Table 5. Comparison of Variables Between Procedures With RPE and Those Without It

	Procedures With RPE of Grade 2 or Higher (n = 53)	Procedures Without RPE (n = 87)	p Value
First session	31 (58.5)	23 (26.4)	0.0003*
Mean RAP, mm Hg	4 (3 to 7)	4 (2 to 6)	0.2022
Mean PAP, mm Hg	42 (38 to 50)	33 (28 to 41)	<0.0001*
Cardiac index, l/min/m^2	2.5 (1.9 to 2.7)	2.6 (2.4 to 3.3)	0.0060*
PVR, Wood units	9.2 (7.0 to 14.6)	6.1 (3.9 to 8.7)	<0.0001*
Number of target vessels	4 (3 to 5)	3 (2 to 5)	0.1128
Sum total change of Pulmonary Flow Grade scores	6.0 (5.0 to 8.5)	4.0 (3.0 to 6.3)	<0.0001*
PEPSI	54.6 (41.9 to 81.5)	24.5 (17.7 to 33.2)	<0.0001*
Hemoglobin, g/dl	12.3 (11.3 to 13.5)	12.2 (10.6 to 13.6)	0.3353
eGFR, ml/min/1.73 m^2	63.4 (52.0 to 80.0)	74.4 (62.6 to 90.3)	0.0186*
BNP, pg/ml	125 (48 to 365)	42 (22 to 70)	<0.0001*

Values are n (%) or median (25th to 75th percentiles). PEPSI (Pulmonary Edema Predictive Scoring Index) = (sum total change of Pulmonary Flow Grade scores in percutaneous transluminal pulmonary angioplasty) × baseline PVR (Wood units). First session, number of procedures performed as first session. *$p < 0.05$.

EGFR = estimated glomerular filtration rate; RPE = reperfusion pulmonary edema; other abbreviations as in Table 2.

(95% CI: 2.9 to 9.6), and likelihood ratio of a negative test of 0.14 (95% CI: 0.04 to 0.32).

Discussion

We proposed Pulmonary Flow Grade scores for the classification of the angiographic flow appearances of target vessels in PTPA, and PEPSI as a marker connecting the Pulmonary Flow Grade scores with the baseline hemodynamic severity of CTEPH. This study demonstrates that the sum total change in Pulmonary Flow Grade scores is a good marker for predicting hemodynamic improvement at follow-up, and that PEPSI is useful to predict the risk of RPE in PTPA.

The present study found significant improvement in hemodynamic parameters, exercise capacity as indicated by 6-min-walk distance, and plasma BNP level after PTPA. In combination with some previous studies (17–20), these findings demonstrate that PTPA is clinically effective for the treatment of CTEPH. Some previous reports have demonstrated that about 45% to 55% of mean PAP and 65% to 70% of PVR decrease by pulmonary endarterectomy (22–24). Furthermore, the outcomes of patients treated medically have been reported sporadically (25–35), suggesting that the clinical efficacy of medical treatment tends to be lower than that of invasive surgical treatment. Meanwhile, in the results of our study, 42% of the mean PAP and 60% of the PVR decreased at about 6 months after PTPA. These findings suggest that the hemodynamic outcomes by PTPA are improved, but are not superior to, the outcomes by pulmonary endarterectomy. A large multicenter collaborative study is required in the future to compare the therapeutic efficacy, mortality, and complications of PTPA with those of pulmonary endarterectomy performed in experienced centers.

We proposed Pulmonary Flow Grade scores, which classify selective pulmonary angiography flow grade based on the flow appearance of the pulmonary veins perfused by the targeted pulmonary arteries. In the present study, the sum total change in Pulmonary Flow Grade scores was significantly correlated with hemodynamic changes of PVR and mean PAP at follow-up. In particular, our previous report demonstrated that the benefits of PTPA cannot be estimated by any immediate hemodynamic changes at the time of the procedure (17), suggesting that the performance guided by Pulmonary Flow Grade could more easily predict

