Journal of Artificial Organs (2018) 21:172–179
https://doi.org/10.1007/s10047-017-1011-4

ORIGINAL ARTICLE

Artificial Heart (Clinical)

Diagnosis, medical treatment, and stepwise mechanical circulatory support for fulminat myocarditis

Shunsuke Saito[1] · Koichi Toda[1] · Shigeru Miyagawa[1] · Yasushi Yoshikawa[1] · Hiroki Hata[1] · Daisuke Yoshioka[1] · Keitaro Domae[1] · Yasumasa Tsukamoto[2] · Yasushi Sakata[2] · Yoshiki Sawa[1]

Received: 5 October 2017 / Accepted: 4 December 2017 / Published online: 13 December 2017

Abstract
Fulminant myocarditis is one of the most challenging diseases. We sought to examine the outcomes of our multidisciplinary treatment strategy for fulminant myocarditis. A retrospective review of consecutive 30 patients with fulminant myocarditis was conducted. Of the 30 patients, 25 required mechanical circulatory support (MCS). Percutaneous extracorporeal membrane oxygenation (ECMO) was the first-line therapy to rescue the patients and inserted in 23 of them. The other 2 were implanted with temporary ventricular assist device (t-VAD) with extracorporeal centrifugal pump(s). Sixteen of the ECMO-supported patients were later transitioned to t-VAD. Of the 18 patients who underwent t-VAD support, heart function recovered and the VAD was explanted in 10. Four patients were bridged to long-term VAD and the other 4 died on t-VAD. Two patients were directly bridged to long-term VAD by ECMO. Heart function recovered only with ECMO in 4 patients and 1 died on ECMO. Overall survival rate was 83.3%. The duration of ECMO support significantly correlated with total bilirubin level, which was a significant risk factor for mortality. Pathologically, 7 patients (23.3%) had eosinophilic myocarditis and 1 (3.3%) had giant-cell myocarditis, and all the 8 patients underwent immunosuppressive therapy including steroids. Heart function recovered to normal level in 7 of them (87.5%). Timely conversion from the percutaneous ECMO to the temporary VAD before elevation of total bilirubin level is crucial for improving the clinical outcomes. Endomyocardial biopsy is needed to be done as soon as possible, because immunosuppressive therapy carries promising outcomes in certain etiologies.

Keywords Fulminant myocarditis · Extracorporeal membrane oxygenation · Temporary left ventricular assist device · Endomyocardial biopsy

Introduction

Myocarditis is an inflammatory condition with various etiologies affecting the myocardial muscle [1]. Regardless of the etiology, myocarditis may cause severe cardiac dysfunction, sometimes with fulminant clinical manifestation. Because of its heterogeneous clinical presentations, clinical practice guidelines regarding its evaluation and treatment are lacking [2, 3].

In the present study, we describe our comprehensive treatment strategy for acute fulminant myocarditis and examine the outcomes of patients, especially in those who deteriorated due to cardiogenic shock and required acute mechanical circulatory support.

Methods

From May 2009 to October 2015, a total of 30 patients (21 males, 9 females, mean age 39.2 ± 16.8 years) were treated for fulminant myocarditis at our institute.

Acute myocarditis was diagnosed based on clinico-pathorogical presentations: cardiogenic shock of acute

✉ Shunsuke Saito
shunsaito@surg1.med.osaka-u.ac.jp

✉ Yoshiki Sawa
sawa-p@surg1.med.osaka-u.ac.jp

[1] Department of Cardiovascular Surgery, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka 565-0871, Japan

[2] Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka 565-0871, Japan

onset in patients with recent history of gastrointestinal or upper respiratory tract infection and the inflammation of the myocardium proved by endomyocardial biopsy. "Fulminant" myocarditis was defined as histologically proven myocarditis with severe hemodynamic compromise requiring high doses of vasopressors (≧5 μg of dopamine or dobutamine per kilogram of body weight per minute) or a mechanical circulatory support [4].

As a mechanical circulatory support (MCS) for acute cardiogenic shock, percutaneous extracorporeal membrane oxygenation (ECMO) with femoral veno-arterial cannulations was the first-line therapy. The most frequently used ECMO system was the Capiox Emergent Bypass System (Capiox EBS; Terumo, Tokyo, Japan). In patients whose end-organ function deteriorated even with percutaneous ECMO support or in patients with complication of percutaneous ECMO, the percutaneous ECMO was converted to temporary ventricular assist device (VAD) using extracorporeal centrifugal pumps such as Rotaflow (Maquet AG, Rastatt, Germany) or Gyro pump (Medtronic Inc. CFP). In most of the cases, patients who require temporary VAD were complicated with multiple organ failure, and required biventricular VAD (BVAD). The site of inflow and outflow was left ventricular apex and ascending aorta, respectively, for left VAD (LVAD) and right atrium and main pulmonary trunk, respectively, for right VAD (RVAD) [5, 6]. An artificial lung (Biocube, Nipro, Tokyo, Japan) was integrated into the LVAD circulation in patients with pulmonary dysfunction. The anticoagulation therapy in temporary VAD patients was started with continuous heparin injection with target activated partial thromboplastin time 150–200% of the normal value. After oral intake or tube feeding was started, heparin was converted to warfarin (target international normalized ration 2.5) and aspirin 100 mg/day.

