

SUPPLEMENTAL MATERIAL

Table S1. Clinical characteristics and strain parameters, with reference value, of healthy controls

	Healthy controls (n=20)	
Demographics		
Age (years)	41 ±12	
Sex	15 (75%)	
BMI (kg/m ²)	25 ±4	
Strain parameter		Reference value
LV GLS	-23.43 ± 2.29	-18.85
LV GCS	-27.54 ± 3.25	-20.04
LV GRS	71.19 ± 10.85	49.49
RV GLS	-27.09 ± 4.22	-18.65
LA reservoir	39.70 ± 8.42	22.86
LA booster	16.60 ± 3.81	8.98
LA conduit	23.10 ± 6.64	9.82

Abbreviations: GCS = global circumferential strain, GLS = global longitudinal strain, GRS = global radial strain, LA = left atrial, LV = left ventricular, RV = right ventricular.

Table S2. Common MACE predictors in acute myocarditis patients from literature

N=162	Clinical parameters + LV GLS		Clinical parameters + LV GCS		Clinical parameters + LV GRS		Clinical parameters + LA reservoir strain		Clinical parameters + LA conduit strain	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	1.05 (1.02-1.07)	< 0.001	1.05 (1.03-1.08)	< 0.001	1.05 (1.02-1.07)	< 0.001	1.05 (1.03-1.08)	< 0.001	1.05 (1.03-1.08)	< 0.001
Male sex	0.68 (0.32-1.47)	0.33	0.58 (0.26-1.29)	0.18	0.72 (0.32-1.61)	0.42	0.65 (0.30-1.40)	0.27	0.65 (0.30-1.40)	0.27
LVEF (%)	1.02 (0.98-1.07)	0.36	1.07 (1.01-1.15)	0.04	1.01 (0.97-1.05)	0.59	0.98 (0.96-1.00)	0.10	0.98 (0.96-1.00)	0.17
LV GLS (%)	1.07 (1.01-1.14)	0.02								
LV GCS (%)			1.17 (1.04-1.32)	0.01						
LV GRS (%)					0.98 (0.96-0.99)	0.03				
LA reservoir strain (%)							0.99 (0.96-1.03)	0.73		
LA conduit strain (%)									1.01 (0.95-1.08)	0.66

Abbreviations: CI = confidence interval, EF = ejection fraction, GCS = global circumferential strain, GLS = global longitudinal strain, GRS = global radial strain, HR = hazard ratio, LA = left atrial, LV = left ventricular.

Table S3. Overview of (suspected) etiologies of myocarditis

(suspected) Etiology of myocarditis	Frequency, n (%)
Viral	80 (49)
Auto-immune disease	15 (9)
Systemic lupus erythematosus	6 (4)
Systemic sclerosis	7 (4)
Eosinophilic granulomatosis with polyangiitis	1 (0.6)
Miller-Fisher syndrome	1 (0.6)
Giant-cell	1 (0.6)
Eosinophilic	3 (2)
Inflammatory presentation of genetic cardiomyopathy	1 (0.6)
Malaria	1 (0.6)
Polymyositis	1 (0.6)
Toxic after chemotherapy	1 (0.6)
Bacterial	4 (3)
Unknown etiology	55 (34)

Table S4. Overview of causes of death

Cause of death	Frequency, n (%)
Sudden or cardiac death	10 (59)
Cancer	2 (12)
Auto-immune disease	4 (24)
Parkinson	1 (6)

