

National Survey of Fulminant Myocarditis in Japan

— Therapeutic Guidelines and Long-Term Prognosis of Using Percutaneous Cardiopulmonary Support for Fulminant Myocarditis (Special Report From a Scientific Committee) —

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Although fulminant myocarditis is known as a fatal disease, patients have been able to recover and return to normal life with the help of mechanical cardiopulmonary support. However, therapeutic guidelines for using percutaneous cardiopulmonary support (PCPS) for fulminant myocarditis have not been established, and the clinical course and long-term prognosis of such patients are still controversial issues. The present national survey considered the current situation of patients as the basis for proposing therapeutic guidelines. Thirty of 52 patients (57.7%) survived and returned to social life. Important factors concerning the prognosis were the severity and grade of cardiac and renal dysfunction, the adjusted support flow rate to enable recovery from circulatory failure, and prevention of circulatory disturbances of the legs and multiple organ failure directly associated with PCPS. With regard to the long-term prognosis of patients treated with PCPS, the readmission rate was 10%, the exacerbation rate was 3.3%, and mortality was 10% during the average follow-up period of 962 days. Optimal management of the mechanical cardiopulmonary support and curative treatment for the myocarditis further improve the outcome of this disease. (*Circ J* 2002; 66: 133–144)

Key Words: Fulminant myocarditis; Long-term prognosis; Percutaneous cardiopulmonary support (PCPS); Therapeutic guidelines

Patients undergoing a cardiopulmonary crisis, who would previously not have survived under conventional emergency treatment, are now saved by mechanical cardiopulmonary support systems [intra-aortic balloon pump (IABP), percutaneous cardiopulmonary support (PCPS) and ventricular assist device (VAS)]. Fulminant myocarditis is one such disease in which patients can recover and return to normal life after being rescued from fatal cardiopulmonary crisis by mechanical cardiopulmonary support.^{1–15} However, this breakthrough in treatment has led to new problems, such as how to manage the mechanical cardiopulmonary support to improve survival, how to monitor the clinical course, and how to enhance the long-term prognosis of fulminant myocarditis.

A national survey was planned to clarify these problems by investigating the current situation of patients with fulminant myocarditis requiring PCPS and thereby formulate therapeutic guidelines for the use of PCPS for this disease. To this end, the investigators (the scientific committee of the Japanese Circulation Society) gathered information on patients with fulminant myocarditis who were treated with

PCPS in Japan for the 3-year period from April 1997 to March 2000.

Methods

Patients

In hospitals affiliated with the investigators or in their referral hospitals, a retrospective cohort study was conducted on fulminant myocarditis patients treated with PCPS. The time of patient enrollment ranged from May 1989 to March 2000. The patients were diagnosed as active myocarditis histologically either from endomyocardial biopsy or from autopsy, and PCPS was regarded as essential for managing the clinical crisis. The primary issues investigated in a questionnaire (Table 1) prepared for cardiologists were (1) clinical features, disease course and patient prognosis in relation to PCPS treatment, (2) indications, management and cessation of PCPS, and avoidance of complications associated with PCPS, and (3) long-term prognosis. The investigators went to the admitting hospital of the patient and directly interviewed the doctors involved. The analyses mainly focused on (1) the clinical features of survivors and non-survivors, (2) the differences in the indications for PCPS and its outcome, (3) the characteristics of potential survivors who could be weaned off PCPS at some stage, and (4) which patients could be weaned off PCPS.

Data were expressed as mean $\pm$ SD. Mann-Whitney's U test was used to compare differences between continuous

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Table 1 Aspects of the Patients, the Disease and the Therapy Included in the Questionnaire*I. Clinical features on admission and before undergoing PCPS.*

1. Age, sex
2. Prognosis
3. Etiology of the myocarditis
4. Method of definitive diagnosis: endomyocardial biopsy or autopsy
5. Period from onset to admission
6. Period from admission to starting PCPS
7. Initial and cardinal symptoms
8. NYHA (New York Heart Association) functional classification
9. Vital signs on admission: BP (blood pressure), HR (heart rate), BT (body temperature)
10. Consciousness
11. Present findings
12. Chest X-ray: CTR (cardiothoracic ratio), congestion
13. Electrocardiogram: rhythm, arrhythmia, ST-T abnormality, abnormal Q, low voltage, poor r-progression, right or left bundle branch block
14. Echocardiogram: wall motion, %FS (percent left ventricular fractional shortening), EF (left ventricular ejection fraction), IVSth (interventricular septum thickness), PWT (posterior wall thickness), LAD (left atrial dimension), LVDd (left ventricular end-diastolic dimension), LVDs (left ventricular end-systolic dimension), pericardial effusion
15. Arterial blood gas analysis: pH, BE (base excess)
16. Full blood count: WBC (leukocyte), Hb (hemoglobin), Plt (platelet)
17. Blood biochemical examination: TP (total protein), Alb (albumin), TB (total bilirubin), DB (direct bilirubin), AST (GOT) (aspartate aminotransferase [glutamic oxaloacetic transaminase]), ALT (GPT) (alanine aminotransferase [glutamic pyruvic transaminase]), LDH (lactate dehydrogenase), CK (creatinine kinase), CK-MB (creatinine kinase-MB), TNT (troponin T), AMY (amylase), BUN (blood urea nitrogen), Cr (serum creatinine), UA (uric acid), Na (sodium), K (potassium), Cl (chloride), Ca (calcium), IP (inorganic phosphorus), Glu (glucose), LA (lactic acid), CRP (C-reactive protein)
18. Paired serum
19. Swan-Ganz catheter: PAs/d (pulmonary artery systolic/diastolic pressure), CVP (central venous pressure), PCWP (pulmonary capillary wedge pressure), CI (cardiac index), SVO₂ (mixed venous blood oxygen saturation)
20. Cardiac catheterization: coronary angiographies, PAs/d, CVP, PCWP, CI, endomyocardial biopsy
21. Instructions of cardiovascular drugs

II. Indications, management, termination and complications associated with PCPS.

1. Indication: LOS (low output syndrome), LTA (life-threatening arrhythmia)
2. Concurrent treatments: IABP (intra-aortic balloon pump), CHF (continuous hemofiltration), steroid pulse therapy, γ -globulin therapy
3. Total operating time
4. Instructions of drugs used for anticoagulation
5. Initial and control flow rate
6. Frequency of PCPS exchange
7. Complications: bleeding, haemolysis, thrombus formation, sepsis, circulatory disturbances of the legs, MOF (multiple organ failure), DIC (disseminated intravascular coagulation)
8. Clinical data immediately before and after undergoing PCPS, progress and maximum and minimum data during PCPS:
 - (1) Vital signs: BP, HR, BT
 - (2) Swan-Ganz catheter: PAs/d, CVP, PCWP, CI, SVI (stroke volume index), SVO₂

variables. Differences between groups were examined by chi-square analysis. A probability value less than 0.05 was considered statistically significant.

