Impact of Pulmonary Artery-to-Aorta Ratio by CT on the Clinical Outcome in Heart Failure

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ABSTRACT

Introduction: Previous studies have indicated that the ratio of pulmonary artery (PA) to ascending aorta (Ao) diameter as measured by computed tomography (PA/Ao) is strongly associated with pulmonary artery pressure. However, the clinical significance of PA/Ao in heart failure (HF) has not been fully characterized. We sought to investigate the prognostic impact of PA/Ao in HF.

Methods: Based on the prospective registry of patients admitted to our institution due to acute decompensated HF (ADHF), the records of the consecutive 761 patients admitted between 2011 and 2016 were reviewed. Thoracic computed tomography data during the hospital stays were obtained from 447 patients (median 78 (70−84) years of age; male, 62.2%). The diameters of PA and Ao were measured at the level of PA bifurcation. The subjects were divided into the H group (PA/Ao $\geq$ 1.0) and the L group (PA/Ao $<$ 1.0) according to the PA/Ao values. The cutoff value was derived from receiver operating curve analysis.

Results: There were no significant differences in age, sex or body mass index between the H and L groups. The H group was associated with significantly larger left atrial dimension (LAD), higher tricuspid regurgitation peak gradient (TRPG) and E/e' (LAD, H, 48 (42−55) mm vs L, 45 (39−50) mm, $P < 0.001$; TRPG, H, 34 (26−48) mm Hg vs L, 28 (22−38) mm Hg, $P < 0.001$; E/e′, H, 23.3 (42−55) vs L, 18.4 (13.9−25), $P < 0.001$). Length of hospital stay was significantly longer in the H group than in the L group (H, 19 (14−32) days vs L, 16 (12−23) days, $P < 0.001$). In-hospital mortality was significantly higher in the H group compared with the L group (H, 5.4% vs L, 1.2%, $P = 0.02$). Age, sex, LAD and TRPG were independently associated with PA/Ao. The primary endpoint, defined as the composite of all-cause death and ADHF rehospitalization during a median of 479 days after discharge, was significantly more common in the H group ($P < 0.001$, log-rank test). PA/Ao was independently associated with the primary endpoint, even after adjusting for the other confounding factors ($P = 0.002$).

Conclusions: PA/Ao is a reliable marker for the prediction of the outcome of patients with ADHF. (*J Cardiac Fail 2019;25:886−893*)

Key Words: Pulmonary artery to aorta ratio, heart failure, pulmonary hypertension, computed tomography.

INTRODUCTION

Pulmonary hypertension (PH) is a life-threatening condition and generally confers a poor prognosis. Among the various etiologies, left-heart disease is the most common cause of the development of PH.[1] The presence of PH in heart failure (HF) is associated with more severe symptom and worse exercise tolerance.[2] PH also has negative impacts on the clinical outcomes in HF with preserved ejection fraction (HFpEF)[3] and reduced ejection fraction (HFrEF).[4] Because the definite diagnosis of PH, defined as mean pulmonary artery pressure more than 25 mm Hg, requires right-heart catheterization, noninvasive methods such as tricuspid regurgitation peak gradient (TRPG) as assessed by echocardiography are often used to predict PH.[1] However, the estimation of PH by echocardiography is commonly affected by biases, including interobserver variability and limited visibility in some patients.[5] Some previous studies have noted that the ratio of pulmonary artery (PA) to ascending aorta (Ao) diameter (PA/Ao) as measured by computed tomography (CT) or magnetic resonance imaging (MRI) correlates with mean pulmonary artery pressure.[6−9] However, the clinical significance of PA/Ao in patients with acute decompensated HF (ADHF) has not been fully characterized. The

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purpose of this study was to elucidate the association between PA/Ao and clinical characteristics and prognosis in patients with HF.

Methods

Study Population

This is a single-center retrospective observational study. We reviewed the data in our registry of people with HF, which enrolled consecutive patients with ADHF admitted to Sakakibara Heart Institute.[10] The diagnosis of ADHF was based on Framingham criteria.[11] The patients with acute coronary syndrome and isolated right-sided HF were excluded. In the present study, we retrospectively reviewed 761 consecutive patients with ADHF between November 2011 and January 2016 in this registry database. The study flow chart is shown in Figure 1. Of 761 patients, those who underwent thoracic CT scans for some clinical reason during the hospital stay (N = 447) were included in the present study (Figure 1). We conducted receiver operating characteristics (ROC) curve analysis for composite endpoint of all-cause death and HF rehospitalization, and the cutoff value of PA/Ao was determined to be 1.0 to minimize the distance to the top-left corner of the ROC curve. Patients were divided into 2 groups by the cutoff value of PA/Ao (H group: PA/Ao $\geq$ 1; L group: PA/Ao $<$ 1). This study was performed in accordance with the Declaration of Helsinki and approved by the institutional review board at Sakakibara Heart Institute. Written informed consent was obtained from all study participants.

