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# Analysis of risk factors affecting prognosis of fulminant myocarditis in children: a ten-year single-center study

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## Abstract

**Objective** The present study aimed to analyze the risk factors affecting the prognosis children with fulminant myocarditis.

**Methods** The medical records of all patients ($n=40$) who were diagnosed with fulminant myocarditis and admitted to the Cardiac Intensive Care Unit (CICU) and Pediatric Intensive Care Unit (PICU) at the Guanzhou Women and Children's Medical Center, Guangzhou Medical University between January 2014 and December 2023 were retrospectively analyzed. Patients were divided into two groups based on their in-hospital prognosis, namely, a survival group ($n=32$) and an non-survival group ($n=8$). Baseline demographics, laboratory findings, electrocardiograms, echocardiograms, and treatment regimens were compared between the two groups via multifactorial analysis.

**Results** The median age of patients in the survival group was 7.8 years (M[5,11.5]), and the median age in the non-survival group was 9.0 years (M[6,11.5]). Compared with those in the survival group, patients in the non survival group had significantly higher levels of extracorporeal cardiopulmonary resuscitation (ECPR) use, ventricular tachycardia/ventricular fibrillation (VT/VF), peak creatine kinase isoenzyme (CK-MB), peak N-terminal B-type natriuretic peptide precursor (NT-proBNP), serum creatinine (Scr) on admission, peak serum Scr, peak aspartate aminotransferase (AST), peak alanine aminotransferase (ALT), peak cardiac troponin I (cTnI), lactate on admission, peak lactate, and extracorporeal membrane oxygenation (ECMO) use (all $p<0.05$). Binary logistic regression analysis revealed that the peak lactate level was an independent risk factor for mortality in patients with fulminant myocarditis (OR = 0.661, 95% CI 0.488–0.897; $p=0.008$).

**Conclusions** The present study demonstrated that the peak lactate level is an independent risk factor for mortality in patients with fulminant myocarditis.

**Keywords** Fulminant myocarditis, Pediatrics, Peak lactate

## Introduction

Acute myocarditis typically presents as an inflammatory heart disease arising from a combination of genetic, infectious, and autoimmune factors. The clinical manifestations vary considerably, with generally favorable prognoses in mild cases. However, fulminant myocarditis, a particularly severe form of acute myocarditis, can lead to cardiogenic shock, ventricular arrhythmias, heart block, multiple organ failure, and even death [1]. Fulminant myocarditis is estimated to account for approximately

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10% to 38% of all acute myocarditis cases [2]. Notably, fulminant myocarditis may be responsible for approximately 10% to 20% of sudden and unexplained deaths in the pediatric population [3].

The present retrospective analysis investigated the clinical data of 40 pediatric patients diagnosed with fulminant myocarditis to identify risk factors affecting the prognosis of fulminant myocarditis in children. The present findings will inform clinical diagnosis and treatment strategies for patients at high risk of fulminant myocarditis.

## Materials and methods

### Research subjects

The present retrospective study employed a grouped case design to analyze patients with fulminant myocarditis admitted to the Cardiac Intensive Care Unit (CICU) and Pediatric Intensive Care Unit (PICU) of the Guangzhou Women and Children's Medical Center, Guangzhou Medical University between January 2014 and December 2023. The inclusion criteria were as follows: (1) age less than 18 years and (2) a diagnosis of fulminant myocarditis. The main clinical diagnoses of the cardiovascular myocarditis group (version 2018) [4] were as follows: (1) cardiac insufficiency or cardiac shock; (2) cardiac enlargement; (3) serum cardiac troponin T (cTnT), serum cardiac troponin I (cTnI) or serum creatine kinase isozyme (CK-MB) with dynamic changes; (4) significant ECG changes (ECG or 24 h Holter); or (5) typical myocarditis in cardiac magnetic resonance imaging. The secondary clinical diagnoses were as follows: (1) a history of prodromal infection, such as a history of upper respiratory tract or gastrointestinal virus infection 1 to 3 weeks before onset; (2) chest tightness, chest pain, palpitations, fatigue, dizziness, pale, or abdominal pain; (3) serum lactate dehydrogenase (LDH), α-hydroxybutyrate dehydrogenase (α-HBDH) or aspartate transaminotransferase (AST); (4) mild abnormal electrocardiogram; or (5) positive anti-myocardial antibody. Myocarditis was clinically diagnosed in accordance with 3 clinical diagnostic bases for the main diagnosis of myocarditis or 2 main clinical diagnostic bases plus 3 secondary clinical diagnostic bases in addition to other diseases. Currently, there are no clear diagnostic criteria for fulminant myocarditis in children; these criteria were based on the Chinese Medical Association Cardiovascular Society guidelines for adult fulminant myocarditis diagnosis and treatment, created with Chinese expert consensus [5]. When acute myocarditis suddenly and rapidly progresses, severe heart failure, hypotension or cardiogenic shock soon appear, and the use of positive inotropic drugs, vascular active drugs or mechanical circulation adjuvant therapy can lead to a diagnosis of fulminant myocarditis. Patients were categorized into survival and non-survival groups based on their in-hospital prognosis. Ethical approval for the present study was granted by the Ethics Committee of Guangzhou Women and Children's Medical Center, Guangzhou Medical University (Approval No. 257A01). Informed consent was obtained from the parents or legal guardians of participants under the age of 16.

