

Characteristics of myocardial injury as revealed by cardiac magnetic resonance in adults with severe myocarditis requiring extracorporeal membrane oxygenation

Supplemental Methods:

1. Initiation criteria of ECMO in patients with severe myocarditis

ECPR criteria: adequate cardiopulmonary resuscitation within 10 min after cardiac arrest. VA ECMO criteria: 1) refractory hypotension remained after traditional treatment, and the dose of vasoactive drugs was continuously increased; 2) persistent worsening lactic acidemia; and 3) bedside UCG suggesting obvious ventricular ejection dysfunction.

2. CMR protocol

CMR was performed using a 3.0-T magnetic resonance scanner (MAGNETOM Skyra and Vida, Siemens Healthcare, Erlangen, Germany). Breath-hold mode retrospectively gated cardiac balanced steady-state free precession cine images were acquired: three-chamber (two-, three-, and four-dimension) long axis and contiguous short axis views covering the left ventricle (LV) from the basal to the apex. The sequence parameters were as follows: repetition time, 3.4 ms; echo time, 1.4 ms; flip angle, 47°; matrix, 208 × 188; slice thickness, 8 mm; inter-slice gap, 2 mm; and 25 frames captured for each cardiac cycle.

Based on using a phase-sensitive inversion recovery gradient echo sequence with the segmented acquisition, LGE images were obtained in the short-axis orientation 8–15 min after the injection of 0.2 mmol/kg of gadodiamide (Magnevist; Bayer HealthCare Pharmaceuticals, Berlin, Germany).

In the basal, mid-, and apical levels of the LV short-axis cine images, T1 mapping was performed at the end-diastolic phase using a modified look locker inversion recovery sequence as has been previously described,^{16,17} with native T1 mapping of 5(3)3 and post-contrast T1 mapping of 4(1)3(1)2 protocol (10–12 min after administration of an intravenous bolus of 0.20 mmol/kg gadopentetate dimeglumine). T2 mapping was performed using a 3-point T2 prepared SSFP sequence before contrast injection in the basal, mid-chamber, and apical short-axis slices at end-diastole with the typical parameters: field of view, 340–360 mm; repetition time, 207.39 ms; echo time, 0, 30, and 55 ms; flip angle, 35°; and voxel size, 1.9 × 1.9 × 8.0 mm.

Supplemental Tables

Table S1 Laboratory data on patients with severe myocarditis supported using ECMO

Laboratory result	All patients (n = 22)
WBC count before ECMO (*10 ⁹ /L)	10.9 (8.6, 19.1)
Neutrophil count before ECMO (*10 ⁹ /L)	9.3 (7.2, 16.9)
Lymphocyte count before ECMO (*10 ⁹ /L)	0.9 (0.5, 1.5)
cTnT before ECMO (pg/mL)	2304.0 (1121.5, 4806.0)

cTnT before CMR (pg/mL)	30.6 (19.5, 63.9)
NT-proBNP before ECMO (pg/mL)	7440.4 (2662.0, 14887.8)
NT-proBNP before CMR (pg/mL)	948.9 (351.6, 1864.5)

Data were presented as median (Q1, Q3).

Abbreviations: WBC, white blood cell; cTnT, cardiac troponin T; NT-proBNP, N-terminal pro-B type natriuretic peptide; ECMO, extracorporeal membrane oxygenation; CMR, cardiac magnetic resonance.

Table S2 LVEF calculated using UCG and CMR

NO. of case	LVEF _{UCG} (%) ^a	LVEF _{CMR} (%)
1	64.40	55.46
2	65.80	56.92
3	69.40	66.83
4	64.40	64.60
5	65.20	50.46
6	60.00	55.89
7	64.40	58.98
8	63.60	59.27
9	63.70	64.97
10	60.20	59.75
11	40.30	15.95
12	55.90	49.64
13	68.50	74.28
14	51.30	29.04
15	64.70	66.60
16	65.40	68.71
17	64.40	57.78
18	66.40	39.92
19	66.30	42.57
20	59.90	42.67
21	55.90	45.13
22	54.40	65.96

^a Biplane Simpson's method was used for the calculation of LVEF using UCG.

Abbreviations: LVEF, left ventricle ejection fraction; UCG, ultrasound cardiography; CMR, cardiac magnetic resonance.