Table 6. Statistical Analysis of Variables Correlated With the Occurrence of RPE

	Univariate Analysis			Multivariate Analysis		
	Odds Ratio	95% CI	p Value	Odds Ratio	95% CI	p Value
First session	3.920	1.918–8.215	0.0002*	1.958	0.692–5.578	0.2037
Mean RAP	1.093	0.970–1.242	0.1423	—	—	—
Mean PAP	1.075	1.038–1.116	<0.0001*	1.117	1.027–1.224	0.0088*
Cardiac index	0.417	0.225–0.723	0.0013*	—	—	—
PVR	1.220	1.120–1.344	<0.0001*	0.571	0.367–0.834	0.0029*
Number of target vessels	1.123	0.925–1.372	0.239	—	—	—
Sum total change of Pulmonary Flow Grade scores	1.284	1.124–1.487	0.0002*	0.642	0.364–1.056	0.0827
PEPSI	1.074	1.048–1.106	<0.0001*	1.162	1.078–1.274	<0.0001*
Hemoglobin	1.138	0.938–1.390	0.1899	—	—	—
eGFR	0.977	0.958–0.995	0.0143*	—	—	—
BNP	1.005	1.002–1.008	<0.0001*	1.002	0.998–1.008	0.2479

Multivariate analysis was made using variables with significant correlation of $p < 0.001$ in univariate analysis. *$p < 0.05$.

CI = confidence intervals; other abbreviations as in Tables 2 and 5.

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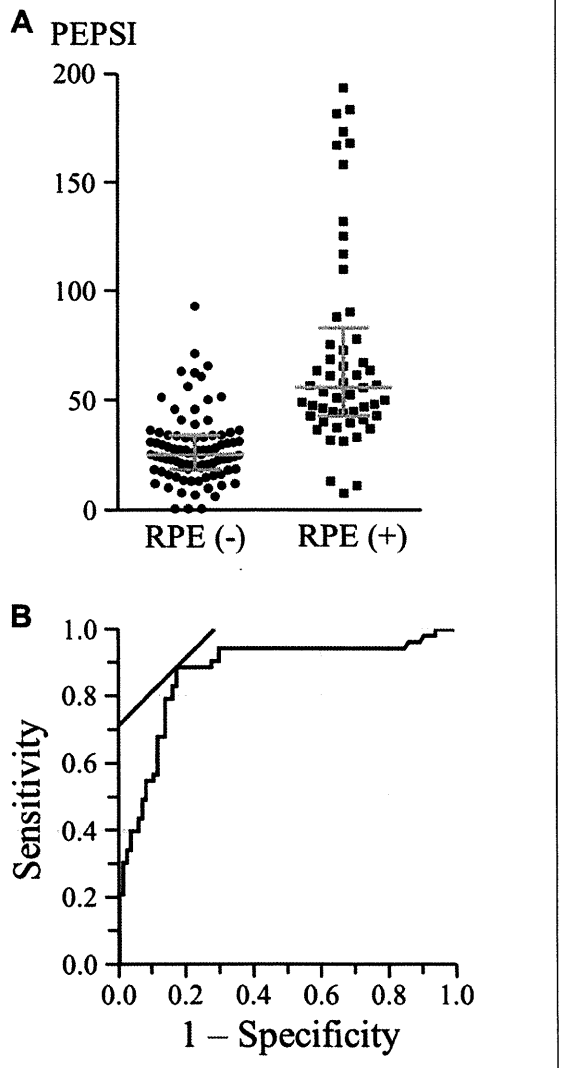

Figure 6. Correlation Between PEPSI and the Occurrence of RPE

(A) Distribution of PEPSI (Pulmonary Edema Predictive Scoring Index) in the presence [RPE (+)] and absence of reperfusion pulmonary edema [RPE (−)]. **(B)** Receiver-operating characteristic curve analysis of PEPSI for prediction of RPE.

the therapeutic efficacy at follow-up. Furthermore, in our results, Pulmonary Flow Grade score was strongly correlated with the ratio of the proximal to the distal pressures of the target lesions obtained by a pressure wire, suggesting that the practical utility of Pulmonary Flow Grade scores is substantiated by these pressure ratios, which is an objective method of measurement of stenosis.

RPE remains the most important complication of PTPA. Indeed, Feinstein et al. (20) experienced RPE in 11 of 18 enrolled patients (61%). In this study, RPE was graded into 5 groups according to severity. As shown in Figure 5, the RPE was recognized even in the opposite lung without angioplasty, in particular in grade 3 or higher. These findings raise the possibility that the occurrence of RPE is mediated, not only by the direct injury or direct exposure of high pressure in pulmonary arteries, but also by the indirect spreading effect of inflammation via cytokines. A more detailed exploration of mechanisms of RPE is desirable. Among the 140 total procedures in this study, 53 procedures (38%) were classified as grade 2 to 5, which indicates clear occurrence of RPE, and all 9 cases with RPE of grade 4 or higher, which indicates severe RPE, needed noninvasive positive-pressure ventilation or artificial respiration. Therefore, it would be highly risky to increase the sum total change of Pulmonary Flow Grade scores blindly without concern for the occurrence of RPE.