### Clinical data collection

The following clinical data were collected: (1) demographic information; (2) hemodynamic parameters and cardiac rhythm; (3) laboratory findings, including peak levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatine kinase-MB isoenzyme (CK-MB), cardiac troponin I (cTnI), serum creatinine (Scr), N-terminal pro-B-type natriuretic peptide (NT-proBNP), and lactate measured on admission; and (4) treatment data, including immunomodulatory therapy and vasoactive medications. A vasoactive-inotropic score (VIS) was calculated using a previously published formula [6] to quantify the degree of vasopressor support needed. A VIS exceeding 20 points indicates severe cardiovascular dysfunction, often necessitating interventions, such as mechanical ventilation, temporary or permanent pacemaker implantation, extracorporeal membrane oxygenation (ECMO) for circulatory support, and continuous renal replacement therapy (CRRT) [6].

3. Statistical methods. Data analysis was performed using SPSS 29.0 statistical software. Categorical variables are expressed as frequencies and percentages, and the chi-square test was used to assess statistically significant differences between groups. When the assumptions for the chi-square test were not met, Fisher's exact probability test was employed. Nonnormally distributed continuous variables are presented as medians with interquartile ranges (M [Q1, Q3]), and the Mann–Whitney U test was used for comparisons between groups. Binary logistic regression analysis was used to identify independent risk factors associated with mortality in patients with fulminant myocarditis. A $p$ value of less than 0.05 was considered statistically significant.

## Results

### Basic clinical data (Table 1)

Forty patients diagnosed with fulminant myocarditis were enrolled in the present study. Patients were categorized into the following two groups on the basis of their in-hospital prognosis: a survival group ($n=32$) and an non-survival group ($n=8$). The median age of the survival group was 7.8 years (M[5,11.5]), whereas the median age of the non-survival group was 9.0 years (M[6,11.5]). Fever was present upon admission in 29 patients. Fever and duration of fever at admission were

**Table 1** Comparison of basic clinical data of patients with fulminant myocarditis

| | survival ($n=32$) | non-survival ($n=8$) | $p$ |
|---|---|---|---|
| Sex (female) | 14 (43.8%) | 3 (37.5%) | 1.0 |
| Age (years) | 7.8 (5,11.5) | 9 (6,11.5) | 0.574 |
| Fever | 24 (75%) | 5 (62.5%) | 0.66 |
| Fever days | 2(2,3) | 2(1.5,3.5) | 0.674 |
| Respiratory symptoms | 8 (25%) | 1 (12.5%) | 0.655 |
| Gastrointestinal symptoms | 19 (59.4%) | 6 (75%) | 0.686 |
| Circulatory symptoms | 5 (15.6%) | 1 (12.5%) | 1.0 |
| Duration of symptoms before admission (days) | 2(2, 4) | 2(2,4.75) | 0.792 |
| ECPR | 7 (21.9%) | 5 (62.5%) | 0.039 |

*ECPR* Extracorporeal cardiopulmonary resuscitation

not significantly different between the two groups. The clinical manifestations at admission varied and included respiratory (cough and shortness of breath), digestive (nausea, vomiting, and abdominal pain), and circulatory (chest tightness and chest pain) symptoms. ECPR was performed prior to ECMO support in 5 patients in the survival group and 4 patients in the non-survival group; this difference in ECPR utilization between the groups was statistically significant ($p<0.05$).

