



The Relationship Between Computed Tomography Derived Thoracic Metrics and Echocardiographic Systolic Pulmonary Arterial Pressure in Patients with Pulmonary Hypertension

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ABSTRACT

Introduction: Doppler echocardiography-derived systolic pulmonary artery pressure (sPAP) is the first-line examination in evaluating patients with suspected pulmonary hypertension (PH). We aimed to determine the relationship between the contrast-enhanced chest computed tomography (CT)-derived dimensions of pulmonary vessels/right heart chambers and echocardiographic sPAP in patients with PH.

Patients and Methods: Overall, 68 patients (44 female, 24 male) with sPAP > 35 mmHg who underwent CT within 3 days of echocardiographic examination were included. The diameters of the main pulmonary artery (MPA), right and left pulmonary arteries, and right and left interlobar branch arteries and the wall thicknesses and diameters of the right ventricle were measured. Pulmonary arterial measurements were adjusted based on diameters of the ascending aorta, descending aorta, and thorax length. The right ventricular measurements were adjusted by left ventricular internal dimensions and wall thicknesses and by thorax length. The relationships between sPAP and all primary and adjusted measurements were assessed by correlation analyses.

Results: The dimensions of MPA, left and right pulmonary arteries, left and right interlobar arteries, right ventricular chamber, and wall thickness were all related to sPAP. Adjustment of these measurements lessened the relationship with sPAP. By multivariate analysis, MPA was the only independent variable related to sPAP ($r=0.65$, $p<0.001$). Subgroup analysis of 48 (71%) patients with sPAP elevation not caused by left heart pathology revealed a stronger correlation between MPA and sPAP ($r=0.72$, $p<0.001$).

Conclusion: MPA was the strongest single independent correlator of sPAP among various CT measurements. The relationship between sPAP and MPA was more pronounced in patients with precapillary PH.

Key Words: Tomography, emission-computed; pulmonary artery; hypertension, pulmonary

Pulmoner Hipertansiyonlu Hastalarda Ekokardiyografik Sistolik Pulmoner Arter Basıncının Bilgisayarlı tomografi ile Ölçülen Torasik Metriklerle İlişkisi

ÖZET

Giriş: Şüpheli pulmoner hipertansiyon (PH)*lu hastaların değerlendirilmesinde Doppler ekokardiyografi ile ölçülen sistolik pulmoner arter basıncı (sPAB) ilk seçenek incelemesidir. Bu çalışmada PH hastalarında kontrastlı toraks bilgisayarlı tomografi (BT) ile elde edilen pulmoner damar ve sağ kalp boşluklarının çapları ile ekokardiyografik sPAB arasındaki ilişkiyi belirlemeyi amaçladık.

Hastalar ve Yöntem: Araştırmaya sPAB > 35 mmHg olup ekokardiyografik inceleme ile 3 gün içerisinde BT çekilmiş olan toplam 68 hasta (44 kadın, 24 erkek) dahil edildi. Ana pulmoner arterler (APA), sağ ve sol pulmoner arterler, sağ ve sol interlobar dal arterlerin çapları ile sağ ventrikül duvar kalınlıkları ve çapları birincil ölçümler idi. Pulmoner damar ölçümleri, asendan aorta, desendan aorta ve toraks çapına oranlanarak ikincil türev ölçümler elde edildi. sPAB ile birincil ve ikincil ölçümler arasındaki ilişki korelasyon analizi ile araştırıldı.

Bulgular: APA, sol ve sağ pulmoner arterler, sol ve sağ interlobar arter çapları ile sağ ventrikül çap ve duvar kalınlığı ölçümlerinin tamamı sPAB ile korele idi. İkincil türev ölçümler ise sPAB ile olan ilişkiyi zayıflattı. Çok değişkenli analizde sPAB ile tek bağımsız ilişkisi olan parametre APA çapı idi ($R=0.65$, $p<0.001$). Sol kalp patolojisine sekonder sPAB artışı olan hastalar hariç tutulduğunda, geriye kalan 48 (%71) hastanın alt grup analizinde APA çapı ile sPAB arasında daha güçlü bir korelasyon olduğu gözlemlendi.

Sonuç: Çeşitli toraks BT ölçütleri arasında sPAB ile en güçlü ve bağımsız ilişkili olanı APA çapıdır. Prekapiler PH hastalarında, sPAB ile APA çapı arasındaki ilişki daha da belirgindir.