Comparison between the procedures with and without RPE of grade 2 or higher demonstrated that the sum total change in Pulmonary Flow Grade scores in cases with RPE was significantly higher than that in those without, and that procedures in cases with greater clinical severity at baseline had a higher risk of RPE. These findings confirm that PTPA should be performed based on the index reflecting both angiographic flow change and baseline severity of pulmonary hypertension so as to obtain maximum therapeutic efficacy and minimal risk of RPE at the same time. The PEPSI, which is calculated by multiplying the sum total change in Pulmonary Flow Grade scores by baseline PVR, could therefore provide a new and useful index in clinical settings. In this study, PEPSI was the strongest factor related to the occurrence of RPE by multivariate analysis, and ROC curve analysis demonstrated that the negative predictive value of the PEPSI for the occurrence of RPE was 92.3% when the cutoff value was 35.4, suggesting the possibility that PEPSI is a useful predictor of RPE.

These findings presuppose the usefulness of PTPA performed based on PEPSI. To cite a case with baseline PVR of 12 Wood units, the targeted value of sum total change in Pulmonary Flow Grade scores is 2.95, because the optimal cutoff value of PEPSI, 35.4, divided by a PVR of 12 Wood units equals 2.95. Thus, in such a case, if the Pulmonary Flow Grade score is changed from 0 to 2 after angioplasty of the first target vessel, the procedure should be stopped without angioplasty of the second target vessel because it would be difficult to maintain the change in Pulmonary Flow Grade score within 0.95 (i.e., 2.95 − 2). Alternatively, the procedure should be carefully continued so as to control the change in Pulmonary Flow Grade score of the second target vessel within 1 (for example, change in Pulmonary Flow Grade score from 0 to 1, 1 to 2, or 2 to 3). To cite another case with a baseline PVR of 5.0 Wood units, the targeted value of the sum total change in Pulmonary Flow Grade scores is 7.1 (i.e., 35.4/5.0). In such a case, if the Pulmonary Flow Grade score is changed from 0 to 3 after angioplasty of the first target vessel and is changed from 0 to 2 after angioplasty of the second target vessel, the change in Pulmonary Flow Grade score of the third target vessel should

be controlled within 2 (for example, change in Pulmonary Flow Grade score from 0 to 2 or 1 to 3). Additionally, because PEPSI is calculated using the baseline PVR, in the patients with lower PVR at baseline, it appears that it is possible to treat more target lesions or reach more changes of Pulmonary Flow Grade scores within 1 procedure, leading to more benefits in reduction in PVR and mean PAP.

Study limitations. The average observation period was not very long, and the number of patients was relatively small. Therefore, a study based on a longer observation period following a greater number of patients is needed to confirm our results. Furthermore, a prospective study should be performed to further demonstrate the predictive value of the PEPSI. This is also a nonrandomized study with no control arm, and these data are subject to selection bias.

Conclusions

PTPA is effective for the treatment of CTEPH, and the sum total change in Pulmonary Flow Grade scores is very useful for predicting the therapeutic efficacy at follow-up. With RPE recognized as the most important complication of PTPA, PEPSI, which reflects both angiographic flow change and the baseline severity of pulmonary hypertension due to CTEPH, could be a useful predictor of RPE. Our findings lead to the following hypothesis: if PTPA is performed guided by PEPSI, the risk of RPE will be minimized and therapeutic efficacy maximized, making PTPA a safe and common therapeutic strategy for CTEPH. However, the usefulness of PEPSI in this study is just a retrospective finding and would need to be tested prospectively to see whether clinical outcome is improved by using the PEPSI as a guide for PTPA.

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Key Words: chronic thromboembolic pulmonary hypertension ■ flow appearance ■ percutaneous transluminal pulmonary angioplasty ■ reperfusion pulmonary edema.

