Original Article

Fulminant Myocarditis Treated with Percutaneous Cardiopulmonary Support System (PCPS)

Kiyohiro Oshima, MD, PhD,[1] Fumio Kunimoto, MD, PhD,[1] Hiroshi Hinohara, MD, PhD,[1] Yoshiro Hayashi, MD, PhD,[1] Junko Hirato, MD, PhD,[2] Yukio Tajima, ME,[3] and Hiroyuki Kuwano, MD, PhD[1]

Purpose: Fulminant myocarditis is characterized by rapid and extensive hemodynamic compromise occurring in a previously healthy patient. The patients sometimes require mechanical circulatory support to maintain systemic perfusion. The purpose of this study was to analyze the clinical course of patients with fulminant myocarditis treated with a percutaneous cardiopulmonary support system (PCPS).

Patients and Methods: From January 1998 to November 2006, four fulminant myocarditis patients were admitted to the intensive care unit (ICU) in Gunma University Hospital and treated with PCPS to support deteriorating hemodynamics. The mean age of the 4 was 38 ± 18 (range 14 to 57) years. None of the patients had a past history of heart disease, and the diagnosis of fulminant myocarditis was made with clinical findings and endomyocardial biopsy. Three patients were successfully removed from PCPS; one was not removed and died from cerebral bleeding. Changes in clinical findings, APACHE II scores, and laboratory data were analyzed in the 3 survivors and 1 nonsurvivor.

Results: Intra-aortic balloon pumping (IABP) was used in all 4 patients. The duration of PCPS support was 141, 228, and 266 h in the survivors and 330 h in the nonsurvivors. The interval between the occurrence of clinical symptoms such as fever and general fatigue and the induction of PCPS in the nonsurvivor was shorter (2 days) than in the survivors (4–6 days). Cardiac troponin I (cTnI) and creatine phosphokinase (CPK)–MB levels were significantly higher in the nonsurvivor compared with those in the survivors. Left ventricular ejection fraction (LVEF) gradually improved, and PCPS flow was decreased at around 120 h after PCPS start in the survivors; however, these improvements did not occur in the nonsurvivor.

Conclusion: PCPS was induced in 4 fulminant myocarditis patients and successfully removed from 3 after long-term PCPS (>5 days). The maintenance of hemodynamics, especially in the acute phase of fulminant myocarditis, is important because the possibility of circulatory recovery is relatively high compared with those having severe cardiac failure resulting from other causes. The prognosis might be poor if the interval between the occurrence of clinical symptoms and PCPS deployment is short. (Ann Thorac Cardiovasc Surg 2008; 14: 75–80)

Key words: fulminant myocarditis, cardiac failure, mechanical circulatory support, percutaneous cardiopulmonary support

From [1]Intensive Care Unit, [2]Department of Pathology, and [3]Supply Center, Gunma University Hospital, Maebashi, Japan

Received April 25, 2007; accepted for publication July 6, 2007
Address reprint requests to Kiyohiro Oshima, MD, PhD: Intensive Care Unit, Gunma University Hospital, 3–39–15 Showa-machi, Maebashi 371–8511, Japan.

Introduction

The clinical features of acute myocarditis are nonspecific, ranging from a subclinical form to cardiopulmonary crisis.[1)] The term “fulminant myocarditis” is used for acute myocarditis that rapidly develops into cardiogenic shock

requiring a mechanical circulatory support system.[2–4] The prognosis of fulminant myocarditis is generally poor. However, the deteriorated cardiac function is reversible if the patients can be carried through the critical phase with the aid of cardiopulmonary support. Moreover, fulminant myocarditis was recently reported to have a more favorable prognosis than acute myocarditis in the United States.[5] Therefore appropriate hemodynamic management in the acute phase influences the prognosis of patients with fulminant myocarditis. It has been reported that a percutaneous cardiopulmonary support system (PCPS) is a convenient and effective mechanical circulatory support for the maintenance of hemodynamics in patients with fulminant myocarditis.[6,7] However, the criteria of initiation and discontinuation of PCPS have not been established, and the prognostic factors predicted from laboratory data are still controversial.

The purpose of this study was to analyze the clinical course of 4 patients with fulminant myocarditis treated with PCPS and to find the prognostic factors.

