Clinical Investigation

Left Atrial Expansion Index Predicts Left Ventricular Filling Pressure and Adverse Events in Acute Heart Failure With Severe Left Ventricular Dysfunction

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ABSTRACT

Background: The power of left atrial (LA) parameters for predicting left ventricular (LV) filling pressure and adverse events in acute heart failure (HF) with severe LV dysfunction, either sinus rhythm or atrial fibrillation (AF), is not fully understood.

Methods and Results: Echocardiography was performed in 141 patients with acute decompensated congestive HF and LV ejection fraction <35%, including 42 with permanent AF. The LA expansion index was calculated as $(Vol_{max} - Vol_{min}) \times 100\%/Vol_{min}$, where Vol_{max} was defined as maximal and Vol_{min} as minimal LA volume. Of 141 patients, invasive LV filling pressures within 12 hours of LA expansion index measurement were available in 109. The end points were 3-year frequencies of HF hospitalization and all-cause mortality. Over a median follow-up of 3.1 years, 74 participants (52.5%) reached the end points (sinus vs AF group: 48.5% vs 61.9%, respectively; $P = .047$). Multivariate analysis revealed that adverse events of both groups were only independently associated with age and LA expansion index. Rates of adverse events were proportional to LA expansion index. There was a good logarithmic relationship between LA expansion index and LV filling pressure, regardless of presence or absence of AF.

Conclusions: LV filling pressure can be estimated well by LA expansion index, with or without AF. The LA expansion index predicts adverse events in HF patients with severe systolic dysfunction. (ClinicalTrials.gov number: NCT01307722). (*J Cardiac Fail 2016;22:272–279*)

Key Words: Adverse event, congestive heart failure, left atrial expansion index, left ventricular filling pressure.

Left ventricular ejection fraction (LVEF) is an accepted prognostic indicator in heart failure (HF) patients.[1] Deaths due to atrial fibrillation (AF), worsening HF, and other cardiac causes are more frequent among patients with lower LVEF. Regarding adverse events and prognosis, left ventricular (LV) diastolic dysfunction is another significant determinant of clinical outcomes in HF patients with systolic dysfunction.[2,3] Although elevation of left ventricular filling pressure (LVFP) induces either LV systolic or diastolic dysfunction, the morphologic changes of the left atrium (LA) are much more obvious than those of the LV during diastolic phase, with mitral valve opening and facing the same pressure loading, because the thickness of the LA is much less than that of the LV. The only way for a thin-wall chamber to adapt to pressure overloading is progressive dilation with increasing interstitial fibrosis in atrial wall, deteriorating contraction function, and the development of AF.[4]

Recent studies with the use of echocardiography show that LA parameter, either LA size or maximal indexed LA volume, may be a useful index of cardiovascular risk.[5–10] The present authors recently showed that the LA expansion index, which accurately reflects instantaneous LVFP (logarithmic correlation) in many disease entities, including stable angina, acute

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Manuscript received July 22, 2015; revised manuscript received December 28, 2015; revised manuscript accepted January 13, 2016.

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Source of Funding: This work was funded by Kaohsiung Veterans General Hospital (VGHKS102-010) and National Ministry of Science and Technology (102-2628-B-650-002-MY3).

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1071-9164/$ - see front matter

http://dx.doi.org/10.1016/j.cardfail.2016.01.009

myocardial infarction, and severe mitral regurgitation, is useful for predicting AF after coronary artery bypass graft surgery, HF rehospitalization, and both short- and long-term mortality in ischemic heart disease.[11–15] However, the prognostic power of LA expansion index in acute HF with severe LV systolic dysfunction, either sinus rhythm or AF, has not been described, and the association between LA expansion index and LVFP in this group is not well validated.

