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Immunogenicity of a Monovalent Pandemic Influenza A H1N1 Virus Vaccine with or without Prior Seasonal Influenza Vaccine Administration

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The immunogenicity of pandemic influenza A H1N1 virus (A/H1pdm) vaccine might be modified by prior seasonal trivalent influenza vaccine (sTIV) administration. We conducted a retrospective analysis of immunogenicity of 243 health care workers (number of sTIV-positive [$sTIV^+$] subjects, 216; number of $sTIV^-$ subjects, 27) by hemagglutination inhibition. There was no significant difference in the ratios of antibody titers of ≥40 (41.2% versus 48.1%; $P = 0.49$) and fold increases in geometric mean titer (3.8 versus 4.5; $P = 0.37$). sTIV injected 7 to 10 days prior to A/H1pdm vaccine administration did not interfere with the immunogenicity of the latter.

Human infections with pandemic influenza AH1N1 virus (A/H1pdm) were identified in April 2009. The availability of safe and effective vaccines was a critical component of efforts to prevent A/H1pdm infection and expansion of the pandemic (1). In Chiba University Hospital (CUH), seasonal trivalent influenza vaccine (sTIV) administration was conducted 7 to 10 days prior to A/H1pdm vaccination because the precise date of the initial A/H1pdm vaccine supply was unclear owing to limitations in the manufacturer's production capacity.

There was uncertainty as to whether prior sTIV administration might interfere with the immunogenicity of A/H1pdm vaccine administered a week later. We undertook a clinical trial with health care workers (HCWs) to examine the immunogenicity of A/H1pdm vaccine (3). This study was a retrospective subgroup analysis of a previous study to evaluate the immunogenicity of a monovalent A/H1pdm vaccine administered with or without previous sTIV vaccination in HCWs aged between 20 and 39 years. All subjects provided written informed consent. The study was approved by the CUH Research Ethics Committee (G21035).

Vaccine. The A/H1pdm vaccine was monovalent, with a single dose containing 15 μg of hemagglutinin antigen. sTIV contained 15 μg of hemagglutinin antigen of each seed virus per single dose. Both vaccines were inactivated, split-virus, unadjuvanted ones produced by the same procedure and with thimerosal added as a preservative. Both vaccines were administered subcutaneously into the external upper arm in a single dose.

The Japanese Ministry of Health, Labor and Welfare initiated A/H1pdm vaccination of HCWs with top priority on 19 October 2009. Between 26 and 30 October, 409 HCWs without prior A/H1pdm infection were enrolled, and peripheral venous blood samples were collected before and 28 days after vaccination. The vaccination was independent of study participation. Of the 409 subjects, 20 were then excluded because 28-day-postvaccination blood samples were not provided. As a result, immunogenicity analysis was performed on data from 389 subjects. Among these, we selected 243 between 20 and 39 years old for this subgroup analysis.

A/H1pdm (A/California/07/09 [H1N1]) was allowed to proliferate in MDCK cells, and then a viral fraction was obtained and inactivated with formalin. Immunogenicity of the A/H1pdm vaccine was evaluated with a hemagglutination inhibition (HI) antibody assay according to standard methods (7), using the inactivated virus as described previously (3).

Statistical analyses were performed with Dr-SPSS II (SPSS Japan Inc., Tokyo, Japan). The statistical significance of the results of comparisons of data between groups was analyzed by a paired *t* test and chi-square test as well as a Wilcoxon signed-rank test when appropriate. *P* values of <0.05 were considered significant. We analyzed three factors as follows: (i) the proportion of subjects with an antibody titer of ≥40, (ii) the proportion of subjects with either seroconversion (prevaccination titer of <10 with postvaccination HI antibody titer of ≥40) or an increase by a factor of 4 or more in antibody titer, and (iii) the fold increase in geometric mean titer (GMT).

At baseline, 6 (3.1%) of 216 subjects with prior sTIV had an antibody titer of ≥40 and 1 (2.8%) of 27 subjects without prior sTIV had an antibody titer of ≥40. There were no significant differences in the proportions of subjects with a baseline antibody titer of >40 or in the baseline GMTs between the groups with and without prior sTIV.