Patients and Methods

From January 1998 to November 2006, four fulminant myocarditis patients were admitted to the intensive care unit (ICU) in Gunma University Hospital and treated with PCPS to support deteriorating hemodynamics (Table 1). Three of the patients were males and one was female, and their mean age was 38 ± 18 (range 14 to 57) years. None of the patients had a past history of heart disease, and the diagnosis of fulminant myocarditis was made on the basis of clinical findings and endomyocardial biopsy. In all 4 cases, an endomyocardial biopsy showed a remarkable degeneration of myocardial cells and a marked invasion of inflammatory cells, such as lymphocytes and monocytes, into edematous interstitial tissue, which was consistent with acute myocarditis (Fig. 1). The results of viral antibody examination are shown in Table 1.

In our hospital, the indication of PCPS for severe cardiac failure is as follows[8]: peak systolic pressure less than 80 mmHg and cardiac index less than 1.8 L/min/m^2 for more than 30 min after the correction of hypovolemia, hypoxemia, and acidosis. A rapid decrease in cardiac output unresponsive to intra-aortic balloon pumping (IABP) was also an indication for PCPS. The decision to initiate PCPS therapy was made by the attending physicians. The PCPS system comprised a hollow-fiber microporous membrane oxygenator, a heat exchanger, a centrifugal pump, arterial and venous cannulae, and standard 3/8-inch tubing. The blood-contact surfaces of these components were heparin-coated. We used a Capiox SP Pump Controller Sp-101 and a Capiox circuit (Terumo Co., Tokyo). PCPS flow was initially maintained in the range 2.0 to 2.5 L/min/m^2, and activated clotting time was controlled to be 150–250 s with the administration of nafamostat mesylate (TORII Pharmaceutical Inc., Osaka Japan), a potent antiplatelet agent, during PCPS use. As regards the termination of PCPS, its flow was gradually decreased with enough preload and the administration of catecholamines for a stabilization of the hemodynamics. When PCPS flow was from 1.5 to 2.0 L/min and hemodynamics were stable, i.e., systolic blood pressure was more than 80 mmHg, central venous pressure less than 15 mmHg, and pulse pressure more than 30 mmHg, PCPS was terminated.

PCPS flow, left ventricular ejection fraction (LVEF) measured with transthoracic echocardiography, APACHE II score, laboratory data such as blood lactate levels, cardiac troponin I (cTnI) levels, and creatine phosphokinase (CPK) and CPK-MB levels before and after PCPS induction were evaluated.

Results

Hemodynamic parameters and the doses of catecholamines before PCPS deployment are shown in Table 2. Ventricular tachycardia (VT)/ventricular fibrillation (VF) was found in 3 patients, and a transvenous temporary pacemaker (tPM) was necessary in the same 3 (Table 1). The mean interval between the occurrence of clinical symptoms, such as fever and general fatigue, and the induction of PCPS was 4.3 ± 1.7 (range 2–6) days, and the mean elapsed time between ICU admission and PCPS induction was 14 ± 14 (2–32) h. No patient required cardiopulmonary resuscitation (CPR) before the deployment of PCPS.

PCPS was established with venous drainage (19.5 Fr or 21 Fr cannula) from the femoral vein (the tip of the cannula was placed in the right atrium), and arterialized blood was returned to the femoral artery using a 15 Fr or 16.5 Fr cannula. The mean duration of PCPS support was 241 ± 79 (range 141–330) h. IABP was used in all 4 patients. Mechanical ventilatory support was also required in all patients, and the mean duration of mechanical ventilatory support was 445 ± 211 (range 276–749) h. No patient underwent a tracheotomy. Three patients (75%) required renal replacement therapy, such as continuous hemodiafiltration (CHDF) and/or hemodialysis (HD).

Table 1. Characteristics and clinical course of patients

Case	Age	Sex	Viral antibody examination	PCPS time (h)	ICU length of stay (days)	VT/VF	tPM	Prognosis
1	14	F	unknown	141	14	(–)	(–)	Alive (91 mon)
2	37	M	CoxakieB3 Echo7	266	47	(+)	(+)	Alive (39 mon)
3	57	M	CoxakieA2	228	19	(+)	(+)	Alive (39 mon)
4	47	M	Adeno1, 3 CoxakieA9	330	15	(+)	(+)	Death

VT, ventricular tachycardia; VF, ventricular fibrillation; tPM, temporary pacemaker.