International Journal of Cardiology xxx (2013) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Letter to the Editor

Detection of right ventricular wall motion asynergy confirmed on four-dimensional 320-slice CT by two-dimensional global longitudinal strain of right ventricle using transthoracic-echocardiography in pulmonary hypertension

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ARTICLE INFO

Article history:
Received 27 July 2013
Accepted 27 September 2013
Available online xxxx

Keywords:
Right ventricular wall motion asynergy
Four-dimensional 320-slice CT
Two dimensional global longitudinal strain of right ventricle

Introduction. Pulmonary hypertension (PH) patients often have an enlarged right ventricle (RV) and right atria (RA) and RV wall motion asynergy. Because the structures of the RV and RA are complex, especially when enlarged, they are often difficult to visualize. Thus it is difficult to evaluate RV wall motion asynergy accurately using transthoracic echocardiogram (TTE).

Computed tomography (CT) is essential in assessing subjects with pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH), for the presence of thrombi in the pulmonary artery (PA). Furthermore, quantitative evaluation of RV function by retrospective electrocardiogram (ECG) gating CT is defined as appropriate in the ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 criteria for cardiac CT [1].

The utility of two-dimensional (2D) speckle tracking using TTE to evaluate RV function [2] and prognosis [3] has been demonstrated as well as left ventricular (LV) function and characteristics [4]. However, little is known, regarding the usefulness of RV global longitudinal strain measurement using TTE for the detection of RV wall motion asynergy.

The aim of this study was to detect RV wall motion asynergy, confirmed by four dimensional 320 slice CT in PH subjects, using TTE to measure 2D global longitudinal RV strain.

Materials and methods. A total of 24 subjects with PH confirmed by right heart catheterization (RHC) within the previous 6 months (8 males, mean age 57 ± 14 years, 15 CTEPH and 9 PAH) underwent TTE (iE33, Philips) and ECG gated 320 slice CT (Aquilion ONE, Toshiba Medical).

TTE protocol. 2D TTE was performed to evaluate RV and RA sizes and RV systolic and diastolic function.

2D global longitudinal strain analysis. TTE (iE-33, Philips) with a S5-1 transducer at 2.4 to 4.2 MHz and high frame rate (50 or more Hz) was used to image the RV in apical views.

We evaluate both global longitudinal strain using the Q-LAB ver. 9.0, one using 7 segments for the whole RV and the other using only 4 segments for the RV free wall only not including the inter-ventricular septum (Fig. 1).

CT protocol. To obtain not only images of the whole heart including RV and coronary arteries, but also images of the PA, all CT scans were obtained using a double volume conventional scan with retrospective ECG-gating using 320-slice CT with a 0.5 mm slice thickness and 0.35 s/rotation with a downward direction. Tube voltage was set at 120 kV and tube current was set at 550 mA with tube current dose modulation [5,6].

We injected 60 ml of contrast material (350mgI/ml) at 3.5 ml/s, followed by injection of a saline-to-contrast material mixture (40 ml contrast material at 2.0 ml/s and 30 ml saline at 1.5 ml/s), followed by injection of 20 ml pure saline at 1.5 ml/s.

All CT examinations were performed for a normal workup to diagnose or evaluate PH, with a scanning delay of 20–30 s for optimal PA visualization.

CT analysis. CT images were reconstructed every 5% from 0 to 95% of the R–R interval (total, 20 phases). Both ventricular volumes in each phase (total 20 phases) were calculated using a computer assisted edge detection algorithm drawing program (Virtual Place, AZE). The RV and RA are divided at the tricuspid valve annulus, and the RV and PA are divided at the pulmonary valve annulus (Fig. 2). We quantified RV end diastolic volume (RVEDV) and end systolic volume (RVESV), and RV ejection fraction (EF) (RV EF). RV EF was calculated by the following formula: RVEDV minus RVESV per RVEDV.

RV wall motion asynergy was defined as an RV wall motion focal abnormality, in which the absence of coordination of RV wall motions that usually work together harmoniously was observed, diagnosed by an experienced cardiologist (N.F.), using four dimensional 320 slice CT (Fig. 3). In this definition, the presence of an abnormal shift of inter-ventricular septum to LV in end-systole, which suggests the presence of RV pressure load, was not included.

