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The Role of Pulmonary Artery Compliance for Predicting Mid-Term Outcome in Patients with Systolic Heart Failure

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A B S T R A C T

Alteration in pulmonary artery compliance and the extent of pulmonary hypertension might be a determinant of morbidity and mortality in patients with heart failure. However, whether reduced pulmonary artery compliance has a prognostic value in patients who have systolic heart failure is unknown. In the present study, we investigated whether pulmonary artery compliance has a prognostic value in these patients. In a prospective cohort study, 107 consecutive patients with systolic heart failure with any etiologies who underwent cardiac catheterization at the Shahid Rajaee hospital between September 2009 and April 2011 and undertreated with optimal medical regimens were included into the study. Cardiac catheterization was performed using Swan Ganz Catheters. Plasma NT-pro BNP level was also measured using enzyme immunoassay. Clinical follow-up examinations were performed at 3 months and 6 months after the initial evaluation and the patients were evaluated regarding occurrence of death, hospitalization, functional class and serum level of Pro-BNP. Among angiographic parameters, pulmonary artery compliance had an adverse relation with left ventricular ejection fraction, peripheral vascular resistance, mean pulmonary artery pressure, systolic and diastolic pulmonary artery pressures, right ventricular systolic and diastolic pressures, central vein pressure, Pulmonary capillary wedge pressure, whereas this parameter was positively correlated with cardiac output, stroke volume, arterial oxygen saturation, and mixed venous oxygen saturation. There was no univariate significant association between pulmonary artery compliance and living status or hospitalization. An adverse association was revealed between pulmonary artery compliance and mid-term functional class. Also, an adverse association was revealed between pulmonary artery compliance and plasma level of Pro-BNP within 6-month follow-up time in the multivariable regression analysis with the presence of cofounders. Pulmonary artery compliance using standard right heart catheterization might be a useful tool for predicting changes in functional class as well as plasma Pro-BNP level in patients with systolic heart failure.

Introduction

The pulmonary circulation is a low-pressure, high-capacity system. At sea level, the normal pulmonary artery systolic pressure is about 25 mm Hg, and the pulmonary vascular resistance (PVR) averages 67±30 dynes, less than one tenth that of the systemic circulation (1). The pulmonary vasculature can accommodate large increases in blood flow, as during exercise or sudden occlusion of a pulmonary artery, with little or no increase in pressure. The pulmonary circulation is a major determinant of right ventricular (RV) after-load and thus determines RV output (2). Although the thin-walled, distensible RV can accommodate large increases in systemic venous return without a rise in pulmonary artery pressures, even modest increases in pulmonary vascular tone, if acute, can result in RV failure (2). The pulmonary circulation also regulates venous return to the left ventricle (LV) and thus protects the LV against excess preload. In pulmonary hypertension associated with chronic heart failure, RV after-load and LV preload are increased, leading to further myocardial dysfunction (2).

The extent of secondary pulmonary hypertension may be a determinant of morbidity and mortality in patients with chronic heart failure. In patients with chronic heart failure, pulmonary artery systolic pressure was an independent predictor of the need for cardiac transplant (3). Likewise, death and hospitalization for heart failure were increased in patients with echocardiographic evidence of pulmonary hypertension (4).

Presumably, a major impact of pulmonary hypertension is on RV function, which is a strong predictor of overall and event-free survival in chronic heart failure (5).

Pulmonary hypertension is an identified indicator of a poor prognosis in patients with various types of heart diseases including dilated cardiomyopathy, functional mitral regurgitation, as well as in heart transplant recipients (6, 7). However, whether reduced pulmonary artery compliance has the same prognostic value in patients who have systolic heart failure is unknown. In the present study, we investigated whether pulmonary artery compliance has a prognostic value in patients with systolic heart failure. In addition, we determined which parameters might function as predictors of adverse mid-term outcome of heart failure such as mortality, hospitalization, reduced function class and serum Pro-BNP level in those patients.

Materials and Methods

In a prospective cohort study, 107 consecutive patients with systolic heart failure with any etiologies who underwent cardiac catheterization at the Shahid Rajaee hospital between September 2009 and April 2011 were included into the study. All patients had a left ventricular ejection fraction (LVEF) of less than 40% in their previous reported echocardiography. The related institutional ethics committees approved the present study and each patient provided written informed consent for the procedure before any intervention. Baseline characteristics were collected through interviewing included demographics, weight, height, and baseline functional class.