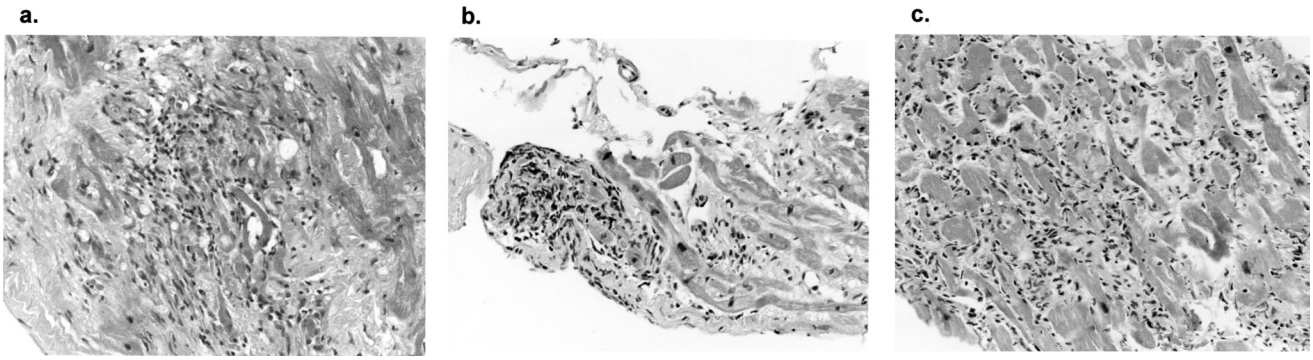

Fig. 1. Microscopic findings of endomyocardial biopsy in 3 patients (cases 2–4) were shown.
An endomyocardial biopsy showed a remarkable degeneration of myocardial cells and a marked invasion of inflammatory cells, such as lymphocytes and monocytes, into edematous interstitial tissue. **a** and **b** are findings of cases 2 and 3, respectively, and **c** is the findings of case 4.

PCPS was successfully removed in three patients (Table 1), and a patient who could not be removed from PCPS died because of massive brain hemorrhage resulting from disseminated intravascular coagulation (DIC). The interval between the occurrence of clinical symptoms such as fever and general fatigue and the deployment of PCPS in the nonsurvivor was shorter than that in the survivors (Fig. 2a). In the nonsurvivor, there was a steep increase in cTnI level (more than 1,000 ng/mL), whereas this did not occur in the survivors (Fig. 2b).

As shown in Fig. 3, a and b, LVEF gradually improved, and PCPS flow started to be weaned at approximately 120 h after PCPS deployment in the survivors, and was finally removed. On the other hand, a patient who show no improvement of LVEF could not be removed from PCPS and died from massive cerebral hemorrhage on the 13th day of PCPS. The APACHE II score gradually increased after PCPS start in the nonsurvivor; however, in the survivors the scores decreased from 120 h after PCPS start (Fig. 4a). There were no notable differences in serum lactate levels and CPK levels in all 4 patients (Figs. 4b and 5a). On the other hand, serum CPK-MB level was markedly elevated at the start of PCPS in the nonsurvivor (Fig. 5b).

Table 2. Hemodynamic parametes and the doses of catecholamines before PCPS deployment

Hemodynamics prior to PCPS start	
HR	83±33 (50–120) bpm
SAP	64±6 (55–77) mmHg
LVEF	13±3 (10%–15%)
CI	1.3±0.4 (0.9–1.8) L/min/m^2
The administered catecholamine dose	
dopamine	9±1 (8–10) μg/kg/min
dobutamine	2±4 (0–8) μg/kg/min
adrenaline	0.025±0.05 (0–0.1) μg/kg/min

HR, heart rate; SAP, systolic arterial pressure; LVEF, left ventricular ejection fraction; CI, cardiac index. Data are shown as mean ± SD.

Necrotomy of the right toe was necessary in one sur-

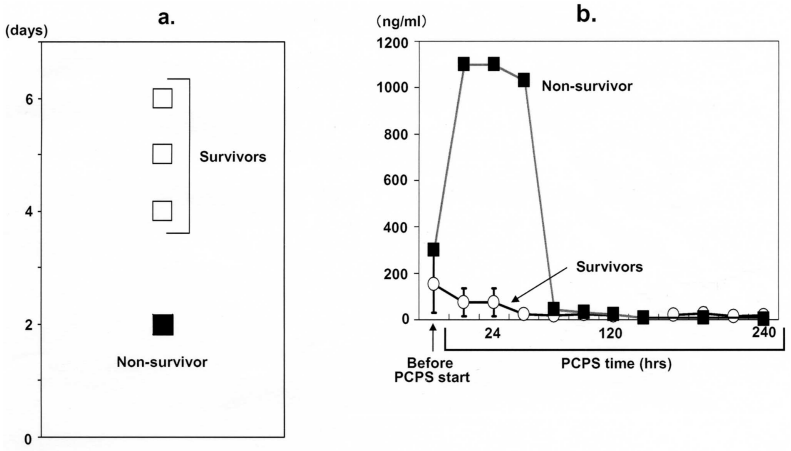

Fig. 2.