Postvaccination titers of ≥40 were observed in 41.2% (95% confidence interval [CI], 34.6 to 47.8) of the subjects with prior sTIV and in 48.1% (95% CI, 29.3 to 66.9) of those without prior sTIV. The proportions of subjects with a postvaccination anti-

Received 22 February 2012 **Returned for modification** 23 March 2012
Accepted 22 July 2012
Published ahead of print 1 August 2012
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doi:10.1128/CVI.00077-12

TABLE 1 Immune responses after A/H1pdm vaccination as measured by hemagglutination inhibition antibody assay[a]

Parameter	Prior seasonal vaccination		P value[b]
	Yes	No	
Total no. of subjects	216	27	
Age (yr) (mean ± SD)	30.0 ± 4.7	30.0 ± 5.3	0.47
Before vaccination (baseline)			
No. (% [95% CI]) of subjects with HI antibody titer ≥ 40	6 (2.8 [0.6–5.0])	1 (3.7 [0.0–10.8])	0.79
Geometric mean titer (mean ± SD)	6.7 ± 1.3	6.1 ± 1.8	0.44
After vaccination			
No. (% [95% CI]) of subjects with HI antibody titer ≥ 40	89 (41.2 [34.6–47.8])	13 (48.1 [29.3–66.9])	0.49
No. (% [95% CI]) of subjects with seroconversion or significant increase in titer[c]	131 (60.6 [54.1–67.1])	16 (59.3 [40.8–77.8])	0.89
Geometric mean titer (mean ± SD)	25.1 ± 5.8	27.9 ± 16.9	0.64
Factor increase in geometric mean titer (mean ± SD)	3.8 ± 2.7	4.5 ± 3.9	0.37

[a] A/H1pdm, pandemic influenza AH1N1 virus; HI, hemagglutination inhibition; CI, confidence interval. Hemagglutination inhibition antibody titer values of <10 were assigned a value of 5 for the purpose of calculating the geometric mean titer.

[b] *P* values were analyzed by *t* test, and the Wilcoxon rank sum test was also used where appropriate.

[c] Data represent the proportion of subjects who had either seroconversion (prevaccination titer of <10 with postvaccination HI antibody titer of ≥40) or an increase by a factor of 4 or more in antibody titer.

body titer of ≥40 did not differ significantly between the two groups ($P = 0.49$) (Table 1). Seroconversion or a significant increase in HI occurred in 60.6% (95% CI, 54.1 to 67.1) of subjects with prior sTIV and in 59.3% (95% CI, 40.8 to 77.8) of subjects without prior sTIV, with no significant difference between the two groups ($P = 0.89$). There was a substantial rise in GMTs after vaccination (for sTIV-positive [$sTIV^+$] subjects, $P < 0.001$; for $sTIV^-$ subjects, $P < 0.001$), but the differences in the values of GMTs and the factor increases in GMTs were not significant between the two groups ($P = 0.64$ and $P = 0.37$, respectively).

This study demonstrated that sTIV injected 7 to 10 days previously did not affect the immunogenicity of A/H1pdm vaccine. Simultaneous administration of sTIV and A/H1pdm vaccine could induce sufficient levels of antibody to both vaccines (8). Ohfuji et al. reported interference with the immune response to the A/H1pdm vaccine by pregnant Japanese women who had recently received sTIV (6). Another study also showed lower GMT levels for A/H1pdm vaccine among seasonally vaccinated groups of infants and children aged 6 months to less than 9 years (5). Our current study, including this subgroup analysis, demonstrated lower immunogenicity among healthy HCWs (3) compared with other studies (2, 4, 9). However, we were able to compare the immunogenicities of A/H1pdm with or without prior sTIV administration because the samples from both groups were tested for the presence of antibodies using the same assay.