### Laboratory data

Table 2 summarizes the results of initial laboratory tests conducted upon admission, alongside the peak levels measured for the same variables. Compared with the survival group, the non-survival group presented significantly greater peak levels of CK-MB, cTnI, NT-proBNP, Scr (both at admission and peak), AST, and lactate (both at admission and peak) ($p<0.05$).

### Etiological data

All patients underwent etiological testing, but etiological data were available for only 9 patients (30%) as follows: influenza B virus for 3 patients, Mycoplasma pneumoniae for 3 patients, influenza A virus for 1 patient, enterovirus for 1 patient, and adenovirus for 1 patient.

### Electrocardiograms and echocardiograms (Table 3)

Twelve-lead electrocardiogram (ECG) examinations were performed on all patients, with most patients undergoing multiple routine ECGs. Electrocardiographic abnormalities were identified in 36 patients (90%), with 29 patients in the survival group and 7 patients in the non-survival group exhibiting these abnormalities. Notably, the prevalence of ventricular tachycardia/ventricular fibrillation (VT/VF) was significantly greater in the non-survival group than in the survival group ($p<0.05$).

Echocardiographic evaluation revealed that all patients exhibited cardiac enlargement. However, no statistically significant differences were observed between the survival and non-survival groups regarding pericardial

**Table 2** Comparison of biochemical test indicators with fulminant myocarditis

| | survival ($n=32$) | non-survival ($n=8$) | $p$ |
|---|---|---|---|
| On admission | | | |
| CK-MB (U/L) | 101 (49.3, 109.5) | 226.8 (57, 290.3) | 0.06 |
| cTnI (ug/L) | 1.1 (0.5, 1.3) | 2.1 (0.9, 3.4) | 0.052 |
| Scr (umol/L) | 70.2 (37, 70) | 120.1 (56.8, 182.8) | 0.016 |
| AST(U/L) | 287.3 (89, 424.5) | 941.6 (102, 2006.8) | 0.12 |
| ALT(U/L) | 150.7 (25, 210) | 711.8 (59.5, 1330.8) | 0.31 |
| Lactate (mmol/L) | 4.8 (2.5, 6.4) | 7 (4.1, 9.1) | 0.048 |
| NT-proBNP (pg/mL) | 24,553.2(4282.5, 27328.8) | 18,375.3 (5156.5, 34480.3) | 0.477 |
| Peak levels | | | |
| CK-MB (U/L) | 178 (50, 160.3) | 1004.8 (264.8, 902.8) | < 0.001 |
| cTnI (ug/L | 1.8 (0.7, 2.3) | 4.4 (2.0, 5.5) | 0.006 |
| Scr (umol/L) | 93.8 (49, 86.5) | 311.6 (122.8, 260.8) | < 0.001 |
| AST(U/L) | 914.4 (116, 1122.5) | 4124 (1144, 4526.5) | 0.003 |
| ALT(U/L) | 764.4 (47.5, 909.8) | 2448.8 (347, 3764.3) | 0.015 |
| Lactate (mmol/L) | 7.8 (4.8, 11) | 13.6 (11.3, 15) | 0.002 |
| NT-proBNP (pg/mL) | 19,856.1(9297.5, 34378.3) | 30,211 (23460.5, 35000) | 0.014 |

*CK-MB* Creatine kinase isoenzyme, *cTnI* Cardiac troponin I, *NT-proBNP* N-terminal B-type natriuretic peptide precursor, *Scr* Serum creatinine, *AST* Aspartate aminotransferase, *ALT* Alanine aminotransferase

**Table 3** Comparison of electrocardiogram and echocardiogram in fulminant myocarditis

| | survival ($n=32$) | non-survival ($n=8$) | $p$ |
|---|---|---|---|
| A-V block | 13 (40.6%) | 1 (12.5%) | 0.222 |
| VT/VF | 3 (9.4%) | 4 (50%) | 0.02 |
| SVT | 13 (40.6%) | 2 (25%) | 0.686 |
| LVEF | 38.7 (26.8, 47) | 33 (23.3, 46.8) | 0.426 |
| LVFS | 18.4 (12.5, 23) | 15.8 (11, 23.5) | 0.487 |
| Pericardial effusion | 10 (35%) | 4 (50%) | 0.416 |
| Ventricular wall motion abnormalities | 8 (25%) | 2 (25%) | 1.0 |
| Mitral regurgitation | 16 (50%) | 4 (50%) | 1.0 |
| tricuspid regurgitation | 16 (50%) | 4 (50%) | 1.0 |