PA/Ao Measurement

Measurements were completed using axial CT images collected by SOMATOM Definition Flash (Siemens Healthcare, Erlangen, Germany) or SOMATOM Sensation 16 (Siemens) CT scanners. The transverse axial diameter of the main PA was manually measured at the level of PA bifurcation, and the ascending aorta diameter was measured at the same level in its minimum diameter (Figure 2). Nonenhanced images were used in all the measurements. PA and Ao were measured by 1 cardiologist who was blinded to the patients' clinical characteristics.

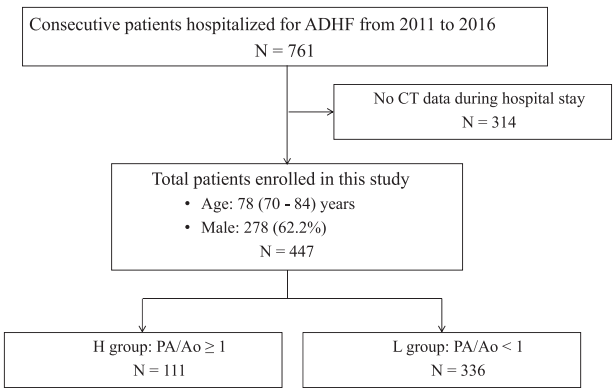

Fig. 1. Study flow chart. ADHF, acute decompensated heart failure; Ao, ascending aorta; CT, computed tomography; PA, pulmonary artery.

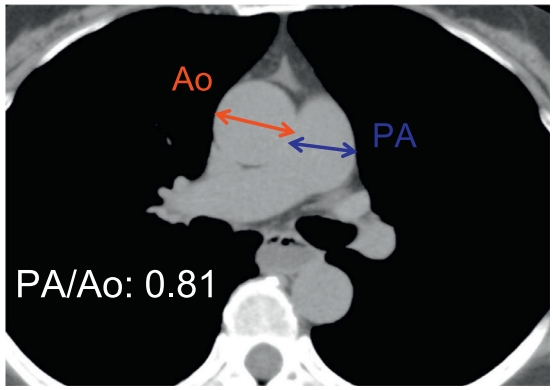

Fig. 2. Measurement of PA and Ao. The transverse axial diameter of the main PA was manually measured at the level of PA bifurcation, and the ascending aorta diameter was measured at the same level in its minimum diameter. Ao, ascending aorta; PA, pulmonary artery.

Clinical Parameters and Outcome Definition

Conventional clinical variables, including age, sex, etiology of HF, risk factors, blood pressure, heart rate, laboratory data, echocardiographic findings, and medications were collected from all study participants. The primary endpoint was defined as the composite of all-cause death and rehospitalization due to ADHF for 1000 days after discharge.

Statistical Analysis

Continuous variables are described as mean ± SD when normally distributed and as median and interquartile range (IQR) 25th percentile−75th percentile) when not normally distributed. Normality was tested by using the Shapiro-Wilk test in each group. Categorical variables are expressed in percentages and total numbers. The differences between the 2 groups were analyzed by using the t test or the Mann-Whitney U test, as appropriate, for continuous variables and the the Fisher exact test or the chi-square test, as appropriate, for categorical variables. The Spearman correlation analysis was conducted to assess the correlation of PA/Ao with TRPG, the ratio of early diastolic mitral inflow velocity to early diastolic velocity of the mitral annulus (E/e′) and left atrial dimension. Multiple linear regression analysis was conducted to assess the variables independently associated with PA/Ao. For survival analysis, the Kaplan-Meier curve was drawn, and the log-rank test was conducted to compare the survival from the primary endpoint, all-cause death and rehospitalization due to ADHF between the 2 groups. We used the multivariable Cox proportional hazards model to estimate the impact of PA/Ao on the primary endpoint, with adjustment for the other clinical variables related to the prognosis of HF, such as age, sex, body mass index (BMI), left ventricular ejection fraction (LVEF), N-terminal pro B-type natriuretic peptide (NT-proBNP), hemoglobin level, and estimated glomerular filtration ratio (eGFR). The presence of atrial fibrillation, TRPG and left atrial dimension (LAD) were found to be associated with PA/Ao; they were also included in the model as independent

variables. Independent variables that showed P values less than 0.10 in the univariate analysis were employed in the multivariable analysis. All analyses were performed by using statistical software (SPSS v 24, IBM). For all tests, a P value of 0.05 or less indicated statistical significance.