Results

Clinical Characteristics and Prognosis of Fulminant Myocarditis Patients

Fifty-two patients were enrolled in the survey and their clinical characteristics are shown in Table 2; 30 (57.7%) patients survived and returned to normal life, 1 (1.9%) patient survived in a vegetative state and remained hospitalized, and 21 (40.4%) patients died. The average period from onset to admission was 4.67 ± 3.46 days, and the period from admission to instituting PCPS was 0.90 ± 1.54 days. On admission, half of the patients showed systolic blood pressure (SBP) of less than 90 mmHg, and approximately 60% of patients showed either tachycardia or bradycardia. Approximately 80% of patients had clear consciousness: 16 of the patients with clear consciousness, 3 with semi-consciousness and 1 who was in a coma on admission survived and returned to normal life. Not all patients were New York Heart Association (NYHA) functional classification IV on admission.

The initial and cardinal symptoms are summarized in

Table 3. Of the initial symptoms, increased fever, general fatigue and coughing were the most common, and of the cardinal symptoms, most were caused by congestive heart failure and low output syndrome. The results of the chest X-ray, electrocardiogram and echocardiogram of patients are shown in Table 4. The chest X-rays were characterized by a slight dilatation of the heart and congestion of the lungs and approximately 80% of patients showed either sinus tachycardia or complete atrioventricular block on the ECG. Abnormal Q, poor r-progression and low voltage were common findings in addition to an ST-T abnormality on admission. The echocardiogram showed left ventricular dysfunction, slight hypertrophy and pericardial effusion without dilatation of the left atrium or ventricle. Table 5 shows the arterial blood gas analysis, full blood count and biochemical examination on admission. Most patients showed respiratory compensation of the metabolic acidosis, markedly increased leukocytes (WBC), increased myocardial releasing enzymes, renal dysfunction, hyponatraemia and increased C-reactive protein (CRP). One-third of the patients had thrombopenia. In particular, qualitative and quantitative analysis of troponin T (TNT) was more useful than creatine kinase (CK), because 19 (57.6%) of 33 patients who had TNT confirmed on admission did not show significant increases of CK or creatine kinase-MB (CK-MB). With

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- (3) Arterial blood gas analysis: pH, BE
 - (4) ETCO_2 (end-tidal carbon dioxide partial pressure)
 - (5) Full blood count: WBC, Plt
 - (6) Blood biochemical examination: TB, AST (GOT), ALT (GPT), LDH, CK, CK-MB, TNT, AMY, BUN, Cr, UA, Na, K, Cl, Glu, LA, CRP
 - (7) ACT (activated clotting time)
 - (8) Chest X-ray: CTR
 - (9) Echocardiogram: %FS, EF, ET, IVSth, PWth, LAD, LVDd, LVDs, pericardial effusion
 - (10) Instructions of cardiovascular drugs: dosages of NA (noradrenaline), DOA (dopamine), DOB (dobutamine)
 - (11) Control flow rate of PCPS

9. Data at termination of PCPS:

- (1) Vital signs: BP, HR, BP
- (2) Swan-Ganz catheter: PAs/d, CVP, PCWP, CI, SVI, SVO₂
- (3) Arterial blood gas analysis: pH, BE, PaCO_2 (arterial blood carbon dioxide partial pressure)
- (4) ETCO_2
- (5) Blood biochemical examination: TB, AST (GOT), ALT (GPT), LDH, CK, CK-MB, TNT, AMY, BUN, Cr, UA, Na, LA, CRP
- (6) Echocardiogram: %FS, EF, ET (ejection time), IVSth, PWth, LAD, LVDd, LVDs
- (7) Instructions of cardiovascular drugs: dosages of NA, DOA, DOB

10. Administration of cardiovascular drugs

III. Condition on discharge.

1. NYHA functional classification
2. Instructions of cardiovascular drugs

IV. Long-term evaluation of patients treated with PCPS.

1. Age, sex
 2. Prognosis
 3. Clinical course after discharge:
 - (1) Physical findings: BP, HR
 - (2) NYHA functional classification
 - (3) Full blood count: WBC
 - (4) Blood biochemical examination: AST (GOT), LDH, CK or CK-MB, TNT, CRP
 - (5) Chest X-ray: CTR
 - (6) Electrocardiogram: rhythm, arrhythmia, ST-T abnormality, abnormal Q, low voltage, poor r progression, right or left bundle branch block
 - (7) Holter electrocardiogram
 - (8) Echocardiogram: %FS, EF, IVSth, PWth, LVDd, pericardial effusion
 - (9) SPECT (single photon emission computed tomography)
 - (10) Cardiac catheterization, endomyocardial biopsy
 - (11) Instructions of cardiovascular drugs
 - (12) Readmission
 - (13) Cardiac event
 - (14) Autopsy
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the paired serum samples, a fluctuation of 4-fold the virus antibody titer was revealed in 14 (26.9%) of 52 patients. In 28 (65.1%) of 43 patients cardiac catheterization was performed within 10 days of admission (Table 6), and a definitive diagnosis was made by endomyocardial biopsy.

The total time required for setting up the PCPS was 186.9 ± 134.4 h (7.8 ± 5.6 days) and there was no significant difference in the time required between the groups.

Comparison of Survivors and Non-Survivors

The patients who survived ($n=31$), including the one non-rehabilitated patient, were compared with the patients who did not ($n=21$) (Table 7). However, there were items that could not be compared by date by a statistical method because of insufficient data: lactic acid (LA), uric acid (UA), ejection time (ET) and arterial blood carbon dioxide partial pressure (PaCO_2). Non-survivors had a lower heart rate on admission and CK before undergoing PCPS, circulatory disturbances of the legs and multiple organ failure (MOF) associated with PCPS, maximum dosage of noradrenaline (NA) during PCPS, steroid pulse therapy or continuous hemofiltration (CHF) as concurrent treatments, the number of exchanges of PCPS, WBC, total bilirubin (TB), lactate dehydrogenase (LDH), CK-MB, TNT and blood urea nitrogen (BUN) during PCPS were significantly

higher than those of the survivors. In the patients who survived, the number given phentolamine mesylate (PM) during PCPS, and the maximum percent left ventricular fractional shortening (%FS) and ejection fraction (EF) were significantly higher than for the non-survivors.

Comparison of the Patient Groups That Underwent PCPS for Low Output Syndrome (LOS) and Life-Threatening Arrhythmia (LTA)

The LOS patient group ($n=28$) included those who, despite cardiotonic or vasopressor drugs and IABP treatment, did not recover from the circulatory failure and then underwent PCPS. Those who did not recover from cardiac arrest or LTA despite every possible treatment and who then underwent PCPS were defined as the LTA group ($n=24$). There were no significant differences other than those shown in Table 8 between the 2 groups, but because of insufficient data, 2 items could not be compared by date by a statistical method: UA and ET. The severity of nausea and vomiting as the cardinal symptoms and the maximum left ventricle end-diastolic dimension (LVDd) during PCPS were higher in the LTA patients than in the LOS patients. The minimum EF during PCPS in the LOS patients was lower than that of the LTA patients.