*A-V block* Atrioventricular block, *VT/VF* Ventricular tachycardia/ventricular fibrillation, *SVT* Supraventricular tachycardia, *LVEF* Left ventricular ejection fraction, *LVFS* Left ventricular fractional shortening

**Table 4** Comparison of treatment in fulminant myocarditis

| | survival ($n=32$) | non-survival ($n=8$) | $p$ |
|---|---|---|---|
| IVIG | 32 (100%) | 7 (87.5%) | 0.2 |
| Corticosteroids | 32 (100%) | 7 (87.5%) | 0.2 |
| VIS (scores) | 18.8 (12.3,23.2) | 23.3 (15.7,32) | 0.37 |
| Temporary pacemaker | 9 (28.1%) | 1 (12.5%) | 0.653 |
| Permanent pacemakers | 2 (6.3%) | 0 (0) | 1.0 |
| CRRT | 3 (13.6%) | 3 (50%) | 0.091 |
| Ventilator | 32 (100%) | 8 (100%) | - |
| ECMO | 11 (34.4%) | 8 (100%) | < 0.001 |

*IVIG* Intravenous immunoglobulin, *VIS* Vasoactive-inotropic score, *CRRT* Continuous renal replacement therapy, *ECMO* Extracorporeal membrane oxygenation

effusion, ventricular wall motion abnormalities, or mitral and tricuspid regurgitation ($p > 0.05$).

#### Treatment of fulminant myocarditis (Table 4)

All patients necessitated mechanical ventilation following admission. Ten patients (25%) required temporary pacemaker implantation due to high-grade atrioventricular block. Unfortunately, one patient in this group with a temporary pacemaker and ECMO support did not survive. The remaining two patients with temporary pacemakers did not experience a return to sinus rhythm within two weeks, necessitating permanent pacemaker placement. Following their diagnosis of fulminant myocarditis upon admission, 39 patients received treatment with intravenous immunoglobulin (IVIG) and corticosteroids.

ECMO was used for circulatory support in 19 patients (47.5%), with a significant difference in utilization between the survival and non-survival groups ($p < 0.05$). Notably, six of these patients also received CRRT.

**Table 5** ECMO situation

| | survival ($n=11$) | non-survival ($n=8$) | $P$ |
|---|---|---|---|
| Shock to ECMO times(h) | 10 (6.0,18) | 8.5(6.5,30.25) | 0.74 |
| ECMO duration (days) | 9.5(6.3, 13) | 7.6(1.4, 24.3) | 0.772 |

**Table 6** Logistic regression analysis of mortality risk factors in fulminant myocarditis

| Risk factor | *B* | *OR* | 95%*CI* | *P* |
|---|---|---|---|---|
| Lactate peak | −0.414 | 0.661 | 0.488, 0.897 | 0.008 |

#### ECMO situation and outcome (Table 5)

Nineteen patients initiated ECMO, and there were no statistically significant differences between the two groups in terms of the time from shock to ECMO initiation or the ECMO maintenance time.

ECMO was used in all 8 patients who died; the survival rate of patients with fulminant myocarditis treated with ECMO was only 42.1% (4 patients died due to cardiogenic shock, 3 patients died due to multiple organ dysfunction syndrome, and 1 patient died due to septic shock).

#### Analysis of independent risk factors for death in patients with fulminant myocarditis (Table 6)

Variables identified in the univariate analysis to have statistically significant differences between the survival and non-survival groups with fulminant myocarditis were included in the subsequent multivariable logistic regression analysis. These variables included ECPR use, VT/VF, peak CK-MB levels, peak NT-proBNP levels, Scr levels at admission, peak Scr levels, peak AST levels, peak ALT levels, peak cTnI levels, lactate levels at admission, peak lactate levels, and ECMO use. The peak lactate level was an independent risk factor for mortality in patients with fulminant myocarditis.

## Discussion

Fulminant myocarditis represents a severe form of viral myocarditis characterized by an abrupt onset and rapid clinical deterioration. Patients swiftly develop hemodynamic compromise (including pump failure and circulatory insufficiency) alongside malignant arrhythmias, resulting in an exceptionally high early mortality rate [7, 8]. Endomyocardial biopsy remains the gold standard for definitive diagnosis. However, owing to its

inherent invasiveness, the diagnosis of fulminant myocarditis often relies on clinical features, biochemical markers, electrocardiographic findings, and echocardiographic characteristics.