Table S5. Clinical characteristics of four risk groups using age and LV GLS

	Age < 40 years		Age ≥ 40 years		p-value
	Good LV GLS	Worse LV GLS	Good LV GLS	Worse LV GLS	
Demographics					
Age (years)	27 ±7*	26 ±6*	53 ±10 [†]	57 ±10 [†]	*0.59/ [†] 0.11
Male	44 (86)	25 (83)	23 (76)	29 (57)	<0.01
BMI (kg/m ²)	25 ±3	26 ±5	25 ±4	25 ±4	NS
Medical history					
Atrial fibrillation	0	0	1 (3)	3 (6)	NS
Pericarditis	2 (4)	0	0	3 (6)	NS
Myocarditis	5 (10)	1 (3)	3 (10)	0	NS
Hypertension	2 (4)	3 (10)	5 (16)	16 (31)	0.001
Hypercholesterolemia	3 (6)	0	3 (10)	8 (16)	NS
Chronic obstructive pulmonary disease	1 (2)	0	3 (10)	3 (6)	NS
Diabetes Mellitus	1 (2)	0	1 (3)	4 (8)	NS
Autoinflammatory disease	3 (5)	3 (10)	5 (16)	13 (25)	<0.05
Clinical presentation					
Chest pain	45 (88)	23 (77)	24 (80)	31 (61)	0.01
Dyspnoea	16 (31)	8 (27)	10 (33)	22 (43)	NS
Collapse	4 (8)	1 (3)	0	7 (14)	NS
Flulike symptoms	36 (71)	21 (70)	14 (47)	27 (53)	NS
Fever	26 (51)	12 (40)	10 (33)	10 (20)	<0.01
Smoking status					NS
Never	37 (73)	21 (70)	21 (70)	32 (63)	
Former smoker	4 (8)	0	5 (17)	11 (22)	
Current smoker	10 (20)	8 (27)	4 (13)	8 (16)	
Heart rate (bpm)	80 ±23	98 ±26	80 ±22	92 ±33	<0.01
Systolic blood pressure (mmHg)	125 ±18	122 ±25	132 ±19	132 ±29	NS
Diastolic blood pressure (mmHg)	74 ±12	75 ±18	81 ±11	82 ±19	0.03
Killip class					NS
Class I	49 (96)	26 (87)	27 (90)	39 (76)	
Class II	1 (2)	2 (7)	2 (7)	10 (20)	
Class III	0	0	1 (3)	0	

Class IV	1 (2)	2 (7)	0	2 (4)	
Laboratory findings					
Creatinine ($\mu\text{mol/L}$) at admittance	77 [69-83]	80 [70-108]	77 [69-91]	81 [67-95]	NS
Elevated troponin (%)	49 (98)	29 (100)	24 (90)	45 (92)	NS
Creatin kinase, maximum (U/L)	529 [363-975]	583 [382-1075]	257 [158-599]	161 [66-485]	NS
NTproBNP, maximum (pmol/L)	167 [36-392]	2226 [537-16650]	199 [5-2650]	1500 [371-4418]	NS
Leucocytes, maximum ($10\text{E}9/\text{L}$)	10.6 [8.2-13.2]	11.7 [7.8-14.7]	11.3 [7.5-15.7]	10.6 [8.2-13.8]	NS
C-reactive protein, maximum (mg/L)	31 [16-88]	91 [27-187]	47 [8-126]	43 [9-96]	0.04
Electrocardiography					
Conduction disorders					
High degree AV-block (2 nd or 3 rd degree)	1 (2)	0	0	1 (2)	NS
Left bundle branch block	0	0	1 (3)	5 (10)	NS
Right bundle branch block	0	2 (7)	2 (7)	2 (4)	NS
ST-segment elevation	38 (76)	21 (75)	15 (50)	14 (24)	<0.001
ST-segment depression	10 (20)	11 (40)	4 (13)	13 (26)	NS
Cardiac MRI					
<i>Left ventricle</i>					
Ejection fraction (%)	58 \pm 7	46 \pm 11	59 \pm 7	43 \pm 14	<0.001
End-diastolic volume, indexed (mL/m^2)	91 \pm 16	101 \pm 24	85 \pm 21	104 \pm 42	0.02
End-systolic volume, indexed (mL/m^2)	38 \pm 9	57 \pm 25	35 \pm 13	62 \pm 41	<0.001
Mass, indexed (g/m^2)	62 \pm 12	63 \pm 18	57 \pm 11	61 \pm 18	NS
Cardiac output (L/min)	7.1 \pm 1.7	6.6 \pm 1.7	6.7 \pm 1.9	5.8 \pm 1.5	<0.01
<i>Right ventricle</i>					
Ejection fraction (%)	56 \pm 5	49 \pm 9	56 \pm 4	51 \pm 13	0.001
End-diastolic volume, indexed (mL/m^2)	93 \pm 15	86 \pm 23	89 \pm 21	76 \pm 29	<0.01
End-systolic volume, indexed (mL/m^2)	41 \pm 9	45 \pm 16	39 \pm 10	38 \pm 21	NS
Late gadolinium enhancement					
Present	47 (94)	27 (90)	27 (90)	42 (84)	NS
Quantification (% of LV mass)	6.3 [3.6-8.4]	7.2 [1.8-11.7]	3.6 [2.8-8.7]	3.9 [1.3-7.5]	NS
T2 weighted imaging					
Performed	50 (98)	28 (93)	30 (100)	49 (96)	NS
Myocardial oedema present	47 (94)	23 (82)	17 (57)	33 (49)	<0.01
Admission					