Table 2 Outline and Clinical Characteristics of the Enrolled Patients

Total no.	52
Age (years)	47.9±16.0
M/F	26/26
Etiology	
Idiopathic	34 (65.4%)
Viral	14 (26.9%)
Eosinophilic	2 (3.8%)
Giant cell	2 (3.8%)
Definitive diagnosis	
Endomyocardial biopsy	43
Autopsy	10
Survivors	
Rehabilitation	30 (57.7%)
Non-rehabilitation	1 (1.95%)
Non-survivors	21 (40.4%)
BP on admission (n=48)	84.4±37.9/50.6±28.6 mmHg
SBP ≥90 mmHg	23 (47.9%)
SBP <90 mmHg	25 (52.1%)
HR on admission (n=47)	91.8±33.1 beats/min
≥100 beats/min	22 (46.8%)
<60 beats/min	7 (14.9%)
Temporary pacemaker	6 (12.8%)
BT on admission (n=38)	36.6±1.2 °C
≥37 °C	14 (36.8%)
<36 °C	12 (31.5%)
Consciousness on admission	
Clear	33 (80.5%)
Semi-conscious	5 (12.2%)
Coma	2 (4.9%)
NYHA (n=37)	
I	1 (2.7%)
II	0
III	2 (5.4%)
IV	34 (91.9%)

Data are mean±SD or number of patients (%). n, total number of patients with confirmed data; BP, blood pressure; SBP, systolic blood pressure; HR, heart rate; BT, body temperature; NYHA, New York Heart Association.

Comparison of the Survivors and Non-Survivors in the LOS Group

The survivors (n=20) and non-survivors (n=8) were compared and the significant differences are shown in Table 9. However, the items that could not be compared by date by a statistical method because of insufficient data were: LA, UA, TNT, central venous pressure (CVP), cardiac index (CI) and pulmonary capillary wedge pressure (PCWP), stroke volume index (SVI), cardiothoracic rate (CTR), end-tidal carbon dioxide partial pressure (ETCO₂), PaCO₂, and echocardiographic data. The level of LDH and CK before undergoing PCPS, circulatory disturbances of the legs, MOF and disseminated intravascular coagulation (DIC) associated with PCPS, and maximum level of WBC, CK-MB and serum creatinine (Cr) during PCPS were higher in the non-survivors than in the patients who survived. In addition, the initial flow rate of PCPS and the minimum of pH during PCPS were lower in the patients who did not survive, and furthermore in the post-PCPS patients, the doses of dobutamine (DOB) (p=0.005) and Cr (p=0.013) were higher in the patients who did not survive than in those who did at the time of completion of PCPS.

Comparison of the Survivors and Non-Survivors in the LTA Group

The survivors (n=11) were compared with non-survivors (n=13) and the significant differences are shown in Table 10. However, because of insufficient data, the following items could not be compared by date by a statistical method: LA,

Table 3 Initial and Cardinal Symptoms

Initial symptoms	(n=52)
Increased fever	32 (61.5%)
General fatigue	12 (23.1%)
Cough	11 (21.2%)
Nausea/vomiting	8 (15.4%)
Arthralgia/myalgia	6 (11.5%)
Headache	6 (11.5%)
Chest pain	3 (5.8%)
Syncope/cramp	3 (5.8%)
Diarrhea	3 (5.8%)
Appetite loss	3 (5.8%)
Pharyngalgia	2 (3.8%)
Palpitation	2 (3.8%)
Abdominal pain	1 (1.9%)
Epigastralgia	1 (1.9%)
Back pain	1 (1.9%)
Dyspnea	1 (1.9%)
Chest discomfort	1 (1.9%)
Common cold	1 (1.9%)
Cardinal symptoms	(n=51)
Dyspnea	20 (39.2%)
Shock	15 (29.4%)
Nausea/vomiting	11 (21.6%)
Increased fever	11 (21.6%)
Syncope/cramp	10 (19.6%)
Chest pain	9 (17.6%)
General fatigue	6 (11.8%)
Abdominal pain	3 (5.9%)
Diarrhea	2 (3.9%)
Palpitation	2 (3.9%)
Coughing	1 (2.0%)
Cyanosis	1 (2.0%)
Headache	1 (2.0%)
Cardiopulmonary arrest	1 (2.0%)
Epigastralgia	1 (2.0%)
Back pain	1 (2.0%)

Number of patients (%).

UA, TNT, mixed venous blood oxygen saturation (SVO₂), CI, ETCO₂, PaCO₂, and ET. In the non-survivors, the period from admission to starting PCPS, the calcium level (Ca) on admission, circulatory disturbances of the legs and MOF associated with PCPS, maximum BUN and Cr during PCPS, the maximum dosage of NA during PCPS, and the number of patients requiring nafamostat during PCPS, γ globulin therapy or CHF as concurrent treatments were higher than in the survivors. The number of patients given PM during PCPS was higher in the survivors than non-survivors. Furthermore, comparison between survivors and non-survivors in the post-PCPS patients showed that CI (p=0.039) and PCWP (p=0.020) were lower in the non-survivors than survivors at the time of PCPS completion. However, CI and PCWP were unrelated to each other. The level of alanine aminotransferase (ALT [glutamic pyruvic transaminase: GPT]) (p=0.007), aspartate aminotransferase (AST [glutamic oxaloacetic transaminase: GOT]) (p=0.015) and BUN (p=0.020) in the non-survivors was higher than in the survivors at the time of PCPS completion.

Comparison of Patients Who Could and Those Who Could Not Be Weaned Off PCPS

Patients who could (n=42) and those who could not (n=10) be weaned off PCPS were compared and the significant differences are shown in Table 11. However, because of insufficient data, the items that could not be compared by date by a statistical method were as follows: LA and TNT, CVP and SVO₂, SVI and CVP, and CTR. In those

Table 4 Results of Chest X-Ray, Electrocardiography and Echocardiography on Admission

<i>Chest X-ray</i>	
CTR (n=33)	55.2±5.7%
CTR <50%	5 (15.2%)
Congestion of the lung (n=31)	22 (71.0%)
<i>Electrocardiogram</i>	
Sinus tachycardia (n=48)	20 (41.7%)
Complete atrioventricular block (n=48)	16 (35.4%)
First or second degree atrioventricular block (n=48)	4 (8.3%)
Ventricular tachycardia (n=48)	3 (6.3%)
Atrioventricular junctional rhythm (n=48)	2 (4.2%)
Atrial fibrillation (n=48)	2 (4.2%)
Cardiac arrest (n=48)	1 (2.1%)
Bigeminy (n=48)	1 (2.1%)
ST-T abnormality (n=27)	27 (100%)
Abnormal Q (n=25)	20 (80.0%)
Low voltage (n=31)	18 (58.1%)
Poor r progression (n=17)	16 (94.1%)
Right bundle branch block (n=31)	9 (29.0%)
Left bundle branch block (n=29)	5 (17.2%)
<i>Echocardiogram</i>	
Diffuse-severe hypokinesis (n=41)	19 (46.3%)
Diffuse hypokinesis (n=41)	17 (41.5%)
Slightly hypokinesis (n=41)	1 (2.4%)
Regional asynergy (n=41)	3 (7.3%)
Normal (n=41)	1 (2.4%)
%FS (n=19)	13.9±6.2
EF (n=24)	37.1±12.8%
IVSth (n=30)	11.6±2.6 mm
PWth (n=30)	12.0±2.5 mm
IVSth or PWth >12 mm	20 (66.7%)
LAD (n=19)	32.5±8.2 mm
LAD >40 mm	3 (15.8%)
LVDd (n=26)	47.3±9.3 mm
LVDd >55 mm	3 (11.5%)
LVDs (n=22)	39.7±9.0 mm
Pericardial effusion (n=41)	36 (87.8%)