Ethical committee approval was obtained for this retrospective study, and individual informed consent was waived, because individual patients were not identified in this study.

Statistical analysis

Continuous variables with normal distribution were summarized as means ± standard deviations and continuous variables without normal distribution as median. Categorical variables are summarized as frequencies and proportions. All continuous variables were checked for normality using the Shapiro–Wilk test and normal probability plot. The survival curve was prepared using the Kaplan–Meier method. Risk factor analyses were done using logistic regression model. Optimal cut-off values of peak creatinine kinase MB (CKMB) level and total bilirubin level at percutaneous ECMO removal to predict the recovery of heart function and patient death, respectively, were determined by receiver-operating characteristics (ROC) curve analysis. The optimal cut-off value was defined as that providing maximal accuracy to distinguish between responders and non-responders. Correlations between the serum total bilirubin level and the duration of ECMO support were analyzed using Pearson's correlation coefficient. Values of $p < 0.05$ were considered to indicate statistical significance. Statistical analyses were performed using SPSS 19.0 software (SPSS Inc., Chicago, IL).

Results

Initial symptoms at onset

All the patients experienced flu-like symptoms within 1 week prior to the onset of heart failure symptoms. Twenty-four patients (80%) had fever, pharyngalgia, arthralgia, and cough, and 17 patients (57%) had digestive symptoms such as diarrhea, vomiting, and abdominal pain. Only 4 patients (13%) experienced chest pain. Other minor symptoms included exanthema in 2 patients, dyspnea in 1, and syncope in 1. The median duration from the initial symptoms to the onset of the heart failure was 3 days (0–7 days).

Electrocardiographic changes

Patients showed various and dynamic changes in electrocardiogram (ECG) during the course. The initial ECG abnormalities were wide QRS complex and ST elevation in 15 patients (50%), complete atrioventricular (AV) block in 11 (37%), atrial fibrillation in 2 (7%), and ventricular fibrillation in 1 (3%). Wide QRS complex and ST elevation later developed into complete AV block in 5 patients and cardiac standstill in 3. Of the 11 patients who showed complete AV block at the beginning, 5 later suffered from cardiac standstill. One of the two patients who initially showed atrial fibrillation later developed complete AV block. The median duration from the onset of heart failure symptom to lethal ECG abnormalities (complete AV block, ventricular fibrillation, or cardiac standstill) was 0.5 days (0–6 days).

Mechanical circulatory support

A total of 25 patients (83%) required MCS due to profound cardiogenic shock. Of the 25 patients, 23 underwent emergent implantation of percutaneous ECMO at bed-side or in the cath-lab. The other 2 were directly taken to the operating room and underwent temporary VAD implantation (1 LVAD and 1 BVAD). The median duration from the onset of heart failure symptom to the establishment of initial MCS was 1 day (0–12 days). Of the 23 patients who were rescued with percutaneous ECMO, 18 patients later required conversion to central cannulation. Percutaneous ECMO was converted to temporary BVAD in 15 patients, paracorporeal BVAD

(Nipro VAD, Nipro, Tokyo, Japan) in 2, and central ECMO in 1. In the patient who received central ECMO, pulmonary circulation could not be established due to massive airway bleeding.

Limitation of percutaneous ECMO

Our treatment policy was the early conversion from percutaneous ECMO to central cannulation before the occurrence of irreversible complications by the peripheral cannulation. The median duration of the percutaneous ECMO support before the conversion to temporary VAD was 2.0 days (0–12 days). The signs that limit the continuation of percutaneous ECMO include lung congestion due to increase in left ventricular afterload, progressive deterioration of renal and/or liver function, or complications of the cannulation site such as bleeding or limb ischemia. Figure 1a, b shows the changes in serum creatinine and serum total bilirubin levels, respectively, in patients in whom percutaneous ECMO were successfully removed due to the recovery of heart function ($n=4$) and in patients in whom percutaneous ECMO was converted to the central cannulations ($n=18$). In patients who required conversion to the central cannulations, serum creatinine level was already high before percutaneous ECMO support (Cr 1.45 ± 0.99 mg/dL). Creatinine and total bilirubin levels elevated further even with the ECMO support. On the other hand, in patients who were successfully weaned off percutaneous ECMO support, mean serum creatinine and total bilirubin levels were within normal limit before ECMO support, and remained so during the ECMO

