

Supplementary Materials

A synopsis of the guidelines for diagnosis and treatment of fulminant myocarditis

**Zheng Wen^{1,#}, Zuowen He^{1,#}, Hongyang Shu¹, Jiangang Jiang¹, Chenze Li²,
Jiahui Fan¹, Xiao Ran³, Dao Wen Wang¹**

¹Division of Cardiology, Department of Internal Medicine and Hubei Key Laboratory of Genetics and Molecular Mechanism of Cardiologic Disorders, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, Hubei, China.

²Department of Cardiology, Zhongnan Hospital of Wuhan University, Wuhan 430071, Hubei, China.

³Department of Intensive Care Unit, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, Hubei, China.

[#]These authors contributed equally to this work.

Correspondence to: Prof. Dao Wen Wang, Division of Cardiology, Department of Internal Medicine and Hubei Key Laboratory of Genetics and Molecular Mechanism of Cardiologic Disorders, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, Hubei, China. E-mail: dwwang@tjh.tjmu.edu.cn

ORCID: Dao Wen Wang (0000-0002-9774-3980)

Supplementary Table 1. Evidence table for Table 1-Recommendations for laboratory examinations for patients with FM

Relevant topic	First author surname and publication year	PMID	Study type	Number of enrolled cases	Research design	Main relevant findings
Hs-cTnI / cTnI	Artico 2023 ^[1]	36705028	Prospective observational study	342 patients with COVID-19 and an elevated troponin level (COVID+/troponin+), with two prospective control groups comprising 64 patients with COVID-19 and normal troponin levels (COVID+/troponin-) and 113 patients without COVID-19 or elevated troponin level	Regression modeling was performed to identify predictors of major adverse cardiovascular events at 12 months.	More cases than controls had ventricular impairment (17.2% versus 3.1% and 7.1%) or scar (42% versus 7% and 23%; P<0.001 for both).
Hs-cTnI / cTnI	Liu 2021 ^[2]	34847863	Retrospective study	83 FM patients	The value of cardiac troponin was recorded after patients admitted to hospital in succession. The absolute and relative changes in hs-cTnI within 24 h and 48 h were described as range distributions.	69 patients survived and 14 patients died in hospital. In the survival group, 78% of patients experienced a decline in hs-cTnI within 24 h, while 36% of the mortality group exhibited a declining tendency in hs-cTnI (P=0.003). Multivariable logistic analysis revealed that the declining tendency of hs-cTnI within 24 h were associated with the in-hospital mortality of FM (OR=0.10, 95% CI 0.02–0.68, P=0.018).
Hs-cTnI / cTnI	Perelman 2025 ^[3]	40579948	Retrospective observational study	455 patients treated with ICIs	Patients were performed baseline (T1) and follow-up hs-TnI (T2) assessments. The primary endpoint was all-cause mortality, and the secondary endpoint was cardiovascular events, defined as the composite of myocarditis, pericarditis, acute coronary syndrome, HF, or arrhythmias.	T2 > 8 ng/L was significantly associated with increased all-cause mortality (64% vs 48%, P < 0.001) and cardiovascular events (22% vs 9%, P < 0.001), notably HF (12% vs 4%, P = 0.003) and myocarditis (3% vs 0%, P = 0.038). A multivariable analysis confirmed that T2 > 8 ng/L was an independent predictor for all-cause mortality (HR 1.67, 95% CI: 1.29-2.17, P < 0.001) and cardiovascular events (HR 2.59, 95% CI: 1.50-4.46, P = 0.001).

NT-pro BNP/ BNP	Ukena 2014 ^[4]	24781421	Prospective observational study	70 patients with clinically suspected myocarditis underwent EMB	At the time of EMB, blood samples to evaluate concentrations of hs-TnT, Copeptin, NT-proBNP and mid-regional pro-adrenomedullin were collected. The patients were followed for 7.5 (2-21) months.	During follow-up, only NT-proBNP in the highest quartile (>4,225 ng/ml) was predictive for cardiac death or heart transplantation (HR 9.2; 95% CI 1.7-50; p = 0.011).
NT-pro BNP/ BNP	Ekström 2016 ^[5]	27407025	Prospective observational study	46 patients with GCM	The association of transplant-free survival with patient characteristics, laboratory data on admission, and myocardial histology in the 38 patients diagnosed prior to death or transplantation was examined at long-term follow-up.	By Cox regression analysis, HR for death or transplantation was 0.87 (95% CI 0.75-0.99) per +5% difference in LVEF, 1.06 (95% CI 1.03-1.10) per + 1000 ng/L difference in NT-proBNP, and 4.57 (95% CI 1.63-11.28) for cardiac troponin-T above the median of 85 ng/L at presentation.
NT-pro BNP/ BNP	McDonagh 2021 ^[6]	34447992	Guidelines	/	/	Plasma NP levels (BNP or NT-proBNP or MR-proANP) should be measured if the diagnosis of AHF is uncertain and a POC assay is available. Normal concentrations of NPs make the diagnosis of AHF unlikely. Cut-offs for acute HF are: BNP <100 pg/mL, NT-proBNP <300 pg/mL and MR-proANP <120 pg/ mL.
Coagula tion function	Saracoglu 2024 ^[7]	38744017	Systematic review and meta-analysis	A total of 1718 records were retrieved from the searches. Fifteen studies that enrolled a total of 583 participants met the inclusion criteria. Of those, 3 studies enrolling 181 subjects were eligible for meta-analysis.	It aimed to assess the efficacy and safety of viscoelastic POC-guided coagulation management in adult patients on ECMO.	In patients managed with POC-guided algorithms, the odds were coherently lower for bleeding (OR 0.71, 95%CI 0.36-1.42), thrombosis (OR 0.91, 95%CI 0.32-2.60), and in-hospital mortality (OR 0.54, 95%CI 0.29-1.03), but not for circuit change or failure (OR 1.50, 95%CI 0.59-3.83).
Coagula tion function	Zhu 2024 ^[8]	39246243	Systematic review and meta-analysis	Nineteen studies encompassing 10,767 participants were identified and included in the analysis.	This study investigates the prevalence and risk factors associated with venous thrombotic events in patients receiving ECMO support.	The pooled prevalence of venous thrombotic events among patients receiving ECMO support was 48% (95% CI 0.37-0.60, I2 = 97.18%). Factors associated with increased incidence rates included longer duration of ECMO support (OR 1.08, 95% CI

