Tricuspid Regurgitation Pressure Gradient as a Useful Predictor of Adverse Cardiovascular Events and All-Cause Mortality in Patients With Atrial Fibrillation

Po-Chao Hsu, MD, PhD[1,3], Wen-Hsien Lee, MD[1,2,3], Chun-Yuan Chu, MD[1], Wei-Chung Tsai, MD[1,3], Hung-Hao Lee, MD[1,2], Chee-Siong Lee, MD[1,3], Hsueh-Wei Yen, MD[1,3], Tsung-Hsien Lin, MD, PhD[1,3], Wen-Chol Voon, MD[1,3], Wen-Ter Lai, MD[1,3], Sheng-Hsiung Sheu, MD[1,3] and Ho-Ming Su, MD[1,2,3]

[1]Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, Republic of China; [2]Department of Internal Medicine, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, Republic of China; [3]Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, Republic of China

ABSTRACT

Background: Tricuspid regurgitation pressure gradient (TRPG) is reportedly a predictor of cardiovascular (CV) mortality in patients without atrial fibrillation (AF); its relationship with cardiac outcomes in patients with AF has never been evaluated. This study aimed to examine the ability of TRPG to predict CV events and all-cause mortality in patients with AF.

Materials and Methods: Comprehensive echocardiography was performed in 155 patients with persistent AF. Combined CV events were defined as CV mortality, stroke and hospitalization for heart failure.

Results: During an average follow-up period of 27 months, 57 CV events and 31 all-cause deaths occurred. According to multivariate analysis, predictors of CV events included diuretic use, decreased left ventricular ejection fraction (LVEF), increased ratio of transmitral E velocity (E) to early diastolic mitral annular velocity (E′) and TRPG. Predictors of all-cause mortality included old age, decreased LVEF, increased E/E′ and TRPG. Notably, the addition of TRPG to a model containing clinical significant parameters, LVEF and E/E′ significantly improved the values in predicting adverse CV events and all-cause mortality.

Conclusions: The TRPG is not only a useful predictor of adverse CV events and all-cause mortality in patients with AF, it may also provide additional prognostic values for CV outcome and all-cause mortality over conventional parameters in such patients.

Key Indexing Terms: Tricuspid regurgitation pressure gradient; Atrial fibrillation; Cardiovascular events. **[Am J Med Sci 2018;356(2):147–151.]**

INTRODUCTION

Tricuspid regurgitation is commonly observed during echocardiographic evaluation, and tricuspid regurgitation pressure gradient (TRPG) reportedly has a strong correlation with pulmonary artery systolic pressure (PASP).[1] Tricuspid regurgitation is usually functional rather than organic. Symptoms of patients with tricuspid regurgitation are often nonspecific and become clinically significant only after irreversible dysfunction of the right ventricle.[2] Because it is not considered a clinically significant parameter, tricuspid regurgitation has not been extensively discussed in the literature. However, tricuspid regurgitation severity is reportedly associated with poorer prognosis, independent of left ventricular ejection fraction (LVEF) or pulmonary hypertension.[3] High PASP is also reported to be a mortality predictor in many diseases, including coronary artery disease, myocardial infarction, aortic stenosis, end stage renal disease, primary pulmonary hypertension, and so on.[4–8] However, no studies have discussed whether TRPG can predict cardiovascular (CV) outcomes or all-cause mortality in patients with atrial fibrillation (AF). Therefore, the aim of this study was to examine the ability of TRPG to predict adverse CV events or total mortality in AF patients.

METHODS

Study Patients

This prospective observational cohort study consecutively enrolled patients with persistent AF (defined as AF lasting for at least 7 days) referred for echocardiographic examinations at Kaohsiung Municipal Hsiao-Kang Hospital from April 2010 to June 2012. After excluding 35 patients without tricuspid regurgitation, the final analysis included 155 patients with AF. The study methods were carried out in accordance with the approved guidelines.

Ethics Statement

The study protocol was approved by the institutional review board committee of the Kaohsiung Medical University Hospital (KMUH-IRB). Informed consent was obtained in written form from patients and all clinical investigation was conducted according to the principles expressed in the Declaration of Helsinki.