Anahtar Kelimeler: Tomografi, emisyon-bilgisayarlı; pulmoner arter; hipertansiyon, pulmoner

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Submitted: 04.10.2015

Accepted: 08.10.2015

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Available on-line at
www.kosuyoluheartjournal.com

INTRODUCTION

Pulmonary hypertension (PH) is defined as mean pulmonary artery pressure (PAP) being greater than or equal to 25 mmHg at rest, as assessed by right heart catheterization⁽¹⁾. It is a syndrome characterized by increased vascular resistance, constriction, remodeling, and thrombosis in the pulmonary circulation⁽²⁾. Persistent elevation of PAP progressively deteriorates right heart function and causes significant morbidity and mortality⁽³⁾. Although right heart catheterization is the gold standard for the definitive diagnosis of PH, it has recognized risks because of its invasive nature and high cost⁽⁴⁾. Thus, echocardiography is widely used as a noninvasive screening tool in this regard and also in the assessment of response to therapy⁽⁵⁾. The pressure gradient derived from tricuspid regurgitation jet, added to echocardiographically-estimated right atrial pressure, has been reported to correlate well with catheterization-derived PA systolic pressure^(6,7). Elevated systolic PAP (sPAP) (sPAP > 35 mmHg) caused by heart and lung diseases is frequently encountered in echocardiography examinations⁽⁸⁻¹⁰⁾. Contrast-enhanced chest computed tomography (CT) discriminates patients with or without PH by using the diameter of the central pulmonary artery and assessing cardiac morphology⁽¹¹⁻¹³⁾. However, the superiority of one vascular or cardiac dimension over another to predict sPAP has not been widely studied. Moreover, because pulmonary vascular and cardiac dimensions are affected by factors other than PH degree, whether an internal correction of these measurements provides a more strong relation to sPAP is unknown. In this study, we retrospectively investigated the relationship between several predefined primary and adjusted measurements of major cardiac and pulmonary vascular structures with echocardiographic sPAP.

PATIENTS and METHODS

Study Population

The institutional database was retrospectively examined for 2 years, and 451 patients who underwent both echocardiography and contrast-enhanced chest CT within the same day for various reasons between May 2010 and March 2012 were identified. An sPAP > 35 mmHg was present in 81 patients. Patients with motion artifacts on CT imaging were excluded. Finally, 68 out of 81 patients who had adequate CT image quality were included in the study. Age, sex, past medical history (i.e., diabetes, hypertension, coronary artery disease, arrhythmia, renal failure, and lung disease), and echocardiographic and CT findings were recorded. The study was approved by the local ethics board.

Echocardiography

Standard echocardiography (Esaote Mylab-50) was performed using a 3-MHz transducer while the patients were at rest and in the left lateral decubitus position. Routine M-Mode, 2-dimensional, continuous wave, and color Doppler echocardiography were performed in all patients. The peak value of the Doppler trace of the tricuspid regurgitation jet was used in the modified Bernoulli

equation ($\Delta P = 4V^2$) to calculate the pressure gradient between the right ventricle and atrium. The right atrial pressure was estimated according to the contemporary guidelines⁽¹⁴⁾. sPAP was acquired with the addition of the estimated right atrial pressure to this gradient.

Computed Tomography

The CT scans were performed with Siemens Somatom Sensation 64-slice system while the patients held their breath. All patients were in an asymptomatic and fasting condition and lying in a supine position during the scan. Somatom 64 is a scanner with a 0.33 s gantry rotation time, 0.75 mm of slice thickness, and 0.6 mm collimation. The non-electrocardiographically gated scans were triggered automatically when a predefined contrast enhancement was reached in the descending aorta. The tube voltage and current were 120 kV and 250 mAs, respectively. The pitch value was 0.75, and the reconstruction interval was 0.5 mm. A contrast agent including iopromide (Ultravist 300, Bayer Healthcare, Berlin, Germany) was infused at a rate of 3-4 mL/s by intravenous automatic injection system for contrast enhancement.

The images were analyzed on a dedicated workstation using the original axial slices a long with, oblique and curved multiplanar (MPE) and maximum intensity of projection (MIP) reformatted images. The images of all patients were interpreted by an experienced radiologist blinded to the clinical and echocardiographic data.

We were aware that the predefined primary CT measurements could be affected by age, sex, body surface area, scanning moment during the cardiac cycle, and variations in contrast enhancement. Therefore, we divided each primary CT measurement by relevant adjustment factors to provide an internal correction for potential confounders.