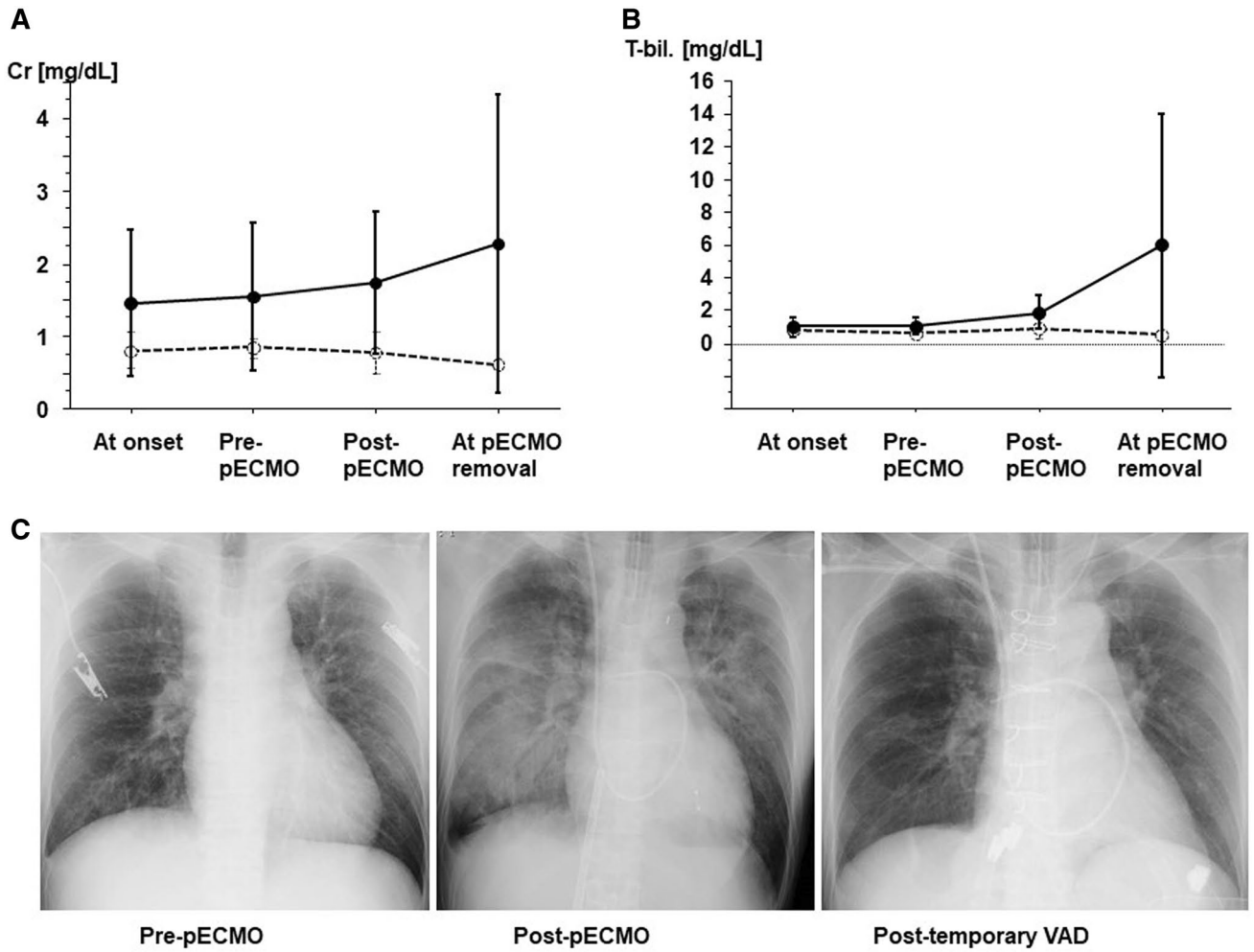

Fig. 1 Changes in serum creatinine (**a**) and serum total bilirubin (**b**) levels in patients in whom percutaneous extracorporeal membrane oxygenation (ECMO) was successfully removed ($n=4$, open circles with dashed line) and in patients in whom percutaneous ECMO was converted to the central cannulations ($n=18$, closed circles with solid line). In patients who required conversion to central cannulations, renal and hepatic function deteriorated even under the ECMO support. **c** Characteristic changes in chest X-ray before and after percutaneous ECMO insertion and after conversion to temporary ventricular assist device (VAD). The lung congestion caused by percutaneous ECMO was improved by left ventricular drainage by the temporary VAD. *Cr* creatinine, *T-bil* total bilirubin, *pECMO* percutaneous ECMO

support. Figure 1c shows the characteristic changes in chest X-ray in patients with near-cardiac arrest who were supported with percutaneous ECMO. The retrograde perfusion of the aorta causes increase in left ventricular afterload, and that results in lung congestion. In all the 4 patients who were successfully weaned off percutaneous ECMO support, the pulmonary congestion never occurred.