a: The interval between the occurrence of clinical symptoms such as fever and general fatigue and the start of PCPS.

b: Changes of cTnI levels before and after PCPS start. Data for survivors are shown as mean ± SD.

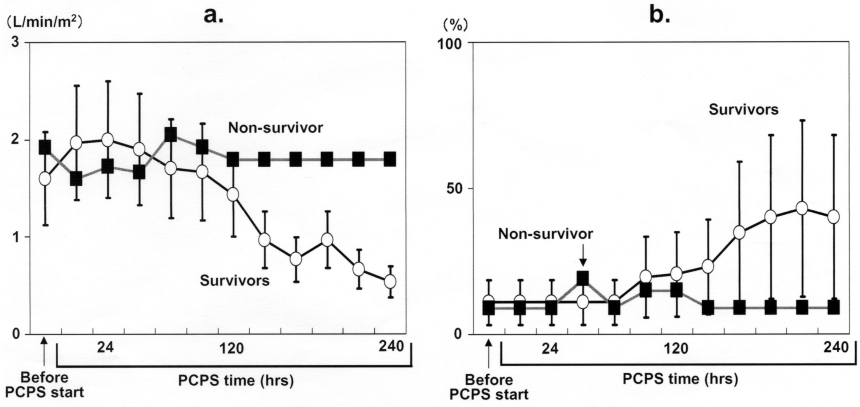

Fig. 3.

a: Changes of PCPS flow before and after PCPS start. Data for survivors are shown as mean ± SD.

b: Changes of LVEF before and after PCPS start. Data for survivors are shown as mean ± SD.

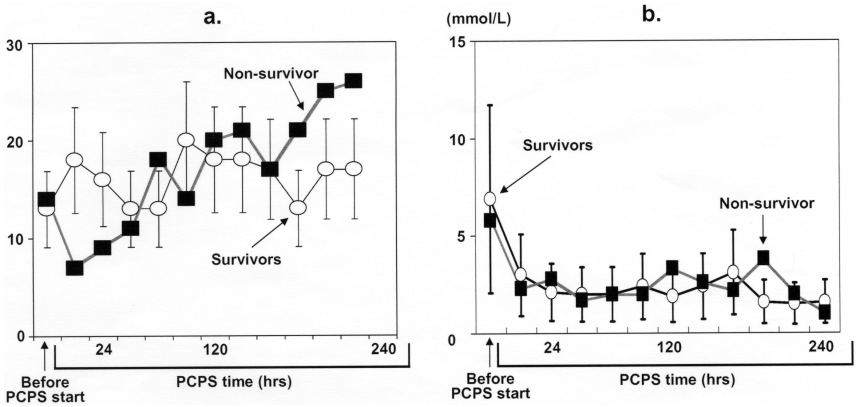

Fig. 4.

a: Changes of APACHE II score before and after PCPS start. Data for survivors are shown as mean ± SD.

b: Changes of serum lactate levels before and after PCPS start. Data for survivors are shown as mean ± SD.

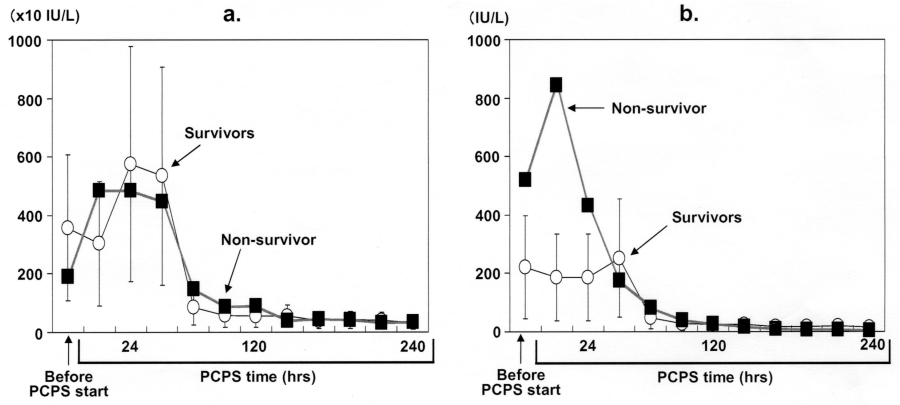

Fig. 5.
a: Changes of CPK levels before and after PCPS start. Data for survivors are shown as mean ± SD.
b: Changes of CPK-MB before and after PCPS start. Data for survivors are shown as mean ± SD.