Results

Patient Characteristics

In the consecutive 761 patients with ADHF, a total of 447 patients (median age, 78 (70−84) years; 62.2% male) who underwent thoracic CT scans during their hospital stays were included in the present study. The baseline characteristics of those who underwent CT scans and those who did not are summarized in Supplementary Table 1. The reasons the CT scans were performed were as follows: 11% for coronary evaluation (coronary CT angiography), 36% for evaluation of lung field or search for the origin of inflammation, 18% for diagnosing the etiology of dyspnea, 16% for preoperative screening, and 19% for other reasons. The mean time between admission and the CT scan was 7.8 days, and the median was 4 days. In the whole study population, the mean value of PA/Ao was 0.902 ± 0.164, and the median value was 0.877. ROC analysis was performed to evaluate the sensitivity and specificity of PA/Ao for the primary endpoint. The area under the curve was 0.60. According to the ROC curve, the cutoff value of PA/Ao was defined as 1.0. Baseline characteristics of the study population divided by the defined cutoff PA/Ao value are listed in Table 1. Males were significantly less common among the patients with PA/Ao ≥ 1 (H group, 111 patients, 54%) than among those with PA/Ao < 1 (L group, 336 patients, 65%). There were no significant differences in the histories of chronic obstructive pulmonary disease or smoking habits in the 2 groups. Previous histories of hospitalization for HF were significantly more common in the H group than in the L group (53% vs 33%, $P < 0.001$). Atrial fibrillation was more common in the H group than in the L group (68% vs 54%, $P = 0.014$). There was no significant difference in the etiology of HF or the proportion of HFrEF (LVEF < 40%), HF with midrange EF (HFmrEF, 40% ≤ LVEF < 50%), or HFpEF (LVEF ≥ 50%). The H group was associated with lower blood pressure at admission, lower hemoglobin (Hb), lower serum sodium level (Na) and higher total bilirubin (Hb, H 11.6 (9.8−13.1) g/dL vs L 12.1 (10.5−13.6) g/dL, $P = 0.012$; Na, H 139 (136−142) mEq/L vs L 140 (137−142) mEq/L, $P = 0.035$; total bilirubin, H 1.1 (0.8−1.6) mg/dL vs L 1.0 (0.7−1.3) mg/dL, $P = 0.009$). Plasma NT-pro BNP and eGFR were similar in the 2 groups. The H group was associated with significantly larger LAD, higher TRPG and E/e′ (LAD, H, 48 (42−55) mm vs L, 45 (39−50) mm, $P < 0.001$; TRPG, H, 34 (26−48) mm Hg vs L, 28 (22−38) mm Hg, $P < 0.001$; E/e′, H, 23.3 (17.3−32.2) vs L, 18.4 (13.9−25.0), $P < 0.001$). The lengths of hospital stays were significantly longer in the H group than in the L group (H, 19 (14−32) days vs L, 16 (12−23) days, $P < 0.001$). In-hospital mortality was significantly higher in the H group than in the L group (H, 5.4% vs L, 1.2%, $P = 0.02$). Although thiazide diuretics were more commonly prescribed in the H group than in the L group at discharge (H, 23% vs L, 8%, $P < 0.001$), there were no significant differences in the other kind of cardiovascular medications, such as angiotensin converting enzyme inhibitors, angiotensin receptor blockers or β-blockers, etc.

The Variables Associated With PA/Ao

Correlation analysis was conducted to examine the correlation of PA/Ao with the other clinical variables related to pulmonary artery pressure and/or left ventricular end-diastolic pressure. PA/Ao showed a modest positive correlation with TRPG, LAD and E/e′ (TRPG, $\rho = 0.224$, $P < 0.001$; LAD, $\rho = 0.240$, $P < 0.001$; E/e', $\rho = 0.189$, $P < 0.001$) (Figure 3). Multiple linear regression analysis was conducted to examine the variables independently associated with PA/Ao. PA/Ao was independently associated with age, sex, TRPG, and LAD but not with either LVEF or E/e' (Table 2).

PA/Ao and Clinical Outcome

During a median of 479 days (IQR 273−741) of follow-up, 265 events (all-cause death and ADHF rehospitalization) were recorded. The patients in the H group had a significantly higher rate of primary endpoint than the L group ($P < 0.001$, log-rank test) (Figure 4A). All-cause death and HF rehospitalization were also more common in the H group than in the L group (all-cause death, $P = 0.015$) (Figure 4B); ADHF rehospitalization, $P = 0.003$) (Figure 4C).

