

## **Study Title:**

Multicenter Retrospective Observational Study of  
Acute Myocarditis in Korea

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## **Study protocol**

### **Background**

Acute myocarditis is divided into fulminant or non-fulminant myocarditis depending on the presence or absence of hemodynamic stability. It is known that the prognosis of fulminant myocarditis is poorer than that of non-fulminant. In addition, additional research is needed on the risk factors contributing to the deterioration of the clinical course. In particular, studies on acute myocarditis published in renowned international journals have only been conducted with a small number of patients, ranging from dozens to hundreds of patients, so it is more necessary to conduct studies that include a large number of patients with public confidence on the overall clinical course and prognosis of myocarditis.

### **Objective**

In this study, we investigated the clinical characteristics of patients with acute myocarditis in Korea and sought to find out the treatment results and prognosis of fulminant myocarditis requiring vasopressors or mechanical assist devices.

### **Design**

Patients diagnosed with acute myocarditis from January 2004 to December 2021 at 6 domestic institutions were investigated for baseline characteristics and clinical course.

### **Method**

#### 1) Analysis method

- Review medical records and reanalyze previously performed blood tests, electrocardiograms, echo-cardiographic tests, imaging tests, and biopsies.
- Clinical results (in hospital mortality, death from any cause, heart transplantation, permanent left ventricular assist device insertion, hospitalization) and changes in echocardiographic findings of patients treated for myocarditis should be confirmed prior to the clinical trial approval date.

#### 2) Observational data and Clinical test

##### (1) Observational data

- ① General characteristics: patient identification code, time of visit (year/month), age, sex, height, weight, vital signs upon admission, symptoms
- ② Underlying diseases: diabetes, hypertension, chronic kidney disease, coronary artery disease, peripheral vascular disease
- ③ Causes of myocarditis: Myocarditis caused by viral, giant cell, immune checkpoint inhibitors
- ④ Conservative treatment of myocarditis and treatment with immunosuppressants and vasopressors
- ⑤ ECMO treatment: date of insertion of ECMO, date of ECMO removal, whether or not venting is performed during ECMO maintenance, date of venting
- ⑥ Clinical results: in-hospital mortality, all-cause mortality, heart transplant, left ventricular assist device insertion, re-hospitalization

## (2) Clinical test

- ① Laboratory test: cardiac enzyme, NT-proBNP, hemoglobin, platelet count, Aspartate Aminotransferase (AST), alanine aminotransferase (ALT), Blood Urea Nitrogen (BUN), Creatinine
- ② Cardiac echocardiography: LVEF, TAPSE, TV s', LV dimension, IVS thickness, LV posterior wall thickness, E flow, e velocity, RVSP, LAVI
- ③ Heart magnetic resonance imaging (MRI): presence of late gadolinium enhancement, edema

## **Statistical Analysis Plan (SAP)**

All data for statistical test are analyzed using SPSS and R. All measurements for continuous variables are expressed as mean  $\pm$  standard deviation, and measurements for discrete variables are expressed as percentages. Student's t-test is used for comparative analysis of continuous variables, and  $\chi^2$ -test is used for comparison between two groups for discrete variables. After treatment for myocarditis, recovery of myocardial function and correlation with clinical results were analyzed using paired t test and Kaplan-Meier survival analysis. Predictors of death and factors requiring ECMO treatment were identified through binary logistic regression analysis. Binary logistic regression

analysis requires the occurrence of 10-15 events per independent variable, but in this study, about 30%, or about 270 people, are expected to die, so enough risk factors can be studied. The goodness of fit of the risk prediction model will be tested by C-statistic and Hosmer-Lemeshow tests. In addition, death or re-hospitalization during follow-up will be estimated by the Cox survival analysis method. After checking the fitness of the model by checking Schoenfeld's residual, the hazard of each risk factor is identified. A case of  $P < 0.05$  is considered statistically significant.