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0167-5273/$ – see front matter
http://dx.doi.org/10.1016/j.ijcard.2013.09.007

Please cite this article as: Ozawa K, et al, Detection of right ventricular wall motion asynergy confirmed on four-dimensional 320-slice CT by two-dimensional global longitudinal strain of right ventricle ..., Int J Cardiol (2013), http://dx.doi.org/10.1016/j.ijcard.2013.09.007

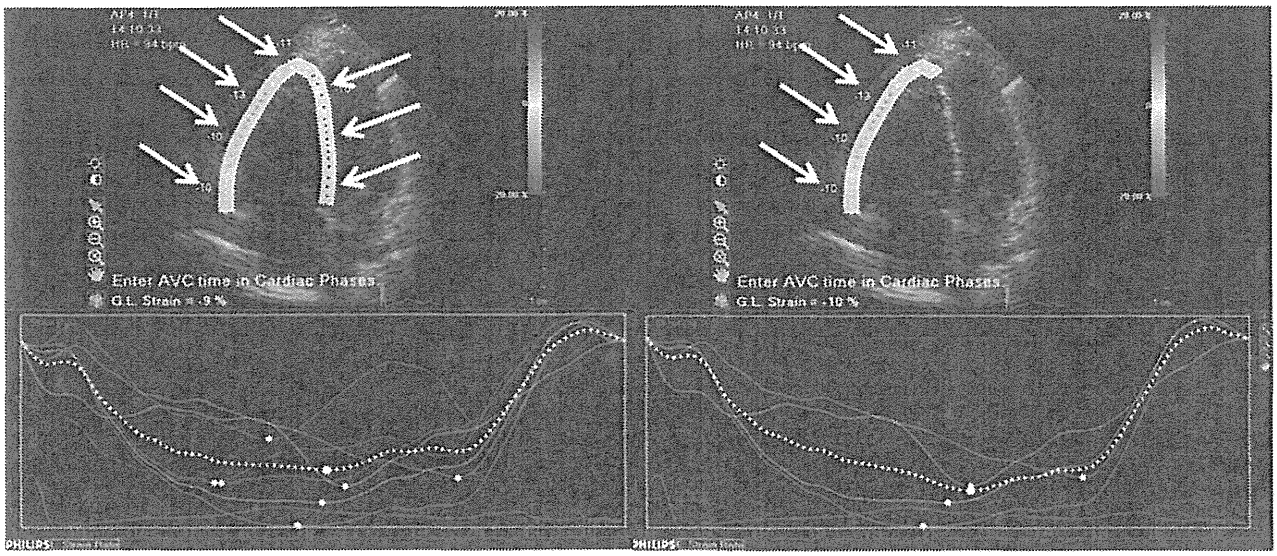

Fig. 1. Measurement of two dimensional (2D) global longitudinal strain analysis using transthoracic echocardiogram (TTE) for the whole right ventricle (RV) (left figure) and RV free wall only (right figure). 2D global longitudinal strain images (upper images) and chart (bottom images) were acquired using TTE. TTE (iE-33, Philips) with a S5-1 transducer at 2.4 to 4.2 MHz and high frame rate (50 or more Hz) was used to image the RV in apical views. We evaluate both of the 2D global longitudinal strain using the Q-LAB ver. 9.0, one using 7 segments (arrows, left figure) for whole RV and the other using only 4 segments (arrows, right figure) for RV free wall only not including inter-ventricular septum.

RHC protocol. All RHCs were performed by pneumologists with more than 5 years experience in managing PH subjects. A Swan–Ganz thermodilution catheter was used and a jugular approach was preferred. Systolic, diastolic and mean PA pressure, RA pressure, cardiac output and cardiac index were measured by a thermodilution method and pulmonary vascular resistance.

Statistical analysis. Statistical analysis was performed using SPSS statistical software (SPSS Japan, Inc., version 17.0).