Two-dimensional and Doppler transthoracic echocardiographies were performed at baseline for all participants. All echocardiographic studies were performed using commercially available 3.75-MHz transducers by the same echocardiographic expert examiner who was unaware of the clinical status of the patients.

Cardiac catheterization was performed using Swan Ganz Catheters to measure the following routine cardiac hemodynamic parameters: LV end-diastolic volume index, LV end-systolic volume index, LV systolic pressure, LV end-diastolic pressure, pulmonary capillary wedge pressure, systolic, diastolic, and mean PAP, transmitral diastolic pressure gradient (pulmonary capillary wedge pressure minus the LVend-diastolic pressure), right atrial pressure, systemic vascular resistance ((mean arterial pressure minus right atrial pressure) multiplied by 80 and divided by the cardiac output), and pulmonary vascular resistance (PVR) ((mean PAP minus pulmonary capillary wedge pressure) multiplied by 80 and divided by the cardiac output). Cardiac output was measured by Thermodilution method and by Vigilence monitors (Edwards Lifescience Inc.). In those with severe tricuspid regurgitation, cardiac output was also measured using Fick formula. Pulmonary arterial compliance defined as the ratio of stroke volume to pulmonary pulse pressure (SV/PP). Plasma NT-pro BNP concentration was measured using enzyme immunoassay at baseline.

Clinical follow-up examinations were performed at 3 months and 6 months after the initial evaluation and the patients were evaluated regarding occurrence of death, hospitalization, functional class and serum level of Pro-BNP. The primary endpoint of the study was assessing relationship between pulmonary arterial compliance and other clinical and angiographic parameters. The secondary endpoint of the study was to determining value of pulmonary arterial compliance for predicting outcome of the study population within 3 and 6 months of the follow-up time including occurrence of death, hospitalization, functional class and serum level of Pro-BNP.

Results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than 5 were observed. Quantitative variables were also compared using t test or ANOVA test. Multivariate logistic regression analysis was used to determine predictive role of pulmonary arterial compliance with the presence of study confounders including demographics parameters and baseline hemodynamic indices. For the statistical analysis, the statistical software SPSS version 19.0 for windows (SPSS Inc., Chicago, IL) was used. P values of 0.05 or less were considered statistically significant.

Results and Discussion

In current study, totally, 107 patients were assessed that among them, 78 patients had the primary etiology of heart failure (HF) and 29 patients were admitted with pulmonary artery hypertension (PAH) (Table 1). The mean age of the patients was 39.0 ± 13.22 years (40.73 ±12.62 years for HF group and 35.31±14.21 years for PAH group, p = 0.078) and 69.2% of them were men (80.8% for HF group and 37.9% for PAH group, p< 0.001). Mean body mass index was significantly higher in HF THAN PAH group (23.78 ± 5.31 kg/m^2 versus 21.53 ± 3.74, p = 0.038). With regard to the baseline functional class, 18.7% were in class I, 43.0% were in class II, 27.1% in class III, and 11.2% were in class IV. Function class in PAH group was significantly higher than the HF group. With respect to the echocardiographic and angiographic parameters, the indices of PVR, RVDP, mean PAP, systolic and diastolic PAP were higher in PAH group

than the HF ones, while PCWP and SAO2 were higher in HF than another group (Table 2). The mean pulmonary artery compliance was totally 2.75 ± 2.45 that significantly higher in HF compared with PAH group (3.14 ± 2.58 versus 1.67 ± 1.71, p = 0.001). Men and women had a similar pulmonary artery compliance (men 2.95 ± 2.71, women 2.28 ± 1.70, p = 0.122). Also, pulmonary artery compliance was not correlated with patients' age, but this pulmonary artery parameter had an adverse relationship with functional class (3.93 ± 3.48 for class I, 3.20 ± 2.39 for class II, 1.81 ± 1.41 for class III, and 1.30 ± 0.78 for class IV, p = 0.002). This negative relation was observed in both group with HF or PAH. Also, pulmonary artery compliance was positively correlated with body mass index (Beta = 0.296, p = 0.002). Furthermore, among angiographic parameters, pulmonary artery compliance had an adverse relation with LVEF, PVR, mean PAP, systolic PAP, diastolic PAP, RVSP, CVP, RVDP, and PSWP, whereas this parameter was positively correlated with cardiac output, SV, SAO2, and MVO2 (Table 3).