						1.07-1.09, I2 = 49%), abnormal anti-coagulation monitoring indicators (OR 1.02, 95% CI 1.00-1.04, I2 = 84%), and type of ECMO cannulation (OR 1.77, 95% CI 1.14-3.34, I2 = 64%).
Inflamm atory cytokine s	Cain 1999 ^[9]	10446825	Prospective, randomized, controlled study	Human atrial trabeculae obtained at the time of cardiac surgery	TNF-alpha (1.25, 12.5, 125, or 250 pg/mL for 20 mins), IL-1beta (6.25, 12.5, 50, or 200 pg/mL for 20 mins), or TNF-alpha (1.25 pg/mL) plus IL-1beta (6.25 pg/mL) were added to the bath containing human atrial trabeculae, and function was measured for the subsequent 100 minutes after the 20-minute exposure.	TNF-alpha and IL-1beta each depressed human myocardial function in a dose-dependent fashion (maximally depressing to 16.2 + 1.9% baseline developed force for TNF-alpha and 25.7 + 6.3% baseline developed force for IL-1beta), affecting systolic relatively more than diastolic performance (each p < 0.05). However, when combined, TNF-alpha and IL-1beta at concentrations that did not individually result in depression (p > 0.05 vs. control) resulted in contractile depression (p < 0.05 vs. control).
Inflamm atory cytokine s	Wang 2020 ^[10]	31998421	Prospective, multicenter, observational study	536 patients with newly diagnosed viral myocarditis	Demographics and clinical characteristics at baseline and after three months were collected, including laboratory blood tests, ECG, echocardiography, and drug treatment in each participating site. The plasma anti-viral Abs, anti-heart autoimmune Abs, and cytokines were detected by ELISA.	The plasma levels of IFN-γ, c were continually higher in patients with incident DCM than in those without incident DCM at baseline, from the 1st month and the 3rd month; all had a P value of <0.0001. There was a positive correlation between IL-4 and LVEDd (r = 0.30, P < 0.0001) and between IL-17 and LVEDd (r = 0.11, P = 0.02). IL-4 and IL-17 were independent predictors for the progression from viral myocarditis to DCM.
Inflamm atory cytokine s	Wang 2025 ^[11]	40927299	Retrospective study	185 patients diagnosed with acute myocarditis	The related values of NPAR, SII, SIRI, and AISI were computed based on the pertinent blood indices that were acquired within 12 hours of admission.	Patients with fulminant myocarditis exhibited significantly higher NPAR, SII, SIRI, and AISI values compared to those with mild myocarditis. These inflammatory biomarkers show associations with the severity of acute myocarditis.
sST2	Coronado 2019 ^[12]	30638108	Retrospective study	303 Adults with a diagnosis of clinically suspected myocarditis	Sera sST2 levels were examined.	SST2 levels were elevated in patients with myocarditis and NYHA class III - IV heart failure (P=0.002), predominantly in men (P=0.0003). Sera sST2 levels were associated with NYHA

						class in men with myocarditis who were ≤ 50 years old ($r=0.231$, $P=0.0006$), but not in women ($r=0.172$, $P=0.57$).
sST2	Wang 2022 ^[13]	35377184	Retrospective study	76 patients with FM and 56 patients with non-FM	The relationship between sST2 and FM was investigated.	Receiver operating characteristic curve analyses suggested that plasma sST2 level was able to differentiate FM from non-FM or other FM-unrelated AHF. The cutoff value of plasma sST2 for optimal diagnosis of FM was established at 58.39 ng/mL, where a sensitivity of 85.7% and specificity of 94.7% were achieved.
sST2	Hou 2023 ^[14]	37653801	Retrospective observational study	203 patients with myocarditis, 22 of whom were diagnosed with FM	The relationship between sST2 and FM was investigated.	The level of sST2 was positively correlated with NT-proBNP (R = 0.5588, $P < 0.0001$). After including multiple factors, creatinine (OR 0.911; 95% CI 0.842-0.986; $P= .021$), NT-proBNP (OR 1.000; 95% CI 1.000-1.000; $P = 0.01$), left ventricular ejection fraction (OR 1.306; 95% CI, 1.153-1.478; P < 0.001) and sST2 (OR 0.982; 95% CI 0.965-0.999; $P = 0.038$) were still risk factors for FM.
sST2	Shi 2024 ^[15]	38807947	Retrospective cohort study	252 patients aged ≤ 14 years diagnosed with myocarditis	Events during the hospitalization were defined as MACEs (all-cause death > new heart failure > ventricular arrhythmia).	After including these risk factors in a multivariate logistic regression analysis, NT-proBNP (OR 4.323; 95% CI, 2.433-7.679; $p < 0.001$) and sST2 (OR 1.020; 95% CI, 1.003-1.037; $p = 0.022$) remained statistically significant and were independent risk factors for MACEs during hospitalization.
PCT	Daubin 2018 ^[16]	29663044	Randomized multicenter study	302 patients with severe acute exacerbations of COPD were randomized into the PCT ($n = 151$) and control ($n = 151$) groups	The antibiotic therapy was differently guided in 2 groups: (1) a 5-day PCT algorithm with predefined cutoff values for the initiation or stoppage of antibiotics (PCT group); (2) standard guidelines (control group).	Among patients without antibiotic therapy at baseline ($n = 119$), the use of PCT significantly increased 3-month mortality [19/61 (31%) vs. 7/58 (12%), $p = 0.015$]. The in-ICU and in-hospital antibiotic exposure durations, were similar between the PCT and control group (5.2 ± 6.5 days in the PCT group vs. 5.4 ± 4.4 days in the control group, $p = 0.85$ and 7.9 ± 8 days in the PCT group vs. 7.7 ± 5.7 days in the control group, $p = 0.75$, respectively).
PCT	Huang 2018 ^[17]	29781385	Randomized controlled trial	1656 patients with a suspected lower respiratory tract infection were included	The antibiotic therapy was differently guided in 2 groups:(1) PCT group, in	There was no significant difference between the PCT group and the usual-care group in antibiotic-days (mean, 4.2 and 4.3 days,

