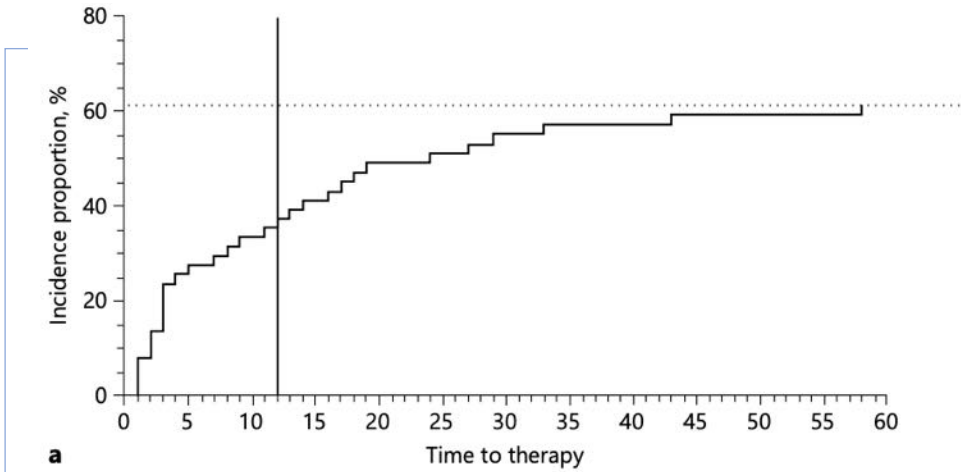
Cardio-myopathy	Patients with VT (n)	Total episodes of VT (n)	Sustained VT (n)	Non-sustained VT (n)	VT duration (seconds)	VT frequency (bpm)	Morphology	Maximal number of morphologies per patient	Therapy (shocks)
DCM	1	1	0	1	Min: 14 Max: 14	Min: 187 Max: 187	Mono: 1 Poly: 0	1	0
MC	7	41	6 in 3 patients	35	Min: 1 Max: 80	Min: 130 Max: 260	Mono: 25 Poly: 16	2	2 in 1 patient
P value	0.03	0.03	0.09	0.10	-	-	-	-	-

3/39 patients avec TV soutenue

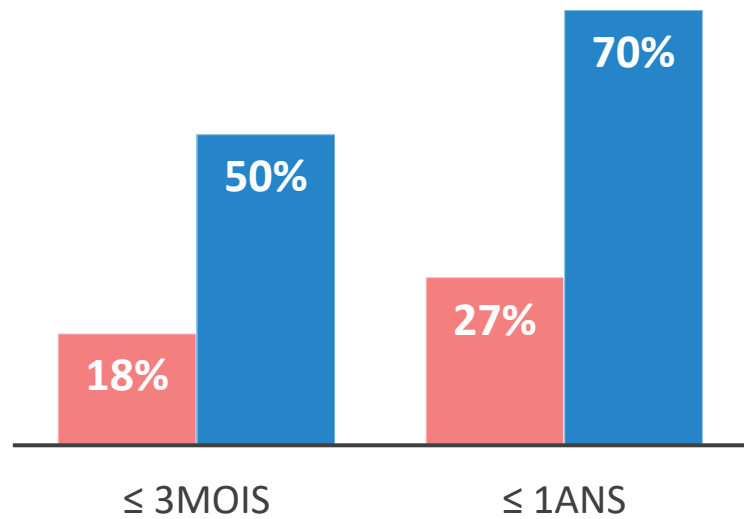
8%

www.pratico-rythmo.com

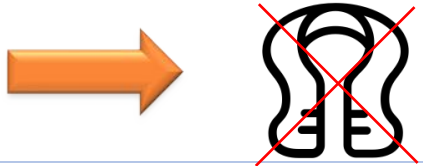
Intérêt de la life vest ?