Data are mean±SD or number of patients (%). n, total number of patients with confirmed data; CTR, cardiothoracic ratio; %FS, percent left ventricular fractional shortening; EF, left ventricular ejection fraction; IVSth, interventricular septum thickness; PWth, posterior wall thickness; LAD, left atrial dimension; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension.

patients who could not be weaned off, the levels of CK-MB before undergoing PCPS, and circulatory disturbances of the legs and MOF associated with PCPS, and maximum AST, ALT, LDH, CK, CK-MB, Cr, EF and activated clotting time (ACT) during PCPS, and the maximum dosage of NA during PCPS, and the number of patients given isosorbide dinitrate (ISDN) during PCPS, and CHF as concurrent treatment, and minimum flow rate of PCPS were higher, and minimum pH, base excess (BE) and BPs during PCPS were lower than in those patients who could.

Comparison of the Survivors and Non-Survivors in the Post-PCPS Patients

Survivors (n=31) and non-survivors (n=11) in post-PCPS patients were compared and the significant differences are shown in Table 12. However, because of insufficient data, the items that could not be compared by date by a statistical method were: LA, UA, SVO₂, SVI, TNT, PaCO₂ and ET. In the non-survivors, low voltage on admission, and circulatory disturbances of the legs and MOF associated with PCPS, and maximum levels of BUN and Cr during PCPS, and AST, ALT, BUN and Cr were higher and the initial flow rate of PCPS, PCWP and CK were lower than those of

Table 5 Arterial Blood Gas Analysis, Full Blood Count and Biochemistry on Admission

<i>Arterial blood gas analysis</i>	
pH (n=41)	7.423±0.096
BE (n=39)	-4.4±5.9 mmol/L
<i>Full blood count</i>	
WBC (n=46)	12.165±13.242×10 ³
Hb (n=46)	12.8±2.2 g/dl
Plt (n=45)	17.3±8.6×10 ⁴
<i>Blood biochemistry</i>	
TB (n=40)	0.84±0.56 mg/dl
AST (GOT) (n=46)	1,102±1,900 IU/L
ALT (GPT) (n=45)	743±1,135 IU/L
LDH (n=45)	2,718±3,910 IU/L
CK (n=44)	1,049±1,071 IU/L
CK-MB (n=33)	97.0±89.1 IU/L
TNT (n=11)	14.13±15.45 ng/dl
AMY (n=23)	118.1±111.1 IU/L
BUN (n=45)	33.2±15.5 mg/dl
Cr (n=45)	1.35±0.67 mg/dl
Na (n=45)	132.7±6.9 mmol/L
K (n=46)	4.5±0.8 mmol/L
CRP (n=31)	6.11±5.51 mg/dl

Data are mean±SD. n, total number of patients with confirmed data; BE, base excess; WBC, leukocyte; Hb, hemoglobin; Plt, platelet; TB, total bilirubin; AST (GOT), aspartate aminotransferase (glutamic oxaloacetic transaminase); ALT (GPT), alanine aminotransferase (glutamic pyruvic transaminase); LDH, lactate dehydrogenase; CK, creatine kinase; CK-MB, creatine kinase-MB; TNT, troponin T; AMY, amylase; BUN, blood urea nitrogen; Cr, serum creatinine; Na, sodium; K, potassium; CRP, c-reactive protein.

Table 6 Cardiac Catheterization (n=43)

<i>Normal coronary arteries (n=35)</i>		35
PAs/d (n=14)	29.5±8.4/16.1±6.2 mmHg	
CVP (n=8)	13.4±4.5 mmHg	
PCWP (n=15)	19.1±8.6 mmHg	
CI (n=14)	2.16±0.72 L·min ⁻¹ ·m ⁻²	
<i>Forrester subset (n=11)</i>		
I	2 (18.2%)	
II	1 (9.1%)	
III	1 (9.1%)	
IV	7 (63.6%)	

Data are mean±SD or number of patients (%). n, total number of patients with confirmed data; PAs/d, pulmonary artery systolic/diastolic pressure; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; CI, cardiac index.

survivors at the time of PCPS completion.

Long-Term Prognosis

The 30 survivors who returned to normal life (n=30) comprised the study group (Table 13). In the average follow-up period of 962 days, the readmission rate was 10%, exacerbation rate 3.3%, and mortality was 10% (Table 14).

Of the readmitted patients (n=3), 2 had congestive heart failure and 1 had recurrence of the myocarditis. All readmitted patients had abnormally increased WBC and CRP during follow-up; one showed poor r-progression on the ECG, a decrease of EF on the echocardiogram and exacerbation of ¹²³I-metaiodobenzyl-guanidine (MIBG) and ¹²³I-β-methyl-iodophenyl pentadecanoic acid (BMIPP) on single photon emission computed tomography (SPECT), and 2 showed dilatation of LVDd on the echocardiogram. Of the non-survivors (n=3), 2 died of congestive heart failure, and 1 died of exacerbation of rheumatoid arthritis.

Concerning medication, 12 patients had none at dis-

Table 7 Comparison of Survivors and Non-Survivors

	Surviving patients	Non-surviving patients	p value
HR on admission (beats/min)	100.0±29.4 (n=27)	80.8±36.7 (n=20)	0.008
CK before PCPS starting (IU/L)	944.0±880.3 (n=26)	1734.8±1545.7 (n=18)	0.037
Complications associated with PCPS			
Circulatory disturbances of the legs	2 (n=29)	10 (n=21)	0.0009
MOF	0 (n=29)	13 (n=21)	8.0×10 ⁻⁷
Maximum dosage of NA during PCPS (μg)	0.14±0.37 (n=28)	0.91±1.68 (n=17)	0.023
Administration of PM during PCPS	10 (n=16)	2 (n=11)	0.020
Steroid pulse therapy	6 (n=25)	10 (n=17)	0.023
CHF	8 (n=24)	15 (n=21)	0.011
Exchange of PCPS	3 (n=15)	7 (n=11)	0.024
Data during PCPS			
Maximum of %FS	22.5±2.4 (n=14)	16.5±15.2 (n=7)	0.033
Maximum of EF (%)	46.5±13.2 (n=15)	27.3±8.5 (n=7)	0.004
Maximum of WBC (×10 ³)	16.7±5.2 (n=29)	25.0±12.6 (n=16)	0.006
Maximum of TB (mg/dl)	4.47±5.61 (n=29)	7.54±6.98 (n=15)	0.016
Maximum of LDH (IU/L)	5,020±6,568 (n=29)	11,912±12,813 (n=19)	0.031
Maximum of CK-MB (IU/L)	97±90 (n=21)	248±246 (n=13)	0.020
Maximum of TNT (ng/dl)	3.56±3.62 (n=3)	43.34±6.60 (n=3)	0.0495
Maximum of BUN (mg/dl)	48.3±30.0 (n=29)	78.1±37.8 (n=19)	0.014