				(826 randomly assigned to the PCT group and 830 to the usual-care group)	which the treating clinicians were provided with PCT assay results and an antibiotic use guideline with graded recommendations based on four tiers of PCT levels; (2) the usual-care group.	respectively; difference, -0.05 day; 95% CI -0.6 to 0.5; P=0.87) or the proportion of patients with adverse outcomes (11.7% [96 patients] and 13.1% [109 patients]; difference, -1.5 percentage points; 95% CI, -4.6 to 1.7; P<0.001 for noninferiority) within 30 days.
PCT	Kyriazopoulou 2021 ^[18]	32757963	Randomized controlled Trial	266 patients with sepsis with lower respiratory tract infections, acute pyelonephritis, or primary bloodstream infection were enrolled.	The patients were randomized (1:1) to receive either PCT-guided discontinuation of antimicrobials or standard of care. The discontinuation criterion was ≥80% reduction in PCT levels or any PCT ≤0.5 µg/L at Day 5 or later.	infection-associated adverse events was 7.2% (95% CI 3.8-13.1%; 9/125) versus 15.3% (95% CI, 10.1-22.4%; 20/131) (HR 0.45; 95% CI, 0.20-0.98; P = 0.045); 28-day mortality 15.2% (95% CI, 10-22.5%; 19/125) versus 28.2% (95% CI, 21.2-36.5%; 37/131) (HR 0.51; 95% CI, 0.29-0.89; P = 0.02); and median length of antibiotic therapy 5 (range, 5-7) versus 10 (range, 7-15) days (P < 0.001) in the PCT and standard-of-care arms, respectively.

FM, fulminant myocarditis; hs-cTnI, high-sensitivity cardiac troponin I; cTnI, cardiac troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide; BNP, B-type natriuretic peptide; COVID, corona virus disease; HR, hazard ratio; OR, odds ratio; CI, confidence interval; ICI, immune checkpoint inhibitor; HF, heart failure; EMB, endomyocardial biopsy; GCM, giant cell myocarditis; LVEF, left ventricular ejection fraction; NP, natriuretic peptide; MR-proANP, midregional pro-atrial natriuretic peptide; AHF, acute heart failure; POC, point-of-care; ECMO, extracorporeal membrane oxygenation; TNF, tumor necrosis factor; IL, interleukin; IFN, interferon; DCM, dilated cardiomyopathy; ECG, electrocardiography; Abs, antibodies; ELISA, enzyme-linked immunosorbent assay; LVEDd, left ventricular end-diastolic dimension; NPAR, neutrophil-percentage-to-albumin ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; AISI, aggregate index of systemic inflammation; NYHA, New York Heart Association; sST2, soluble growth stimulating expressed gene 2; MACE, major adverse cardiovascular events; PCT, procalcitonin; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit.

Supplementary Table 2. Evidence table for Table 2-Recommendations for treatment of FM in the acute phase

Relevant topic	First author surname and publication year	PMID	Study type	Number of enrolled cases	Research design	Main relevant findings
IABP	Uil 2019 ^[19]	31147306	Randomized controlled trial	Patients (n=32) with DHF-LO	Patients (n=32) with DHF-LO despite IV diuretics were randomised to primary 50 mL IABP or inotropes (enoximone or dobutamine). The primary endpoint was the improvement of organ perfusion assessed by Δ SvO ₂ at 3 hours; secondary endpoints included Δ CPO, NT-proBNP proportional change, cumulative fluid balance and Δ dyspnoea severity score, all at 48 hours.	Δ SvO ₂ was higher in the IABP group (+17 [+9; +24] vs. +5 [+2; +9]%, p<0.05). IABP patients had a higher Δ CPO, a greater relative reduction in NT-proBNP, a more negative cumulative fluid balance, and a greater reduction in dyspnoea severity score. There were no IABP-related serious adverse events. Thirty-day mortality was 23% (IABP) vs. 44% (inotropes).
IABP	Deppe 2017 ^[20]	28247473	Meta-analysis	9,212 high-risk patients before CABG surgery, from 23 studies	Group comparison of patients with prophylactic IABP implantation before CABG with a control group was analyzed. Pooled treatment effects (OR or weighted mean difference, and 95% CI) were assessed using a fixed or random effects model.	Prophylactic IABP use before CABG surgery also decreased the risk for myocardial infarction (OR 0.58; 95%CI 0.43-0.78; p = 0.004), CVA (OR 0.67; 95%CI 0.47-0.97; p = 0.042), and renal failure (OR 0.62; 95%CI 0.47-0.83; p = 0.0014). Length of intensive care unit stay (p < 0.0001) and length of hospital stay (p < 0.0001) were significantly reduced in patients with preoperative IABP use.
IABP	Chu 2021 ^[21]	34155835	Nationwide registry	30106 patients with CS	Ischaemic heart disease was the leading cause of CS (73.9%). Hypertension, cardiomyopathy, myocarditis, valvular, and congenital heart disease were seen in 36.0%, 7.5%, 2.6%, 7.3%, and 2.4% of the population. IABP was employed in 2320 (7.7%) subjects.	IABP support was not associated with reduced mortality in the overall CS population in multivariate regression analysis (OR 1.05, 95% CI 0.95–1.17], except for subgroups with myocarditis (OR 0.61, 95% CI 0.39–0.95, P for interaction = 0.010) and those who did not receive the early percutaneous coronary intervention (OR 0.86, 95% CI 0.75–0.97, P for interaction < 0.001).
IABP	Kang 2024 ^[22]	38012086	Retrospective observational study	128 patients with CS	71 (55.5%) patients received VA-ECMO due to AMI-induced CS, and the remaining 57 (44.5%) received VA-ECMO due to non-AMI-induced CS.	In the AMI-induced CS group, LV unloading with IABP did not reduce 90-day mortality (adjusted hazard ratio 1.96, 95% confidence interval 0.90-4.27, P = 0.089). However, in the