Effective circulatory support with temporary VAD

Figure 2a–c show changes in serum creatinine, aspartate transaminase (AST), and total bilirubin levels in patients who were supported with temporary VAD ($n = 18$). Patients showed improvement in renal and liver function promptly after temporary VAD implantation, and they were normalized before the VAD explantation. The lung edema caused by percutaneous ECMO also improved by the left ventricular drainage with temporary VAD (Fig. 1c). Of the 18 patients supported by temporary VAD, the native heart function recovered and the temporary VAD was removed in 10 (Fig. 2d). The recovery of heart function was not sufficient and the temporary VAD was converted to long-term VAD in 4 patients. The other 4 patients died on temporary VAD support due to cerebrovascular events. The mean duration of the temporary VAD support in the 18 patients was 28.1 ± 26.0 (6–105) days. The mean duration was 16.7 ± 10.4 (6–38) days in the 10 patients who were successfully weaned off temporary

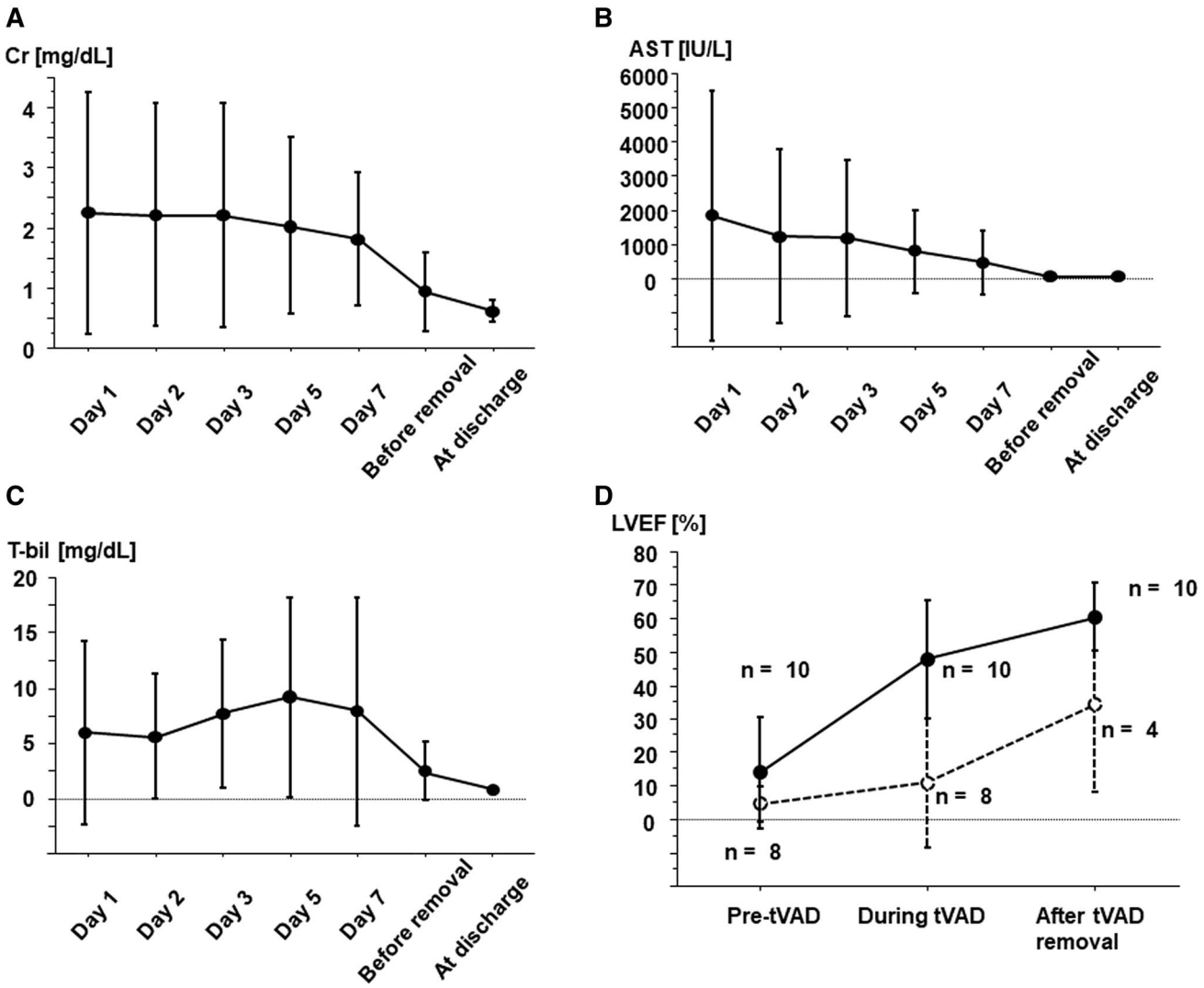

Fig. 2 Changes in serum creatinine (**a**), aspartate transaminase (**b**), and total bilirubin (**c**) levels in patients who were supported with temporary ventricular assist device (VAD, $n = 18$). **d** Changes in the left ventricular ejection fraction assessed by echocardiography in patients who were successfully explanted with temporary VAD ($n = 10$, closed circles with solid line) and in patients in whom temporary VAD was converted to long-term VAD ($n = 4$) or who died on temporary VAD ($n = 4$, open circles with dashed line). *Cr* creatinine, *AST* aspartate transaminase, *T-bil* total bilirubin, *t-VAD* temporary VAD

VAD, and 52.0 ± 36.2 (23–105) days in the 4 patients in whom the temporary VAD was converted to the long-term VAD.

