Supplementary Table S1. Detailed administration of IVIG and concomitant pharmacological treatments.

A. IVIG treatment and exposure

Item	Cohort-specific information
Patients treated	184/316 patients
Product and source	Human Immunoglobulin (pH4) for Intravenous Injection; Hualan Bio, Xinxiang, China; 5% solution, 2.5 g/50 mL. The same formulation and primary manufacturer/source were used at both centers.
Daily dose and treatment duration	Actual daily dose: 5–20 g/day; treatment duration: 1–5 days. IVIG was physician-directed and no study-mandated fixed dose or duration was imposed.
Cumulative exposure	Median cumulative dose: 15.0 g (Q1, Q3: 5.0, 17.5). Dose categories used in the study: <10 g, n=65; 10 to <20 g, n=83; ≥20 g, n=36.
Body weight and weight-adjusted exposure	Median admission body weight: 61.9 kg (56.6, 67.4). Median cumulative IVIG exposure: 0.21 g/kg (0.10, 0.28). IVIG was not prescribed according to a fixed weight-based protocol; g/kg exposure was calculated retrospectively using admission body weight.
Treatment timing	First IVIG administration ≤4 days after admission: n=105; >4 days: n=79. Alternative 3- and 5-day definitions were used only in sensitivity analyses.
Infusion procedure	Infusion was initiated at approximately 20 drops/min for the first 15 min and gradually increased if tolerated; the maximum infusion rate did not exceed 3.0 mL/min.
Interrupted/incomplete treatment definition	A temporary infusion interruption was defined as an unplanned suspension of an ongoing infusion because of suspected infusion-related intolerance or a clinical/hemodynamic concern, followed by clinical reassessment and possible resumption. No “incomplete-treatment” exposure category was used. The <10-g category represents low observed cumulative exposure and does not imply failure to complete a predetermined course.
Safety monitoring	Routine monitoring included temperature and hemodynamic observations during infusion and review for chills/fever, rash or other hypersensitivity reactions, dyspnea, anaphylaxis, renal dysfunction, hemolysis, and thromboembolic events. IVIG-related adverse events were identified from clinical and medication records and were not prospectively adjudicated.

B. Concomitant methylprednisolone, antiviral, and antibacterial therapy

Treatment	Patients receiving treatment	Regimen and implementation	Clinical indication / center consistency
Methylprednisolone	244/316: IVIG, 184/184; non-IVIG, 60/132	Intravenous methylprednisolone 200–500 mg/day for 3–5 days, generally initiated on the day of FM diagnosis or within the first 24 h after admission. The initial course was followed by stepwise dose reduction, typically to 120–200 mg/day for 1–2 days, 80 mg/day for 1–2 days, and 40 mg/day for 1–2 days. When continued corticosteroid therapy was clinically required, patients were converted before discharge to oral prednisone 20–40 mg/day, followed by an individualized taper.	Both centers used the same overall treatment framework. The speed of tapering could be individualized according to hemodynamic recovery, ventricular function, and myocardial-injury/inflammatory markers.
Neuraminidase inhibitor	232/316: IVIG, 147/184; non-IVIG, 85/132. Oseltamivir, n=214; peramivir, n=18.	Oseltamivir: 75 mg orally or by nasogastric tube twice daily, generally for 5 days. Peramivir: 300 mg IV, with 600 mg/day used in selected critically ill patients when clinically indicated; repeated administration was based on clinical response. Doses were adjusted for renal dysfunction when required.	Used for suspected or confirmed influenza-associated viral illness and could be initiated empirically in patients with a compatible viral prodrome. Influenza A/B nucleic-acid or antigen testing was available in 181/232 treated patients; 29/181 (16.0%) were positive. Treatment was therefore not restricted to laboratory-confirmed influenza. The same clinical criteria were applied irrespective of IVIG exposure.
Empirical antibacterial therapy	197/316: IVIG, 115/184; non-IVIG, 82/132	Principal initial agents were piperacillin/tazobactam, cefoperazone/sulbactam, ceftriaxone, or meropenem. Standard adult starting regimens were selected according to infection site, illness severity, renal function, and local practice; treatment was generally 5–7 days and was subsequently de-escalated, changed, or discontinued according to microbiological results and clinical response.	Reserved for clinically suspected concomitant bacterial infection, including compatible pulmonary imaging/respiratory findings, persistent fever with supporting infection markers, or microbiological evidence. It was not a mandatory component of FM treatment, and selection criteria did not differ according to IVIG exposure.

Note: Treatment exposure reflects physician-directed routine clinical care rather than protocol-assigned therapy. Dose adjustment for renal dysfunction was performed when clinically indicated. FM, fulminant myocarditis; IVIG, intravenous immunoglobulin; IV, intravenous.