Primary CT Measurements

- MPA: Main pulmonary artery diameter measured from the largest diameter at the level of bifurcation.
- LPA: Left pulmonary artery diameter measured from the largest inner diameter along its course.
- RPA: Right pulmonary artery diameter measured from the inner diameter.
- LIBA: Left interlobar branch artery inner diameter measured from posteromedial of the left upper lobe bronchus.
- RIBA: Right interlobar branch artery inner diameter measured from anterolateral of the middle lob bronchus.
- RVW: Free wall thickness of the mid-right ventricle.
- RVD: Intracavitary diameter of the mid-right ventricle.

Adjustment Factors

- AA: Ascending aorta measured from the largest diameter between the annulus and arcus.

- DA: Descending aorta measured from the largest diameter at the level of PA bifurcation.
- TL: Thorax length measured from the largest inner diameter between the right and left ribs where the heart is seen as a four-chamber structure.
- LVW: Free wall thickness of the mid-left ventricle.
- LVD: Intracavitary diameter of the mid-left ventricle.

Secondary derivatives

- MPA/AA, MPA/DA, MPA/TL
- LPA/AA, LPA/DA, LPA/TL
- RPA/AA, RPA/DA, RPA/TL
- LIBA/AA, LIBA/DA, LIBA/TL
- RIBA/AA, RIBA/DA, RIBA/TL
- RVW/LVW, RVD/LVD, RVD/TL

Statistics

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) ver. 19.0. Descriptive statistics were reported as mean, standard deviation, median, and minimum and maximum values for continuous variables and as frequency with percentages for categorical variables. The relationship between sPAP and CT measurements were investigated using correlation analyses. The variables that significantly related to PAP were included in the multivariate analysis model. In case of a strong intercorrelation ($R > 0.70$) between two CT measurements that related to sPAP, the weaker one was excluded from the model. In addition, when a primary measurement had a stronger relationship than its relevant secondary derivative or vice versa, the latter was excluded from the model. Ultimately, a stepwise linear regression method was conducted using appropriate covariates. Intra-class correlation coefficients (ICCs) were used to assess the intraobserver reproducibility. The significance level was accepted as $p < 0.05$ in all statistical analyses.

RESULTS

Overall, 68 patients (44 female; median age 71 years, range 25-93 years) were included in the study. Most of the individuals were in-patients (82.4%), and the remaining (17.6%) were under follow-up as out-patients for various reasons. The indications for chest CT scans were to rule out pulmonary infection in 35% patients, interstitial edema or pleural effusion in 26%, pulmonary embolism in 24%, and mediastinal great vessel disease in 15%. Although right heart catheterization was not performed in any patient for a certain diagnosis of PH, the reasons for elevated sPAP were categorized according to the Dana Point classification (Table 1). According to this classification, 70.6% patients had suspected precapillary PH (Dana Point Groups I, III, IV, and V). Overall, 20 patients had elevated sPAP due to left-sided

Table 1. Frequency of patients according to the Dana Point classification

Dana point group	n	%
I	4	5.9
II	20	29.4
III	33	48.5
IV	9	13.2
V	2	2.9
Total	68	100

* The classification was performed according to the consensus of an international group of experts during the 4th World Symposium on pulmonary hypertension held in 2008 in Dana Point, California.

heart pathology (Dana Point Group II), including 10 patients with reduced ejection fraction, 5 with isolated severe left-sided valvular heart disease with preserved ejection fraction, and 5 with hypertensive heart disease. Past medical history of the patients revealed systemic hypertension in 64.7% patients, diabetes mellitus in 23.5%, coronary artery disease in 22.1%, atrial fibrillation in 45.6%, and chronic lung disease in 44.1%.

Echocardiographic Results

The median left ventricular ejection fraction was 60% (range between 20% and 72%). Only 10 (14.7%) patients had reduced ($< 50\%$) left ventricular ejection fraction. Severe left-sided valvular heart disease was present in 14.7% patients. The tricuspid regurgitation was moderate or severe in 87.7% patients. The mean of estimated sPAP was 48 mmHg (range between 36 and 81 mmHg).

Computed Tomography Results

The mean, median, and minimum and maximum values of primary CT measurements are represented in Table 2. A substantial level of intraobserver reproducibility was found for all CT measurements (Table 3).

There was a moderate positive correlation between MPA and sPAP ($r = 0.64$, $p < 0.001$). The relationships between other primary measurements and sPAP were all significant but weak (Table 2). None of the secondary derivative measurements had a moderate or strong relationship with PAP. Furthermore, the relation between all primary measurements and sPAP were higher than all relevant secondary derivatives.