Endomyocardial biopsy and immunosuppressive therapy

All the 30 patients underwent endomyocardial biopsy at the time of admission to our hospital or at the time of referral to our team. The diagnosis of myocarditis was done according to the Dallas histopathological criteria [7]; 22 (73.3%) were diagnosed with lymphocytic myocarditis, 7 (23.3%) with eosinophilic myocarditis, and 1 (3.3%) with giant-cell myocarditis. All the 8 patients diagnosed with eosinophilic or giant-cell myocarditis underwent immunosuppressive treatments. The immunosuppressive treatment for eosinophilic myocarditis consisted of pulse methylprednisolone (1 g/day × 3 days, intravenous injection) followed by oral prednisone (60 mg/day, tapered 10 mg/week until 10 mg/day, and then tapered 2.5 mg/week). In the patient with giant-cell myocarditis, oral cyclosporine (target trough level 200 ng/mL) was added to the steroid therapy. The heart function recovered in the 6 out of 7 patients with eosinophilic myocarditis and in the patient with giant-cell myocarditis. The other patient with eosinophilic myocarditis died on temporary VAD support due to cerebral bleeding. In the patients with eosinophilic myocarditis, the eosinophilic cationic protein (ECP) level in the peripheral blood was markedly elevated (314.9 ± 543.6 μg/L) at the time of diagnosis, and it decreased below the normal limit (14.9 μg/L) in all the patients after the immunosuppressive therapy (Fig. 3).

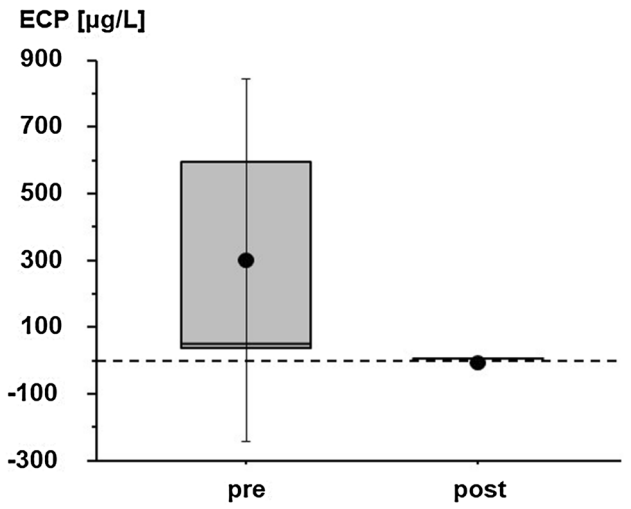

Fig. 3 Serum level of eosinophilic cationic protein before and after immunosuppressive treatment in patients with eosinophilic myocarditis

Clinical outcomes and risk analysis

As a total, heart function recovered enough for hospital discharge in 19 out of 30 patients (63.3%, Fig. 4a). Long-term VAD was implanted as a bridge to heart transplantation in 6 (20%). Five patients died due to cerebrovascular events (16.7%). Overall survival was 83.3% at 12 months (Fig. 4b). By univariate logistic regression model analysis, peak creatinine kinase MB (CKMB) level was detected as the predictor of cardiac functional recovery (odds ratio 0.972, 95% confidential interval 0.946–1.000, and *p* value 0.046). However, by ROC analysis, area under the curve (AUC) was only 0.25, and peak CKMB level was not clinically useful to predict the cardiac functional recovery. On the other hand, univariate logistic regression model detected serum total bilirubin level at the time of percutaneous ECMO removal (i.e., at the time of weaning or at the time of temporary VAD conversion)

