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# Predictors of Left Ventricular Functional Recovery and Their Impact on Clinical Outcomes in Patients With Newly Diagnosed Dilated Cardiomyopathy and Heart Failure

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- Q5 **Background** To identify the predictors of left ventricular functional recovery (LVFR) and its impacts on clinical outcomes in acute heart failure (AHF) patients with newly diagnosed dilated cardiomyopathy (DCM).
- Q6 **Methods** A total of 175 consecutive patients with newly diagnosed DCM and AHF were divided into 2 groups according to LVFR on follow-up echocardiography; the recovered group (n = 54, 54.3 ± 18.5 years, 31 males) vs. the non-recovered group (n = 121, 60.5 ± 15.1 years, 79 males). Clinical, laboratory, and echocardiographic findings were compared, and major adverse cardiac and cerebrovascular events (MACCE) including death, rehospitalisation, and stroke were analysed.
- Q7 **Results** Left ventricular function was normalised in 54 patients (30.8%) on follow-up echocardiography. The change in the level of N-terminal pro-B-type natriuretic peptide ( $\Delta$ NT-proBNP) between initial presentation and discharge >1633.5 pg/mL was an independent predictor of LVFR, whereas diabetes and LV end-systolic diameter >50 mm were negative predictors of LVFR on multivariate analysis. During five years of clinical follow-up, MACCE developed in 91 patients: 58 deaths, 29 rehospitalisations, and 4 strokes. On multivariate analysis, baseline LVEF <30% and no LVFR were independent predictors of MACCE.
- Q8 **Conclusion** Left ventricular functional recovery was not uncommon in newly diagnosed DCM with AHF. The changes in NT-proBNP level during hospitalisation, diabetes, and larger initial LV size were independent predictors of LVFR, and LVFR was an independent predictor of future MACCE. Serial monitoring of NT-proBNP and LV function would be useful in the risk stratification of newly diagnosed DCM with AHF.
- Keywords** Left ventricle • Dilated cardiomyopathy • Recovery • Echocardiography

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## Introduction

Dilated cardiomyopathy (DCM) is defined as a disease of the heart muscle characterised by dilation and depressed systolic function of one or both ventricles [1]. A wide variety of cardiac or systemic diseases may result in DCM, but there are no identifiable causes in many cases of DCM, the so-called idiopathic DCM [2].

Acute heart failure (AHF) associated with DCM is not uncommon in clinical practice [3,4]. The prognosis of DCM with AHF is known to be poor in general, with 25% mortality at one year and 50% mortality at three years [5]. Despite the dismal prognosis of DCM, left ventricular functional recovery (LVFR) or reverse LV remodelling has been described in some aetiologies of DCM when the underlying causes or predisposing conditions are resolved. Because of the advancement of medical treatment, recent studies have suggested that LV function may be normalised after several months of optimal medical treatment for HF in some patients with DCM [6,7]. Several predictors including duration of symptoms, age, comorbidity such as hypertension and diabetes, and imaging characteristics were suggested as independent predictors of LVFR in patients with DCM [6,8]. However, it is challenging to define the incidence or predictors of LVFR in DCM because the definition of the improvement of LV function or LVFR differs between studies. Although some studies have suggested that LVFR or LV reverse remodelling is related to favourable long-term prognosis [9,10], the impact of LVFR on long-term prognosis in DCM has been poorly studied. Therefore, the present study aimed to determine the incidence of normalisation of LV systolic function and identify the useful predictors of LVFR in AHF patients with newly diagnosed DCM. In addition, the impact of this LVFR on long-term major adverse cardiac and cerebrovascular events (MACCE) including death, HF rehospitalisation, and stroke in patients with DCM was also investigated.

## Materials and Methods

### Study Design and Subjects

The present study was a single-centre, prospective, observational study, and the Institutional Review Board of our institution approved the study protocol.

From January 2010 to December 2011, we prospectively enrolled consecutive newly diagnosed DCM patients who presented with AHF and had survived until the time of follow-up echocardiography at six months. Dilated cardiomyopathy was diagnosed using a combination of the following echocardiographic findings in the absence of exclusion criteria in the present study: ventricular dilatation defined by the LV end-diastolic dimension (LVEDD) >55 mm and depressed LV systolic function defined by the LV ejection fraction (EF) <45% by the 2D area-length method [11]. Exclusion criteria were as follows: 1) significant coronary artery disease defined as diameter stenosis >50% in any of the major

coronary arteries on coronary angiography; 2) prior history of percutaneous coronary intervention or coronary artery bypass graft; 3) significant valvular heart disease; 4) congenital heart disease; 5) previous history of HF; 6) previous history of significant arrhythmia except atrial fibrillation (AF); 7) renal replacement therapy associated with end-stage renal disease; and 8) miscellaneous conditions including acute myocarditis, infiltrative myocardial disease, connective tissue disease, endocrine dysfunction, neuromuscular disease, general systemic disease, sensitivity/toxic reactions, or a history of excessive alcohol intake.

The primary end-point was LVFR on follow-up echocardiography at six months after discharge from the index AHF. Left ventricular functional recovery was defined as LVEF  $\geq$ 50% on follow-up echocardiography at six months in the present study [12]. The secondary end-point was the development of major adverse cardiac and cerebrovascular events (MACCE) during five years of clinical follow-up. Death, HF rehospitalisation, or stroke during clinical follow-up was defined as MACCE in the present study, and clinical follow-up ended in the case of death.

Newly diagnosed DCM with AHF was identified in 190 patients during the enrolment period. After excluding 15 cases of death before performing follow-up echocardiography, 175 newly diagnosed DCM patients who survived and finished follow-up echocardiography at six months after the index HF admission were finally enrolled (Figure 1). The patients were divided into two groups according to the presence of LVFR on follow-up echocardiography: the recovered group ( $n = 54$ ,  $54.3 \pm 18.5$  years, 31 males) vs. the non-recovered group ( $n = 121$ ,  $60.5 \pm 15.1$  years, 79 males). Baseline characteristics and the development of MACCE were compared between the groups.

### Echocardiographic Measurements

Comprehensive echocardiographic studies including Doppler studies were performed according to the current recommendations of the American Society of Echocardiography [13]. Baseline echocardiographic examination was performed at initial presentation, and follow-up echocardiography was performed at six months after discharge from the index AHF. Echocardiographic images from various windows were obtained by using a digital echocardiography equipment system (Vivid 7, GE Vingmed Ultrasound, Horten, Norway), and Doppler studies were recorded at a sweep speed of 50 mm/s. Digital cine loops were obtained and stored for subsequent offline analysis, and all of the data were analysed in the computerised offline software package (EchoPAC PC 6.0.0, GE Vingmed Ultrasound, Horten, Norway) by an expert cardiologist in the field of echocardiography. Left ventricular end-systolic and end-diastolic dimensions, inter-ventricular septal and posterior wall thicknesses, and left atrial anteroposterior diameter were determined from two-dimensional images. Ejection fraction was measured by using modified Simpson's method. The intra-observer and inter-observer variabilities of modified Simpson's method were  $4\% \pm 5\%$  and  $5\% \pm 4\%$  (absolute difference divided

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