						non-AMI-induced CS group, LV unloading combined with VA-ECMO significantly reduced 90-day mortality (adjusted HR 0.37, 95% CI 0.14-0.96, P = 0.041; P for interaction = 0.029) as compared with those who received VA-ECMO alone.
ECMO	Duan 2021 ^[23]	33337786	Network meta-analysis	38 studies into this analysis, including a total of 11,270 patients from five interventions (pharmacotherapy, IABP, pMCS, ECMO, and ECMO+IABP)	The short-term efficacy was determined by 30-day or in-hospital mortality.	ECMO+IABP significantly reduced mortality compared with pMCS and ECMO alone (OR = 1.85, 95% CI [1.03-3.26]; OR = 1.89, 95% CI [1.19-3.01], respectively). ECMO+IABP did not show reduced mortality when compared with pharmacotherapy and IABP (OR = 1.73, 95% CI [0.97-3.82]; OR = 1.67, 95% CI [0.98-2.89], respectively).
ECMO	Benenati 2022 ^[24]	33677732	Meta-analysis	24 studies (7 RCTs and 17 non-RCTs) involving 11,117 patients	The primary endpoint was 30-day mortality. Secondary endpoints were stroke and bleeding.	Compared with no MCS, ECMO reduced 30-day mortality when used both alone (OR 0.37, 95% CI 0.15-0.90) and together with the micro-axial pump Impella (OR 0.13, 95% CI 0.02-0.80) or IABP (OR 0.19, 95% CI 0.05-0.63). Consistent results were obtained in a sensitivity analysis including only studies of CS due to myocardial infarction. After halving the weight of studies with a non-RCT design, only the benefit of ECMO + IABP on 30-day mortality was maintained (OR 0.22, 95% CI 0.057-0.76).
ECMO	Low 2024 ^[25]	38206381	Network meta-analysis of randomized controlled trials and propensity score-matched	It included 38 studies (48,749 patients), mostly reporting on patients with Society for Cardiovascular Angiography and	The authors conducted frequentist network meta-analysis, investigating mortality (either 30 days or in-hospital) as the primary outcome.	Compared with no MCS, ECMO-IABP (network OR: 0.54, 95% CI: 0.33-0.86, moderate certainty) was associated with lower mortality. There were no differences in mortality between ECMO, IABP, mVAD, ECMO-mVAD, centrifugal VAD, or mVAD-IABP and no MCS (all very low certainty). Our one-stage survival meta-analysis based on the stratified Cox model found only ECMO-IABP was associated with lower mortality (HR, 0.55, 95% CI 0.46-0.66).

			studies	Intervention shock stages C-E cardiogenic shock.		
Impella	Schrage 2020 ^[26]	33032450	Multicenter cohort study	686 consecutive patients with cardiogenic shock treated with VA-ECMO with or without Impella	The association between left ventricular unloading and 30-day mortality was assessed by Cox regression models in a 1:1 propensity score-matched cohort.	In the matched cohort, left ventricular unloading with Impella was associated with lower 30-day mortality (HR, 0.79 [95% CI, 0.63-0.98]; P=0.03) without differences in various subgroups. Complications occurred more frequently in patients with left ventricular unloading: severe bleeding in 98 (38.4%) versus 45 (17.9%), access site-related ischemia in 55 (21.6%) versus 31 (12.3%), abdominal compartment in 23 (9.4%) versus 9 (3.7%), and renal replacement therapy in 148 (58.5%) versus 99 (39.1%).
Impella	Drazner 2025 ^[27]	39665703	Expert Consensus	/	/	Unloading of the LV via axial flow devices, such as the IMPELLA, may contribute to myocardial recovery.
Glucocorticoids	Lu 2016 ^[28]	25003999	Meta-analysis of randomized controlled trials	Nine articles were finally selected	342 patients with myocarditis were in immunosuppressive treatment group and 267 patients in conventional treatment group.	The immunosuppressive treatment group showed a significant improvement in left ventricular ejection fraction at both short-term (≤ 3 months) [difference: 0.08, 95% CI: 0.05-0.10) and long-term (difference: 0.10, 95% CI: 0.00-0.21)] follow-up. Moreover, left ventricular end-diastolic dimension decreased significantly in the immunosuppressive treatment group after short-term follow-up (difference: -1.85 mm, 95% CI: -3.18 to -0.52 mm), but a long-term beneficial effect was not sustained (difference: -5.79 mm, 95% CI: -15.30 to 3.72 mm).
Glucocorticoids	Aziz 2010 ^[29]	20584348	Prospective randomised study	68 children with acute viral myocarditis	68 children were available for randomisation into a prednisolone-treated group of 44 and a control group of 24.	Compared with controls, 1 month after randomisation significantly more children in the prednisolone-treated group increased their ejection fraction to more than 40% (p = 0.029). At the end of the follow-up visits, a significantly larger number of children in the prednisolone-treated group had an ejection fraction of more than 60% compared with the control group (p = 0.049).