Supplementary Table S2. Variable-level missing-data patterns.

Variable	Missing n	Missing %
cTnI, pg/mL	10	3.16
NT-proBNP, pg/mL	12	3.80
hsCRP, mg/L	13	4.11
IL-1β, pg/mL	15	4.75
IL-2R, IU/mL	14	4.43
IL-6, pg/mL	15	4.75
IL-8, pg/mL	15	4.75
IL-10, pg/mL	14	4.43
TNF-α, pg/mL	14	4.43
Admission LVEF, %	6	1.90
Symptom-to-admission interval, days	8	2.53
Admission lactate, mmol/L	11	3.48
Admission SOFA score	7	2.22
Vasoactive-inotropic score within 24 h	9	2.85

Note: Only variables with missing observations are shown. Missing values were handled using multiple imputation by chained equations; no listed variable exceeded 5% missingness. cTnI, cardiac troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide; hsCRP, high-sensitivity C-reactive protein; LVEF, left ventricular ejection fraction; SOFA, Sequential Organ Failure Assessment.

Supplementary Table S3. Exact specifications of time-to-event and adjusted statistical analyses.

Outcome / analysis	Analysis population and model	Time origin, event definition, censoring, and competing events	Exact covariates
In-hospital mortality: unadjusted curves	Overall cohort (N=316); Kaplan–Meier estimator with log-rank test	Time origin: hospital admission. Event: all-cause in-hospital death. Patients discharged alive were censored on their actual date of hospital discharge.	None
In-hospital mortality: primary analysis	Overall cohort (N=316; 68 deaths); multivariable Cox proportional-hazards model	Same mortality time scale and censoring definition as above.	Age; sex; study center; admission year; symptom-to-admission interval; admission LVEF; admission lactate; admission SOFA score; methylprednisolone treatment; MCS initiated within 24 h
In-hospital mortality: time-dependent exposure analysis	Overall cohort (N=316; 68 deaths); time-dependent Cox proportional-hazards model	Same mortality time scale and censoring definition. IVIG exposure was coded as 0 before the first IVIG administration and changed to 1 from the time of the first IVIG dose onward.	Age; sex; study center; admission year; symptom-to-admission interval; admission LVEF; admission lactate; admission SOFA score; methylprednisolone treatment; MCS initiated within 24 h
In-hospital mortality: methylprednisolone-restricted analysis	Methylprednisolone-treated cohort (N=244; 35 deaths); multivariable Cox proportional-hazards model	Time origin: hospital admission. Event: all-cause in-hospital death. Discharge alive was censored on the actual discharge date.	Age; study center; admission year; admission LVEF; admission lactate; admission SOFA score; MCS initiated within 24 h
In-hospital mortality: overlap-weighted analysis	Methylprednisolone-treated cohort (N=244; 35 deaths); propensity-score overlap-weighted Cox model	Same mortality time scale and censoring definition. Propensity scores for IVIG treatment were estimated by logistic regression; the weighted outcome model included IVIG exposure without additional covariate adjustment.	Propensity-score model: age; sex; study center; admission year; symptom-to-admission interval; interhospital transfer; rural residence; urban employee/commercial insurance; SBP; DBP; admission LVEF; log-transformed cTnI; log-transformed NT-proBNP; WBC; hsCRP; ALT; AST; creatinine; admission lactate; admission SOFA score; vasoactive-inotropic score within 24 h; MCS initiated within 24 h
ALI/AKI: unadjusted cumulative incidence	Overall cohort and prespecified methylprednisolone/MCS strata; Aalen–Johansen cumulative-incidence estimator with Gray's test	Time origin: hospital admission. Event: first occurrence of ALI/AKI during hospitalization. In-hospital death before ALI/AKI and discharge alive without prior ALI/AKI were treated as competing events.	None
ALI/AKI: adjusted analysis	Overall cohort (N=316; 125 events); cause-specific Cox proportional-hazards model	Time origin: hospital admission. Event: first ALI/AKI. Patients experiencing a competing event were removed from the risk set at the time of that event.	Age; sex; study center; admission year; admission LVEF; admission ALT; admission AST; admission creatinine; admission lactate; admission SOFA score; methylprednisolone treatment; MCS initiated within 24 h
Successful ECMO weaning with survival to discharge: unadjusted cumulative incidence	ECMO-supported cohort (N=79; 56 successful events); Aalen–Johansen estimator with Gray's test	Time origin: ECMO cannulation. Event time: date of ECMO decannulation in patients who subsequently survived to hospital discharge. Death before qualifying successful weaning was treated as a competing event.	None
Successful ECMO weaning with survival to discharge: primary adjusted analysis	ECMO-supported cohort (N=79; 56 events); Fine–Gray subdistribution hazards model	Same ECMO time origin and event definition. Death before qualifying successful weaning was the competing event.	Age; study center; admission LVEF; admission lactate; admission SOFA score; vasoactive-inotropic score within 24 h