We also compared the primary endpoints between those who underwent CTs and those who did not. There was no significant difference between the 2 groups in terms of primary endpoint ($P = 0.074$, log-rank test) (Supplementary Figure 1).

Cox proportional hazard model analysis was conducted to identify independent predictors of the primary endpoint (Table 3). In the univariate analysis, age, BMI, LVEF, NT-pro BNP, Hb, eGFR, and PA/Ao were significantly associated with the primary endpoint. LAD was not a significant predictor of the primary endpoint and TRPG was of borderline significance. In the multivariable analysis, PA/Ao remained an independent predictor of the primary endpoint, whereas TRPG was no longer significant (Table 3). The survival curve at the mean of covariates, which remained significant (age, LVEF and eGFR), was drawn (Supplementary Figure 2), and Cox proportional hazard model analysis employing PA/Ao as a dichotomous variable is shown in Supplementary Table 2.

DISCUSSION

In the present study, we explored the clinical significance of PA/Ao as assessed by CT in patients with ADHF. The main findings of the present study were: 1) higher PA/Ao (≤ 1) was associated with higher TRPG, LAD and E/e′ at baseline (Table 1), and PA/Ao was independently associated with TRPG and LAD (Table 2); 2) higher PA/Ao was associated with worse short-term prognosis in terms of length of hospital