Glucocorticoids	Chan 1991 ^[30]	1991904	Clinical trial	13 children with biopsy-proved myocarditis	Prednisone was administered to all patients; one patient also received azathioprine.	Repeat myocardial biopsy in eight patients demonstrated improvement in all eight and elimination of the inflammatory infiltrate in six.
Glucocorticoids	Kanyo 2026 ^[31]	41850419	Retrospective cohort study	2294 children with acute, non-COVID-19 myocarditis	Treatment groups were (1 - none) 8% (189/2294); (2-steroids) 20% (450/2294); (3-IVIg) 25% (578/2294); and (4-IVIg and steroids) 47% (1077/2294).	The receipt of IVIg alone (OR 0.24, 95% CI 0.13-0.42) or the combination of IVIg and steroids (OR 0.60, 95% CI 0.42-0.87) was independently associated with decreased mortality compared with steroid use alone. These associations were also seen in a subgroup of children with acute FM.
IVIg	Huang 2019 ^[32]	30745539	Meta-analysis	13 studies containing 1534 cases with acute myocarditis were incorporated into this meta-analysis	Eligible studies were clinical trials of patients with acute myocarditis who received IVIg therapy. Pooled ORs and 95% CIs were used to estimate the outcomes.	IVIg therapy significantly reduced in-hospital mortality (OR: 0.44, 95% CI 0.17 to 0.71, P < 0.001) and improved the LVEF (OR: 1.73, 95% CI 1.34 to 2.13, P < 0.001) in acute myocarditis patients. Furthermore, patients with acute FM exhibited a significantly higher survival rate (OR: 2.80, 95% CI 1.16 to 6.77, P = 0.022) in the IVIg group.
IVIg	Pan 2023 ^[33]	37898763	Meta-analysis	31 randomized controlled trials were included with a sample size of 6,276 participants with sepsis	Subgroup analyses were conducted according to different IVIg types, ages and economic regions.	IVIg could reduce the mortality (RR 0.86, 95% CI: 0.77-0.95, p = 0.005), the hospital stay (MD - 4.46, 95% CI: - 6.35 to - 2.57, p = 0.00001), and the APACHE II scores (MD - 1.65, 95% CI: - 2.89 to - 0.63, p = 0.001). Additionally, the results showed that IgM-enriched IVIg was effective in treating sepsis (RR 0.55, 95% CI: 0.40 - 0.76; p = 0.0003), while standard IVIg failed to be effective (RR 0.91, 95% CI: 0.81-1.02, p = 0.10). And the effect of IVIg in reducing neonatal mortality was inconclusive (RR 0.93, 95% CI: 0.81-1.05, p = 0.24), but it played a large role in reducing sepsis mortality in adults (RR 0.70, 95% CI: 0.57-0.86, p = 0.0006).
IVIg	Kishimoto 2014 ^[34]	23702697	Clinical trial	41 patients with acute myocarditis	15 patients were treated with IVIg (1-2 g/kg, over 2 days), whereas 26 were untreated.	There was a statistically significant difference between the survival curves of the patients treated with IVIg and the survival curves of those not treated with IVIg.
IVIg	Chou	32220770	Retrospective	88 adults with acute	The primary endpoint was heart recovery without heart	The overall survival of patients was 55.7%. Multivariate logistic

	2020 ^[35]		observational study	FM and ECMO support	transplantation or long-term LVAD support.	regression revealed that peak CK-MB level, severe intraventricular conduction disturbance (asystole) and malignant arrhythmia (VT or VF) were prognostic factors for nonrecovery (P = 0.027 and 0.017, respectively), while early IVIG use before ECMO was highly likely to have a protective effect with a trend toward statistical significance (P = 0.079).
IVIG	Drucker 1994 ^[36]	8281654	Comparative Study	21 children with acute myocarditis and 25 recent historical control patients	21 consecutive children presenting with presumed acute myocarditis with IVIG, 2 g/kg, over 24 hours, in addition to anticongestive therapies. A comparison group comprised 25 recent historical control patients meeting identical eligibility criteria but not receiving IVIG therapy.	Compared with the non-IVIG group, those treated with IVIG had a smaller mean adjusted left ventricular end-diastolic dimension and higher fractional shortening in the periods from 3 to 6 months (P = 0.008 and P = 0.033, respectively) and 6 to 12 months (P = 0.072 and P = 0.029, respectively). When adjusting for age, biopsy status, intravenous inotropic agents, and angiotensin-converting enzyme inhibitors, patients treated with IVIG were more likely to achieve normal left ventricular function during the first year after presentation (P = 0.03).
Neuramini dase inhibitor	Li 2019 ^[37]	30850929	Multi-center retrospective study	169 FM patients	Patients with FM were divided into two groups: patients receiving LSBCTR (81 cases), which includes (i) mechanical life support (positive pressure respiration, intra-aortic balloon pump with or without extracorporeal membrane oxygenation), (ii) immunomodulation therapy using sufficient doses of glucocorticoids and immunoglobulins, and (iii) application of neuraminidase inhibitors, and those receiving conventional treatment (88 cases).	Oral oseltamivir (75 mg, twice a day) significantly decrease the in-hospital death rate in patients with FM (20.8% vs. 38.8%; adjusted OR, 0.22; 95% CI, 0.07–0.65; P=0.008).
Neuramini dase inhibitors	Lee 2020 ^[38]	32547116	Retrospective cohort study	542 adult patients with laboratory-confirmed seasonal influenza	Of the 542 enrolled patients, 251 were administered the standard dose of peramivir (300 mg, single dose), 42 were administered peramivir at doses exceeding 300 mg, and 249 were administered oseltamivir (75 mg,	There were no significant differences in defervescence rates within 3 days between the three groups. The mortality and duration of hospital and ICU stays also did not differ significantly. Treatment of influenza with either peramivir or oseltamivir in hospitalized adults

