



Clinical Research

Sex Differences in Left Ventricular Cavity Dilation and Outcomes in Acute Heart Failure Patients With Left Ventricular Systolic Dysfunction

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ABSTRACT

Background: In this study we evaluated the influence of sex on the left ventricular end-diastolic dimension (LVEDD) and adverse outcomes in patients hospitalized for acute decompensated heart failure (HF) with a reduced ejection fraction (EF).

Methods: Among the 4842 patients enrolled in the Acute Decompensated Heart Failure Syndromes (ATTEND) registry, 2367 patients (1607 men and 760 women) discharged alive after hospitalization for acute decompensated HF with a reduced EF (defined as a left ventricular EF < 50%) were investigated to assess the association of sex and LVEDD with the primary end point (all-cause death and readmission for HF after discharge). Men and women were separately divided into LVEDD quartiles at discharge (men: LVEDD ≤ 54, 55-60, 61-65, and ≥ 66 mm; women: LVEDD ≤ 48, 49-54, 55-60, and ≥ 61 mm). The median follow-up period after discharge was 524 (range, 385-785) days.

Results: Occurrence of the primary end point did not differ between men and women (37.0% vs 37.2%; $P = 0.921$). After adjustment for multiple comorbidities including left ventricular EF, men with an LVEDD of 61-65 and ≥ 66 mm had a significantly higher risk of the primary

RÉSUMÉ

Introduction : Dans la présente étude, nous avons évalué l'influence du sexe sur la dimension du ventricule gauche en fin de diastole (DVGFD) et l'évolution défavorable des patients hospitalisés en raison d'une insuffisance cardiaque (IC) décompensée associée à une fraction d'éjection (FE) réduite.

Méthodes : Parmi les 4842 patients inscrits au registre ATTEND (Acute Decompensated Heart Failure Syndromes), 2367 patients (1607 hommes et 760 femmes) qui sont sortis de l'hôpital en vie après l'hospitalisation en raison d'une IC aiguë décompensée associée à une FE réduite (c'est-à-dire une FE du ventricule gauche < 50 %) ont fait l'objet de l'étude sur l'évaluation de l'association du sexe et de la DVGFD au critère d'évaluation principal (la mortalité toutes causes confondues et la réadmission en raison d'une IC après la sortie de l'hôpital). Nous avons réparti les hommes et les femmes en quartiles distincts de DVGFD à la sortie de l'hôpital (les hommes ayant une DVGFD ≤ 54, de 55 à 60, de 61 à 65 et ≥ 66 mm; les femmes ayant une DVGFD ≤ 48, de 49 à 54, de 55 à 60 et ≥ 61 mm). La période médiane de suivi après la sortie de l'hôpital était de 524 (étendue, de 385 à 785) jours.

In patients with heart failure (HF), left ventricular (LV) cavity dilation has an important influence on mortality and the death rate increases as LV cavity dimensions become larger.¹⁻⁵ Recently, it was suggested that assessment of LV cavity dilation could be used for risk stratification in relation to

serious ventricular arrhythmias or sudden cardiac death independently of LV systolic dysfunction.^{6,7} It was also reported that a larger LV volume is associated with a higher risk of death after myocardial infarction in men, but not in women, suggesting that deterioration of LV function might be more marked in men despite similar structural remodelling.⁸ In addition, previous studies have shown that concentric hypertrophy was more common in women, whereas eccentric hypertrophy was more frequent in men.⁹⁻¹¹ It is well documented that approximately half of all patients hospitalized for acute decompensated HF are women.¹²⁻¹⁵ However, little is known about the influence of sex on LV cavity dilation and outcomes in acute decompensated HF patients. Therefore,

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end point than men with an LVEDD ≤ 54 mm, indicating a positive association between a larger LVEDD and adverse outcomes. In contrast, in women, the adjusted risk of the primary end point was comparable among the LVEDD quartiles.

Conclusions: Men and women with acute decompensated HF and a reduced EF might show important differences in relation to the association between left ventricular cavity dilation and outcomes.

this study was performed to evaluate sex differences in the association between the LV end-diastolic dimension (LVEDD) and outcomes in patients hospitalized for acute decompensated HF with a reduced LV ejection fraction (EF).