Precapillary and Postcapillary PH Subgroups

Correlation analysis was performed in the precapillary PH subgroup. Similar to the whole series, MPA again remained as the strongest correlator of sPAP ($r = 0.74$, $p < 0.001$). All other primary measurements were significantly but weakly correlated to sPAP. Multivariate analysis revealed that MPA was the single independent predictor of sPAP ($r = 0.74$; $B = 16.2$; 95% confidence interval 11.6-20.8; $p < 0.001$). The best-fit equation to calculate sPAP was. The change in MPA explained the 54% of the total variation in sPAP.

Table 2. Relation between sPAP and CT measurements*

Primary measurements	Mean (cm)	Median (cm)	Standard deviation	Minimum (cm)	Maximum (cm)	Correlation coefficient (R)	p
MPA	3.29	3.19	0.49	2.31	4.3	0.65	< 0.001
LPA	2.55	2.48	0.39	1.77	3.52	0.35	0.003
RPA	2.61	2.64	0.42	1.61	3.52	0.40	0.001
RDPA	1.54	1.53	2.49	1	2.42	0.34	0.004
LDPA	1.76	1.74	0.31	1	2.69	0.34	0.004
RVW	0.59	0.6	0.11	0.37	0.85	0.37	0.002
RVD	3.77	3.8	0.59	2.43	5	0.35	0.005
Adjustment factors	Mean (cm)	Median (cm)	Standard deviation	Minimum (cm)	Maximum (cm)		
AA	3.84	3.78	0.55	2.1	5.37	-	-
DA	2.94	2.91	0.43	1.68	4.24	-	-
TL	24.1	23.86	2.93	17.2	32	-	-
LVW	1	0.98	0.17	0.64	1.35	-	-
LVD	4.62	4.57	0.66	3.44	6.22	-	-
Derivative measurements	Mean (cm)	Median (cm)	Standard deviation	Minimum (cm)	Maximum (cm)		
MPA/AA	0.87	0.88	0.14	0.52	1.2		
MPA/DA	1.14	1.13	0.2	0.71	1.59	0.43	< 0.001
MPA/TL	0.14	0.14	0.26	0.09	0.22	0.43	< 0.001
LPA/AA	0.67	0.67	0.11	0.44	0.98	0.21	0.09
LPA/DA	0.88	0.87	0.13	0.63	1.31	0.23	0.06
LPA/TL	0.1	0.11	0.02	0.001	0.16	0.25	0.04
RPA/AA	0.69	0.7	0.1	0.47	0.96	0.29	0.02
RPA/DA	0.9	0.9	0.12	0.6	1.18	0.34	0.005
RPA/TL	0.11	0.11	0.02	0.07	0.15	0.26	0.03
LDPA/AA	0.46	0.46	0.08	0.3	0.79	0.34	0.004
LDPA/DA	0.61	0.6	0.09	0.36	0.87	0.27	0.03
LDPA/TL	0.07	0.07	0.02	0.001	0.12	0.28	0.02
RDPA/AA	0.41	0.41	0.06	0.28	0.58	0.20	0.1
RDPA/DA	0.53	0.53	0.08	0.37	0.78	0.23	0.06
RDPA/TL	0.06	0.07	0.02	0.01	0.11	0.25	0.04
RVW/LVW	0.6	0.6	0.1	0.38	0.89	0.1	0.45
RVD/LVD	0.82	0.81	0.13	0.47	1.17	0.15	0.23
RVD/TL	0.14	0.16	0.06	0.001	0.27	0.17	0.17

* All the abbreviations are mentioned and defined in the text.

The subgroup analysis of patients with postcapillary PH revealed that neither the primary measurements nor their relevant secondary derivatives were related to sPAP.

DISCUSSION

Echocardiography is the cornerstone imaging modality for screening PH in suspected patients. Contrast-enhanced chest CT is also a valuable noninvasive diagnostic tool that

is generally integrated to the diagnostic algorithm of PH for the detection of both parenchymal and vascular changes of the lungs^[15-18]. Various parameters as assessed by CT have been reported to predict PH such as MPA diameter > 29 mm, MPA/AA > 1, or segmentary pulmonary artery diameter/related bronchus diameter > 1.25^[12,13,19]. These cut-off values are used to discriminate patients with PH from those without. In the current study, however, a simple measurement of MPA was the