vivor because of leg ischemia due to PCPS cannulation. There was no other complication resulting from PCPS use. The 3 patients removed from PCPS did not need permanent pacemakers and had no neurological complications. At 56 months (range 39–91) of follow-up, these 3 patients have returned to full-time work.

Discussion

In this study, the mean duration of PCPS support was 241 ± 79 h, and the rate of PCPS removal and survival was 75% (3/4) in patients with fulminant myocarditis requiring PCPS to maintain hemodynamics. In our previous study[8] the mean duration of PCPS support was 134 ± 117 h, and the PCPS removal rate was 38% in patients who required PCPS because of severe cardiac failure resulting from various causes. Fulminant myocarditis is a condition in which patients can recover and return to normal life after being rescued from fatal cardiopulmonary crisis by mechanical cardiopulmonary support.[9] Kato et al.[10] suggested that there might be a normalization of cardiac function, making a resumption of normal daily life possible if the patient diagnosed with fulminant myocarditis survives the acute phase. Our results and those of others noted above indicate that the recovery rate in patients with fulminant myocarditis requiring PCPS is high compared with that in patients with cardiac failure resulting from other causes, and relatively long-term support with mechanical circulatory assist is necessary.

In three patients removed from PCPS, LVEF gradually recovered and PCPS flow could be gradually decreased starting at approximately 120 h after PCPS induction. Therefore it is important to maintain hemodynamics strictly with inotropics and/or mechanical circulatory supports, taking care that complications such as limb ischemia, bleeding, and decrease in platelet count do not occur for at least 120 h after PCPS start. LVAD was used in none of the patients in this study; however, in patients in whom PCPS flow cannot be weaned until 120 h after PCPS start and PCPS support is prolonged, LVAD might be necessary because PCPS is not suitable for long-term use.[11,12] It cannot augment coronary blood flow, and substantial regional myocardial necrosis can occur.[13] Moreover, PCPS may increase the left ventricular afterload without any venting of the left atrium or ventricle. Scholz et al.[14] suggested the need for active left ventricular decompression during PCPS use. The combination of PCPS and IABP has important advantages over PCPS alone in postischemic, dilated, poorly contracting hearts.[15] Lazar and associates[16] also reported that optimal salvage of the ischemic myocardium was achievable by the addition of IABP support to PCPS. In our study, IABP was employed in all 4 patients.

In this study, a patient in whom the interval between the occurrence of clinical symptoms and the deployment of PCPS was short and whose condition progressed rapidly to fulminating myocarditis had a poor prognosis. In this patient, the levels of cTnI and CPK-MB increased rapidly and reached a remarkably high level compared with patients removed from PCPS. The interval between the onset of fulminant myocarditis and the PCPS start might be related with the prognosis of patients with fulminant myocarditis, and the prognosis might be poor if that interval is relatively short. Also, the changes in cTnI

and CPK-MB might be useful in evaluating the severity and the prognosis of patients with fulminant myocarditis; however, the paucity of the number of patients makes it prudent to recognize this as a limitation of the study. Lee et al.[17] reported that prolongations of the QRS complex and depressed LVEF on admission were independent positive predictors for the development of acute fulminant myocarditis, based on an analysis of 35 patients with acute myocarditis. Further studies, including multicenter analysis, are required to identify the risk factors of clinical symptoms and/or laboratory data that could predict the fulminant course of acute myocarditis.

In conclusion, we treated 4 patients with fulminant myocarditis using PCPS for the maintenance of hemodynamics. PCPS was successfully removed in 3 patients, and they returned to full-time work. The maintenance of hemodynamics, especially in the acute phase of fulminant myocarditis, is important because the possibility of circulatory recovery in patients with fulminant myocarditis is relatively high compared with those with severe cardiac failure as a result of other causes. However, the prognosis might be poor if the interval between the occurrence of clinical symptoms and PCPS deployment is short.