Table S3 Comparison of clinical characteristics and laboratory results between younger and older groups

Characteristics	Younger group (n = 11)	Older group (n = 11)	P
Age (years), median (Q1, Q3)	22 (20, 26)	50 (40, 60)	<0.001
Gender (Male), n (%)	6 (54.5)	5 (45.5)	0.670

Clinical features, n (%) ^a			
Chest tightness	7 (63.6)	10 (90.9)	0.311
Fever	7 (63.6)	6 (54.5)	1.000
Dyspnea	5 (45.5)	4 (36.4)	1.000
Chest pain	2 (18.2)	2 (18.2)	1.000
Palpitations	2 (18.2)	1 (9.1)	1.000
Recent viral history	6 (54.5)	3 (27.3)	0.387
ECMO duration (days), median (Q1, Q3)	7 (5, 9)	6 (5, 7)	0.526
ECG abnormalities, n (%) ^a			
III° AVB	4 (36.4)	5 (45.5)	1.000
VT	0 (0)	2 (18.2)	0.476
VF	4 (36.4)	2 (18.2)	0.635
CA	1 (9.1)	2 (18.2)	1.000
APACHE II, median (Q1, Q3)	23 (16, 27)	27 (16,31)	0.490
Laboratory result, median (Q1, Q3)			
WBC count before ECMO (*10 ⁹ /L)	14.0 (8.9, 22.3)	10.6 (8.0, 13.5)	0.279
Neutrophil count before ECMO (*10 ⁹ /L)	11.7 (7.5, 19.9)	9.0 (7.1, 11.9)	0.279
Lymphocyte count before ECMO (*10 ⁹ /L)	1.0 (0.8, 1.3)	0.7 (0.4, 1.2)	0.158
cTnT before ECMO (pg/ml)	2725.0 (1754.0, 5232.0)	1625.0 (533.4, 2844.0)	0.123
cTnT before CMR (pg/ml)	30.8 (21.3,81.6)	30.4 (18.8,38.9)	0.200
NT-proBNP before ECMO (pg/ml)	6605.1 (2002.1,12111.6)	9271.6 (6105.8,14221.7)	0.341
NT-proBNP before CMR (pg/ml)	965.0 (405.5,1281.2)	932.8 (419.2,2164.9)	0.922

^a Differences between groups were tested by Fisher's exact probability method.

Abbreviations: ECMO, extracorporeal membrane oxygenation; ECG, electrocardiogram; III° AVB, third-degree atrioventricular block; VT, ventricular tachycardia; VF, ventricular fibrillation; CA, cardiac arrest; APACHE II, Acute Physiology and Chronic Health Evaluation II; WBC, white blood cell; cTnT, cardiac troponin T; CMR, cardiac magnetic resonance; NT-proBNP, N-terminal pro-B type natriuretic peptide.

Table S4 Comparison of CMR parameters between short-term and long-term follow-up groups

CMR parameters	Short-term group (n = 11)	Long-term group (n = 11)	P
LVEF (%)	56.9 (42.6, 65.5)	59.0 (52.6, 62.2)	0.652
EDV (ml/m ²)	120.1 (96.1, 150.6)	122.1 (117.3, 144.8)	0.606
ESV (ml/m ²)	51.8 (42.1, 59.4)	52.1 (43.1, 70.5)	0.949
SV (ml/m ²)	53.4 (44.8, 73.5)	72.9 (65.6, 80.1)	0.088
CO (L/min/m ²)	5.0 (4.2, 6.2)	5.2 (4.8, 6.2)	0.748
CI (L/min/m ²)	3.4 (2.3, 3.8)	3.0 (2.7, 3.8)	0.898
EDV/BSA (ml/m ²)	73.7 (61.3, 82.5)	79.6 (65.5, 89.7)	0.365
ESV/BSA (ml/m ²)	30.5 (26.1, 34.8)	32.0 (23.1, 43.3)	0.898

SV/BSA (ml/m ²)	35.6 (23.7, 45.2)	43.6 (36.1, 51.0)	0.270
Myo mass /BSA(D) (g/m ²)	56.0 (51.1, 59.3)	47.5 (45.6, 54.3)	0.076
Myo mass /BSA(S) (g/m ²)	53.5 (50.0, 60.6)	48.6 (47.8, 56.6)	0.243
Mean T1 (ms)	1438.5 (1353.8, 1462.5)	1391.2 (1309.4, 1439.8)	0.270
Mean T2 (ms)	43.7 (41.5, 50.2)	44.0 (42.2, 48.4)	0.949
Mean ECV (%)	36.1 (33.7, 39.3)	33.5 (31.1, 36.1)	0.217
Mean LGE (%)	11.2 (7.7, 18.2)	9.0 (3.3, 13.5)	0.438

Data were presented as median (Q1, Q3).

In short-term follow-up group, CMR examinations were performed within 8 days after ECMO withdrawal while in long-term follow-up group, CMR examinations were performed 8 to 30 days after ECMO withdrawal.

Abbreviations: CMR, cardiac magnetic resonance; LVEF, left ventricle ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; CO, cardiac output; CI, cardiac index; BSA, body surface area; ECV, extracellular volume fraction; LGE, late gadolinium enhancement.