Methods

Study design and data collection

The Acute Decompensated Heart Failure Syndromes (ATTEND) registry is a prospective nationwide hospital-based observational cohort study that accumulates data on patients with acute decompensated HF admitted to 53 hospitals between April 2007 and December 2011 throughout Japan. The study design, methods, and patient characteristics have been described previously.¹⁶ In brief, the ATTEND registry study is being performed to clarify the profile of acute decompensated HF, including demographic and clinical characteristics, current treatment, hospital mortality, and morbidity/mortality after discharge. The present study using the ATTEND registry data was conducted according to the principles of the Declaration of Helsinki. Institutional review board approval was obtained at each participating hospital before commencing the study, and all patients gave written informed consent. The end point classification committee (2 experienced cardiologists who were not investigators) reviewed all data and asked the primary physician to confirm the cause of death if clarification was required.

Patients and definitions

In the ATTEND registry, only patients with a discharge diagnosis of acute decompensated HF fitting the modified Framingham criteria are eligible for enrollment. Accordingly, patients with predominantly non-cardiac reasons for hospitalization, such as lung disease or renal dysfunction, were excluded from this registry. Patients younger than 20 years old and those with acute coronary syndrome were also excluded from this registry. Furthermore, patients were enrolled at the first admission and then followed up; thus, data collection was patient-based and not event-based. We reviewed patients discharged after admission for acute decompensated HF who had echocardiographic data (LVEDD, LV end-systolic dimension, and LVEF) at discharge and follow-up data after discharge. LVEF was calculated from the LV end-diastolic and

Résultats : La survenue du critère d'évaluation principal ne différait pas entre les hommes et les femmes (37,0 % vs 37,2 %; $P = 0,921$). Après l'ajustement des comorbidités multiples, dont la FE du ventricule gauche, les hommes ayant une DVGFD de 61 à 65 et ≥ 66 mm étaient exposés à un risque significativement plus élevé du critère d'évaluation principal que les hommes ayant une DVGFD ≤ 54 mm, ce qui montre une association positive entre une plus grande DVGFD et une évolution défavorable. En revanche, nous avons observé que le risque ajusté du critère d'évaluation principal chez les femmes était comparable dans tous les quartiles de DVGFD.

Conclusions : Les hommes et les femmes ayant une IC aiguë décompensée et une FE réduite montreraient des différences importantes en ce qui concerne l'association entre la dilatation de la cavité ventriculaire gauche et l'évolution de la maladie.

end-systolic dimensions using the Quinones method or was calculated using the modified Simpson method.¹⁷ LV dimensions were obtained using 2-dimensional M-mode echocardiography.¹⁷ To investigate the association of LVEDD at discharge with postdischarge outcomes in acute decompensated HF patients with a reduced EF (defined as a LVEF $< 50\%$), men or women were divided into quartiles of LVEDD at hospital discharge (men: LVEDD ≤ 54 , 55-60, 61-65, and ≥ 66 mm; women: LVEDD ≤ 48 , 49-54, 55-60, and ≥ 61 mm). The primary end point of this study was a composite of all-cause death and readmission for HF after discharge, whereas the secondary end points were all-cause death and cardiac death (defined as HF death, sudden cardiac death, or other cardiac death) after discharge.

Statistical analysis

Data are presented as the mean (SD), as the median with interquartile range, or as proportions. One-way analysis of variance was used for between-group comparison of continuous variables with a normal distribution, whereas the Kruskal-Wallis H test was used for skewed continuous or discrete variables. The χ^2 test was used to compare categorical variables. Univariable and multivariable analyses were performed with Cox proportional hazards models to test the association of candidate variables with the primary or secondary end points. Multivariable models included potential confounders such as age, etiology of HF (ischemic or nonischemic), LVEF, hypertension, diabetes, readmission for HF, atrial fibrillation, body mass index, systolic blood pressure, blood urea nitrogen, serum creatinine, serum sodium, hemoglobin, and use of the following medications at discharge: loop diuretic, spironolactone or eplerenone, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and β -blocker, according to directed acyclic graphs.¹⁸ Event-free survival curves or survival curves after adjustment for the previously mentioned variables were constructed for the quartiles of each sex obtained through stratification by LVEDD at discharge. The influence of profile, interaction, and multicollinearity was examined using regression diagnostic analysis. We also carried out sensitivity analyses (such as the cutoff value of LVEF for classification of patients as having a preserved or reduced EF). A 2-tailed P value < 0.05 was considered to indicate statistical significance. An independent statistical data centre (STATZ Institute, Inc, Tokyo,

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