Délai implantation DAI-1er ERM



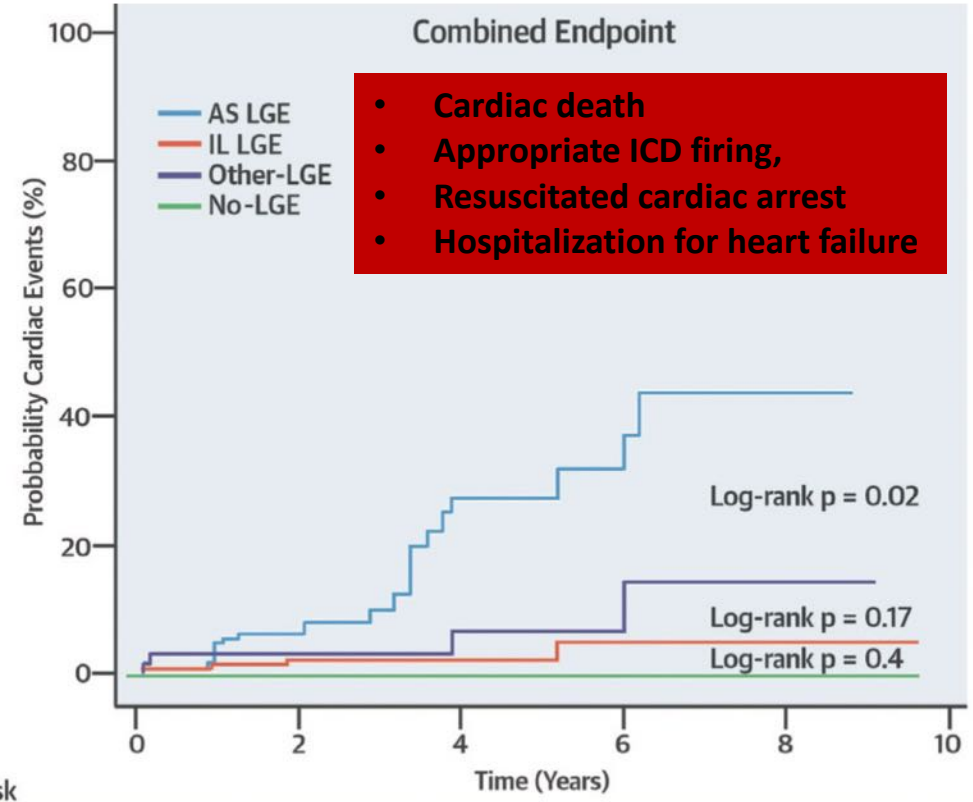
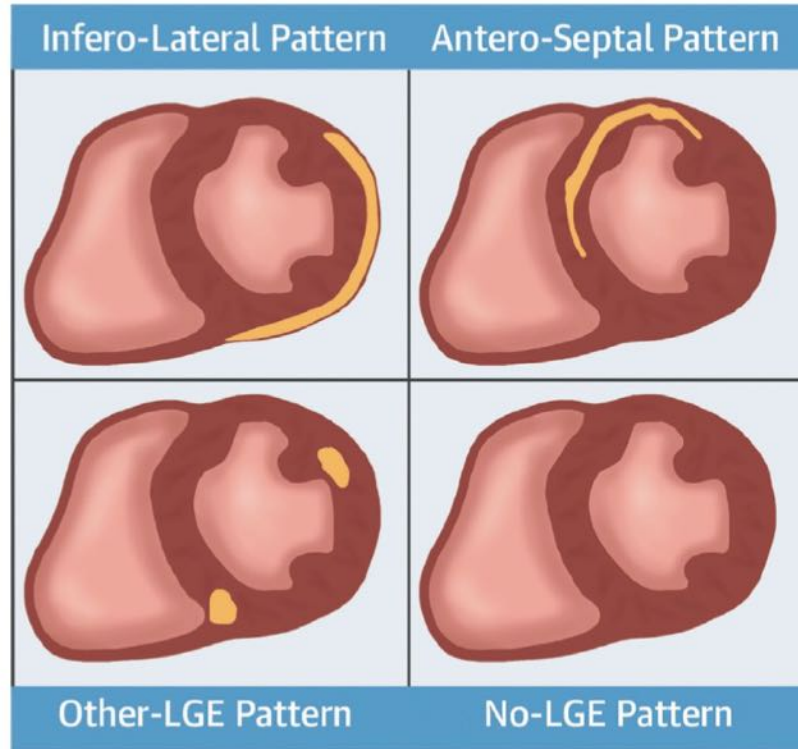
82 % des ERM surviennent après 3 mois en post myocardite aigue



Sasko et al Cardiology 2021;146:213–221

Rosier et al. J. Clin. Med. 2020, 9, 848

CENTRAL ILLUSTRATION Prognostic Role of Different LGE Patterns in Patients With AM and Preserved EF



- Cardiac death
- Appropriate ICD firing,
- Resuscitated cardiac arrest
- Hospitalization for heart failure

	At Risk	0	2	4	6	8	10
AS LGE	135	60	27	11	1	0	0
IL LGE	154	92	52	21	6	0	0
Other-LGE	59	44	24	11	6	0	0
No-LGE	26	19	7	1	1	0	0

Aquaro, G.D. et al. J Am Coll Cardiol. 2017;70(16):1977-87.

In a population of patients with acute myocarditis (AM) and preserved ejection fraction (EF), we identified 4 main patterns of distribution of late gadolinium enhancement (LGE) (**left**). The antero-septal pattern of late gadolinium enhancement was associated with a worse prognosis than the other patterns (**right**). AS = antero-septal; IL = inferolateral.

Prédire les arythmies ventriculaires?

IRM après TV/FV sur myocardite aigue

Variable	Univariate			Multivariate		
	HR	95% CI	<i>p</i>	HR	95% CI	<i>p</i>
Sequelae group (vs. acute myocarditis)	2.26	1.04–4.91	0.041	2.88	1.29–6.44	0.010
LVEF < 50%	1.76	0.87–3.58	0.119			
Wide QRS	1.94	0.83–4.53	0.124			
Anterior LGE location	2.05	1.01–4.17	0.047	2.60	1.28–5.59	0.009

CI: confidence interval; HR: hazard ratio; LGE: late gadolinium enhancement; LVEF: left ventricular ejection fraction.