Data are mean±SD or number of patients. n, total number of patients with confirmed data; HR, heart rate; CK, creatine kinase; MOF, multiple organ failure; NA, noradrenaline; PM, phentolamine mesylate; CHF, continuous hemofiltration; %FS, percent left ventricular fractional shortening; EF, left ventricular ejection fraction; WBC, leukocyte; TB, total bilirubin; LDH, lactate dehydrogenase; CK-MB, creatine kinase-MB; TNT, troponin T; BUN, blood urea nitrogen.

Table 8 Comparison of LOS and LTA Groups

	LOS patients	LTA patients	p value
Nausea and vomiting	1 (n=27)	11 (n=23)	0.0004
Data during PCPS			
Maximum of LVDd (mm)	52.5±6.5 (n=17)	55.5±8.0 (n=12)	0.034
Minimum of EF (%)	17.8±16.8 (n=13)	18.7±10.2 (n=11)	0.018

Data are mean±SD or number of patients. n, total number of patients with confirmed data; LVDd, left ventricular end-diastolic dimension; EF, left ventricular ejection fraction.

Table 9 Comparison of Survivors and Non-Survivors in the LOS Group

	Surviving patients (n=20)	Non-surviving patients (n=8)	p value
Data before undergoing PCPS			
LDH (IU/L)	2,428±2,850 (n=19)	2,953±2,426 (n=6)	0.0486
CK (IU/L)	972±993 (n=19)	2,022±1,773 (n=6)	0.0417
Initial flow rate of PCPS (L/min)	2.894±0.684 (n=20)	2.225±0.388 (n=8)	0.0236
Complications associated with PCPS			
Circulatory disturbances of the legs	1 (n=18)	4 (n=8)	0.008
MOF	0 (n=18)	6 (n=8)	0.00003
DIC	1 (n=18)	3 (n=8)	0.022
Data during PCPS			
Minimum of pH	7.380±0.085 (n=13)	7.214±0.142 (n=7)	0.007
Maximum of WBC (×10 ³)	17.122±5.030 (n=18)	27.351±12.080 (n=7)	0.034
Maximum of CK-MB (IU/L)	93±81 (n=14)	371±278 (n=7)	0.007
Maximum of Cr (mg/dl)	1.50±0.67 (n=18)	4.53±1.33 (n=8)	0.002

Data are mean±SD or number of patients. n, total number of patients with confirmed data; LDH, lactate dehydrogenase; CK, creatine kinase; MOF, multiple organ failure; DIC, disseminated intravascular coagulation; pH, arterial pH; WBC, leukocyte; CK-MB, creatine kinase-MB; Cr, serum creatinine.

charge, and 5 discontinued medication during follow-up. None of these 17 patients were readmitted, died or had a recurrence of myocarditis during follow-up.

Discussion

Clinical Features, Clinical Course and Prognosis of the Patients Treated With PCPS

Fever, general fatigue, coughing, nausea or vomiting,

arthralgia or myalgia and headaches were often the initial symptoms and particular attention should be paid to patients with the common cold accompanied by general fatigue or digestive symptoms. Of the cardinal symptoms, the most frequent were dyspnea, shock, nausea or vomiting, fever, syncope or cramps, chest pain and general fatigue. The period from onset to admission was 4.67 days and most patients rapidly developed severe peripheral circulatory failure, cardiac arrest or LTA. Of the vital signs on admis-

Table 10 Comparison of Survivors and Non-Survivors in the LTA Group

	Surviving patients (n=11)	Non-surviving patients (n=13)	p value
Period from admission to starting PCPS (days)	0.27±0.47 (n=11)	1.76±2.49 (n=13)	0.046
Ca on admission	6.85±1.53 (n=6)	8.33±0.13 (n=4)	0.011
Complications associated with PCPS			
Circulatory disturbances of the legs	1 (n=11)	6 (n=13)	0.047
MOF	0 (n=11)	7 (n=13)	0.004
Data during PCPS			
Maximum of BUN (mg/dl)	44.8±33.6 (n=11)	73.8±41.7 (n=11)	0.045
Maximum of Cr (mg/dl)	1.58±1.03 (n=11)	2.94±1.63 (n=11)	0.020
Maximum dosage of NA (μg)	0.02±0.06 (n=10)	0.39±0.39 (n=10)	0.049
Administration of nafamostat	3 (n=3)	2 (n=3)	0.029
γ globulin therapy	0 (n=11)	3 (n=9)	0.038
CHF	2 (n=8)	9 (n=13)	0.049
Administration of PM during PCPS	4 (n=5)	1 (n=6)	0.036

Data are mean±SD or number of patients. n, total number of patients with confirmed data; Ca, calcium; MOF, multiple organ failure; BUN, blood urea nitrogen; Cr, serum creatinine; NA, noradrenaline; CHF, continuous hemofiltration; PM, phentolamine mesylate.

Table 11 Comparison of Patients Who Could and Could Not Be Weaned Off PCPS

	Potential patients (n=42)	Non-potential patients (n=10)	p value
CK-MB before PCPS starting (IU/L)	134±262 (n=27)	250±118 (n=3)	0.041
Complications associated with PCPS			
Circulatory disturbances of the legs	6 (n=40)	6 (n=10)	0.003
MOF	5 (n=40)	8 (n=10)	0.00001
Data during PCPS			
Minimum of pH	7.362±0.096 (n=33)	7.227±0.149 (n=6)	0.032
Minimum of BE	-3.11±5.77 (n=31)	-11.7±8.70 (n=6)	0.021
Maximum of AST (GOT) (IU/L)	2,298±4,796 (n=39)	8,519±7,639 (n=9)	0.007
Maximum of ALT (GPT) (IU/L)	1,376±2,278 (n=39)	3,553±2,548 (n=7)	0.009
Maximum of LDH (IU/L)	5,682±8,017 (n=39)	16,702±13,126 (n=9)	0.010
Maximum of CK (IU/L)	6,137±11,157 (n=39)	9,324±9,116 (n=8)	0.015
Maximum of CK-MB (IU/L)	129±159 (n=29)	302±239 (n=5)	0.024
Maximum of Cr (mg/dl)	2.08±1.54 (n=39)	3.55±1.29 (n=9)	0.010
Maximum of EF (%)	20.6±13.7 (n=20)	6.5±7.9 (n=4)	0.006
Maximum of ACT (s)	294±80 (n=33)	378±152 (n=7)	0.046
Maximum dosage of NA (μg)	0.26±0.47 (n=38)	1.38±2.58 (n=7)	0.017
Administration of ISDN	12 (n=22)	0 (n=5)	0.027
CHF	15 (n=35)	8 (n=10)	0.038
Minimum flow rate of PCPS (L/min)	0.98±0.57 (n=38)	2.29±0.94 (n=9)	0.010
Minimum BPs during PCPS (mmHg)	86±16 (n=35)	55±19 (n=8)	0.027