Echocardiographic Evaluation

All echocardiographic examinations were performed by a single experienced cardiologist with a VIVID 7 (General Electric Medical Systems, Horten, Norway). The cardiologist was blinded to all clinical data. Pulsed tissue Doppler imaging was obtained with the sample volume placed at the lateral and septal corners of the mitral annulus in apical 4-chamber view. Early diastolic mitral annulus velocity (E′) was averaged from septal and lateral velocities. The wall filter settings were adjusted to exclude high-frequency signals and the gain was minimized. The LVEF was measured by modified Simpson method.

Left ventricular dimensions and LVEF were measured by the index beat method.[9,10] Because the E, E-wave deceleration time and E′ could be obtained quickly and easily, these measurements were obtained from 5 beats and then averaged for later analysis.[11] If the cardiac cycle length was too short to complete the diastolic process, this beat was skipped. Thus, the selection of E, E-wave deceleration time and E′ was not always consecutive. Heart rate was determined from 5 consecutive beats.

The tricuspid regurgitation jet was traced with color flow imaging and TRPG was measured by continuous wave Doppler. The TRPG obtained from 5 beats was averaged for subsequent analysis.

Collection of Demographic, Medical, and Laboratory Data

Collection of demographic and medical data included age, sex, and history of diabetes mellitus, hypertension, coronary artery disease and stroke. All data were obtained from either medical records or from interviews with patients. Laboratory data collection included total cholesterol and triglyceride. Information about medications taken during the study period was obtained from medical records.

Definition of CV Events

A CV event was defined as CV mortality, hospitalization for heart failure or stroke. Hospitalization for heart failure was defined as admission due to dyspnea with chest radiographic evidence of pulmonary congestion and treatment with intravenous diuretics. The CV events were ascertained and adjudicated by 2 cardiologists. In the case of disagreement, a CV event was adjudicated by a third cardiologist based on the hospital treatment course and medical record. In patients with multiple CV events, only the first event was coded. However, a death from heart failure or stroke during the same admission was coded as CV death. Patients who reached the study end points, were followed up until the first episode of adverse events. All other patients were followed until March, 2014.

Statistical Analysis

All statistical analyses were performed with SPSS 18.0 software (SPSS, Chicago, IL). Follow-up data were expressed as mean ± standard deviation, percentage or median (25^{th}-75th percentile). Continuous and categorical variables among groups were compared by 1-way analysis of variance followed by a *post hoc* test adjusted with a Bonferroni correction and chi-square test, respectively. The relationship between 2 continuous variables was assessed by a bivariate correlation method (Pearson correlation). The significant variables in the univariate analysis were selected for multivariate analysis. Time to the adverse events and covariates of risk factors were modeled using a Cox proportional hazards model with forward selection. A significant improvement in model prediction was based on the −2 log likelihood ratio statistic, which followed a difference in −2 log likelihood value and the *P* value was based on the incremental value compared with the previous model. All tests were 2-sided and a *P* value less than 0.05 was considered statistically significant.

RESULTS

Table 1 compares the clinical and echocardiographic characteristics of the different TRPG groups. The patients were divided into 5 groups according to TRPG value: 10-20 mm Hg (group 1), 20-30 mm Hg (group 2), 30-40 mm Hg (group 3), 40-50 mm Hg (group 4) and >50 mm Hg (group 5). The TRPG groups significantly differed in age, systolic blood pressure (SBP), total cholesterol, use of calcium channel blockers and E/E′.

In all patients, the follow-up period to CV events was 27 months (25^{th}-75^{th} percentile: 15-36 months). During the follow-up periods, 57 CV events were documented, including hospitalization for heart failure ($n = 31$), CV death ($n = 17$) and stroke ($n = 9$). Table 2 shows the results of a Cox proportional hazards regression analysis of CV events. Multivariate analysis showed that increased CV events had significant associations with diuretic use, low LVEF, high E/E′ and TRPG (hazard ratio = 1.029; 95% CI: 1.006-1.052; $P = 0.011$).