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Original article

Prevalence, clinical characteristics, and outcome of atrial functional mitral regurgitation in hospitalized heart failure patients with atrial fibrillation

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ABSTRACT

Background: Functional mitral regurgitation (MR) caused by reduced left ventricular ejection fraction (EF) and tethering, termed ventricular functional MR (VFMR), is associated with worse outcomes. Atrial functional MR (AFMR) caused by left atrial enlargement and annular dilatation was also recently described in patients with atrial fibrillation (AF). However, the clinical profiles of AFMR in hospitalized heart failure (HF) patients are unclear. We investigated the prevalence, clinical characteristics, and prognosis of AFMR in hospitalized HF patients with AF.

Methods: We analyzed 189 hospitalized HF patients with AF. The prevalence, clinical characteristics, and prognosis were compared between 4 groups: patients with EF ≥50% and no/mild MR (pEFnoMR), patients with EF <50% and no/mild MR (rEFnoMR), patients with EF ≥50% and moderate/severe MR (AFMR), and patients with EF <50% and moderate/severe MR (VFMR).

Results: The prevalence of AFMR was 15.9% in hospitalized HF patients with AF. AFMR patients were older and more likely to have an enlarged left atrium, lower tenting height, and moderate/severe tricuspid regurgitation than VFMR patients. There were no differences in all-cause death after discharge among pEFnoMR, rEFnoMR, and AFMR patients. AFMR patients were associated with a higher rate of a composite of cardiac death and readmission for HF compared with pEFnoMR and rEFnoMR patients (log-rank $p = 0.046$ and $p = 0.004$). There were no differences in composite endpoints between AFMR and VFMR patients (log-rank $p = 0.507$).

Conclusions: AFMR was present in a proportion of elderly hospitalized HF patients with AF, and was a condition requiring attention because of readmission for HF in a hospitalized HF cohort.

Introduction

Atrial fibrillation (AF) is the most common cardiac supraventricular sustained arrhythmia [1–3]. AF and heart failure (HF) frequently coexist, and the presence of AF leads to poor prognosis in HF patients [4–6]. AF causes left atrial (LA) remodeling and enlargement, and LA enlargement may result in mitral annular dilatation [7]. Further, mitral annular dilatation may cause progressive mitral regurgitation (MR), which is a potential mechanism by which AF causes HF with preserved ejection fraction (HFpEF) [7,8]. Gertz et al. reported that AF patients with a moderate or higher degree of MR showed significant improvement following restoration of sinus rhythm, and that AF can result in 'atrial functional MR' (AFMR) [9]. In that study, AFMR was defined as patients with AF, an ejection fraction (EF) ≥50%, and moderate/severe MR.

MR can be categorized according to mitral leaflet motion using Carpentier's classification as normal (Type I), excessive (Type II), and restrictive (Type III) [10]. A complimentary method of classifying MR involves the presence of an abnormality in the mitral valve leaflets (primary/organic or secondary/functional) [11]. AFMR, through a mechanism of atrial remodeling leading to mitral annular dilatation, can be categorized as functional type I

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MR. By contrast, conventional functional MR caused by reduced left ventricular EF and tethering, which we termed ventricular functional MR (VFMR) in the present study, can be categorized as functional type III MR [12]. Several studies have also reported that VFMR in HF patients with reduced ejection fraction (HFrEF) is associated with worse outcomes [13,14]. However, to the best of our knowledge, there are no reported data on AFMR in HF patients. Thus, in the present study we examined the prevalence, clinical characteristics, and prognosis of AFMR in hospitalized HF patients with AF.

Methods

Patients

This retrospective study selected 362 hospitalized HF patients with AF out of 910 consecutive hospitalized patients with HF from July 2013 to June 2016 at Tokyo Women's Medical University Hospital, Tokyo, Japan. The disposition of the study population is shown in Fig. 1. Hospitalized HF patients with AF were defined as patients with AF rhythm at the time of admission. After excluding patients who died during hospitalization (n = 18), with missing EF measurements (n = 19), or with structural mitral leaflet abnormality, mitral annular calcification, previous mitral surgery, moderate or severe aortic valve disease, hypertrophic cardiomyopathy, or congenital heart disease (total n = 136), 189 patients were included in our final analysis. Among the 189 patients, 28 patients (14.8%) were recovered to sinus rhythm during hospitalization, and these patients were also included in this analysis. These patients were divided into pEFnoMR (EF ≥50% and no/mild MR), rEFnoMR (EF <50% and no/mild MR), AFMR (EF ≥50% and moderate/severe functional MR) [8,9], and VFMR (EF <50% and moderate/severe functional MR). The diagnosis of HF was defined by modified Framingham criteria [15], and we enrolled patients with established HF sufficient to warrant hospitalization for therapy and evaluation. Long-standing persistent AF was defined as continuous AF >12 months in duration. Permanent AF was defined when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm [1,3]. This study was an observational study in which information was collected within clinical practice, and there were no specific interventions. Treatment of HF and AF was not specified and was selected by each attending physician. This study was conducted according to the principles of the Helsinki Declaration. The review board of Tokyo Women's Medical University Hospital approved the protocol.