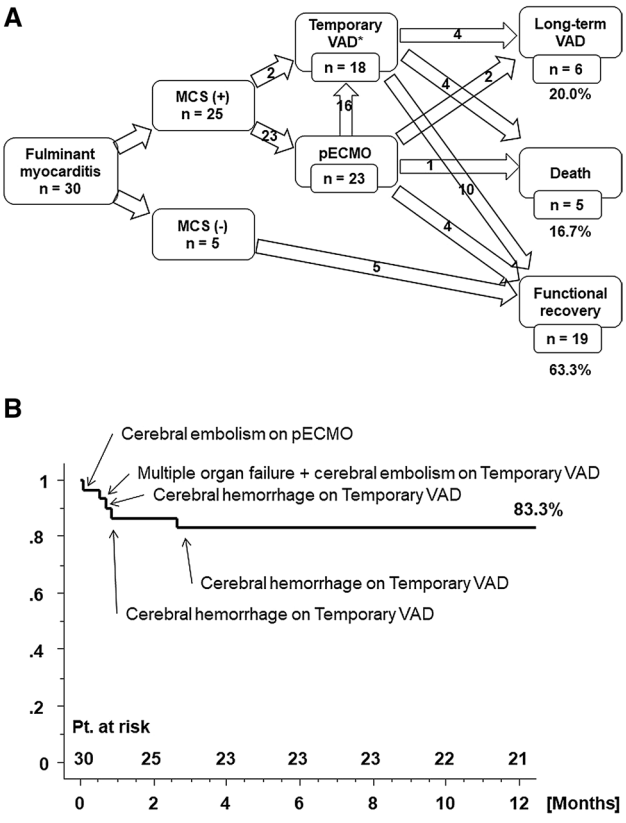

Fig. 4 **a** Clinical course of the 30 patients with fulminant myocarditis treated at Osaka University Hospital between May 2009 and October 2015. *MCS* mechanical circulatory support, *VAD* ventricular assist device, *pECMO* percutaneous extracorporeal membrane oxygenation. *One patient with central ECMO is included here. **b** Kaplan–Meyer survival curve of the 30 patients. All the five deaths were due to cerebrovascular events

as the risk factor for patient death (odds ratio 1.357, 95% CI 1.015–1.814, and p value 0.039). The cut-off value of serum total bilirubin level was 4.65 mg/dL by ROC analysis (AUC 0.80, sensitivity 0.80, and specificity 0.83). The correlation analysis showed that the serum total bilirubin level correlated significantly with the duration of ECMO support ($p < 0.001$, $r = 0.63$, Fig. 5).

Discussion

The 30 patients included in the present study are those who presented the most severe clinical course of myocarditis. The time course of the 25 patients who required mechanical circulatory support in this study was compatible to that of previous reports. In a study of 27 patients with acute myocarditis, Asaumi and coworkers reported that 14 patients required circulatory support with ECMO, and the average time from onset of heart failure symptoms to ECMO placement was 17 h, with a range of 7–36 h [8]. In another study of 41 patients with fulminant myocarditis, the reported average time after onset of heart failure symptoms before initiation of ECMO was 2.6 ± 5.4 days [9].

The frequency of the patients requiring MCS in the present study was higher than that of previous reports [4, 8]. This is because our patients were sent to us only after their hemodynamics deteriorated and became unable to be managed at the regional hospitals, even though the survival rate of the patients in our study (83.3%) was equivalent or even higher than that of previous reports (60.0–87.5% [4, 8–13]).

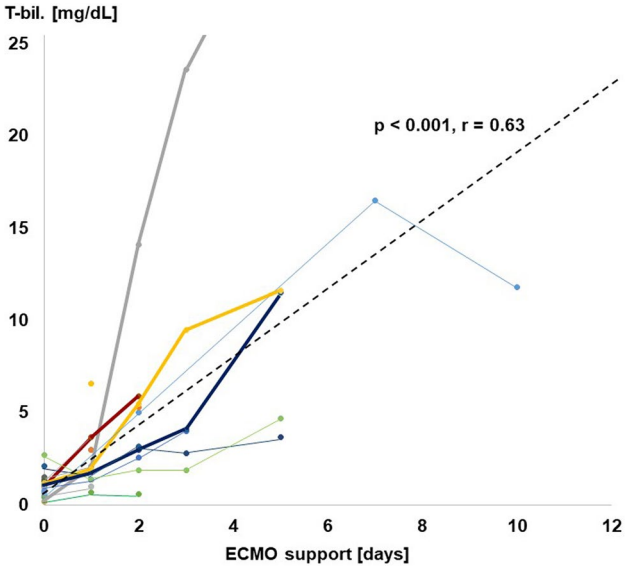

Fig. 5 Serum level of total bilirubin correlated significantly with the duration of percutaneous ECMO support. The death cases are marked with bold line. *T-bil* total bilirubin, *ECMO* extracorporeal membrane oxygenation