Table 1. Baseline Characteristics of the Study Population Divided by PA/Ao

	All patients	H group (PA/Ao ≥ 1)	L group (PA/Ao < 1)	
	N = 447	n = 111	n = 336	*P* value
Age (years)	78 (70−84)	77 (69−84)	78 (70−84)	0.84
Sex (male) [%]	62.2 (278/447)	54% (60/111)	65% (218/336)	0.04
BMI (kg/m^2)	23.1 (20.9−25.9)	22.9 (20.9−25.4)	23.1 (20.9−26)	0.51
Previous HF hospitalization [%]	37.8 (169/447)	53% (58/110)	33% (111/335)	< 0.001
AF [%]	57.7 (258/447)	68% (75/111)	54% (183/336)	0.01
PM [%]	8.3 (37/447)	12% (13/111)	7% (24/336)	0.14
ICD [%]	4.0 (18/447)	3% (3/111)	4% (15/336)	0.39
CRT [%]	1.1 (5/447)	2% (2/111)	1% (3/336)	0.45
Stroke/TIA [%]	13.6 (60/440)	18% (20/109)	12% (40/331)	0.11
Hemodialysis [%]	0.4 (2/447)	0.9% (1/111)	0.3% (1/336)	0.44
COPD [%]	3.8 (17/446)	4% (4/111)	4% (13/335)	0.89
HTN [%]	68.0 (304/447)	59% (66/111)	71% (238/336)	0.03
DL [%]	40.3 (180/447)	36% (40/111)	42% (140/336)	0.32
DM [%]	29.5 (132/447)	24% (27/111)	31% (105/336)	0.16
Smoking [%]	53.2 (237/445)	48% (53/111)	55% (184/334)	0.18
Etiology				0.2
ICM [%]	27.1 (121/447)	23% (25/111)	29% (96/336)	
DCM [%]	8.7 (39/447)	6% (7/111)	10% (32/336)	
VHD [%]	41.6 (186/447)	47% (52/111)	40% (134/336)	
Other [%]	22.6 (101/447)	24% (27/111)	22% (74/336)	
Vital signs and symptoms at admission				
SBP (mm Hg)	137 (120−156)	134 (111−151)	138 (122−159)	0.01
DBP (mm Hg)	78 (66−95)	74 (65−85)	80 (66−97)	0.002
HR (/min)	88 (71.5−109.5)	81 (69−108)	90 (74−110)	0.11
NYHA III or IV [%]	74.7 (334/447)	74%	75%	0.81
Laboratory data				
Hb (g/dL)	12 (10.4−13.4)	11.6 (9.8−13.1)	12.1 (10.5−13.6)	0.012
BUN (mg/dL)	20.9 (16.1−27.9)	21.3 (17.3−30.6)	20.8 (15.6−27.6)	0.1
Na (mEq/L)	140 (137−142)	139 (136−142)	140 (137−142)	0.035
K (mEq/L)	4.3 (4−4.7)	4.5 (4.1−4.9)	4.3 (4−4.7)	0.006
TB [mg/dL]	1 (0.7−1.4)	1.1 (0.8−1.6)	1 (0.7−1.3)	0.009
AST [U/L]	31 (25−43)	33 (25.5−44)	30.5 (23−43.8)	0.51
ALT [U/L]	22 (13−37)	21 (12−26)	22 (13−47.75)	0.3
Alb [g/dL]	3.6 ± 0.5	3.9 ± 0.3	3.5 ± 0.5	0.009
UA [mg/dL]	6.3 (5.3−7.8)	6.3 (5.2−7.8)	6.3 (5.3−7.8)	0.8
NT-proBNP [pg/uL]	3628 (1796−7354)	3762 (1796−7250.5)	3524 (1784−7470)	0.97
CRP [mg/dL]	0.5 (0.15−2.16)	0.57 (0.16−2.69)	0.48 (0.15−2.03)	0.31
eGFR [mL/min/1.73 m^2]	53.3 (37.7−67.5)	52.6 (33.7−66.7)	53.5 (39.2−67.6)	0.49
Echocardiography				
LVDs [mm]	38 (30−48)	37 (28−50)	38 (31−48)	0.43
LVDd [mm]	52 (45−58)	50 (43−60)	52 (45−58)	0.62
LVEF [%]	50 (33−60)	56 (37−62)	48 (32−59)	0.02
rEF/mrEF/pEF [%]	35.7/13.1/51.2	49%/13%/39%	58%/14%/29%	0.16
LAD [mm]	45 (40−51.5)	48 (42−55)	45 (39−50)	< 0.001
E/e'	19.3 (14.7−26.8)	23.3 (17.3−32.2)	18.4 (13.9−25)	< 0.001
TRPG [mm Hg]	30 (23−39.5)	34 (26−48)	28 (22−38)	< 0.001
In-hospital outcome				
In-hospital mortality [%]	2.2 (10/447)	5.4% (6/111)	1.2% (4/336)	0.02
Hospital stay (days)	17 (12−24)	19 (14−32)	16 (12−23)	< 0.001
Medication at discharge				
Thiazide [%]	11.4 (51/447)	23% (24/105)	8.2% (27/331)	< 0.001
ACEi [%]	24.2 (108/447)	23% (24/106)	25% (84/335)	0.61
ARB [%]	38.3 (171/447)	34% (36/106)	40% (135/335)	0.24
Aldosterone antagonist [%]	30.9 (138/447)	34% (36/106)	30% (102/335)	0.5
β blocker [%]	72.7 (325/447)	69% (73/106)	75% (252/335)	0.2
Amiodarone [%]	5.8 (26/447)	7.5% (8/106)	5.4% (18/335)	0.42
Loop diuretics [%]	81.4 (364/447)	87.6% (92/105)	81.2% (272/335)	0.14
CT parameters				
PA [mm]	32 (28.8−36)	37.9 (35.3−41)	30.4 (28.1−33.3)	< 0.001
Ao [mm]	36.2 (33.8−38.9)	34.3 (32−37.1)	36.7 (34.3−39.7)	< 0.001
PA/Ao	0.88 (0.79−1)	1.1 (1.04−1.18)	0.83 (0.77−0.9)	< 0.001

ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; Alb, albumin; ALT, alanine transaminase; Ao, ascending aorta diameter; ARB, angiotensin II receptor blocker; AST, aspartate transaminase; BMI, body mass index; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CRT, cardiac resynchronization therapy device; DBP diastolic blood pressure; DCM, dilated cardiomyopathy; DL, dyslipidemia; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HF, heart failure; HR, heart rate; HTN, hypertension; ICD, implantable cardioverter defibrillator; ICM, ischemic cardiomyopathy; K, potassium; LAD, left atrial dimension; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; Na, Sodium; NYHA, New York Heart Association functional class; PA, pulmonary artery diameter; PM, pacemaker; SBP, systolic blood pressure; TB, total bilirubin; TIA, transient ischemic attack; TRPG, tricuspid regurgitation peak gradient; UA, urinary acid; VHD, valvular heart disease.