Echocardiography

A comprehensive transthoracic echocardiography (TTE) study that included 2-dimensional, M-mode, Doppler echocardiography and tissue Doppler imaging was performed at the time of discharge according to the American Society of Echocardiography recommendations [16–19]. TTE examinations were performed using a Vivid 7 ultrasound (GE Healthcare, Horten, Norway) or an iE33 ultrasound (Philips Healthcare, Bothell, WA, USA). LA dimension at end-systole was measured in the parasternal long-axis view, and LA volume at end-systole was measured in the apical 2-chamber and 4-chamber views using the modified Simpson's method of discs. From the parasternal long-axis view, we recorded LV end-diastolic and end-systolic diameters. The LVEF was calculated by the modified Simpson's method. Diastolic function was described with the E/e' ratio, where E was measured using pulsed Doppler of the mitral inflow from the 4-chamber views, and e' reflects the septal mitral annular diastolic velocities measured using tissue Doppler imaging.

Tenting height at mid-systole was measured as the distance between the point of coaptation and the mitral annulus line in the apical 4-chamber and 3-chamber views [20,21]. The color Doppler scale of MR and tricuspid regurgitation (TR) were determined by the clinical ultrasonographer, and in general were set to 50–60 cm/s. The severity of MR was determined by the ratio of the MR color jet area to the LA area (MR/LA ratio). The MR color jet area was measured in the apical 4-chamber, apical 2-chamber, and long-axis views. The MR/LA ratio was then calculated, using the largest measured values for both. Mild MR was defined as an MR/LA ratio of ≥0.1 to <0.2, moderate MR as ≥0.2 to <0.4, and severe as ≥0.4.

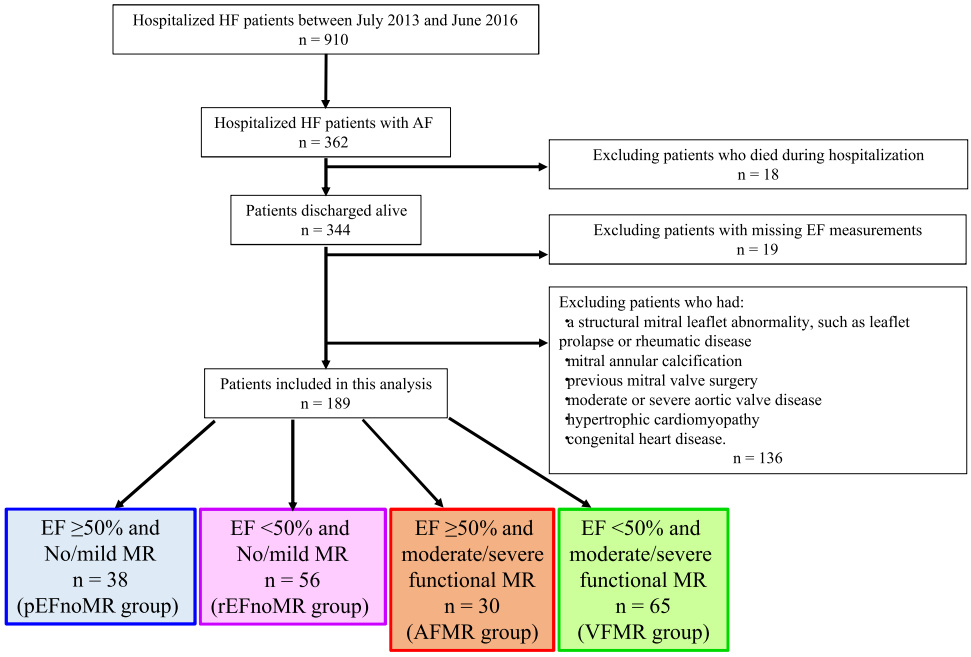

Fig. 1. Disposition of the study patients. The 189 hospitalized heart failure (HF) patients with atrial fibrillation (AF) were divided into 4 groups: 38 patients with an ejection fraction (EF) ≥50% and no/mild mitral regurgitation (MR) (pEFnoMR group), 56 patients with an EF <50% and no/mild MR (rEFnoMR group), 30 patients with an EF ≥50% and moderate/severe functional MR (AFMR group), and 65 patients with an EF <50% and moderate/severe functional MR (VFMR group).

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