Admission duration (days)	5 [4-8]	6 [3-11]	6 [3-12]	9 [6-15]	NS
Transfer to intensive care unit	4 (8)	6 (20)	2 (7)	6 (12)	NS
Start of immunosuppressive therapy	4 (8)	5 (17)	5 (17)	9 (18)	NS
Events					
All-cause death	2	1	3	12	<0.01
HF hospitalization	0	1	1	5	NS
Life threatening arrhythmias	1	0	2	8	0.02
MACE ‡	3	2	4	20	<0.01

* = good versus low GLS in patients with age <40 years, † = good versus low GLS in patients with age >40 years, ‡ When more than 1 event, the first event was included for the combined endpoint 'MACE'.

NS = not significant.

Data is presented as mean ± standard deviation, median (interquartile range) or number (%).

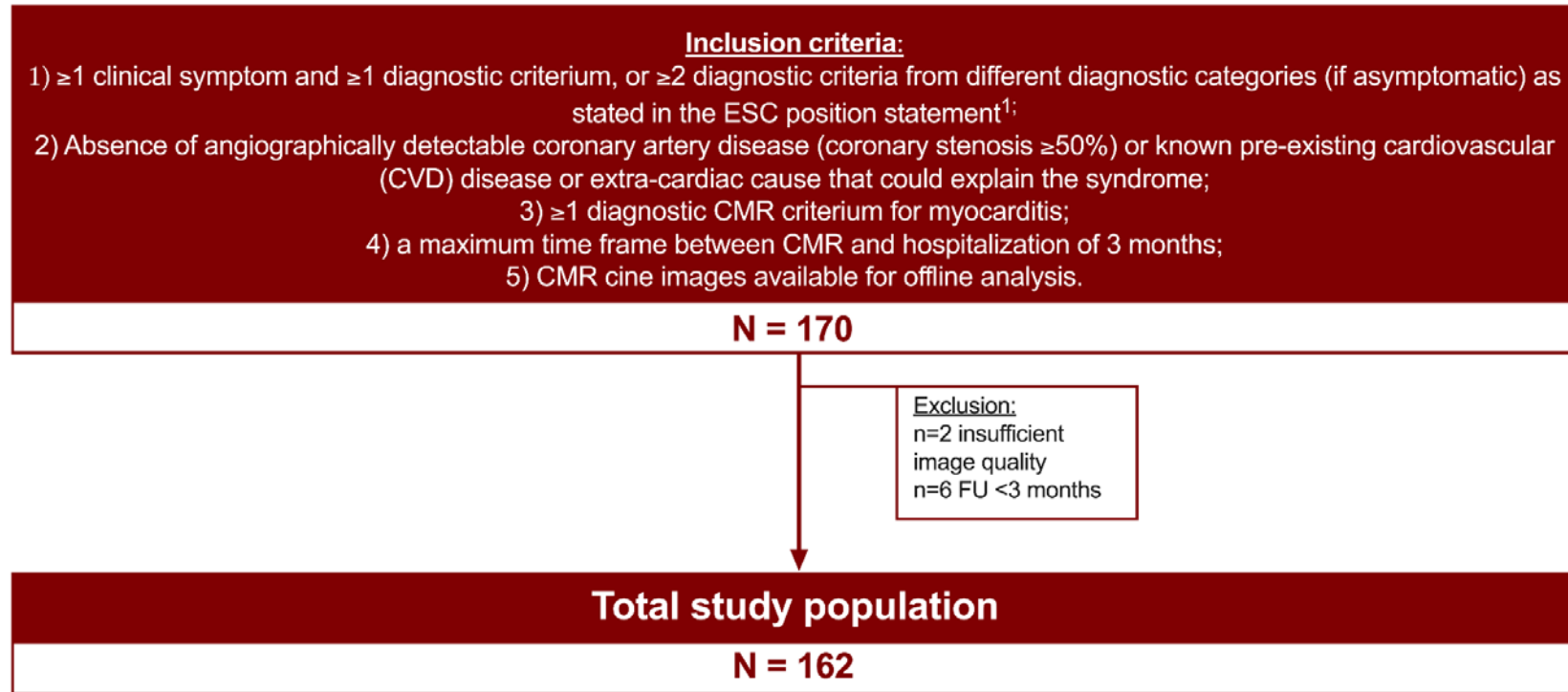
Abbreviations: BMI = body mass index, MACE = major adverse cardiovascular events.