					twice daily for 5 days).	resulted in generally similar clinical outcomes.
Maintenance of MAP	Lamontagne 2016 ^[39]	26891677	Randomized Controlled Trial	118 critically ill patients who were presumed to suffer from vasodilatory shock	The patients were randomly assigned to 2 groups with a lower (60-65 mmHg) versus a higher (75-80 mmHg) MAP target. The between-group separation in MAP was 9 mmHg (95% CI 7-11).	Risks of cardiac arrhythmias (20 versus 36%, $p = 0.07$) and hospital mortality (30 versus 33%, $p = 0.84$) were not different between lower and higher MAP arms. Among patients aged 75 years or older, a lower MAP target was associated with reduced hospital mortality (13 versus 60%, $p = 0.03$) but not in younger patients.
Maintenance of MAP	Lamontagne 2020 ^[40]	32049269	Randomized Controlled Trial	2600 patients aged 65 years or older with vasodilatory hypotension	Patients were randomized 1:1 to vasopressors guided either by MAP target (60-65 mm Hg, permissive hypotension) ($n = 1291$) or according to usual care (at the discretion of treating clinicians) ($n = 1307$).	Patients randomized to the permissive hypotension group had lower exposure to vasopressors compared with those in the usual care group (median duration 33 hours vs 38 hours; difference in medians, -5.0; 95% CI, -7.8 to -2.2 hours; total dose in norepinephrine equivalents median, 17.7 mg vs 26.4 mg; difference in medians, -8.7 mg; 95% CI, -12.8 to -4.6 mg). At 90 days, 500 of 1221 (41.0%) in the permissive hypotension compared with 544 of 1242 (43.8%) in the usual care group had died (absolute risk difference, -2.85%; 95% CI, -6.75 to 1.05; $P = .15$) (unadjusted relative risk, 0.93; 95% CI, 0.85-1.03). When adjusted for prespecified baseline variables, the odds ratio for 90-day mortality was 0.82 (95% CI, 0.68 to 0.98).
Maintenance of MAP	Asfar 2014 ^[41]	24635770	Randomized Controlled Trial	776 patients with septic shock	Patients were randomly assigned to undergo resuscitation with a mean arterial pressure target of either 80 to 85 mm Hg (high-target group) or 65 to 70 mm Hg (low-target group). The primary end point was mortality at day 28.	At 28 days, there was no significant between-group difference in mortality, with deaths reported in 142 of 388 patients in the high-target group (36.6%) and 132 of 388 patients in the low-target group (34.0%) (HR in the high-target group, 1.07; 95% CI, 0.84 to 1.38; $P=0.57$). There was also no significant difference in mortality at 90 days, with 170 deaths (43.8%) and 164 deaths (42.3%), respectively (HR, 1.04; 95% CI, 0.83 to 1.30; $P=0.74$).
Inotropic drugs	Vally 2019 ^[42]	30707314	Retrospective cohort study	150 patients undergoing VA-ECMO	38 propensity-matched patients were evaluated in the levosimendan group and 65 in the non-levosimendan group.	After propensity score matching, levosimendan was the only factor associated with a significant reduction in VA-ECMO weaning failure rates (HR = 0.16; 95% CI = 0.04-0.7; $P = 0.01$). Kaplan-Meier survival curves showed that survival rates at 30 days

						were 78.4% for the levosimendan group and 49.5% for the non-levosimendan group (P = 0.02).
Inotropic drugs	Kim 2022 ^[43]	36078888	Retrospective study	496 patients who underwent VA-ECMO	191 matched pairs of patients were selected (who did or did not receive inodilators) to adjust for baseline clinical characteristics after 1:1 propensity score matching.	The univariate and multivariate analyses showed that the inodilator group (dobutamine and milrinone) had significantly lower in-hospital mortality than the no-inodilator group (unadjusted HR, 0.768; 95% CI, 0.579-1.018; p = 0.066, adjusted HR, 0.702; 95% CI, 0.552-0.944; p = 0.019).
Inotropic drugs	Cholley 2019 ^[44]	31783891	Expert opinion	/	/	Currently, levosimendan is recommended as a “rescue” therapy in cardiogenic shock after dobutamine failure and before veno-arterial extracorporeal membrane oxygenation.
PPI	Pahuja 2022 ^[45]	35523591	Retrospective study	466627 patients with pMCS devices during the index hospitalization	The analysis was conducted using the National Inpatient Sample. Multivariate logistic regression analysis was performed to determine independent predictors of GIB in these patients.	In comparison to patients without GIB, those with GIB had significantly higher in-hospital mortality, length of stay, and hospitalization cost.
PPI	Hickman 2019 ^[46]	30527506	Observational cohort study	138 patients with ventricular assist devices	The association between acid suppressing drug regimen and the number of GIB events within 30 d after VAD implantation was analyzed: PPI, H2RA, or neither.	Both H2RA and PPI use were associated with reduced GIB compared with the cohort with no acid suppressive therapy. In the multivariate analysis, the PPI cohort showed a statistically significant reduction in GIB (Odds ratio 0.18 [95% confidence interval 0.04-0.79] P = 0.026).
Antibiotics	Pieri 2013 ^[47]	23040766	Observational study	61 patients requiring mechanical circulatory support	46 patients with ECMO and 15 patients with VAD.	39% of the 46 patients with ECMO and 69% of the 15 patients with VAD developed infection.
Antibiotics	Aslam 2024 ^[48]	38691077	Consensus statement	/	/	Patients receiving MCS for a variety of indications are a growing population globally that are vulnerable to infectious complications. Infection is associated with significant morbidity and mortality and impacts the long-term success of MCS therapy.
Antifungals	Evans 2021 ^[49]	34599691	Guideline	/	/	For adults with sepsis or septic shock at low risk of fungal infection, we suggest against empiric use of antifungal therapy.