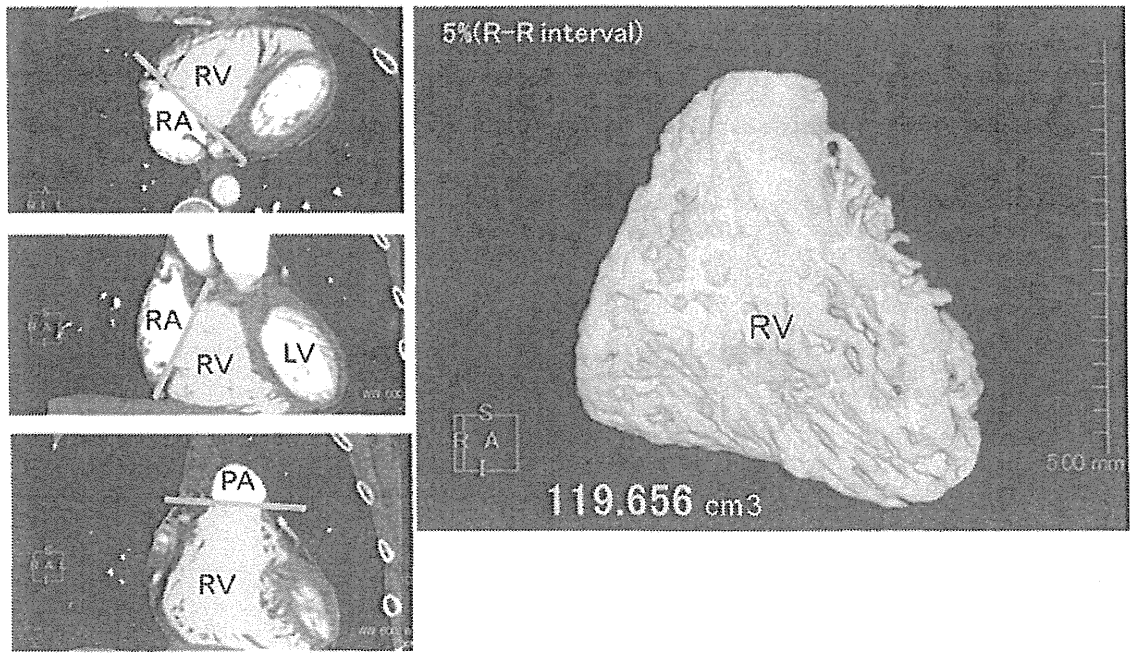

Fig. 2. Actual computed tomography (CT) images used to determine right ventricular (RV) volume. CT images were reconstructed every 5% from 0 to 95% of the R–R interval (total, 20 phases). Both ventricular volumes in each phase (total 20 phases) were calculated using a computer assisted edge detection algorithm drawing program (Virtual Place, AZE). The RV and right atria (RA) are divided at the tricuspid valve annulus (left upper and left middle images), and the RV and pulmonary artery (PA) are divided at the pulmonary valve annulus (left bottom image). And finally three dimensional volume rendered images were generated (right figure) with determination of RV volume (in this case 119.656 cm^3).

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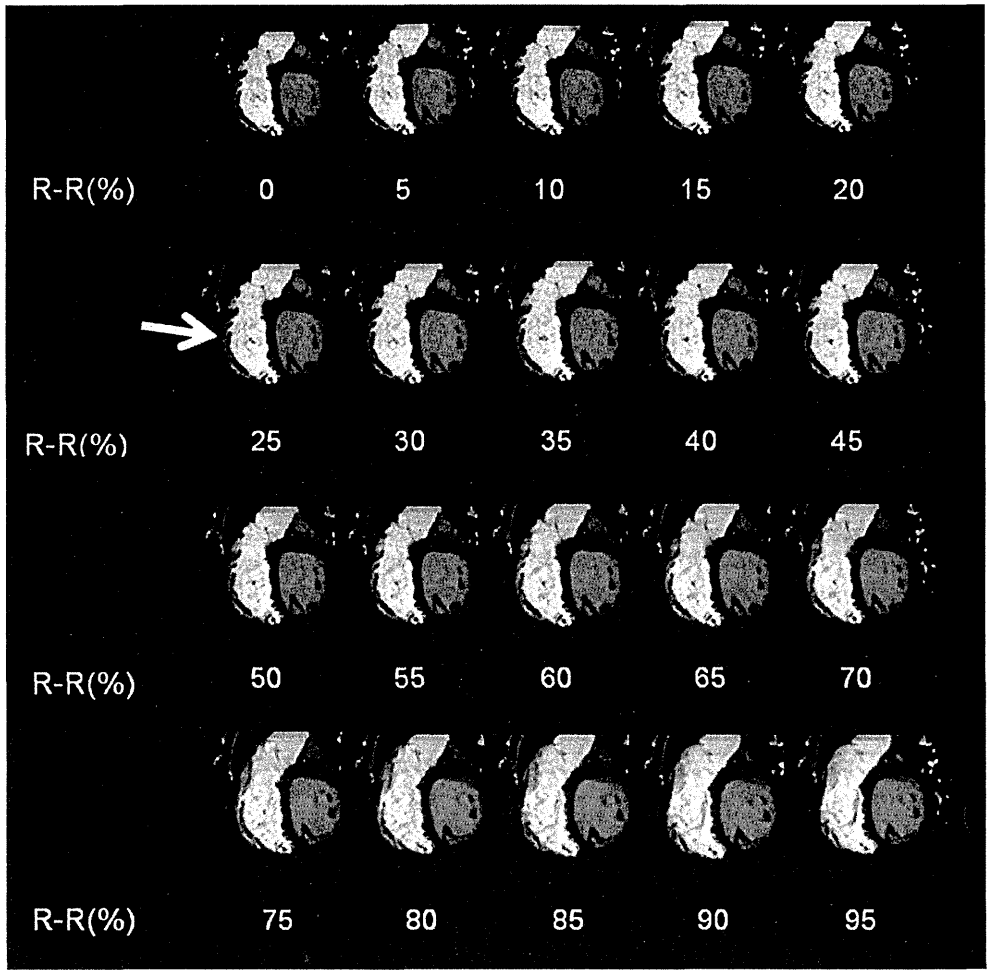