Regarding the differing results of the former two studies (5, 6), we speculate that the immunogenicity of infants and pregnant women is possibly modified in comparison with that of healthy HCWs. Since our subjects were healthy, relatively young HCWs, trials need to be conducted in other populations that may have different responses to the vaccine, such as the elderly, children, and those with impaired immunity. In the study of the immunogenicity of Australian infants (5), A/H1pdm vaccination was conducted in August and early September, with seasonal influenza vaccination having been conducted more than 2 months earlier. In the study of pregnant Japanese women (6), lower immunogenicity was demonstrated in subjects receiving sTIV vaccination within 19 days prior to A/H1pdm vaccination. The interval between sTIV and A/H1pdm vaccinations was slightly longer than ours, allowing us to speculate that a shorter interval between the two types of influenza vaccines might prevent an interference effect. Further testing is required to confirm this hypothesis. This study was a retrospective subgroup analysis, and the two groups with and without sTIV were not assigned to this study. The number of sTIV-vaccinated HCWs was 216, and the number of sTIV-unvaccinated ones was 27. Because of the small sample size, the statistical power to ascertain a difference between the two groups might be insufficient and results need to be interpreted cautiously.

In conclusion, sTIV injected 7 to 10 days prior to a single dose of A/H1pdm vaccine did not interfere with the immunogenicity of the latter, according to HI antibody assays.

ACKNOWLEDGMENTS

We thank the subjects for their critical role in this study and the staff of Chiba University Hospital, including the following: Yasunori Sato at the Division of Clinical Research Center, Kyoko Shoji and Hitoshi Chiba at the Division of Control and Treatment of Infectious Diseases, Chiba University Hospital, and Naruhiko Ishiwada, Junko Ogita, and Haruka Hishiki at the Department of Pediatrics, Graduate School of Medicine, Chiba University.

This study was funded by Chiba University.

None of us has any potential conflict of interest relevant to this article.

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Word counts (body of text 3146, abstract 205)

Role of 320-Slice computed tomography in the diagnostic workup of patients with chronic thromboembolic pulmonary hypertension

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Running Head: 320-Slice CT in the diagnostic workup for CTEPH

Conflict of interests and grants: Dr. Tatsumi was supported by a grant to the Respiratory Failure Research Group from the Ministry of Health, Labor and Welfare, Japan (No 21590962) ; and Dr. Tanabe was supported by a research grant from the Ministry of Education, Culture, Sports, Science and Technology of Japan (No 22590849)

ABSTRACT

***Background*:** Right heart catheterisation (RHC) and pulmonary digital subtraction angiography (PDSA) are the standard method used to diagnose patients with suspected or definite chronic thromboembolic pulmonary hypertension (CTEPH). The aim of this study was to evaluate the ability of 320-slice computed tomography (CT) for simultaneous diagnosis of chronic thoromboembolic findings in the pulmonary arteries and pulmonary hemodynamics based on the curvature of the interventricular septum (IVS) in CTEPH.

***Methods*:** Forty-four patients with high clinical suspicion of CTEPH underwent RHC, PDSA and enhanced double volume retrospective electrocardiogram-gated 320-slice CT. We measured the sensitivity and specificity of CT to detect thrombi in the pulmonary arteries compared with PDSA. We also compared IVS bowing (expressed as curvature) measured on the short-axis cine heart image with pulmonary arterial pressure (PAP) obtained by RHC.

Results: Compared with PDSA, the sensitivity and specificity of CT to detect chronic thromboembolic findings were 97.0% and 97.1% at the main/lobar level and 85.8% and 94.6% at the segmental level, respectively. The correlation coefficients of IVS curvature with systolic PAP and mean PAP were -0.79 ($P<0.001$) and -0.86 ($P<0.001$), respectively.

***Conclusions*:** The use of 320-slice CT allows less invasive and simultaneous detection of thrombi and evaluation of pulmonary hemodynamics for the diagnostic workup of CTEPH.