Rosier et al. *J. Clin. Med.* 2020, 9, 848

IRM après TV/FV sur myocardite aigue

Table 2 Univariable and multivariable analysis for baseline prediction model of major arrhythmic events at follow-up

	HR (95% CI) for MAEs ^a			
	Unadjusted HR	P-value	Adjusted HR	P-value
Epoch of enrolment (1995–2004 vs. 2005–2019)	0.18 (0.03–1.32)	0.09		
Male sex	0.38 (0.18–0.81)	0.012		
Family history of cardiomyopathy	2.31 (1.04–5.15)	0.04		
Sustained ventricular tachycardia at presentation	2.24 (1.20–4.17)	0.011	2.90 (1.38–6.11)	0.005
LVEDV	1.01 (0.99–1.01)	0.07		
LGE involving ≥2 myocardial segments at CMR	3.56 (1.75–7.23)	<0.001	4.51 (2.39–8.53)	<0.001
Absence of positive STIR at CMR	1.90 (1.05–3.44)	0.033	2.59 (1.40–4.79)	0.002
Cardiac sarcoidosis	12.95 (2.69–62.34)	0.001		

All tested variables with P-values >0.1 are not shown.

CI, confidence interval; CMR, cardiac magnetic resonance; HR, hazard ratio; LGE, late gadolinium enhancement; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; MAE, major arrhythmic event; STIR, short-tau inversion recovery.

^aThe independent predictors of MAEs during follow-up were studied in the population with available CMR data (n = 117/156, 75%; 44 events).

Gentile et al. European Journal of Heart Failure (2021) 23, 2045–2054

Voltage bipolaire après TV/FV sur myocardite aigue

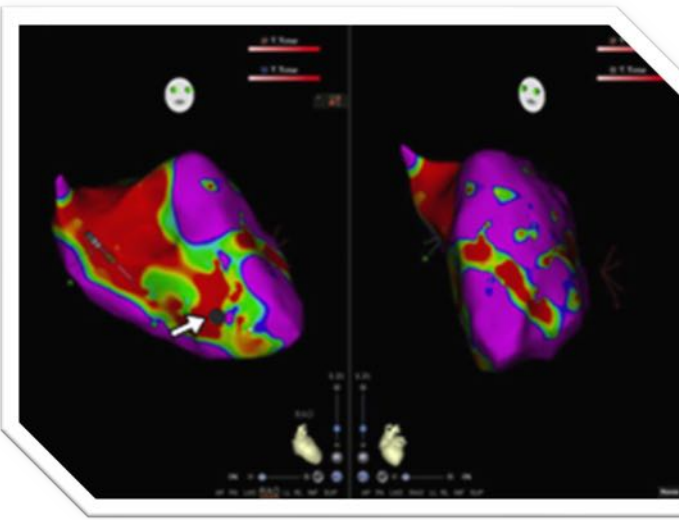


TABLE 4 HR for Time to Appropriate ICD Intervention

	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Age	1.010 (0.970-1.050)	0.60	1.100 (0.100-15.000)	0.98
Male	1.120 (0.380-3.340)	0.83	0.670 (0.100-3.000)	0.88
QRS duration	1.020 (0.990-1.040)	0.10	1.200 (0.400-9.000)	0.65
Sustained VT	6.900 (1.600-28.000)	0.007	13.000 (2.000-35.000)	0.032
Active myocarditis	0.810 (0.380-1.730)	0.58	0.980 (0.100-32.000)	0.98
LVEF	1.001 (0.970-1.035)	0.90	0.810 (0.200-26.000)	0.99
LGE (CMR)	1.120 (0.220-4.460)	0.53	1.220 (0.070-41.000)	0.98
Abnormal BI area	1.104 (1.004-1.214)	0.041	1.200 (1.040-1.370)	0.013
VT inducibility	2.680 (0.89-8.13)	0.08	1.700 (0.200-10.000)	0.62

Pelargonio et al J Am Coll Cardiol EP 2020;6:574-82

Conclusion

- TV/FV sur myocardite aigüe :
 - Risque rythmique persiste après la phase aigüe (> prévention primaire CMD)
 - TV +++ au suivi
 - Life vest inutile
 - DAI si mal tolérée (ESC 2022)
- TV/FV sur séquelle de myocardite :
 - TV +++ : privilégier endocavitaire (et/ou ablation?)
 - Biopsie pour confirmer le diagnostic ?
- Stratifier le risque avant le trouble du rythme :
 - nouveaux marqueurs pronostiques : IRM +++, voltage bipolaire ?



UBFC
UNIVERSITÉ
BOURGOGNE-FRANCHE-COMTE

UFR
SCIENCES
DE SANTÉ
DIJON



PEC
ÉQUIPE D'ACCUEIL - EA 7460
Hépatologie & Entérologie, Gastro-Cardiovasculaires

CHU
Centre Hospitalier Universitaire
Dijon Bourgogne