Methods

Subject and Study Protocol

From August 2011, this prospective study recruited patients aged ≥18 years with LVEF < 35% and 1st hospitalization to Kaohsiung Veterans General Hospital due to acute decompensated congestive HF. All participants were scheduled for echocardiography immediately followed by cardiac catheterization if they had not undergone cardiac catheterization before. Exclusion criteria included any history of the following: 1) mitral stenosis or prosthetic mitral valve, 2) atrial septal abnormality (eg, atrial septal defect or aneurysm), 3) acute myocardial infarction, 4) severe renal dysfunction with creatinine clearance rate (CCr) <30 mL/min, 5) poor echocardiographic image quality, or 6) lack of written informed consent. In total, 141 patients were enrolled for final analysis. Histories of hyperlipidemia, hypertension, and smoking were recorded. Diabetes mellitus was defined according to American Diabetes Association criteria.[16] Based on earlier chart and electrocardiography/Holter recordings, permanent AF was defined as continuous AF which had occurred for >1 year. At enrollment, CCr was estimated by means of the Cockroft-Gault equation, and renal dysfunction was defined as CCr <60 mL/min.[17] The end points for the current study were HF rehospitalization and all-cause mortality. Patients with adverse events underwent echocardiography checkups again during hospital readmission. Patients without events underwent annual echocardiography checkups. The study protocol was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital. Patients were enrolled in this study only after giving written informed consents.

Echocardiography and Invasive Catheterization

Conventional Echocardiographic and Tissue Doppler Measurements. LVEF was calculated by means of the Simpson biplane technique. Pulsed-wave tissue Doppler (TDI) was performed in apical views, and a pulsed-wave Doppler sample volume was placed at the level of the mitral annulus over the septal and lateral borders. The pulsed-wave TDI tracing recorded over 5 cardiac cycles at a sweep speed of 100 mm/s was used for offline calculations. The average early-diastolic velocity (e′) of the septal and lateral mitral annuli was used to estimate LV diastolic filling by E/e′ method.[18] The severity of mitral regurgitation, which was evaluated semiquantitatively from the area of regurgitant jet with the use of color Doppler, was classified as absent or trivial (0), mild (1+), moderate (2+), or severe (3+). Diastolic dysfunction was assessed as described previously.[19,20] Based on Doppler measurements of mitral inflow and TDI,[21] diastolic function was classified into 4 categories: normal, mild (impaired relaxation without evidence of increased filling pressures), moderate (pseudonormal with moderately elevated filling pressures), and severe (restrictive with advanced reduction in compliance).

LA Volume Parameter Measurements. All volume measurements were calculated by means of the biplane area-length method in apical 4- and 2-chamber views.[22] The LA volumes were measured at 2 points, immediately before mitral valve opening (maximal LA volume or Vol_{max}) and at mitral valve closure (minimal LA volume or Vol_{min}). The LA expansion index was calculated as $(Vol_{max} - Vol_{min}) \times 100\% / Vol_{min}$. For patients with AF, LA expansion index was calculated as the average of measurements in 5 consecutive beats. In all patients, LA volumes were indexed to BSA.[15]

Left Ventricular Filling Pressure Measurements. Besides 32 participants who had previously undergone cardiac catheterization, all participants underwent cardiac catheterization examination including LVFP (pre–A-wave LV pressure) measurements during the index hospitalization. The measurements of LVFP were performed with the use of a 6-F pigtail catheter before any interventions, including percutaneous coronary intervention (PCI) or left ventriculography. The 4th intercostal space in the midaxillary line was used as the zero level. The LVFP was continuously recorded (50 mm/s) by a 6-F pigtail catheter placed at mid-LV cavity with the use of fluoroscopic screening. Digital records of rapid-acquisition LV pressure tracings were recorded. Measurements were made offline from the digitized recordings. The average value of pre-A pressure over 5 cardiac cycles was used as LVFP.[23] LVFP >15 mm Hg was considered to be elevated.

Clinical Follow-Up

Patients were followed at our cardiovascular clinic. A follow-up survey was performed to assess HF rehospitalization and all-cause mortality. Rehospitalization for HF was defined as a hospital stay of ≥1 night for treatment of a clinical syndrome with ≥2 of the following symptoms: paroxysmal nocturnal dyspnea, orthopnea, elevated jugular venous pressure, pulmonary rales, or pulmonary edema according to chest radiography. These clinical signs and symptoms represented a change from the normal clinical state of the patient and were accompanied by either failing cardiac output, as determined by peripheral hypoperfusion (in the absence of other causes such as sepsis or dehydration), or peripheral or pulmonary edema requiring treatment with intravenous diuretics, inotropes, or vasodilators. Supportive documentation of decreased cardiac index, increased pulmonary capillary wedge pressure, decreasing oxygen saturation, and/or end-organ hypoperfusion, if available, were included in the adjudication. Follow-up included medical record reviews and patient interviews. Medical assistants checked medical records every 3 months. In patients lost to follow-up, assistants contacted and interviewed patients by telephone or, if necessary, by visiting patients at their homes. The certification of death was