References

1. Kohno K, Aoyama N, Shimohama T, Yoshida M, Machida Y, et al. Resuscitation from fulminant myocarditis associated with refractory ventricular fibrillation. *Jpn Circ J* 2000; **64**: 139–43.
2. Morishima I, Sassa H, Sone T, Tsuboi H, Kondo J, et al. A case of fulminant myocarditis rescued by long-term percutaneous cardiopulmonary support. *Jpn Circ J* 1994; **58**: 433–8.
3. Kawahito K, Murata S, Yasu T, Adachi H, Ino T, et al. Usefulness of extracorponeal membrane oxygenation for treatment of fulminant myocarditis and circulatory collapse. *Am J Cardiol* 1998; **82**: 910–1.
4. Kato S, Morimoto S, Hiramitsu S, Nomura M, Ito T, et al. Use of percutaneous cardiopulmonary support of patients with fulmonant myocarditis and cardiogenic shock for improving prognosis. *Am J Cardiol* 1999; **83**: 623–5.
5. McCarthy RE 3rd, Boehmer JP, Hruban RH, Hutchins GM, Kasper EK, et al. Long-term outcome of fulminant myocarditis as compared with acute (nonfulminant) myocarditis. *N Engl J Med* 2000; **342**: 690–5.
6. Inoue Y, Kaneko H, Yoshizawa Y, Morikawa A. Rescue of a child with fulminant myocarditis using percutaneous cardiopulmonary bupport. *Pediatr Cardiol* 2000; **21**: 158–60.
7. Leung MCH, Harper RW, Boxall J. Extracorporeal membrane oxygenation in fulminant myocarditis complicating systemic lupus erythematosus. *Med J Aust* 2002; **176**: 374–5.
8. Oshima K, Morishita Y, Hinohara H, Hayashi Y, Tajima Y, et al. Factors for weaning from a percutaneous cardiopulmonary support system (PCPS) in patients with severe cardiac failure: a comparative study in weaned and nonweaned patients. *Int Heart J* 2006; **47**: 575–84.
9. Aoyama N, Izumi T, Hiramori K, Isobe M, Kawana M, et al. National survey of fulminant myocarditis in Japan: therapeutic guidelines and long-term prognosis of using percutaenous cardiopulmonary support for fulminant myocarditis (special report from a scientific committee). *Circ J* 2002; **66**: 133–44.
10. Kato S, Morimoto S, Hiramitsu S, Uemura A, Ohtsuki M, et al. Risk factors for patients developing a fulminant course with acute myocarditis. *Circ J* 2004; **68**: 734–9.
11. Muehrcke DD, McCarthy PM, Stewart RW, Seshagiri S, Ogella DA, et al. Complications of extracorporeal life support systems using heparin-bound surfaces. The risk of intracardiac clot formation. *J Thorac Cardiovasc Surg* 1995; **110**: 843–51.
12. Zwischenberger JB, Nguyen TT, Upp JR Jr, Bush PE, Cox CS Jr, et al. Complications of neonatal extracorporeal membrane oxygenation. Collective experience from the Extracorporeal Life Support Organization. *J Thorac Cardiovasc Surg* 1994; **107**: 838–49.
13. Lazar HL, Treanor P, Rivers S, Bernard S, Shemin RJ. Combining percutaneous bypass with coronary retroperfusion limits myocardial necrosis. *Ann Thorac Surg* 1995; **59**: 373–8.
14. Scholz KH, Schröder T, Hering JP, Ferrari M, Figulla HR, et al. Need for active left-ventricular decompression during percutaneous cardiopulmonary support in cardiac arrest. *Cardiology* 1994; **84**: 222–30.
15. Bavaria JE, Furukawa S, Kreiner G, Gupta KB, Streicher J, et al. Effect of circulatory assist devices on stunned myocardium. *Ann Thorac Surg* 1990; **49**: 123–8.
16. Lazar HL, Treanor P, Yang XM, Rivers S, Bernard S, et al. Enhanced recovery of ischemic myocardium by combining percutaneous bypass with intraaortic balloon pump support. A*nn Thorac Surg* 1994; **57**: 663–8.
17. Lee CH, Tsai WC, Hsu CH, Liu PY, Lin LJ, et al. Predictive factors of a fulminant course in acute myocarditis. *Int J Cardiol* 2006; **109**: 142–5.