Table S6. Inter- and intraobserver variability of strain parameters

Strain parameters	Interobserver variability		Intraobserver variability	
	ICC (95% CI)	p-value	ICC (95% CI)	p-value
Left ventricular GLS (%)	0.94 (0.86-0.98)	<0.001	0.92 (0.82-0.97)	<0.001
Left ventricular GCS (%)	0.82 (0.61-0.93)	<0.001	0.91 (0.80-0.97)	<0.001
Left ventricular GRS (%)	0.99 (0.97-1.00)	<0.001	0.91 (0.79-0.97)	<0.001
Right ventricular GLS (%)	0.90 (0.76-0.96)	<0.001	0.95 (0.88-0.98)	<0.001
Left atrial reservoir strain (%)	0.97 (0.92-0.98)	<0.001	0.90 (0.76-0.96)	<0.001
Left atrial conduit strain (%)	0.96 (0.89-0.98)	<0.001	0.96 (0.89-0.98)	<0.001
Left atrial booster strain (%)	0.89 (0.75-0.96)	<0.001	0.88 (0.73-0.95)	<0.001

Abbreviations: GCS = global circumferential strain, GLS = global longitudinal strain, GRS = global radial strain

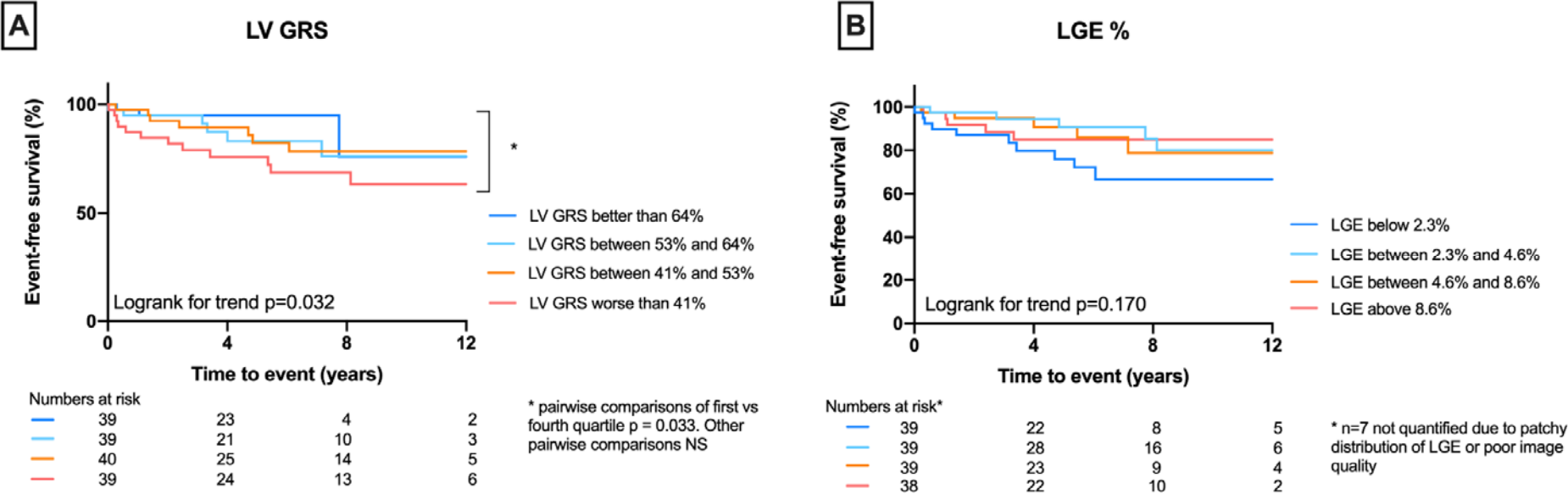
Figure S1. Flowchart of the study population



Suspected acute myocarditis patients who underwent CMR between 2005 and 2019 were retrospectively screened in four Dutch centers. Patients were included when they fulfilled the ESC position statement criteria including a diagnostic CMR criterium and had a maximum timeframe of 3 months between CMR and hospitalization. Patients were excluded if all cine images (short- and both long-axis) were unavailable for offline analysis, of insufficient quality or had no or too short follow-up. A total of 162 patients was included.

Abbreviations: CMR = cardiovascular magnetic resonance, ESC = European Society of Cardiology, FU = follow-up.

Figure S2. Kaplan Meier survival analysis of phasic strain parameters and LGE %



Abbreviations: GRS = global radial strain, LGE = late gadolinium enhancement, LV = left ventricular.

(A) LV-GRS is associated with event-free survival; (B) LGE extent is not associated with event-free survival