The present study revealed a diverse range of clinical presentations upon admission, with predominant extracardiac manifestations (gastrointestinal and respiratory) compared with circulatory symptoms. This aligns with previous international studies reporting that fulminant myocarditis often manifests primarily through extracardiac symptoms [2]. Owing to the nonspecificity and symptoms of myocarditis, approximately 71% of children are misdiagnosed with sepsis or pneumonia [9, 10]. These initial symptoms may delay the diagnosis of myocarditis and lead to delayed hospitalization, thereby increasing mortality. The present analysis compared duration of symptoms before admission of the two groups of patients, but the difference was not statistically significant, owing to the small sample size. However, a high index of suspicion for fulminant myocarditis should be carefully maintained in patients with a history of infection after alternative explanations for these extracardiac manifestations are ruled out. ECPR, also known as venoarterial ECMO, has demonstrated promising outcomes in fulminant myocarditis treatment. International studies have reported a wider range of survival rates (33%–79%) for patients with fulminant myocarditis who underwent ECPR and were subsequently discharged [11–13]. However, the observed survival rate of 21.9% following ECPR in the present study is less than that reported internationally. This statistically significant difference ($p < 0.05$) may be attributed to the relatively recent development and potentially limited experience with ECMO technology in China.

The pathogenesis of fulminant myocarditis may be related to direct damage from the virus or excessive immunity to the virus [14] which is commonly observed with Coxsackievirus. During the coronavirus disease 2019 (COVID-19) pandemic, multiple studies have shown that COVID-19 is associated with a high incidence of myocarditis. Amrei R et al. [15] reported that SARS-CoV-2 causes vascular damage either directly or indirectly by stimulating the immune response, which leads to the overproduction of cytokines (cytokine storms), ultimately causing blood vessel damage. Vascular damage caused by SARS-CoV-2, alone or in combination with preexisting endothelial dysfunction, can lead to multisystem organ failure and death. In the present study, all patients underwent etiological testing, but etiological data were detected in only 9 patients (30%) as follows: influenza B virus for 3 patients, mycoplasma pneumoniae for 3 patients, influenza A virus for 1 patient, enterovirus for 1 patient, and adenovirus for 1 patient. None of the patients contracted SARS-CoV-2.

Myocardial enzymes are proteins located within heart muscle cells. When these cells are damaged or die (necrose or rupture), myocardial enzymes are released into the bloodstream. The levels of these enzymes indirectly reflect the extent of myocardial injury. CK-MB is a dimeric enzyme found predominantly in myocardial tissue, and the serum concentration of CK-MB significantly increases 3–8 h after myocardial injury. The severity of the injury often correlates with the level of CK-MB, with values potentially exceeding those of healthy individuals by several-fold. Cardiac troponin I is a myocardial cell-specific protein that binds calmodulin, and it exists in both free and complex forms within human cardiomyocytes. Myocardial injury triggers the release of cardiac troponin I into the bloodstream, leading to significantly higher serum levels than normal. While cTnI is highly sensitive, its ability to return to normal levels can last 7–10 days. In the present study, the peak CK-MB and cTnI levels in the survival group differed significantly from those in the non-survival group. This finding suggested that a continuous increase in myocardial injury markers indicates disease deterioration, highlighting the importance of early intervention [16]. Furthermore, elevated AST and ALT levels were observed in most patients in the present study. This elevation may be associated with shock, congestive heart failure, or the viral triggers responsible for myocarditis itself. A pediatric study supporting this association has reported elevated AST levels in children with myocarditis [9, 17].

NT-proBNP has gained widespread use in clinical practice in recent years because of its high degree of cardiac specificity and sensitivity; this biomarker reflects left ventricular end-diastolic pressure, a measure of filling pressure within the main pumping chamber of the heart. When the ventricular volume or pressure load increases, leading to elevated wall tension, the synthesis and secretion of NT-proBNP increases accordingly. Consequently, NT-proBNP serves as an accurate indicator of changes in left ventricular function and is a key prognostic factor for assessing disease severity and patient outcomes [16]. Notably, the present study revealed a significant difference ($p < 0.05$) in peak NT-proBNP levels between the survival and non-survival groups.