Outcome / analysis	Analysis population and model	Time origin, event definition, censoring, and competing events	Exact covariates
Successful ECMO weaning: cause-specific sensitivity analysis	ECMO-supported cohort (N=79; 56 events); cause-specific Cox proportional-hazards model	Same ECMO time origin and successful-weaning definition. Competing deaths were removed from the risk set when they occurred.	Age; study center; admission LVEF; admission lactate; admission SOFA score; vasoactive-inotropic score within 24 h
ECMO support duration: sensitivity analysis	ECMO-supported cohort (N=79); accelerated failure-time model	Time from ECMO cannulation to termination of ECMO support. All 79 patients had a documented ECMO termination date.	Age; study center; admission LVEF; admission lactate; admission SOFA score; vasoactive-inotropic score within 24 h
Successful ECMO weaning: binary sensitivity analysis	ECMO-supported cohort (N=79); penalized logistic regression with 1,000-bootstrap 95% CI	Binary outcome: successful ECMO decannulation followed by survival to hospital discharge versus failure to meet this composite endpoint.	Age; study center; admission LVEF; admission lactate; admission SOFA score; vasoactive-inotropic score within 24 h
IVIG initiation-timing analyses	IVIG-treated cohort (N=184); Cox proportional-hazards models comparing initiation ≤3 vs >3 days, ≤4 vs >4 days, and ≤5 vs >5 days	Time origin: hospital admission. Event: in-hospital death. Discharge alive was censored on the actual discharge date.	Age; admission lactate; MCS initiated within 24 h
Day-4 landmark cumulative-dose analysis	IVIG-treated patients alive and under observation at day 4; landmark Cox proportional-hazards model	Landmark time origin: day 4 after admission. Exposure: cumulative IVIG dose received by day 4 (<10 g, 10 to <20 g, or ≥20 g). Subsequent in-hospital death was the event; subsequent discharge alive was censored at the actual discharge date.	Age; admission lactate; MCS initiated within 24 h

Note: Clinical subgroup analyses of in-hospital mortality according to WBC, ALT, AST, and creatinine used the primary mortality adjustment framework, with the subgroup-defining variable excluded from the corresponding model. These analyses were exploratory; no formal interaction-based claim of effect modification was made. Missing covariate values were handled using multiple imputation by chained equations with 20 imputed datasets, and estimates were pooled using Rubin's rules. Proportional-hazards assumptions were evaluated using Schoenfeld residuals. cTnI and NT-proBNP were log-transformed where included. No patient in the ECMO cohort underwent heart transplantation before weaning, was transferred or discharged while receiving ECMO, or died after ECMO decannulation but before hospital discharge. CI, confidence interval; IVIG, intravenous immunoglobulin; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; SOFA, Sequential Organ Failure Assessment; SBP, systolic blood pressure; DBP, diastolic blood pressure; cTnI, cardiac troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide; WBC, white blood cell count; hsCRP, high-sensitivity C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALI, acute liver injury; AKI, acute kidney injury; ECMO, extracorporeal membrane oxygenation.

Supplementary Table S4. Covariate balance before and after propensity-score overlap weighting in methylprednisolone-treated patients (N=244).

Covariate	Absolute SMD before weighting	Absolute SMD after overlap weighting
Age, years	0.135	0.007
Male sex	0.222	0.007
Center: First Affiliated Hospital of Zhengzhou University	0.023	0.002
Admission year	0.364	0.015
Symptom-to-admission interval, days	0.408	0.009
Interhospital transfer	0.374	0.017
Rural residence	0.353	0.012
Urban employee/commercial insurance	0.248	0.010
SBP, mmHg	0.282	0.008
DBP, mmHg	0.290	0.012
Admission LVEF, %	0.411	0.013
Log-transformed cTnI	0.009	0.001
Log-transformed NT-proBNP	0.079	0.003
WBC, 10^9/L	0.053	0.006
hsCRP, mg/L	0.180	0.009
ALT, IU/L	0.477	0.084
AST, IU/L	0.149	0.006
Creatinine, μmol/L	0.043	0.004
Admission lactate, mmol/L	0.044	0.006
Admission SOFA score	0.024	0.000
Vasoactive-inotropic score within 24 h	0.237	0.013
MCS initiated within 24 h	0.300	0.013

Note: SMD, standardized mean difference. An absolute SMD <0.10 was considered evidence of adequate covariate balance. SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; cTnI, cardiac troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide; WBC, white blood cell count; hsCRP, high-sensitivity C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SOFA, Sequential Organ Failure Assessment; MCS, mechanical circulatory support.