Mechanica 1 ventilation	McDonagh 2021 ^[6]	34447992	Guidelines	/	/	Non-invasive positive pressure ventilation should be considered in patients with respiratory distress (respiratory rate >25 breaths/ min, SpO2< 90%) and started as soon as possible in order to decrease respiratory distress and reduce the rate of mechanical endotracheal intubation.
CRRT	Xie 2022 ^[50]	34130280	Retrospective observational study	117 patients with cardiorenal syndrome after acute decompensated heart failure	54 patients in the early GDRRT group and 63 patients in the late GDRRT group. Baseline characteristics, clinical data at initiation renal replacement therapy time, and the clinical outcome were collected and several parameters were compared and analyzed between 2 groups.	Hemodynamic parameters such as mean artery pressure were higher (70.06 ± 32.99 vs. 54.34 ± 40.88 mm Hg, p = 0.012), the heart rate was slower (80.17 ± 15.26 vs. 99.21 ± 25.45 bpm, p = 0.002), and the diameter of inferior vena cava was narrower (22.00 ± 1.91 vs. 25.77 ± 5.5 mm, p = 0.04) in early GDRRT. Primary end point was inhospital all-cause mortality and cardiovascular mortality, which was obviously lower in the early GDRRT group (respectively 24.1 vs. 60.3%, p = 0.002 and 20.3 vs. 50.8%, p = 0.005). The second end point of kidney recovery in the early GDRRT group was much better than that in the latter GDRRT group (p = 0.018). Moreover, urine volume after GDRRT of the early group was more significant than that of the late group (1,432 ± 172 vs. 702 ± 183 mL, p = 0.005).
CRRT	McDonagh 2021 ^[6]	34447992	Guidelines	/	/	Main treatment for AHF include diuretics, Inotropic agents/ vasopressors (if peripheral hypoperfusion/ hypotension), short-term MCS or RRT if needed.
Manageme nt of arrhythmia s	Glikson 2022 ^[51]	34455427	Guidelines	/	/	CRT should be considered for patients with HF and LVEF <_35% in NYHA class III or IV despite OMT if they are in AF and have intrinsic QRS >_130 ms, provided a strategy to ensure biventricular capture is in place, in order to improve symptoms and reduce morbidity and mortality.
Manageme nt of	Wang 2025 ^[52]	40275132	Observational study	43 patients with ICI-associated	Baseline clinical characteristics and initial temporary pacing therapy were evaluated. Follow-up assessments	A total of 11 (11/43, 25.6%) patients (mean age 64.5 ± 8.6 years, female 18.2%) were diagnosed with advanced or complete AVB and

arrhythmias	myocarditis	were conducted to evaluate the survival rate and the recovery of atrioventricular conduction.	subsequently underwent pacing therapy. Short-term (within 90-days after procedure) survival rate was 72.7% (8/11). Atrioventricular conduction recovered in 4 (4/11, 36.4%) patients, without AVB recurrence after temporary pacemaker removal.
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FM, fulminant myocarditis; IABP, intra-aortic balloon pump; VA-ECMO, venoarterial-extracorporeal membrane oxygenation; DHF-LO, decompensated heart failure and low output; SvO2, mixed-venous oxygen saturation; CPO, cardiac power output; NT-proBNP, N-terminal pro-B-type natriuretic peptide; CABG, coronary artery bypass grafting; HR, hazard ratio; OR, odds ratio; CI, confidence interval; RR, relative risk; CVA, cerebrovascular accident; CS, cardiogenic shock; AMI, acute myocardial infarction; LV, left ventricle; pMCS, percutaneous mechanical circulatory support; RCT, randomized controlled trial; mVAD, microaxial ventricular assist device; COVID, corona virus disease; IVIG, intravenous immunoglobulin; LVEF, left ventricular ejection fraction; MD, mean difference; APACHE, acute physiology and chronic health evaluation; LVAD, left ventricular assist device; CK-MB, creatine kinase-MB; VT, ventricular tachycardia; VF, ventricular fibrillation; LSBCTR, life support-based comprehensive treatment regimen; ICU, intensive care unit; MAP, mean arterial pressure; GIB, gastrointestinal bleeding; PPI, proton pump inhibitors; H2RA, H2 receptor antagonist; SpO2, blood oxygen saturation; CRRT, continuous renal replacement therapy; GDRRT, goal-directed renal replacement therapy; AHF, acute heart failure; OMT, optimal medical therapy; AF, atrial fibrillation; QRS, Q, R, and S waves; ICI, immune checkpoint inhibitor; AVB, atrioventricular block.

Supplementary Table 3. Evidence table for Table 3-Recommendations for convalescent management for patients with FM