Abbreviation list

confidence interval (CI)

cardiac output (CO)

chronic thromboembolic pulmonary hypertension (CTEPH)

computed tomography (CT)

computed tomography pulmonary angiography (CTPA)

electrocardiogram (ECG)

interventricular septum (IVS)

pulmonary digital subtraction angiography (PDSA)

pulmonary endarterectomy (PEA)

left ventricle (LV)

magnetic resonance imaging (MRI)

mean pulmonary artery pressure (mPAP)

pulmonary artery pressure (PAP)

pulmonary hypertension (PH)

pulmonary vascular resistance (PVR)

right heart catheterisation (RHC)

right ventricle (RV)

systolic pulmonary artery pressure (sPAP)

ventilation/perfusion (V/Q)

Background

Chronic thromboembolic pulmonary hypertension (CTEPH) is a very severe disease caused by non-resolving thromboemboli in the pulmonary arteries and can potentially be cured by pulmonary endarterectomy (PEA). If left untreated, depending on the extent of the obstruction of the vascular bed and vascular remodelling in the unobstructed distal pulmonary arteries, there may be increased right ventricular afterload and progression of pulmonary hypertension (PH) (1-3).

Invasive pulmonary digital subtraction angiography (PDSA) is a standard diagnostic tool used to assess patients with suspected or definite CTEPH, both to establish the diagnosis and to assess operability (3,4). In contrast to PDSA, ventilation/perfusion (V/Q) lung scintigraphy and enhanced helical computed tomography (CT) are recommended as primary, less invasive substitutes for vascular imaging (5~8). In addition, previous studies have shown that contrast multislice CT angiography can be used to evaluate the pulmonary artery and can serve as a less invasive alternative to PDSA for the diagnosis of CTEPH (9-11). However, CT angiography is less sensitive than V/Q lung scintigraphy for the diagnosis of CTEPH (5,6).

Invasive pulmonary artery pressure (PAP) measurement using right heart catheterisation (RHC) is the "gold standard" for the diagnosis of PH (1-4). Currently, less invasive PAP estimation using transthoracic Doppler echocardiography is recommended to screen for PH (12,13). In the presence of increased systolic pressure in the right ventricle (RV), the interventricular septum (IVS) flattens and sometimes even

bows leftward into the left ventricle (LV). Earlier studies showed that the IVS curvature on cardiac magnetic resonance imaging (MRI) was well correlated with PAP in patients with PH (14).

Recently, because of advances in CT technology, electrocardiogram (ECG)-gated multislice CT has been used to image the heart with high spatial and temporal resolution. Taylar et al. reported the possibility of quantitative evaluation of RV function and morphology using ECG-gated 64-slice CT (15). The more recent introduction of 320-slice CT affords 16 cm craniocaudal coverage and allows volumetric imaging of the entire heart with only a single gantry rotation (16). In addition, a series of two gantry rotations (double volume scan) with ECG-gated 320-slice CT can acquire simultaneous images of the pulmonary arteries and the entire heart.

The purpose of this study was to measure the sensitivity and specificity of 320-slice CT to detect chronic thromboembolic findings in the pulmonary arteries, and to evaluate the relationship between IVS curvature on 320-slice CT and PAP measured by RHC. Our hypothesis was that 320-slice CT could be used for less invasive and simultaneous evaluation of the pulmonary artery and hemodynamics in the diagnostic workup of patients with CTEPH.

Materials and Methods

Patients

The study group consisted of 44 consecutive patients (28 women, 16 men; mean age 59 years; range, 33-78 years) with high clinical suspicion of CTEPH based on V/Q lung scintigraphy and transthoracic echocardiography. All patients were enrolled from March 2009 to April 2012 and underwent enhanced retrospective ECG-gated 320-slice CT, RHC and PDSA. The shortest and longest intervals between CT and RHC plus PDSA were two days and two weeks, respectively.

The study was approved by the ethics committee of Chiba University (approval number 826), and written informed consent was obtained from each patient before CT, RHC and PDSA.