Fig. 3. Typical images of right ventricular (RV) wall motion asynergy on four dimensional computed tomography (CT) analysis. Multiplanar reconstruction images of short axis of left ventricle were reconstructed every 5% from 0 to 95% of the R–R interval (total, 20 phases). In this subject, impaired wall motion was observed mainly in a mid level of RV free wall (arrow).

Results. RV wall motion asynergy was detected in 15 subjects (63%) on CT.

Frequencies of RV wall motion asynergy on CT were 73% in CTEPH subjects and 44% in PAH subjects and there were no significant differences between these frequencies in groups with and without RV wall motion asynergy (Chi square test, $P = 0.157$).

Baseline characteristics. There were no significant differences in all these parameters between groups with and without RV wall motion asynergy (Table 1).

ECG gated CT findings. On CT, RV EDV and ESV were significantly greater (188.4 ± 99.8 cm^3 vs. 97.9 ± 14.2 cm^3, and 139.8 ± 83.1 cm^3 vs. 59.1 ± 21.5 cm^3, both $P < 0.01$) and RV EF was significantly lower

Table 1
Baseline characteristics in groups with and without right ventricular (RV) wall motion asynergy on computed tomography (CT). There were no significant differences in all these parameters between groups with and without RV wall motion asynergy. NYHA indicates New York Heart Association.

	RV wall motion asynergy (+) N = 15	RV wall motion asynergy (−) N = 9	P value
Age (years)	58 ± 15	57 ± 13	0.654
Males (%)	6 (40.0%)	2 (22.2%)	0.371
Systolic blood pressure (mm Hg)	111 ± 14	114 ± 16	0.788
Diastolic blood pressure (mm Hg)	70 ± 10	67 ± 9	0.511
Brain natriuretic peptide (pg/ml)	188 ± 258	205 ± 405	0.27
Six minute walk test (m)	353 ± 78	424 ± 90	0.123
NYHA			0.141
Class 1	0 (0%)	0 (0%)	-
Class 2	4 (26.7%)	6 (66.7%)	-
Class 3	10 (66.7%)	3 (33.3%)	-
Class 4	1 (6.7%)	0 (0%)	-

Table 2
Electrocardiography (ECG) gated computed tomography (CT) findings in groups with and without right ventricular (RV) wall motion asynergy on CT. On CT, RV end diastolic volume (EDV) and end systolic volume (ESV) were significantly greater (188.4 ± 99.8 cm^3 vs. 97.9 ± 14.2 cm^3, and 139.8 ± 83.1 cm^3 vs. 59.1 ± 21.5 cm^3, both $P < 0.01$) and RV ejection fraction (EF) was significantly lower ($26.7 \pm 8.4\%$ vs. $40.8 \pm 15.2\%$, $P = 0.016$) in groups with RV wall motion asynergy than in those without RV wall motion asynergy. RA indicates right atria.

ECG gated CT findings	RV wall motion asynergy (+) N = 15	RV wall motion asynergy (−) N = 9	P value
RV free wall thickness (diastolic) (mm)	3.89 ± 1.32	3.17 ± 1.48	0.151
RV free wall thickness (systolic) (mm)	5.87 ± 2.21	4.67 ± 1.48	0.296
RV EDV (cm^3)	188.4 ± 99.8	97.9 ± 14.2	<0.001
RV ESV (cm^3)	139.8 ± 83.1	59.1 ± 21.5	0.001
RV EF (%)	26.7 ± 8.4	40.8 ± 15.2	0.016
RA EDV (cm^3)	137.9 ± 82.1	96.3 ± 27.2	0.297
RA ESV(cm^3)	113.2 ± 76.7	72.7 ± 27.4	0.18
RA EF (%)	19.4 ± 13.5	25.9 ± 10.6	0.245