Within the follow-up time, mortality was reported in a patient within 3 month (in HF group) and 2 patients (in both groups) within 6 months of follow-up. Also, 3-month hospitalization rate was totally 23.3% (17.9% in HF group and 37.9% in PAH group) and 6-month hospitalization rate was totally 31.8% (28.2% in HF group and 41.4% in PAH group). Both indices of function class and Pro-BNP level were gradually reduced within the follow-up period, but the trend of these changes was not different between the HF and PAH groups. There were no univariate significant association between pulmonary artery compliance and two variables of living status and hospitalization (Table 4). Although an adverse association was revealed between pulmonary artery compliance and functional class (Figure 1), but this association was not confirmed within 3 months (Beta = -0.032, p = 0.309) and 6 months (-0.053, p = 0.107) of follow-up in the multivariable regression analysis with the presence of cofounders. Also, although an adverse association was revealed between pulmonary artery compliance and plasma level of Pro-BNP (Figure 2), but this association was only observed within 6-month follow-up in the multivariable regression analysis with the presence of cofounders (Beta = -208.188, p = 0.020).

This study aimed to determine role of pulmonary artery compliance for predicting adverse outcome of systolic heart failure including mortality, hospitalization, and functional class as well as plasma level of BNP. Our study is the first one to our knowledge to look into pulmonary artery compliance with regard to some aspects of outcome such as changes in functional class and plasma pro-BNP. Our study has the following main findings: first, we showed that pulmonary artery compliance could not predict mid-term mortality in those with systolic heart failure. This finding can be influenced by a short time of following-up, low mortality rate within the follow-up period and more important, the potential role of other underlying factors such as cardiac risk factors or failure-related complications which affecting mortality in study subjects. In a study by Mahapatra (8), relationship between pulmonary artery compliance and mortality in patients with idiopathic pulmonary hypertension was proved. In that study, 102 patients were followed for 4 years with a mortality rate higher that found in our study.

Table.1 Baseline characteristics and clinical data of the study population

Characteristics	Total group (n = 107)	HF group (n = 78)	PAH group (n=29)	P-value
Male gender	74 (69.2)	63 (80.8)	11 (37.9)	< 0.001
Age (year)	39.00 ± 13.22	40.73 ± 12.62	35.31 ± 14.21	0.078
Body mass index (kg/m^2)	22.67 ± 5.02	23.78 ± 5.31	21.53 ± 3.74	0.038
Function class				
I	20 (18.7)	11 (14.1)	9 (31.1)	
II	46 (43.0)	40 (51.3)	6 (20.7)	0.003
III	29 (27.1)	22 (28.2)	7 (24.1)	
IV	12 (11.2)	5 (6.4)	7 (24.1)	

Table.2 Angiographic parameters in study groups

Characteristics	Total group (n = 107)	HF group (n = 78)	PAH group (n=29)	P-value
PVR	7.87 ± 6.23	3.27 ± 4.94	14.20 ± 8.80	< 0.001
COt	4.02 ± 1.00	3.99 ± 0.97	4.11 ± 1.11	0.603
COf	4.28 ± 4.21	4.43 ± 4.88	3.86 ± 1.11	0.338
SV	49.16 ± 15.61	49.23 ± 15.44	48.97 ± 16.33	0.940
LVEF	27.12 ± 11.77	21.18 ± 7.42	43.10 ± 3.11	< 0.001
CVP	9.84 ± 4.44	9.99 ± 4.69	9.41 ± 3.72	0.509
RVDP	12.23 ± 8.11	11.18 ± 6.96	15.07 ± 10.22	0.027
PAP mean	40.49 ± 21.33	35.01 ± 16.28	55.22 ± 26.18	< 0.001
Systolic PAP	59.87 ± 33.72	48.35 ± 22.64	90.86 ± 39.11	< 0.001
Diastolic PAP	31.33 ± 16.92	25.71 ± 11.94	46.45 ± 19.16	< 0.001
PCWP	18.41 ± 9.27	20.02 ± 9.24	14.07 ± 8.00	0.002
SVR	19.84 ± 8.15	19.72 ± 8.68	20.16 ± 6.64	0.779
MVO2	59.38 ± 9.58	58.68 ± 9.70	61.28 ± 9.13	0.204
SAO2	91.98 ± 6.13	93.86 ± 2.75	86.93 ± 9.22	< 0.001
HR	83.28 ± 12.92	83.05 ± 13.05	83.90 ± 12.76	0.763
SBP	113.49 ± 16.80	111.95 ± 16.45	117.62 ± 7.34	0.134
DBP	73.89 ± 13.04	73.37 ± 12.95	75.28 ± 13.40	0.513

Table.3 Correlation between angiographic parameters and pulmonary artery compliance