End-organ perfusion, a marker of tissue oxygenation, reflects the severity of hypoperfusion and aids in assessing circulatory shock. The kidneys, which are highly sensitive to ischemia and reperfusion injury, serve as indicators of circulatory compromise. Scr is a well-established clinical measure of renal function. In fulminant myocarditis, reduced cardiac output, the use of vasoactive medications, infection, hemolysis, and decreased

blood volume can all contribute to renal dysfunction. Studies have demonstrated an association between Scr changes and mortality in adult fulminant myocarditis patients [18]. The present study revealed that some patients received ECPR prior to ECMO, suggesting rapid disease progression in the early stages, potentially leading to multiorgan dysfunction, particularly affecting the kidneys. Hypotension and systemic hypoperfusion before ECMO support in fulminant myocarditis patients can cause acute renal ischemia–reperfusion injury. Additionally, virus-mediated immune responses following initial viral infection can also contribute to acute kidney injury. Consequently, changes in Scr may reflect both the severity of hypoperfusion and the intensity of the immune response, both of which can be confounding factors associated with poor prognosis [18].

Lactate, a byproduct of anaerobic glycolysis, plays a crucial role in metabolism and exercise. Lactate levels not only reflect abnormalities in the respiratory and circulatory systems but also reflect the severity of various conditions [19]. In critical care medicine, lactate has emerged as a risk factor for predicting patient mortality and a critical prognostic indicator [20, 21]. Elevated lactate levels exacerbate heart failure and cardiogenic shock, ultimately contributing to increased patient mortality [22]. The literature on the prediction of the prognosis of patients with fulminant myocarditis is limited, and the conclusions are controversial. Merkle-Storms et al. [23] reported that pre-ECMO lactate levels in pediatric patients are similar between survivors and non-survivors, but Laimod et al. [24] reported that in adult patients receiving ECMO, lactate levels are similar in patients with fulminant myocarditis. The pre-ECMO lactate level is significantly lower in survivors than in non-survivors. A previous meta-analysis study [25] has reported no statistically significant difference in lactate levels between survivors and non-survivors in adult and child populations, but the pooled analysis revealed that lactate levels in survivors are significantly lower than those in non-survivors. The present study revealed a continuous increase in lactate levels within the nonsurvival group, with admission and peak levels exceeding those of the survival group ($p < 0.05$). Furthermore, logistic regression analysis identified the peak lactate level as an independent risk factor for mortality in patients with fulminant myocarditis. This finding is partially similar with previous findings suggesting that peak lactate signifies severe myocardial damage and adversely affects patient outcomes [26, 27].

ECG serves as a vital adjunct test in the diagnosis of fulminant myocarditis. In the present study, approximately 90% of patients presented with abnormal ECG findings. While previous studies have suggested that a high degree of atrioventricular block on initial ECG may correlate with improved survival [2], Miyake et al. reported a poorer prognosis in patients with arrhythmias [28]. Notably, the present study revealed a statistically significant difference ($p < 0.05$) in the incidence of VT/VF between the nonsurvival and survival groups, suggesting a potential association with worse outcomes in patients experiencing these arrhythmias. Echocardiography plays a valuable role in the early detection of cardiac enlargement, aiding in the diagnosis of fulminant myocarditis. This imaging modality allows for the evaluation of cardiac function and the exclusion of alternative etiologies, such as heart failure secondary to rheumatic or congenital heart disease, as well as valvular dysfunction. International studies have reported a poor long-term prognosis for patients with a reduced left ventricular ejection fraction (LVEF) [22, 29]. While the present data revealed a lower LVEF and left ventricular fractional shortening (LVFS) in the nonsurvival group than in the survival group, these differences did not reach statistical significance, which may be attributed to the relatively small sample size of the present study.