As MCS for acute cardiogenic shock, percutaneous ECMO was the first choice, because it is easy to set up and quick insertion at bed-side is possible in emergent settings. Especially, the Capiox EBS is designed for rapid induction. Its priming volume is 480 mL and can be set up in 5 min with auto-priming [8]. On the other hand, percutaneous ECMO has critical drawbacks such as inadequate flow, pulmonary congestion due to increase in left ventricular afterload, and limb ischemia. Especially, in emergent settings under cardiopulmonary resuscitation, small cannulae tend to be chosen, because the priority is given to quick and safe insertion of the cannulae. This results in an inadequate support flow, especially in patients with multiple organ failure who require higher flow than usual to reverse the deteriorating end-organ function. Moreover, the retrograde flow in the aorta by the percutaneous ECMO hinders the opening of the aortic valve, and increases the afterload of the left ventricle. Together with the inadequate decompression of the right heart, this results in severe pulmonary congestion and lung edema. If the ECMO support with peripheral cannulation is continued in such a case, severe airway bleeding and irreversible pulmonary dysfunction may occur, as we have experienced in the case with central ECMO, in whom pulmonary circulation could not be established. The increase in left ventricular afterload may also hinder the recovery of the native heart function. If any of these drawbacks of percutaneous ECMO appears, we did not hesitate to bring the patient into the operating room, and converted the percutaneous cannulation to the central cannulation. As a result, the median duration of the percutaneous ECMO support before the conversion to the central cannulation was only 2 days in this series. The risk analysis with univariate logistic regression model in the present 30 cases revealed that serum total bilirubin level at the time of percutaneous ECMO removal/conversion was the risk factor for patient death. Moreover, we found a significant correlation between the ECMO duration and the serum total bilirubin level. This may indicate that a delay in decision to upgrade percutaneous ECMO to temporary VAD may result in poor prognosis. All the five deaths in the present study were due to cerebrovascular events. In general, there is no direct association between cerebrovascular events and serum total bilirubin levels. In this series, all the four patients who died on temporary VAD support had very high level of serum total bilirubin at the time of conversion (5.9, 11.5, 11.6, and 33.1 mg/dL, Fig. 5), and the level went even higher after LVAD conversion. They were obviously complicated with multiple organ failure and their hemodynamic status were septic under LVAD support. In patients with mechanical circulatory support, it is well known that MOF and sepsis are significant risk factors of cerebrovascular events.

There are a lot of evidence that a significant proportion of the patients with fulminant myocarditis may recover their

heart function with the early utilization of MCS in combination with appropriate medical therapy and neurohormonal blockade [4, 11–13]. For the devices used as "bridge to recovery", the following characteristics are required: they should be able to provide biventricular unloading and adequate systemic flow support, they should be cost-effective, and the implantation procedure should be simple and as less invasive as possible. Our percutaneous ECMO–temporary VAD protocol meets all these demands. The ECMO system is the most cost-effective, and the peripheral cannulation is the least invasive procedure. When the percutaneous ECMO fails to provide adequate flow support and adequate ventricular unloading, temporary VAD with extracorporeal centrifugal pumps may cover these problems more cost effectively and less invasively than implantable VAD. Minimally invasive implantation technique of the temporary VAD is also reported [14], and may be utilized in a selected proportion of the patients.

On the other hand, if the recovery of the heart function does not occur, it is also known that a considerable percentage of patients are left with severe dilated cardiomyopathy and may ultimately require heart replacement therapy [15, 16]. There are also good reasons to use temporary VAD in such patients. Most of the 30 patients in the present study were sent to our institution from other hospitals after the patients' condition had already deteriorated to The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile 1. The clinical outcomes of primary permanent LVAD implantation are known to be poor in patients classified as INTERMACS profile 1 (critical cardiogenic shock) and profile 2 (Progressive decline) [17]. Therefore, we used the temporary VAD as "bridge to candidacy" [5, 6, 14]. Despite the progress in pharmacological therapy and increasing knowledge about cardiac assist devices, a substantial number of patients are still referred too late, after they have already reached a critical condition. They may present with contraindications for heart transplantation or the implantation of a permanent VAD, but these conditions may be acute and reversible. Short-term low-cost devices that can be inserted with minimal surgical invasiveness may provide immediate hemodynamic stability and recovery for future assessment of these patients [6].

The importance of endomyocardial biopsy can never be overestimated. All the 30 patients in this study underwent the endomyocardial biopsy and 8 of them (26.7%) were diagnosed with eosinophilic or giant-cell myocarditis. Immunosuppressive treatments are known to be effective only in these two subtypes of myocarditis, but not in lymphocytic myocarditis, and the definitive diagnosis can be made only with histopathological analysis [18]. Therefore, the early histological diagnosis with endomyocardial biopsy followed by timely and appropriate decision to administer immunosuppressive medications is critical to improve the clinical outcomes of fulminant myocarditis. All the eight patients in this study received aggressive immunosuppressive treatment including steroids and cyclosporine, and the heart function recovered in 7 (87.5%) of them. The rate of cardiac functional recovery in patients with lymphocytic myocarditis was 12/22 (54.5%).

ECP is one of the eosinophilic granule proteins, and is known to play major roles in the pathogenesis of eosinophilic myocarditis [19, 20]. As with our patients, elevated ECP during active disease and subsequent reductions in ECP with immunosuppressive therapy suggest that ECP may be responsible for the degranulation of eosinophils. Therefore, monitoring of serum ECP levels, which are derived from degranulation of eosinophils, is one of the valuable parameters which may contribute to a prompt diagnosis of eosinophilic myocarditis [21].

Our study has several limitations, including those related to a retrospectively performed analysis of a single-center experience. A relatively small number of the patients precluded the possibility to do the multivariate analysis of the risk factors related to myocardial recovery and patient mortality. The effectiveness of the immunosuppressive therapy in eosinophilic and giant-cell myocarditis should be confirmed in larger series, ideally in a randomized manner.