320-slice CT

All CT scans were obtained with retrospective ECG-gated enhanced volume scanning using 320-slice CT (Aquilion One, Toshiba Medical, Tochigi, Japan) with a 0.5 mm slice thickness and 0.35 sec/rotation. To acquire simultaneous images of the pulmonary arteries and the entire heart, an axial series of two gantry rotations in a cranio-to-caudal direction was performed (double volume scan). The resulting dual volume data sets were stitched automatically. Since the most cranial and caudal parts of each volume data set (both 1.6cm) were not used to create images, the effective scan length was 25.6cm. The tube voltage was set at 120kV and the tube current was set at 580mA with tube current dose modulation. Using a mechanical injector (Dual Shot, Nemoto Tokyo, Japan), 100 ml of contrast media (Iomeron 350 mg/ml, Eisai, Tokyo, Japan) was injected at 3.5 ml/s, followed by the injection of a saline-contrast media

mixture that consisted of 40 ml contrast media at 2.0 ml/s and 30 ml saline at 1.5 ml/s. Time-resolved (every 1 s) single-section CT scans were acquired at the level of the bifurcation of the pulmonary artery without a breath hold. Ascending aortic time-resolved attenuation was then measured using the time-attenuation evaluation program accessible on the scanner. When the CT values in the ascending aorta had increased to 200 HU, we started the actual examination scan while the subject held their breath.

The CT images for a normal workup to diagnose pulmonary thrombi were reconstructed at 75% of the R-R interval with 0.5-mm slice thickness at 0.5-mm intervals using a standard algorithm. The CT images were digitally stored and analysed at a dedicated workstation. All arteries were interactively analysed on two split screens showing axial, coronal or sagittal views by two independent observers. The two observers were blinded to the patient's baseline characteristics and RHC results. Final evaluations were achieved by consensus.

Calculation of IVS curvature on 320-slice CT

The CT images were reconstructed every 5% from 0 to 95% of the R–R interval. Then short-axis cine images of the heart were acquired using double oblique multiplanar reformation. The IVS curvature was measured in the short-axis image plane at the midventricular level (at least one papillary muscle visible). At this level, the cine image with the most deformation of the septum was used for quantification. IVS bowing was quantified by the curvature (defined as 1 divided by the radius of curvature in cm), and this was calculated by entering coordinates (x, y) from three different points on the

midwall septal image into an analytical fitting routine. The method is depicted in Figure 1. The sign of the curvature was dependent on the convexity of the septum. A rightward (physiologic) curvature was denoted as a positive value, and a leftward curvature as a negative value.

All IVS curvature measurements were performed by a reader blinded to the patient's identity. To assess the inter-observer reproducibility of the IVS curvature measurements, two independent observers measured the IVS curvature.

The correlation of IVS curvature measured by 320-slice CT with systolic PAP (sPAP) and mean PAP (mPAP) obtained by RHC was evaluated.

Right heart catheterisation (RHC)

A 7.5 Fr Swan-Ganz thermodilution catheter (Edwards Lifescience, USA) was used, and a jugular approach was preferred. Pressure measurements were taken from the right atrium, RV and main pulmonary artery at end-expiration. Cardiac output (CO) was determined using the thermodilution method by averaging a minimum of three measurements. Left-to-right shunting was ruled out by oximetry.

Pulmonary digital subtraction angiography (PDSA)

For PDSA (Infinix, Toshiba Medical, Japan) the right and left pulmonary arteries were selectively catheterized using a 7 Fr Berman angiographic balloon catheter

(Arrow International, USA). Arteriograms were acquired at 3 frames per second. Postero-anterior projections of each lung, a right lateral projection of the right lung and a left anterior oblique or lateral projection of the left lung were obtained. The contrast bolus consisted of 18 ml of Iomeprol for each of the four series. The flow rate was 9 ml/s.

PDSA images were digitally stored and analysed at a PACS workstation (DrABLE-EX, Fujitsu Limited, Japan). All arteries were interactively analysed by two independent observers using two split screens to show the right- and left-sided projections. The two observers were blinded to the patient's baseline characteristics and CT results. Final evaluations were achieved by consensus.

Assessment of chronic embolic findings by CT and PDSA

The observers reviewed the main pulmonary arteries, and the right and left lobar and segmental arteries. This resulted in 14 vessel segments on each side (the lingula artery was considered a lobar artery and the intermediate artery was considered part of the right main artery) on both 320-slice CT and PDSA. Each vessel segment was judged as positive or negative for the presence of chronic thromboembolic findings.