Data are mean±SD or number of patients. n, total number of patients with confirmed data; CK-MB, creatine kinase-MB; MOF, multiple organ failure; pH, arterial pH; BE, base excess; AST (GOT), aspartate aminotransferase (glutamic oxaloacetic transaminase); ALT (GPT), alanine aminotransferase (glutamic pyruvic transaminase); LDH, lactate dehydrogenase; CK, creatine kinase; Cr, serum creatinine; EF, left ventricular ejection fraction; ACT, activated clotting time; NA, noradrenaline; ISDN, isosorbide dinitrate; CHF, continuous hemofiltration; BPs, systolic blood pressure.

sion, half of the patients had a SBP less than 90 mmHg, and approximately 60% of the patients had either tachycardia or bradycardia. The ECG on admission revealed that approximately 80% of patients had either sinus tachycardia or complete atrioventricular block, and an ST-T abnormality, abnormal Q wave, low voltages or poor r-progression were often present as well. On the chest X-ray on admission, about 70% of the patients showed congestion of the lungs and slight dilatation of the heart. Echocardiography showed left ventricular dysfunction, slight hypertrophy and pericardial effusion without dilatation of the left atrium or ventricle. Arterial blood gas analysis, full blood count and biochemical examination revealed that respiratory compensation for the metabolic acidosis, markedly increased WBC, increased myocardial releasing enzyme, renal dysfunction, hyponatraemia and increased CRP were common findings.

Even if the vital signs are stable on admission, a few patients can suddenly LOS or LTA, so it is necessary to closely observe all such patients with periodic Swan-Ganz catheterization, ECG, echocardiography, full blood count and blood biochemistry, and to prepare for life-support systems. It is important to rapidly confirm the diagnosis with coronary angiography and endomyocardial biopsies, without jeopardizing the patient's clinical condition, because a positive indication for mechanical cardiopulmonary support is required to avoid overuse and a possible negative result.

Comparison Between Each Patient Group and the Prognosis Relation Factor

Differences Between Survivors and Non-Survivors The differences can be summarized as follows.

Table 12 Comparison of Survivors and Non-Survivors in the Post-PCPS Group

	Surviving patients (n=31)	Non-surviving patients (n=11)	p value
Low voltage on admission	13 (n=19)	1 (n=7)	0.009
Initial flow rate of PCPS (L/min)	2.894±0.708 (n=30)	2.390±0.797 (n=11)	0.031
Complications associated with PCPS			
Circulatory disturbances of the legs	2 (n=29)	4 (n=11)	0.020
MOF	0 (n=29)	5 (n=11)	0.0001
Data during PCPS			
Maximum of BUN (mg/dl)	48.3±30.0 (n=29)	89.1±47.2 (n=10)	0.034
Maximum of Cr (mg/dl)	1.53±0.81 (n=11)	3.67±2.04 (n=10)	0.008
Data at the time of the cessation from PCPS			
PCWP (mmHg)	14.5±7.1 (n=10)	4.7±0.6 (n=3)	0.043
AST (GOT) (IU/L)	153±183 (n=26)	193±147 (n=7)	0.028
ALT (GPT) (IU/L)	203±297 (n=25)	239±353 (n=7)	0.026
CK (IU/L)	893±1,987 (n=24)	193±147 (n=7)	0.023
BUN (mg/dl)	38.8±33.2 (n=25)	76.1±45.2 (n=7)	0.034
Cr (mg/dl)	1.17±0.69 (n=24)	2.94±1.89 (n=7)	0.018

Data are mean±SD or number of patients. n, total number of patients with confirmed the data; MOF, multiple organ failure; BUN, blood urea nitrogen; Cr, serum creatinine; PCWP, pulmonary capillary wedge pressure; AST (GOT), aspartate aminotransferase (glutamic oxaloacetic transaminase); ALT (GPT), alanine aminotransferase (glutamic pyruvic transaminase); CK, creatine kinase.

(1) The occurrence of complications associated with PCPS, especially circulatory disturbances of the legs and MOF, affect the prognosis, and symptomatic treatment for MOF was frequently performed in the non-survivors.

(2) The myocardial damage in the non-survivors was more severe than in the survivors.

(3) The improvement of left ventricular contractility during PCPS in the survivors was better than in the non-survivors.

(4) In the non-survivors, steroid pulse therapy was frequently administered as a concurrent treatment, but whether it made the myocarditis worse or not was uncertain.

Differences Between the Survivors and Non-Survivors in Each Group Classified by Indication for PCPS The differences between the survivors and non-survivors in the LOS group are summarized as follows.

(1) In the non-survivors, LDH and CK before undergoing PCPS were higher than in the survivors. High levels of LDH and CK in LOS patients before undergoing PCPS were reliable indicators of a poor prognosis.

(2) In the non-survivors, it was necessary to frequently adjust the support flow rate during PCPS to that which would facilitate recovery from circulatory failure.

(3) The occurrence of complications associated with PCPS, especially circulatory disturbances of the legs and MOF, affected the prognosis.

(4) The myocardial damage in the non-survivors was more severe than in the survivors.

The differences between the survivors and non-survivors in the LTA group are as follows.

(1) The occurrence of complications associated with PCPS, especially circulatory disturbances of the legs and MOF, affected the prognosis, and symptomatic treatment and CHF or nafamostat for MOF were more frequently required by non-survivors.

(2) In the non-survivors, γ globulin therapy was frequently required as a concurrent treatment, but whether it made the myocarditis worse or not was uncertain.

Differences Between Patients Who Could and Could Not Be Weaned Off PCPS The differences are summarized as follows.

(1) The occurrence of complications associated with PCPS, especially circulatory disturbances of the legs and

MOF, affected the prognosis, and symptomatic treatment for MOF was frequently performed in the patients who could not be weaned off PCPS.

(2) Myocardial damage in the patients who could not be weaned off PCPS was more severe than in the patients who could complete PCPS.

(3) Improvement of EF during PCPS in the patients who could complete PCPS was better than in the patients who could not.

Differences Between the Survivors and Non-Survivors in the Post-PCPS Patient Group The differences are summarized as follows.

(1) In the non-survivors, it was necessary to frequently adjust the support flow rate that facilitated recovery from circulatory failure.

(2) The occurrence of complications associated with PCPS, especially circulatory disturbances of the legs and MOF, affected the prognosis.

(3) Renal dysfunction during PCPS in the non-survivors was more serious than in the survivors.