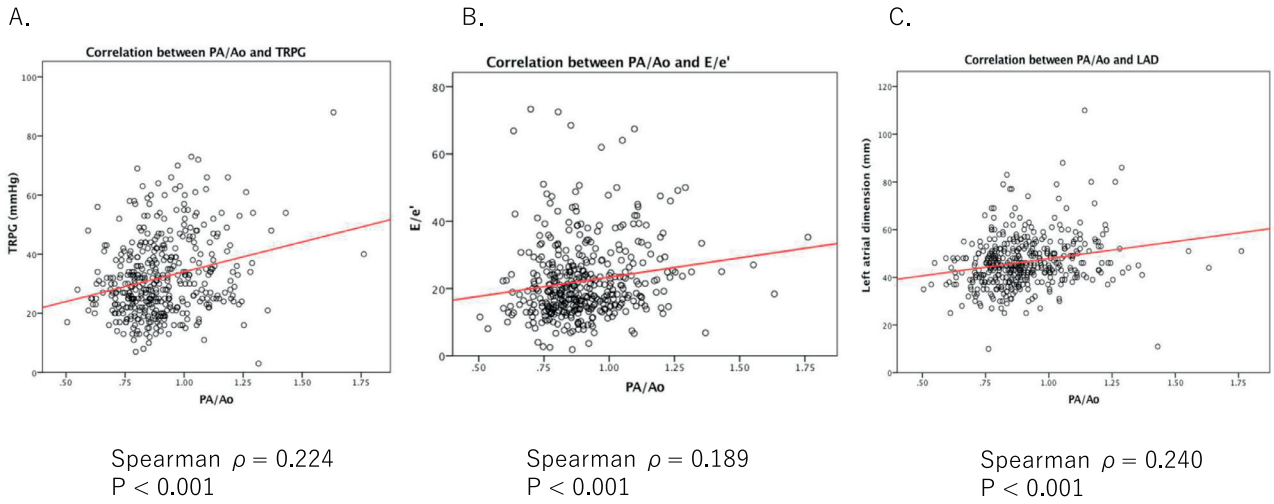

Fig. 3. Correlation between PA/Ao and echocardiographic parameters. Ao, ascending aorta; TRPG (A); E/e′ (B); and LAD (C). LAD, left atrial dimension; PA, pulmonary artery; TRPG, tricuspid regurgitation peak gradient.

Table 2. Multiple Linear Regression Analysis for Assessing the Association Between PA/Ao and the Clinical Variables

	β	95% CI	P value
Age [years]	−0.0020	−0.003 ~ −0.0005	0.007
Sex	0.0227	0.006 ~ 0.039	0.008
TRPG [mmHg]	0.0028	0.002 ~ 0.004	<0.001
LAD [mm]	0.0024	0.0009 ~ 0.004	0.002
E/e′	0.0008	−0.0006 ~ 0.002	0.25
LVEF [%]	0.0005	−0.0005 ~ 0.002	0.33

Ao, ascending aorta diameter; CI, confidence interval for β; LAD, left atrial dimension; LVEF, left ventricular ejection fraction; PA, pulmonary artery diameter; TRPG, tricuspid regurgitation pressure gradient.

stay and in-hospital death (Table 1) and long-term prognosis in terms of the incidence of primary endpoint during a median of 479 days (Figure 4) (Table 3). Based on these findings, we conclude that PA/Ao is a reasonable and reliable surrogate for pulmonary artery pressure and is valuable in terms of prediction of the clinical outcome in patients with ADHF.

Detection of PH by PA/Ao in HF

PA enlargement is a marker for increased pulmonary artery pressure,[6] and PA/Ao measured by CT or MRI was shown to be positively correlated with PAP.[12–14] There has been no consensus on the cut-off value of PA/Ao to estimate the presence of PH. In previous studies that have examined the correlation of PA/Ao and pulmonary artery pressure, a PA/Ao of 0.84[7] and 0.83[12] were reported to be cut-off values for detecting PH. However, PA/Ao = 1 was also used as a cut-off value for detecting PH in patients with chronic obstructive pulmonary disease.[9] Detecting PH in patients with HF is important for the management of HF. The remote monitoring of pulmonary artery pressure using implantable devices provides clinicians with hemodynamics information in patients with HF