Supplementary Table S5. Sensitivity analyses for IVIG initiation timing and cumulative dose.

A. Alternative definitions of early IVIG initiation

Timing comparison	Early n	Delayed n	Adjusted HR (95% CI)	P value
≤3 days vs >3 days after hospital admission	76	108	0.16 (0.04-0.72)	0.017
≤4 days vs >4 days after hospital admission	105	79	0.15 (0.04-0.53)	0.003
≤5 days vs >5 days after hospital admission	130	54	0.27 (0.10-0.73)	0.010

B. Day-4 landmark analysis of cumulative IVIG dose

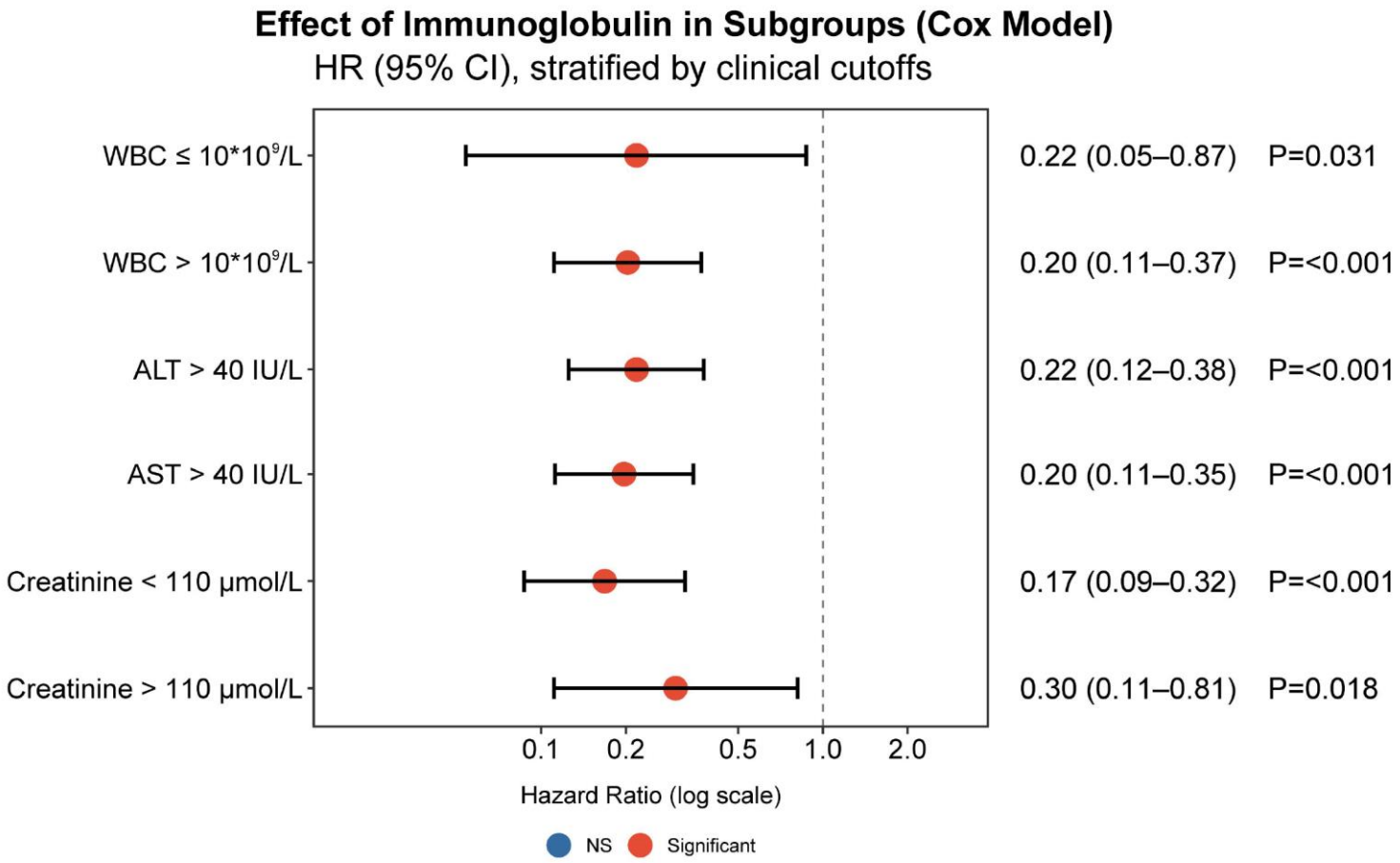
Dose comparison	Adjusted HR (95% CI)	P value
10 to <20 g vs <10 g	0.26 (0.08-0.82)	0.022
≥20 g vs <10 g	0.26 (0.03-1.99)	0.193