Both domestic and international studies have demonstrated the efficacy of mechanical circulatory support therapy in reducing mortality rates for patients with fulminant myocarditis [30]. ECMO remains the most effective treatment option for fulminant myocarditis in children due to limitations in the pediatric medical device market and a paucity of relevant clinical research. Survival rates for patients with fulminant myocarditis treated with ECMO range from 64 to 83% [31–33]. The present study revealed a slightly lower survival rate (57.9%) following ECMO treatment for fulminant myocarditis than previously reported. Early identification of prognostic risk factors associated with fulminant myocarditis in patients receiving ECMO support and subsequent interventions is critical for improving outcomes in these at-risk patients. Currently, there is no consensus on the ideal time to start ECMO. Various medical centers have different time strategies, which are guided mainly by the patient's hemodynamic status and individual institutional criteria to implement ECMO. A multicenter study by Lee et al. [34] divided patients into early (< 0.9 h), middle (1–2.2 h), and late (> 2.2 h) groups on the basis of the time from the onset of shock to ECMO. The results highlighted that patients in the early group (0.6 h) have significantly better outcomes than those in the middle (1.4 h) and late (5.1 h) groups. Early initiation of ECMO does not increase the rate of complications, such as hemorrhagic or ischemic events, but delayed initiation of ECMO support (admission > 24 h) is associated with poor prognosis, with a mortality of up to 75% reported in patients with delayed initiation of ECMO [2]. In our study, a total of 19 patients with fulminant myocarditis required ECMO

support; the shock to ECMO durations were 10 (6, 18) and 8.5 (6.5, 30.25) in the survival and non-survival groups, respectively, but the differences were not statistically significant. It has been reported that the duration of ECMO in the non-surviving patients is longer than that in surviving patients, which may be due to these patients having more severe disease and the myocardium being not fully recovered, suggesting that the ECMO time needs to be extended to ensure adequate tissue perfusion [35]. In our study, there was no significant difference in the duration of ECMO between the two groups, but the duration of ECMO in the non-survival group was shorter than that in the survival group, which may be attributed to the patients being critically ill and parents stopping the treatment.

Early and adequate administration of corticosteroids effectively suppresses the immune response and potentially limits further myocardial cell damage [36]. While gamma globulin is currently used as an immunoregulatory support therapy for fulminant myocarditis in children, existing evidence suggests that neither corticosteroids nor IVIG have a significant effect on mortality rates [37, 38]. In the present study, one patient presented with rapid disease progression upon admission. Despite the implementation of ECMO circulatory support following ECPR, the patient developed multiple organ failure, precluding the use of corticosteroids therapy or IVIG.

### Study limitations

Owing to the single-center, retrospective design and limited sample size, the present study was susceptible to missing data and selection bias, potentially limiting the generalizability of the findings. Additionally, the absence of follow-up data precluded an evaluation of long-term outcomes in surviving patients after hospital discharge.

## Conclusions

The present study identified peak lactate level as an independent risk factor affecting the prognosis of fulminant myocarditis in children. This finding underscores the importance of early recognition, prompt diagnosis, and timely intervention to improve overall patient outcomes.

#### Abbreviations

| | |
|---|---|
| CICU | Cardiac Intensive Care Unit |
| PICU | Pediatric Intensive Care Unit |
| ECPR | Extracorporeal cardiopulmonary resuscitation |
| VT | Ventricular tachycardia |
| VF | Ventricular fibrillation |
| CK-MB | Creatine kinase isoenzyme |
| NT-proBNP | N-terminal B-type natriuretic peptide precursor |
| Scr | Serum creatinine |
| AST | Aspartate aminotransferase |
| ALT | Alanine aminotransferase |
| cTnI | Cardiac troponin I |
| ECMO | Extracorporeal membrane oxygenation |
| CRRT | Continuous renal replacement therapy |
| A-V block | Atrioventricular block |
| SVT | Supraventricular tachycardia; |
| LVEF | Left ventricular ejection fraction; |
| LVFS | Left ventricular fractional shortening |
| IVIG | Intravenous immunoglobulin |
| VIS | Vasoactive-inotropic score |
| COVID-19 | Coronavirus disease 2019 |
| cTnT | Cardiac troponin T |
| LDH | Lactate dehydrogenase |
| α-HBDH | α-Hydroxybutyrate dehydrogenase |

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#### Author's contributions

J Y was responsible for the writing of the article and analyzed the data. L-J L, F-X Land M L performed the experiments and collected data. L M was responsible for the placement of ECMO. N Z designed the research study. All authors have read and approved the final version of this manuscript.

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#### Data availability

No datasets were generated or analysed during the current study.

## Declarations

#### Ethics approval and consent to participate

This study was performed with the ethics approval from the Institutional Committee of Guangzhou Women and Children's Medical Center, Guangzhou Medcial University. The study obtained informed consent from parents or legal guardians of participants under the age of 16.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare no competing interests.

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