Statistical analysis

Sensitivity, specificity, and positive and negative predictive values for the diagnosis of chronic embolic findings by 320-slice CT were calculated using PDSA as the gold standard. All images were evaluated in random order and CTPA and PDSA images were not analysed in pairs. For comparing CTPA and PDSA, the level of

agreement was determined using Cohen's Kappa and its 95% confidence interval (CI). A Kappa value greater than 0.81 was interpreted as excellent agreement, values of 0.61 to 0.80 were interpreted as good, values of 0.41 to 0.60 as moderate, values of 0.21 to 0.40 as fair and values less than 0.20 as poor agreement.

The level of inter-observer agreement of CTPA and PDSA was also determined using Cohen's Kappa and its 95% CI.

To determine the inter-observer variation of the measurement of IVS curvature, Pearson's correlation analysis and Bland-Altman analysis were used. The correlation of IVS curvature measured by 320-slice CT with hemodynamic data was performed by Pearson's correlation analysis.

All results are expressed as the mean ± standard deviation unless otherwise indicated. For all statistical analyses, a P value < 0.05 was considered significant. All statistical analyses were performed using SAS 8.0 software (Cary, NC, USA).

RESULTS

Forty-four consecutive patients (mean age, 59.2 ± 11.3; female, 64%) with CTEPH based on RHC and PDSA were included (Table 1). One patient did not undergo PDSA because of an allergic reaction to contrast media. Thus, there were 86 main arteries, 258 lobar arteries and 860 segmental arteries that were included in the statistical analysis. CT pulmonary angiography (CTPA) showed chronic thromboembolic findings in 73 of 344 arteries at the main/lobar level and 199 of 860 arteries at the

segmental level. The sensitivity and specificity of CTPA to detect chronic thromboembolic findings were 97.0% and 97.1% at the main/lobar level and 85.8% and 94.6% at the segmental level, respectively. CTPA showed excellent agreement compared with PDSA at the main/lobar level (Kappa=0.91) and good agreement at the segmental level (Kappa=0.79) (Table 2).

The inter-observer agreement between the two observers for PDSA was as follows: Kappa=0.938 (95% CI: 0.892, 0.983) at the main and lobar level, and Kappa=0.821 (95% CI: 0.776, 0.867) at the segmental level. The inter-observer agreement for CTPA was similar at the main and lobar levels (Kappa=0.947 (95% CI: 0.906, 0.989) and at the segmental level, Kappa=0.809 (95% CI: 0.763, 0.855).

Evaluation of IVS curvature was feasible in all patients. The maximum septum displacement ranged from a curvature of +0.394 cm^{-1} to severe leftward IVS bowing with a curvature of -0.339 cm^{-1}. There was a close correlation between the separate measurements of IVS curvature by two independent observers ($r = 0.93$, $P < 0.001$). A Bland-Altman analysis showed that the mean inter-observer difference in IVS curvature was 0.00 (95% CI: -0.03, 0.02) (Figure 2).

As shown in Figure 3, there was a strong correlation between IVS curvature and sPAP measured by RHC (r=-0.79, P <0 .001, n = 44). The sPAP showed a linear variation with IVS curvature, with a slope of -74.368 (95% CI: -92.172, -56.564) and a y-intercept of 74.518 (95% CI: 70.899, 78.136). As shown in Figure 4, there was also a strong correlation between IVS curvature and mPAP obtained by RHC (r=-0.86, P <0

.001, n = 44). The mPAP showed a linear variation with IVS curvature, with a slope of -41.519 (95% CI: -49.190, -33.847) and a y-intercept of 41.961 (95% CI: 40.401, 43.520).

DISCUSSION

To our knowledge this is the first study to assess the ability of 320-slice CT to diagnose CTEPH. There are three main findings of our study. First, 320-slice double volume CTPA, as well as PDSA, can yield images that allow the diagnosis of thromboembolic changes in the main, lobar and segmental PA in patients with CTEPH. Second, IVS curvature based on retrospective ECG-gated 320-slice CT can estimate PAP in patients with CTEPH. The third finding is that this modality allows simultaneous and less invasive detection of thrombi and evaluation of pulmonary hemodynamics for the diagnostic workup of CTEPH.