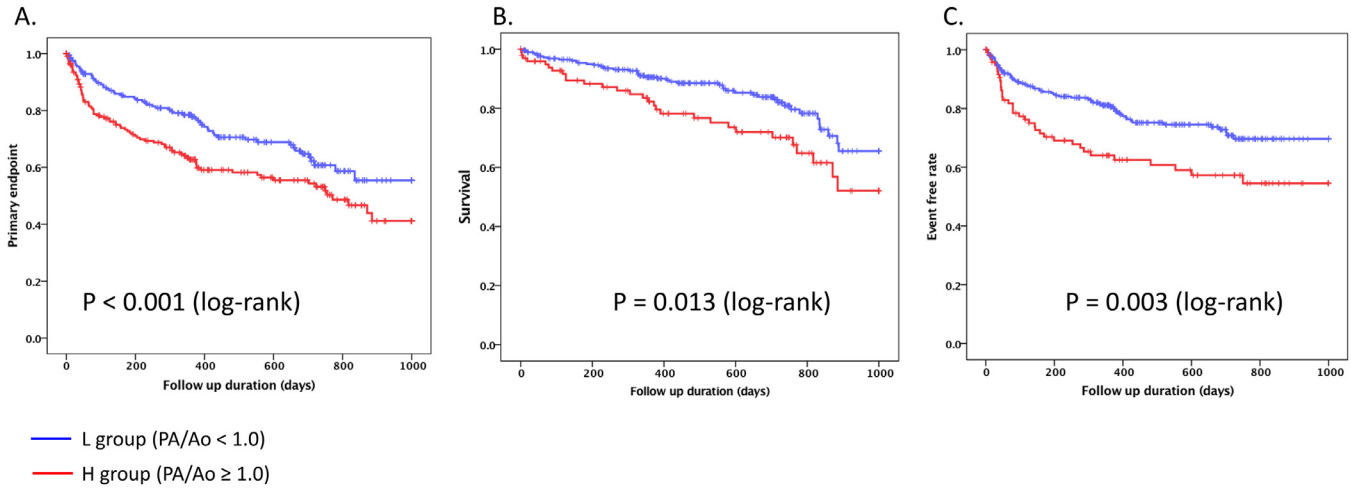

Fig. 4. Kaplan-Meier curve for the primary endpoint (A), all-cause death (B) and rehospitalization for ADHF (C).
The patients in the H group (PA/Ao ≥ 1, red line) had significantly higher rates of the primary endpoint (A), all-cause death (B) and rehospitalization for ADHF (C) compared with the patients in the L group (PA/Ao < 1, blue line).
ADHF, acute decompensated heart failure; Ao, ascending aorta PA; pulmonary artery.

Table 3. Cox Proportional Hazard Model Analysis for the Primary Endpoint

	Univariate				Multivariable			
	HR (per unit)	Lower 95%	Upper 95%	*P* value	HR (per unit)	Lower 95%	Upper 95%	*P* value
Age [years]	1.036	1.023	1.048	< 0.001	1.038	1.017	1.06	< 0.001
Sex [male/female]	0.789	0.622	1.004	0.054	0.87	0.6	1.266	0.47
BMI [kg/m2]	0.936	0.906	0.966	< 0.001	0.977	0.929	1.028	0.38
AF	1.320	0.949	1.856	0.104				
LVEF [%]	0.989	0.981	0.996	0.004	0.983	0.972	0.996	0.009
NT-proBNP [pg/mL]	1.000008	1.000002	1.000012	0.002	1	0.999	1	0.73
Hb [g/dL]	0.86	0.815	0.908	< 0.001	0.935	0.863	1.014	0.1
eGFR [mL/min/1.73m^2]	0.979	0.973	0.985	< 0.001	0.99	0.981	0.999	0.038
TRPG [mm Hg]	1.011	0.999	1.022	0.07	0.999	0.987	1.012	0.95
LAD [mm]	1.007	0.992	1.022	0.35				
PA/Ao	3.503	1.429	8.192	0.005	5.253	1.818	14.93	0.002

AF, atrial fibrillation; Ao, ascending aorta diameter; BMI, body mass index; eGFR, estimated glomerular filtration ratio; Hb, hemoglobin level; LAD, left atrial dimension; LVEF left ventricular ejection fraction; NT-proBNP, N-terminal pro B-type natriuretic peptide; PA, pulmonary artery diameter; TRPG, tricuspid regurgitation peak gradient.

and recently, this device has successfully reduced rehospitalization.[15] In the present study, PA/Ao was significantly correlated with TRPG. Furthermore, in multiple linear regression analysis, PA/Ao was independently associated with TRPG, even after adjusting for the other variables. Based on these findings, PA/Ao can be a reliable surrogate for estimation of PH in patients with HF. Because of its convenient and noninvasive nature, transthoracic echocardiography parameters, including TRPG and inferior vena cava diameter, are often used to estimate pulmonary artery pressure. However, for noncardiologists, the estimation of PH by echocardiography is often difficult to perform technically or to interpret, and it can be affected by biases, including interobserver variability and limited visibility in some patients. On the other hand, estimation of PH by PA/Ao has an advantage because it is easy to measure in conventional axial noncontrast CT images and to interpret, even for noncardiologists. Correction of PA diameter by Ao seems to be reasonable because both are correlated with body surface area[16,17] and, as a result, PA/Ao is not affected by body surface area.[17] However, Ao diameter was significantly smaller in the L group in the present study (Table 1), although the previous study showed no significant difference in Ao between high and low PA/Ao groups.[12,18] Ao diameter was shown to be positively correlated with age and hypertension,[19] so smaller Ao diameter in the H group in the present study might be attributed to the lower proportion of patients with hypertension (Table 1). Although it can be a bias to use PA/Ao as a surrogate for pulmonary artery pressure, lower blood pressure is also 1 of the features of severe HF,[20] and PA/Ao can be a comprehensive marker of the severity of and prognosis for HF.