In conclusion, we reported our stepwise approach for fulminant myocarditis with aggressive MCS therapy using percutaneous ECMO and temporary VAD. The duration of ECMO support significantly correlated with total bilirubin level, which was the significant risk factor for mortality. Therefore, timely conversion from the percutaneous ECMO to the temporary VAD before the elevation of total bilirubin level is crucial for improving the clinical outcomes. Endomyocardial biopsy is very important, because immunosuppressive therapy carries promising outcomes in certain etiologies.

Compliance with ethical standards

Conflict of interest All authors declare no conflict of interest associated with this study.

References

1. Maisch B, Pankuweit S. Standard and etiology-directed evidence-based therapies in myocarditis: state of the art and future perspectives. Heart Fail Rev. 2013;18:761–95.
2. Heart Failure Society of America. HFSA guidelines for the management of patients with heart failure due to left ventricular systolic dysfunction: pharmacological approaches. Congest Heart Fail. 2000;6:11–39.
3. Japanese Circulation Society Task Force Committee on Acute and Chronic Myocarditis. Guidelines for diagnosis and treatment of myocarditis (JCS 2009). http://www.j-circ.or.jp/guideline/pdf/JCS 2009_izumi_h.pdf. Accessed 13 Dec 2017.

4. McCarthy RE 3rd, Boehmer JP, Hruban RH, et al. Long-term outcome of fulminant myocarditis as compared with acute (non-fulminant) myocarditis. N Engl J Med. 2000;342:690–5.
5. De Robertis F, Birks EJ, Rogers P, Dreyfus G, Repper JR, Khaghani A. Clinical performance with the levitronix centrimag short-term ventricular assist device. J Heart Lung Transpl. 2006;25:181–6.
6. De Robertis F, Rogers P, Amrani M, et al. Bridge to decision using the levitronix centrimag short-term ventricular assist device. J Heart Lung Transpl. 2008;27:474–8.
7. Aretz HT, Billingham ME, Edwards WD, et al. Myocarditis: a histopathologic definition and classification. Am J Cardiovasc Pathol. 1987;1:3–14.
8. Asaumi Y, Yasuda S, Morii I, et al. Favourable clinical outcome in patients with cardiogenic shock due to fulminant myocarditis supported by percutaneous extracorporeal membrane oxygenation. Eur Heart J. 2005;26:2185e92.
9. Mirabel M, Luyt CE, Leprince P, et al. Outcomes, long-term quality of life, and psychologic assessment of fulminant myocarditis patients rescued by mechanical circulatory support. Crit Care Med. 2011;39:1029e35.
10. Saito S, Nakatani T, Kobayashi J, et al. Is extracorporeal life support contraindicated in elderly patinets? Ann Thorac Surg. 2007;83:140–5.
11. Acker MA. Mechanical circulatory support for patientswith acute-fulminant myocarditis. Ann Thorac Surg. 2001;71:S73–6.
12. Ginsberg F, Parrillo JE. Fulminant myocarditis. Critic Care Clin. 2013;29:465–83.
13. Mody KP, Takayama H, Landes E, et al. Acute mechanical circulatory support for fulminant myocarditis complicated by cardiogenic shock. J Cardiovasc Trans Res. 2014;7:156–64.
14. Saito S, Fleischer B, Maeß C, Baraki H, Kutschka I. Minimally invasive implantation of an extracorporeal membrane oxygenation circuit used as a temporary left ventricular assist device: a new concept for bridging to permanent cardiac support. J Artif Organs. 2015;18:95–8.
15. Mason JW, O'Connell JB, Herskowitz A, et al. A clinical trial of immunosuppressive therapy for myocarditis. The myocarditis treatment trial investigators. N Engl J Med. 1995;333:269–75.
16. Cooper LT Jr. Myocarditis. N Engl J Med. 2009;360:1526–38.
17. Kirklin JK, Naftel DC, Pagani FD, et al. Seventh INTERMACS annual report: 15,000 patients and counting. J Heart Lung Transplant 2015;34;1495–504.
18. Kawano S, Kato J, Kawano N, et al. Clinical features and outcomes of eosinophilic myocarditis patients treated with prednisolone at a single institution over a 27-year period. Intern Med. 2011;50:975–81.
19. Arima M, Kanoh T. Eosinophilic myocarditis associated with dense deposits of eosinophil cationic protein (ECP) in endomyocardium with high serum ECP. Heart. 1999;81:669–75.
20. Tai PC, Ackerman SJ, Spry CJF, Dunnette S, Olsen EGJ, Gleich GJ. Deposits of eosinophil granule proteins in cardiac tissues of patients with eosinophilic endomyocardial disease. Lancet. 1987;8534:643–7.
21. Arima M, Kanoh T, Kawano Y, Oigawa T, Yamagami S, Matsuda S. Serum levels of eosinophilic cationic protein in patients with eosinophilic myocarditis. Int J Cardiol. 2002;84:97–9.