Noteworthy factors concerning the prognosis are as follows.

(1) The severity and level of improvement of cardiac and renal dysfunction.

(2) Adjustment of the support flow rate.

(3) Prevention of circulatory disturbances of the legs and MOF.

Therapeutic Guidelines for the Use of PCPS for Fulminant Myocarditis

Based on the results of the survey, management guidelines for using PCPS to improve the survival rate of fulminant myocarditis patients were discussed and proposed (Fig 1). In addition, these guidelines were based on recent data of 40 fulminant myocarditis patients treated with PCPS from Japan and overseas¹⁻¹³. The fundamental concepts were appropriate adjustment of the support flow rate that would facilitate recovery from circulatory failure while constantly checking certain indicators of circulatory failure and cardiac function, and prevention of complications associated with PCPS.

The indications for PCPS for fulminant myocarditis

Table 13 Outline and Clinical Characteristics of Patients Investigated for Long-Term Prognosis

Total number of patients	30	
Age (years)	49.5±12.8	
M/F	13/17	
Follow-up period (days)	961.6±780.0	
Etiology		
Idiopathic	21 (70.0%)	
Viral	8 (26.7%)	
Eosinophilic	1 (3.3%)	
	On discharge	On last examination
NYHA functional class		
I	24 (80.0%)	23 (76.7%)
II	4 (13.3%)	1 (3.3%)
III	1 (3.3%)	0
IV	0	1 (3.3%)
Unknown	1 (3.3%)	5 (16.7%)
Chest X-ray		
CTR (%)	47.7±5.7 (n=24)	48.2±5.1 (n=23)
Echocardiogram		
Wall thickness (mm)	10.2±1.5 (n=19)	9.6±1.4 (n=25)
LVDd (mm)	47.0±6.6 (n=18)	48.2±8.6 (n=25)
LVDs (mm)	30.9±7.6 (n=18)	32.2±7.0 (n=25)
EF (%)	60.4±14.0 (n=18)	60.6±10.0 (n=21)
Abnormally increased data		
WBC	4 (n=25)	
AST (GOT)	3 (n=26)	
LDH	2 (n=26)	
CK	1 (n=26)	
CRP	3 (n=20)	
ANP	1 (n=10)	
BNP	2 (n=10)	
Electrocardiogram		
De novo LVH	2 (n=28)	
De novo poor r progression	1 (n=28)	
Appearance of negative T-wave	1 (n=28)	
Disappearance of negative T-wave	2 (n=28)	
Single photon emission computed tomography		
MIBG		
Restoration	3 (n=5)	
Exacerbation	2 (n=5)	
BMIPP		
Exacerbation	1 (n=2)	
Unchanged	1 (n=2)	
Medication		
No medication on discharge	12 (n=30)	
Discontinuance during follow-up	5 (n=18)	
Continued medication		
Digoxin	4	
Ubidecarenone	4	
ACE inhibitor	12	
Ang-II receptor antagonist	1	
Diuretic	8	
Ca-antagonist	3	
β-blockade	5	
Anti-arrhythmic agent	2	

Data are mean±SD or number of patients (%). n, total number of patients with confirmed data; CTR, cardiothoracic ratio; wall thickness, average value of interventricular septum and posterior left ventricular wall thickness; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; EF, left ventricular ejection fraction; WBC, leukocyte; AST (GOT), aspartate aminotransferase (glutamic oxaloacetic transaminase); LDH, lactate dehydrogenase; CK, creatine kinase; CRP, c-reactive protein; ANP, atrial natriuretic polypeptide; BNP, brain natriuretic peptide; LVH, left ventricular hypertrophy; MIBG, I-123-metaiodobenzyl-guanidine; BMIPP, I-123-β-methyl-iodophenyl pentadecanoic acid; ACE, angiotensin converting enzyme; Ang-II, angiotensin II.

were ultimately the development of LTA or LOS, especially those patients who did not recover from cardiac arrest or LTA despite every possible treatment. However, the decision to use PCPS should be made with consideration of the quality of resuscitation in cases of cardiopulmonary arrest that occurred pre-admission. The indication for PCPS in LOS has not been clearly determined yet, so it is important to base the decision on the indicators of circu-

Table 14 Rates of Readmission, Mortality and Recurrence of Patients Investigated for Long-Term Prognosis

Readmission rate	3 (10.0%)
Mortality	3 (10.0%)
Recurrence rate	1 (3.3%)

Data are number of patients (%).