Note: Hazard ratios estimate the association with in-hospital mortality. Treatment timing was measured from hospital admission. In the day-4 landmark analysis, cumulative IVIG dose was defined by the dose received by day 4 among patients alive and under observation at the landmark; the <10 g category served as the reference. These dose- and timing-related analyses were exploratory and were not used to infer a definitive optimal regimen. HR, hazard ratio; CI, confidence interval; IVIG, intravenous immunoglobulin.

Supplementary Table S6. Diagnostic, exposure, endpoint, and exploratory tissue-subset definitions.

Domain	Operational definition or implementation	Cohort-specific information
Fulminant myocarditis diagnosis	Abrupt severe heart failure with cardiogenic shock, hypotension requiring vasoactive/inotropic support, or life-threatening arrhythmia; biochemical evidence of myocardial injury; and exclusion of major alternative causes.	All 316 cases were adjudicated at the two participating centers.
Exclusion of acute coronary syndrome	Coronary angiography or coronary CTA was performed when feasible; otherwise serial ECGs, cardiac biomarkers, echocardiography, and the clinical course were used for adjudication.	Coronary angiography or coronary CTA: 287/316 (90.82%).
Cardiac magnetic resonance	CMR was performed when hemodynamic stability permitted; Lake Louise-compatible findings were supportive but were not mandatory for cohort inclusion.	CMR: 122/316 (38.61%); Lake Louise-compatible findings: 103/122 (84.43%).
Methylprednisolone exposure	Methylprednisolone was administered at 200-500 mg/day for 3-5 days and then tapered according to clinical response.	IVIG group: 184/184; non-IVIG group: 60/132.
MCS and ECMO outcome	IABP and/or VA-ECMO was used for refractory cardiogenic shock, persistent hypoperfusion, malignant arrhythmia, or failure of pharmacological support. Successful ECMO weaning required decannulation and survival to discharge.	Any MCS: 180/316. ECMO: 79/316 (IVIG, 61; non-IVIG, 18). Successful weaning with survival: 56/79 (IVIG, 50; non-IVIG, 6).
ALI/AKI composite and CRRT	The composite comprised persistent ALT or AST elevation >3 times the upper limit of normal and/or Kidney Disease: Improving Global Outcomes-defined acute kidney injury. Every patient receiving CRRT was classified as having acute kidney injury.	ALI/AKI: 125/316 (IVIG, 53; non-IVIG, 72). CRRT: 52/316 (IVIG, 44; non-IVIG, 8).
Exploratory myocardial tissue subset	Clinically indicated endomyocardial biopsy specimens were assessed by two pathologists blinded to treatment group. The analysis was exploratory and not intended for causal inference.	Available specimens: n=11 (IVIG, n=6; non-IVIG, n=5). Median admission-to-biopsy interval: 4.80 days (Q1, 4.05; Q3, 5.85).

Note: CTA, computed tomography angiography; ECG, electrocardiogram; CMR, cardiac magnetic resonance; IVIG, intravenous immunoglobulin; MCS, mechanical circulatory support; IABP, intra-aortic balloon pump; VA-ECMO, venoarterial extracorporeal membrane oxygenation; ALI, acute liver injury; AKI, acute kidney injury; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRRT, continuous renal replacement therapy.



Supplementary Figure S1. Subgroup analysis of the association between IVIG use and in-hospital mortality using Cox proportional hazards models. Forest plot of hazard ratios (HRs) with 95% confidence intervals (CIs) for the effect of IVIG treatment on in-hospital mortality, stratified by clinical subgroups. Subgroups were defined based on the following clinical cutoffs: White blood cell (WBC) count: < 10*10⁹/L vs > 10*10⁹/L; Alanine aminotransferase (ALT): > 40 IU/L; Aspartate aminotransferase (AST): > 40 IU/L; Serum creatinine: < 110 μmol/L vs > 110 μmol/L. Hazard ratios were estimated using Cox proportional hazards regression within each subgroup. Data points are presented as log-scaled HRs with corresponding 95% CIs. Red dots indicate statistically significant results; blue dots indicate non-significant results. P < 0.05 was considered statistically significant.