Supplemental Figures

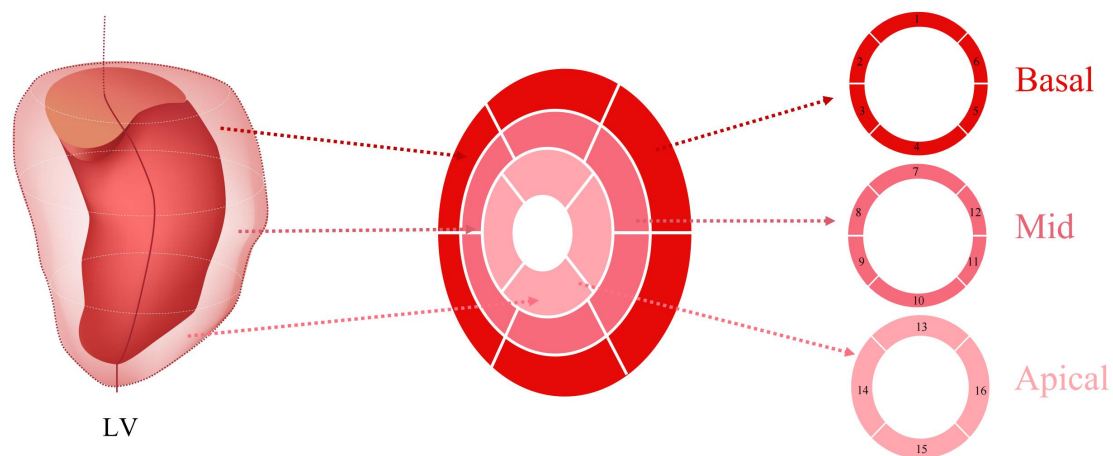


Figure S1. Schematic diagram for standard AHA Guidelines bull's eye plot used for LV assessment. The figure shows the 16 segments within the LV that are separated into three categories based on location: basal (segments 1–6), mid-cavity (segments 7–12), and apical (segments 13–16). Abbreviations: AHA, American Heart Association; LV, left ventricle.

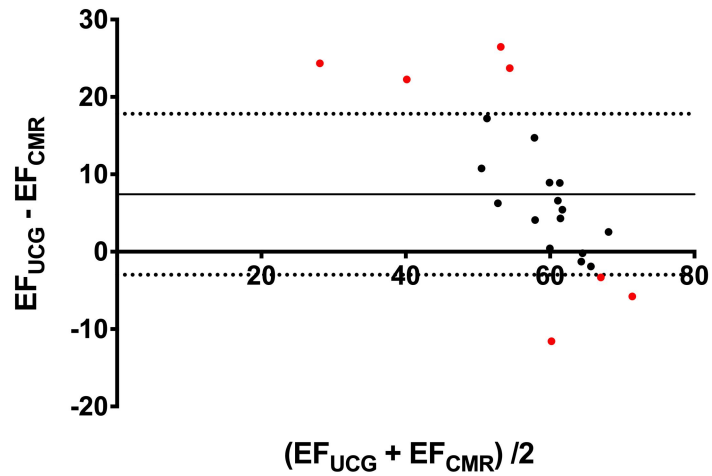


Figure S2. Bland–Altman plot showing agreement between UCG and CMR on the LVEF. In only 68.2% of the cases, the differences (EF_{UCG} vs EF_{CMR}) were within ± 1.96 SD. Abbreviations: UCG, ultrasound cardiography; CMR, cardiac magnetic resonance; LVEF, left ventricle ejection fraction; SD, standard deviation.

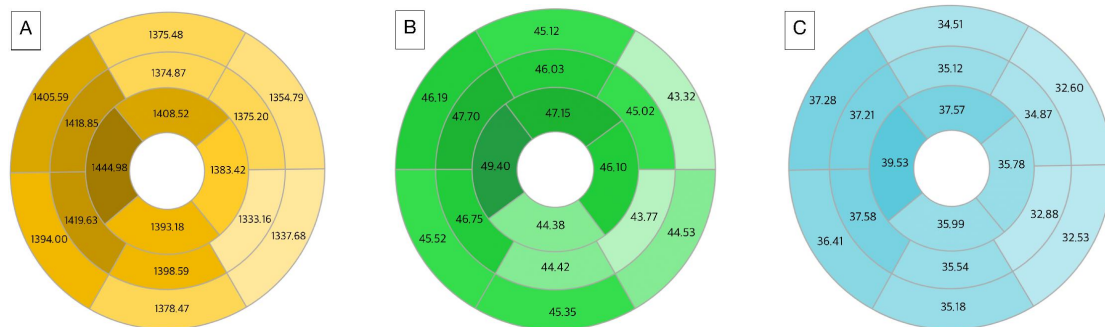


Figure S3. Bull's eye maps of the (A) native mean T1, (B) mean T2, and (C) mean ECV. Abbreviations: ECV, extracellular volume fraction.