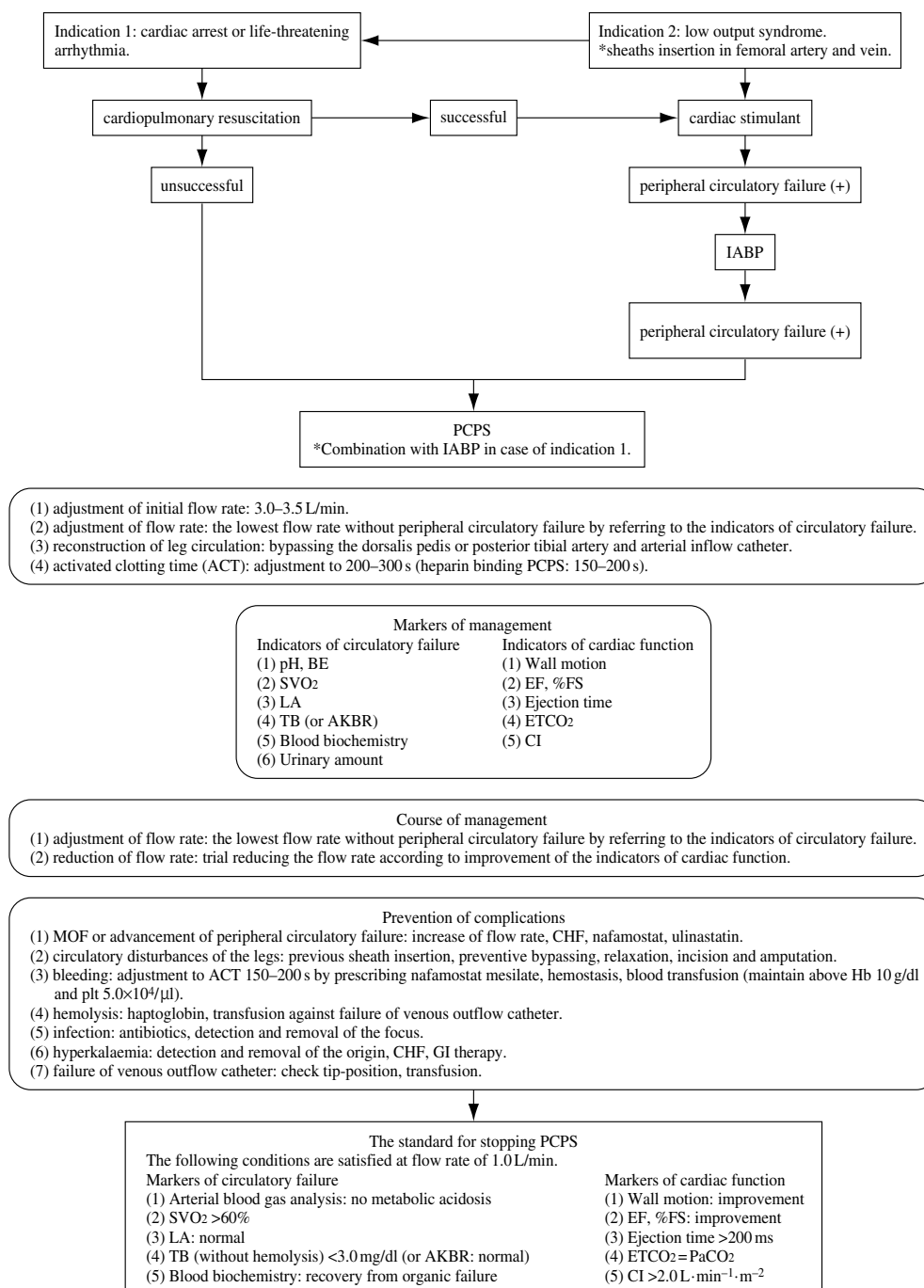


Fig 1. The guidelines of PCPS for acute fulminate myocarditis.

latory failure; that is, if despite cardiogenic or vasopressor drugs and IABP treatment, the patient does not recover from circulatory failure, PCPS should be instituted. Overuse or using PCPS without following this procedure must be avoided, because complications associated with PCPS often become the cause of death.

The initial flow rate is usually 3–3.5 L/min, and then the support flow rate that induces recovery from circulatory failure is determined by referring to the indicators of circulatory failure. After recovery, the lowest flow rate without circulatory failure is usually recommended for possible long-term use. In LOS patients, the initial flow rate in the non-survivors was lower than in the survivors and further-

more, in the post-PCPS patients, renal dysfunction during PCPS in the non-survivors was more serious than in the survivors, and the initial flow rate in the non-survivors was lower than in the survivors. It is paramount to prevent renal dysfunction and MOF by setting the correct initial flow rate.

The present investigation made clear that patients with circulatory disturbances of the legs or MOF associated with PCPS had a poor prognosis. Delay in instituting PCPS or managing the non-recovery from shock often led to MOF. It is necessary to shorten the period of shock, to decide the indication for PCPS appropriately and to correctly adjust the support flow rate. The circulatory disturbances of the

Table 15 Usefulness of the Guidelines in Each Group

	Excellent	Poor	Unknown	p value
Survivors (n=31)	25	2	4	0.000002
Non-survivors (n=21)	4	17	0	
LOS				
Survivors (n=20)	16	2	2	0.00042
Non-survivors (n=8)	0	8	0	
LTA				
Survivors (n=11)	9	0	2	0.0016
Non-survivors (n=13)	4	9	0	
Potential patients weaned off PCPS (n=42)	27	11	4	0.029
Non-potential patients weaned off PCPS (n=10)	3	7	0	
Survivors post-PCPS (n=31)	25	2	4	0.0000068
Non-survivors post-PCPS (n=11)	1	10	0	

Data are number of patients. n, total number of patients with confirmed data; LOS, low output syndrome; LTA, life-threatening arrhythmia.

legs tended to be caused by cannulation during cardiopulmonary resuscitation, so in patients who are candidates for PCPS, sheaths should be previously inserted in the femoral artery and vein and immediately after PCPS is begun, a bypass should be established between the artery of the legs and the arterial inflow catheter, because once ischemic signs appear, establishing such a bypass is useless.

When the indicators of cardiac function have improved, reduction of the support flow rate can be attempted. When the patient's condition can be stabilized to the standards without exacerbation of circulatory failure and cardiac function at the flow rate 1.0L/min, the patient should be re-evaluated for cessation of PCPS. It is also important to try to complete PCPS as soon as possible in order to prevent the development of complications associated with PCPS.

We have also tried to verify whether the proposed guidelines are helpful or not. The enrolled patients with fulminant myocarditis were divided into 3 groups: those subjects who underwent PCPS in accordance with the proposed guidelines were defined as the excellently treated group, and those who did not were defined as the poorly treated group; those who were hard to differentiate because of insufficient data were put into the unknown group. The usefulness of the guidelines has been documented with significant differences in each group (Table 15). In the comparison between the survivors and non-survivors, it was calculated that 25 (86.2%) patients survived in the excellent group (n=29) and 17 (89.5%) patients died in the poor group (n=19). The problems identified in the poor group were: delay in instituting PCPS (6/17 patients: 35.3%), poor adjustment of the flow rate (16/17 patients: 94.1%), non-standard completion of PCPS (4/17 patients: 23.5%), and circulatory disturbances of the legs and MOF associated with PCPS (10/17 patients: 58.8%). Despite a good prediction in the excellent group, 4 patients died because of cardiac dysfunction (half of the patients did not recover full contractility), circulatory disturbances of the legs and MOF. Accordingly, it is important to develop a curative and radical treatment for myocardial inflammation in order to achieve less mortality than is the current status

Long-Term Prognosis of Patients Treated With PCPS

The readmission rate was 10%, exacerbation rate 3.3%, and mortality 10% in the average follow-up period of 962 days (Table 14). The follow-up leukocyte count, CRP, ECG, echocardiogram and ¹²³I-MIBG were good methods for detecting cardiac events. Observation of the clinical course of the 17 patients without medication was carried out, as

well as of the 10 patients who were taking medication for chronic heart failure. However, it is not yet clear whether patients need to continue or discontinue their medication.

McCarthy et al reported the long-term outcome of fulminant myocarditis patients as compared with acute non-fulminant myocarditis patients, and 93% of the patients survived without having received a heart transplant. The use of a circulatory-assist device appeared to be highly beneficial and it seemed that cardiac transplantation could be avoided in most cases! Certainly, fulminant myocarditis can be a clinical entity with an excellent long-term prognosis: in the present survey, 90% of the survivors who were treated with PCPS were reported to be alive, although the survival rate remained at 57.7%. Accurate management of mechanical cardiopulmonary support systems and the development of a cure for myocarditis are the promising influences on the outcome of fulminant myocarditis.

Study Limitations

The patients were divided into different classes and compared by their data. Obvious causes with significant difference by statistical method could hardly be detected, because several causes were compounded, such as association with myocarditis itself, PCPS, side effects of therapy, complications and MOF. The causes were not always conclusive because of insufficient data. However, as far as making a decision according to clinical information and circumstantial evidence, we can conclude that the causes are noteworthy factors affecting the prognosis.

The lack of data for some aspects prevented us from always comparing the data by a statistical method and further analysis is necessary with detailed data.

The proposed therapeutic guidelines also referred to other published data, but we evaluated the guidelines using the present national survey only. We propose carrying out further investigation to verify or improve the guidelines.

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Appendix

Investigators from the Scientific Committee elected by the Japanese Circulation Society (1997–1999) for the study of Fulminant Myocarditis
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