Table 3. Intraobserver reliability of primary measurements*

Primary measurement	ICC	95% CI
AA	0.95	0.91-0.97
DA	0.9	0.85 × 0.94
MPA	0.9	0.84-0.94
LPA	0.89	0.83-0.93
RPA	0.93	0.89-0.95
RDPA	0.87	0.8-0.92
LDPA	0.91	0.86-0.94
RVD	0.93	0.88-0.96
LVW	0.87	0.79-0.92
LVD	0.93	0.89-0.96
TL	0.92	0.88-0.95

*All the abbreviations are mentioned and defined in the text.

only significant predictor of sPAP by multivariate analysis in the whole series. MPA was moderately related to sPAP in the heterogeneous group of PH patients in the current report. This relation was more pronounced in the precapillary PH subgroup in whom MPA strongly correlated to sPAP. Interestingly, an internal correction to MPA did not provide a stronger relationship with sPAP. The MPA/AA or any other derivatives of MPA did not exhibit more than a weak correlation with sPAP.

In certain patient groups in whom echocardiographic calculation of sPAP is inaccurate and a suspicion for pre-capillary PH exists, CT-derived MPA may be useful. For instance, obesity and/or chronic obstructive lung disease may cause low-quality echocardiographic images; thus, Doppler examination of tricuspid regurgitation may be precluded. In one study, most of the patients with connective tissue diseases had no adequate tricuspid regurgitation signal⁽²⁰⁾. Estimation of sPAP with echocardiography is questioned and may be unreliable in patients with trivial or mild tricuspid regurgitation, which is reported to be as high as 20% in patients with PH⁽²¹⁾. Thus, measurement of MPA with CT as a screening tool may be useful in patients with suspected pre-capillary PH and a non-diagnostic Doppler echocardiography. The target patients suggested in the current report to be screened for PH with CT-derived MPA diameter, in whom echocardiography may remain inconclusive for sPAP measurements Chronic obstructive lung disease, connective tissue disorders, obesity, thoracic deformity, etc. are already candidates for precapillary PH.

A significant correlation was not found between MPA and echocardiographic sPAP in patients with elevated sPAP because of left-sided heart diseases (Dana Point Group II). The cause of this discrepancy may be that the mechanism of sPAP elevation in patients with post capillary (i.e., secondary to left-sided heart diseases) PH involves two mechanisms. The first is reactive elevation of sPAP, which may reverse by diuretic and vasodilator therapy over time. The second is fixed sPAP elevation due to vascular remodeling of pulmonary vasculature. Because central

pulmonary artery dilation is caused by persistent elevation of sPAP, it may be within normal limits in patients with transient elevation of sPAP due to pulmonary venous congestion. In the current study, patients with postcapillary PH included a heterogeneous population in terms of fixed or transient elevation of sPAP. Thus, the unrelation of sPAP to the MPA diameter in this subgroup may be attributable to the heterogeneity of patients. However, whether sPAP is related to MPA diameter in those with fixed PH due to left-sided heart diseases is yet to be defined in further studies.

The correlation between sPAP and MPA/AA was reported to be high⁽¹²⁾. However, in the current study, we found a moderate correlation between sPAP and MPA/AA. This may be related to relatively older individuals included in the study and a significantly high proportion of patients having systemic hypertension (64.9%) that gave rise to a high proportion of patients having a dilated ascending aorta. Indeed, more than one-half of the patients had a dilated ascending aorta.

Although we consider that CT-derived MPA may be a potential noninvasive tool for the screening of pre-capillary PH, we are aware that it is the most important contributor to patient radiation exposure in medical imaging^(21,22). Therefore CT-derived MPA measurement for the estimation of sPAP should be reserved for those with inaccurate echocardiographic findings.

Limitations

The major limitations of our study are the retrospective design, a heterogeneous patient population with PH, and the lack of right heart catheterization.

CONCLUSIONS

The strongest correlator of echocardiographic sPAP is CT-derived MPA among various thoracic cardiovascular metrics. The relation between sPAP and MPA diameter is more pronounced in patients with precapillary PH (i.e., Dana Point Groups I, III, IV, and V). However, no significant relationship was observed between MPA diameter and sPAP in patients with postcapillary PH (i.e., Dana Point Group II). CT derived MPA may be used for sPAP calculation and as a screening tool in whom echocardiography is inaccurate. These findings should be supported by studies including relatively a higher number of patients in which right heart catheterization is used as the reference.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: SG, NG, EZ

Analysis/Interpretation: SG, NG, EZ, MY, BŞY, MÖ

Data Acquisition: SG, EZ, NG

Writing: SG, NG

Critical Revision: MÖ, BŞY, EZ, MY

Final Approval: All of authors

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