Parameters	Beta	P value
PVR	-0.364	< 0.001
LVEF	-0.201	0.038
PAP mean	-0.472	< 0.001
PAP systolic	-0.618	< 0.001
PAP diastolic	-0.525	< 0.001
RVSP	-0.611	< 0.001
CVP	-0.274	0.004
RVDP	-0.420	< 0.001
PCWP	-0.300	0.002
COt	0.569	< 0.001
SV	0.649	< 0.001
SAO2	0.324	0.001
MVO2	0.434	< 0.001

Table.4 Relationship between pulmonary artery compliance and study outcome

Compliance	Total group (n = 107)	HF group (n = 78)	PAH group (n=29)
Living status (3-month)			
Alive	2.76 ± 2.46	3.17 ± 2.59	1.67 ± 1.71
Dead	1.72	1.42	0.001
p-value	0.093	0.504	0.620
Living status (6-month)			
Alive	2.78 ± 2.47	3.17 ± 2.59	1.71 ± 1.73
Dead	1.00 ± 0.59	1.42	0.58
p-value	0.081	0.504	0.525
Hospitalization (3-month)			
Hospitalized	2.08 ± 2.06	2.74 ± 2.55	1.20 ± 0.65
No hospitalized	2.95 ± 2.53	3.23 ± 2.59	1.96 ± 2.01
p-value	0.023	0.262	0.438
Hospitalization (6-month)			
Hospitalized	2.32 ± 2.45	3.02 ± 2.79	1.03 ± 0.60
No hospitalized	2.94 ± 2.45	3.19 ± 2.51	2.12 ± 2.08
p-value	0.044	0.567	0.059

Figure.1 Relationship between pulmonary artery compliance and function class

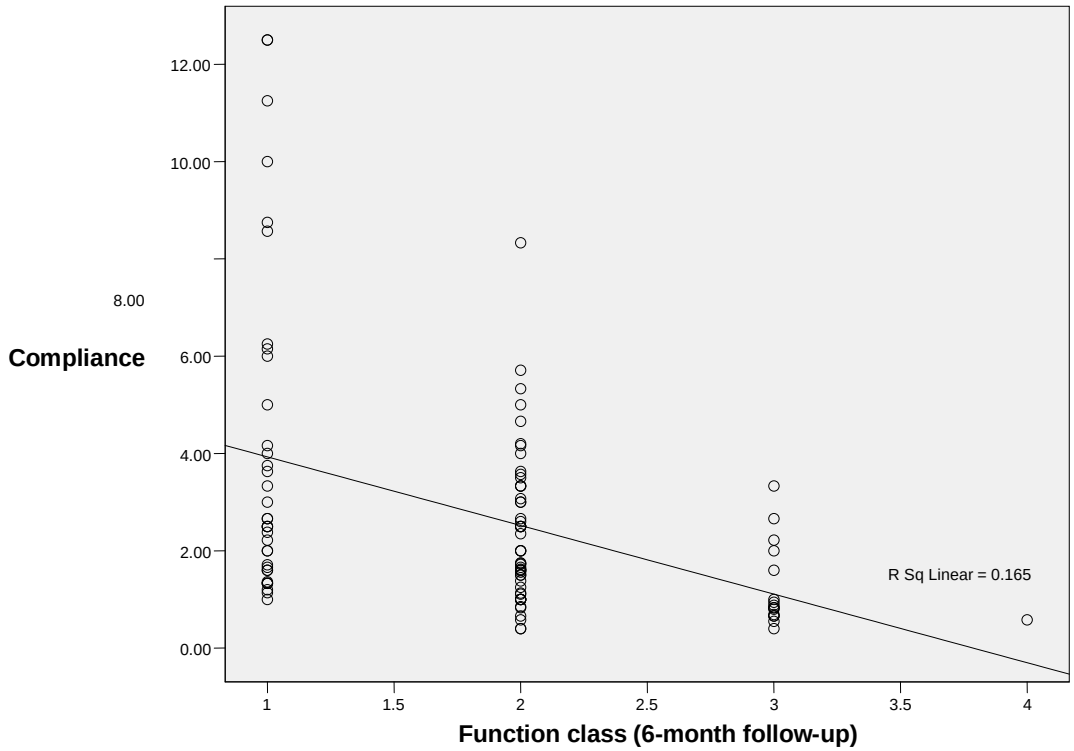
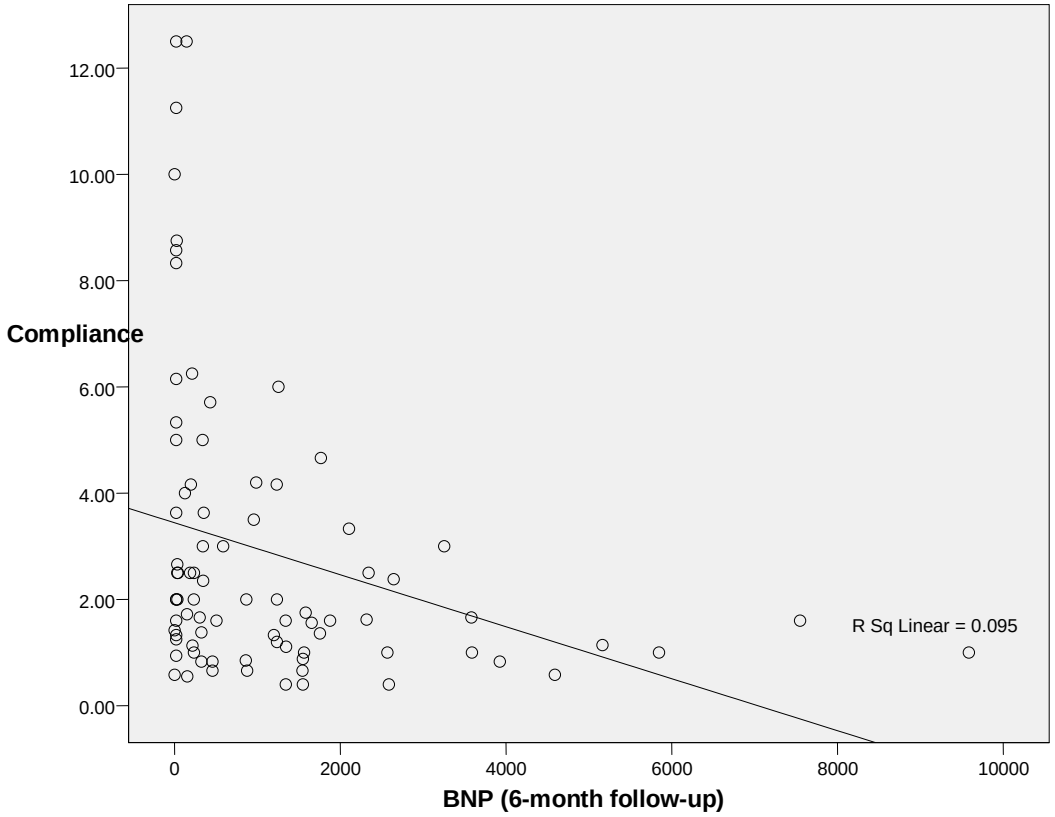