The Prognostic Value of PA/Ao

PA/Ao was shown to predict future adverse events in chronic obstructive pulmonary disease,[9,21,22] idiopathic pulmonary fibrosis,[14] chronic thromboembolic PH,[23] and the cohort of the consecutive patients who underwent cardiac MRI for the evaluation of heart disease.[24] Also, there are some previous studies that investigated the prognostic value of PA/Ao in patients with HF. Karakus et al enrolled 110 patients with HFpEF and showed that PA/Ao was associated with future cardiovascular events.[11] However, Pellicori et al studied 384 patients with chronic HF and 38 healthy controls who underwent cardiac MRI, and PA/Ao was not associated with adverse outcomes.[25] In that study, however, ambulatory patients referred with suspected HF who had undergone cardiac MRI as a part of their investigations were enrolled. Median PA/Ao in patients with HF was comparable to that of the control subjects. Also, PA/Ao values did not differ significantly across the tertiles of PA/Ao.[25] Therefore, these findings suggest less severe conditions of HF in that population, and they are quite different from the findings in our study, which was targeted to patients who were admitted for ADHF. To our knowledge, this is the first study that evaluated the impact of PA/Ao by CT on the clinical outcomes in the population with ADHF.

In the present study, higher PA/Ao was associated with higher in-hospital mortality and the higher incidence of the primary endpoint in the patients with HF. Furthermore, PA/Ao was an independent predictor of the primary endpoint after adjustment for the other variables. Interestingly, TRPG and LAD were not independent predictors of the primary endpoint, even though they were correlated with PA/Ao. The causes of the differing prognostic values among these parameters are uncertain. The previous report showed that PA/Ao assessed by CT in combination with echocardiography were superior to echocardiography alone for PH detection.[14] PA/Ao might provide greater accuracy in PH estimation, possibly due to its simple and easy measurement, which might eventually lead to its high prognostic value. In the present study, higher PA/Ao was associated with the features of more severe disease, such as larger LAD, E/e′, TRPG, in-hospital mortality, and higher incidence of the primary endpoint. However, there was no significant difference in the NT pro-BNP at admission, indicating that PA/Ao does not necessarily reflect the severity of HF in the acute phase, although it remains unknown

whether PA/Ao shows significant changes between the compensated and decompensated phases.

Limitations

There are several limitations in the present study. First, this was a single-center observational study with a relatively small number of patients, and the study findings can potentially include some bias because of its retrospective nature; this study design limits the generalizability of these data. For example, the proportion of dilated cardiomyopathy in the underlying disease was relatively small (9%), and the proportion of valvular heart disease was large (42%) compared to the other multicenter HF registries.[26] The findings of this study may not necessarily be generalized to all populations with HF. Although possible confounders were adjusted for, there may be uncaptured factors that could influence the results. Second, the study population consisted of the patients who underwent thoracic CT scans for some clinical reason during the hospital stay. There was some difference in baseline characteristics between those who underwent CTs and those who did not, so there might be some biases in this study cohort that do not represent the general population with HF. Third, we did not collect the hemodynamic data from right-heart catheterization to estimate the direct correlation between PA/Ao and PA pressure, although PA/Ao was shown to be positively correlated with TRPG, which is an established parameter of pulmonary artery pressure.[12] Fourth, PA and Ao diameter show small changes during the cardiac cycle.[27] Because the scans were not intended specifically to determine PA/Ao in the present study, the majority of CT images were not electrocardiogram-gated. Fifth, although the in-hospital mortality rate was significantly higher in the H group than in the L group, it might not be adequate to draw conclusions from this because the total number of in-hospital deaths was small (10 of 447 patients). Sixth, our data lack the lung-function test, which may have some influence on the PA/Ao.[9,28] Finally, the main PA diameter was shown to increase or decrease over time, and the change in PA diameter was shown to predict the mortality in patients with pulmonary arterial hypertension,[29] but we did not collect the CT data after discharge.

Conclusion

PA/Ao is a parameter easily measurable by CT and can be a reliable marker for the prediction of the outcomes of patients with ADHF.

Conflicts of interest

None.

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Supplementary materials

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