Relevant topic	First author surname and publication year	PMID	Study type	Number of enrolled cases	Research design	Main relevant findings
Exercise and cardiac rehabilitation	Patriki 2021 ^[53]	32367345	Prospective Pilot Study	30 patients with newly diagnosed myocarditis	Cessation of physical activity was recommended for 3 months.	At 6- (n = 26) and 12-month (n = 19) follow-up neither cardiac events nor worsening LVEF were recorded. The risk of cardiac events at 1 year after diagnosis of myocarditis appears to be low after resumption of exercise after 3 months among patients who recover from acute myocarditis.
Exercise and cardiac rehabilitation	Berg 2017 ^[54]	29158437	Observational study	24 patients with myocarditis after discharge	Cardiac CMR was repeated at 3 months. Change in LGE >20% was considered significant.	Absolute levels of cardiac enzymes and inflammatory markers at baseline did not predict change in LGE at 3 months. Cardiac and inflammatory markers had normalized in 21 patients (88%). LGE significantly improved in 16 patients (67%); however, it persisted to a lesser degree in 17 of them (71%) and increased in a small percentage (21%) despite normalization of cardiac enzymes.
Exercise and cardiac rehabilitation	Maron 2015 ^[55]	26621644	Scientific Statement	/	/	The interval between initial assessment and retesting before resumption of sports will vary depending on the severity of the initial illness. A reasonable minimum interval for retesting based on experimental models is 3 to 6 months.
Exercise and cardiac rehabilitation	Schwaab 2022 ^[56]	33638641	Expert opinions	/	/	Patients with ‘healing myocarditis’ and patients after myocarditis (‘healed myocarditis’) should be transferred to cardiac rehabilitation. ‘Healing myocarditis’ can be assumed if clinical, laboratory and imaging findings demonstrate a course towards recovery, while ‘healed myocarditis’ can be assumed if active myocardial inflammation has regressed completely (ideally documented by CMR).
Exercise and cardiac rehabilitation	Kerneis 2025 ^[57]	40198815	Expert practical view	/	/	Moderate to high-intensity training should be avoided for at least 6 months if symptoms are present or in case surrogate symptoms such as increased hs-cTnI, or clinically significant ECG or imaging abnormalities are still

						observed.
Immunomodulatory therapy	Frustaci 2009 ^[58]	19556262	Randomized Controlled Trial	85 patients with myocarditis and chronic (>6 months) heart failure unresponsive to conventional therapy, with no evidence of myocardial viral genomes	Patients received either prednisone 1 mg/ kg/ day for 4 weeks followed by 0.33 mg/ kg/ day for 5 months and azathioprine 2 mg/ kg/ day for 6 months (43 patients, Group 1) or placebo (42 patients, Group 2).	Group 1 showed a significant improvement of LVEF and a significant decrease in left-ventricular dimensions and volumes compared with baseline. None of Group 2 patients showed improvement of ejection fraction, that significantly worsened compared with baseline.
Immunomodulatory therapy	Morimoto 2024 ^[59]	37452820	Randomized Controlled Trial	59 patients with active cardiac sarcoidosis	A 6-month regimen of prednisolone therapy was introduced, followed by a second FDG scan.	56 patients completed the initial 6-month prednisolone therapy regimen, and 47 patients were allocated to the response group, 9 to the poor response group, and 2 to the recurrent group.
Immunomodulatory therapy	Brambatti 2017 ^[60]	29096807	Systematic review	264 patients and included and 179 patients admitted to hospital with histologically proven EM from 443 published manuscripts.	The clinical presentation, treatment, and outcome of EM were described.	Steroids were administered in 77.7% of patients. A temporary MCS (n= 30) was instituted in 16.8% of patients. In-hospital death was 22.3% (n= 40), with the highest occurrence in the hypersensitivity form (36.1%; p = 0.026).
Immunomodulatory therapy	Jühl 1994 ^[61]	7971647	Retrospective study	48 patients with EMB-proven chronic myocarditis	31 of these patients were selected for 6-month treatment period with 6-methylprednisolone.	23 patients showed an improvement according to the NYHA classification. Lymphocytic infiltrates were abolished in 24 patients. Left ventricular systolic function was improved in 20 patients (64%) as indicated by an increased ejection fraction and stroke volume with a concomitant decrease of left ventricular end diastolic pressure.
Immunomodulatory therapy	Kandolin 2013 ^[62]	23149495	Retrospective study	32 patients with histologically verified giant-cell myocarditis	26 patients were treated with combined immunosuppression (2-4 drugs) including cyclosporine in 20 patients.	The Kaplan-Meier estimates of transplant-free survival from symptom onset were 69% at 1 year, 58% at 2 years, and 52% at 5 years. Of the transplant-free survivors, 10/17 (59%) experienced sustained ventricular tachyarrhythmia during follow-up and 3 received intracardiac defibrillator shocks for ventricular tachycardia or fibrillation.
Immunomodulatory therapy	Escher	27312326	Retrospective	114 patients with	The patients were treated with	The patients showed a significant improvement of LVEF compared to

atory therapy	2016 ^[63]	study	EMB-proven virus-negative chronic myocarditis or inflammatory cardiomyopathy	prednisone and azathioprine for 6 months.	baseline after 6-month period (LVEF rising from 44.6 ± 17.3 to 51.8 ± 15.5 %, p = 0.006) and in the 10-year follow-up (LVEF 52.1 ± 15.6 %, p = 0.006).In a subgroup analysis, patients with initial LVEF ≤45 % (n = 53) significantly increased with LVEF at follow-up (29.3 ± 8.8-41.7 ± 13.2-42.1 ± 13.1 %, p < 0.0001, Group I), defined as inflammatory cardiomyopathy. Patients with initial LVEF >45-60 % (n = 25) significantly improved further or recovered completely, regarding LVEF (53.0 ± 3.6-59.0 ± 9.4-59.8 ± 10.0 %, p = 0.03, Group II). Patients with initial LVEF >60 % (n = 36) remained stable and did not deteriorate over long-term follow-up (68.8 ± 6.7-67.5 ± 10.9-68.8 ± 10.7 %, p = 0.5, Group III). Groups II and III were defined as chronic myocarditis.
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FM, fulminant myocarditis; LVEF, left ventricular ejection fraction; CMR, cardiac magnetic resonance; LGE, late gadolinium enhancement; hs-cTnI, high-sensitivity cardiac troponin I; ECG, electrocardiography; FDG, fluorodeoxyglucose; EM, eosinophilic myocarditis; MCS, mechanical circulatory support; EMB, endomyocardial biopsy; NYHA, New York Heart Association.

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