Despite the fact that CTPA has been commonly used method to diagnose acute pulmonary embolism, the sensitivity of CTPA to detect CTEPH has been considered to be lower than V/Q lung scintigraphy and SPECT (5,6,17). Moreover, CTPA can lead to a false-positive diagnosis of CTEPH when there is in situ pulmonary arterial thrombi (18). Nevertheless, previous studies demonstrated the diagnostic accuracy of multislice helical CT pulmonary angiography at the main, lobar and segmental levels in patients with CTEPH (9-11). Our study also demonstrated that 320-slice CTPA is a less invasive alternative to conventional PDSA for the diagnosis of CTEPH.

In this study, subsegmental arteries were not included in the analysis, because the aim of pre-operative imaging was mainly to demonstrate chronic thromboembolic changess in the segmental or more proximal PA for assessing operability (11,19), although we recently reported subpleural capillary perfusion by PDSA (20). Animal experiments with artificial emboli showed that CTPA, as well as PDSA, could detect subsegmental pulmonary emboli (21,22), however there is no reference standard for the assessment of subsegmental alterations in humans (23). In addition, previous studies reported that the inter-observer agreement at the level of the subsegmental arteries using PDSA was limited. (24,25)

During the cardiac cycle, the position of the IVS is primarily determined by the difference in pressure between the LV and the RV (the transseptal pressure gradient). In patients with PH, RV pressure overload causes a decrease in the transseptal pressure gradient, which is associated with IVS flattening or bowing. In previous studies using echocardiography or cardiac MRI, the distortion of the IVS observed in patients with PH was quantified by measuring the IVS curvature (14,26). Roeleveld et al. demonstrated a significant correlation between maximal IVS curvature based on cardiac MRI and sPAP measured by RHC in patients with PH ($r=0.77$, $P<0.001$) (14). Our study extended Roeleveld's findings and validated the method of deriving mPAP and sPAP from IVS curvature using ECG-gated 320-slice CT.

In previous studies, elevation of mPAP was a strong predictor of mortality in non-operated CTEPH patients (27,28). Recently, Saouti et al. demonstrated that mPAP and pulmonary vascular resistance (PVR) at baseline were strongly related to long–term survival in inoperable CTEPH patients after initiation of modern vasoactive treatment

(29). Moreover, some studies reported that high PVR was a significant risk factor for the clinical outcome of PEA (30,31). Because of a significant correlation between IVS curvature and PVR determined by RHC in this study (r=-0.73, P <0 .001), IVS curvature may predict mortality and clinical outcome in patients with CTEPH.

Although several studies have evaluated image quality of 320-slice CT for the heart (16, 32, 33) and brain (34), reports on 320-slice CT for the lung are limited (35-37). Since this imaging modality affords 16 cm craniocaudal coverage, it is possible to image the entire heart (or brain) in a single gantry rotation, but it is technically very difficult to image the whole lung. Therefore, the need for two gantry rotations (double volume scan) may have limited the use of this modality for lung imaging. Recently, Kroft et al. reported that, for small children, the acquisition time with 320-slice CT for thoracic imaging was 5 times faster than that with 64-slice helical CT, and a statistically significant reduction in radiation dose was achieved with 320-slice CT (36).

Although cardiac CT with retrospective ECG-gated scanning can more clearly demonstrate dynamic ventricular morphology than CT with prospective ECG-gated or non-ECG-gated scanning, there is a higher radiation dose with retrospective ECG-gated scanning compared with other methods (15). The radiation burden with 320-slice volume CT is lower than that with helical CT, because it avoids overlapping rotations that are used with helical CT (over-scanning). Bischoff et al. reported that the exposure dose with 320-slice volume CT for coronary angiography was only one quarter of that with 64-slice helical CT (32). In the present study, the total radiation dose was approximately 10-20 millisieverts, but we also evaluated coronary artery disease on CT for assessing necessity of simultaneous coronary artery graft bypass surgery during