Figure.2 Relationship between pulmonary artery compliance and BNP



Thus, it seems that the design further studies with greater sample size and longer follow-up period and with the presence of other effective variables, the role of pulmonary artery compliance for predicting mortality might be more highlighted. With regard to another result, no significant relation was observed between pulmonary artery compliance and incidence rate of hospitalization. It is also believed that more important determinants have been identified which predisposing patients to hospitalization such as heart failure-related complications and function class. In fact, based on the multivariate regression model, the role of baseline functional class and plasma level of pro-BNP seems to be higher than pulmonary artery compliance to predict re-hospitalization.

In the univariate analysis in our study, pulmonary artery compliance was a strong indicator for predicting function class within 3 months and 6 months of follow-up; however this relationship was not be approved in the multivariable analysis. So, it seems that the mid-term function class might be more influenced by other confounding factors including baseline functional class. However, strong linear correlation between pulmonary artery compliance and mid-term functional class should not be ignored. In some previous studies (9–11), reduced pulmonary artery compliance was accompanied with reduced physical activity and therefore with decreased functional capacity and thus ability of pulmonary artery compliance for determining reduced function capacity might be explainable.

Although pulmonary artery compliance could not predict above outcome indices in the multivariable models, but this indicator had a strong role to predict plasma level of Pro-BNP at 6-month follow-up time point even with the presence of confounders. In majority of studies, relationship between Pro-BNP and cardiovascular diseases such as infarction and heart failure has been shown. However, relation between Pro-BNP and pulmonary artery compliance is already questioned. Although some recent studies could not indicate relation between reduced pulmonary artery compliance and changes in plasma Pro-BNP (12), but some evidences are available about this fact that the improvement in plasma Pro-BNP can result in improving pulmonary artery blood flow (13). The present study with emphasize on confirming this relation, can be open new ways for more studying relationship between plasma Pro-BNP measure and pulmonary artery compliance in systolic heart failure patients.

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