Please cite this article as: Ozawa K, et al, Detection of right ventricular wall motion asynergy confirmed on four-dimensional 320-slice CT by two-dimensional global longitudinal strain of right ventricle ..., Int J Cardiol (2013), http://dx.doi.org/10.1016/j.ijcard.2013.09.007

Table 3
Transthoracic echocardiographic (TTE) findings in groups with and without right ventricular (RV) wall motion asynergy on computed tomography (CT). On TTE, RV end diastolic diameter (RVDd), RV end systolic diameter (RVDs) and estimated systolic pulmonary arterial pressure (sPAP) were significantly greater in groups with RV wall motion asynergy than in those without (45.4 ± 8.5 mm vs. 35.3 ± 3.6 mm, P = 0.018, 40.5 ± 8.7 mm vs. 25.5 ± 2.5 mm, P = 0.006, and 79.3 ± 19.5 mm Hg vs. 55.3 ± 22.5 mm Hg, P = 0.016). TAPSE indicates tricuspid annular plane systolic excursion.

TTE findings	RV wall motion asynergy (+) N = 15	RV wall motion asynergy (−) N = 9	P value
RVDd (mm)	**45.4 ± 8.5**	**35.3 ± 3.6**	**0.018**
RVDs (mm)	**40.5 ± 8.7**	**25.5 ± 2.5**	**0.006**
Estimated sPAP (mm Hg)	**79.3 ± 19.5**	**55.3 ± 22.5**	**0.016**
TAPSE (mm)	16.4 ± 5.9	16.7 ± 4.5	0.819
RV outflow AcT/ET	0.27 ± 0.08	0.30 ± 0.07	0.458
Cardiac output (L/min)	3.8 ± 1.1	4.5 ± 1.3	0.177
Tricuspid valve S′	10.5 ± 2.0	11.5 ± 2.7	0.528
Tricuspid valve E/E′	7.0 ± 4.2	5.5 ± 2.2	0.453
Tricuspid regurgitation			**0.029**
Trivial	3 (20%)	7 (77.8%)	-
Mild	10 (66.7%)	1 (11.1%)	-
Moderate	1 (6.7%)	1 (11.1%)	-
Severe	1 (6.7%)	0 (0%)	-

(26.7 ± 8.4% vs. 40.8 ± 15.2%, P = 0.016) in groups with RV wall motion asynergy than in those without RV wall motion asynergy (Table 2).

TTE findings. On TTE, RV end diastolic diameter, RV end systolic diameter, and estimated systolic PA pressure were significantly greater in groups with RV wall motion asynergy than in those without (45.4 ± 8.5 mm vs. 35.3 ± 3.6 mm, P = 0.018, 40.5 ± 8.7 mm vs. 25.5 ± 2.5 mm, P = 0.006, and 79.3 ± 19.5 mm Hg vs. 55.3 ± 22.5 mm Hg, P = 0.016) (Table 3).

2D global longitudinal strain of whole RV and RV free wall only were significantly reduced in subjects with RV wall motion asynergy relative to those without (−9.8% ± 3.4% vs. −13.3% ± 4.1% for whole RV and −10.4% ± 4.3% and −15.5% ± 4.8% for RV free wall only, both P < 0.05) (Fig. 4).

RHC findings. There were no significant differences in RHC results between the two groups (Table 4).

Receiver operating characteristic (ROC) curves for the presence of RV wall motion asynergy on CT. ROC curves of 2D global longitudinal strain for whole RV and RV free wall only, to distinguish subjects with and without RV wall motion asynergy, showed areas under the curve of 0.744 (P = 0.049) (whole RV) and 0.793 (P = 0.019) (RV free wall only), respectively, and best cutoff points of −15.4% (sensitivity 93.3%, specificity 55.6% for whole RV) and −16.3% (sensitivity 93.3%, specificity 44.4% for RV free wall only), respectively (Fig. 5).

Table 4
Right heart catheterization (RHC) findings in groups with and without right ventricular (RV) wall motion asynergy on computed tomography. There were no significant differences in RHC results between the two groups. sPAP, dPAP, mPAP, PCWP, PVR and RAP indicate systolic pulmonary arterial pressure, diastolic pulmonary arterial pressure, mean pulmonary arterial pressure, pulmonary capillary wedge pressure, pulmonary vascular resistance, and right atrial pressure, respectively.

RHC findings	RV wall motion asynergy (+) N = 15	RV wall motion asynergy (−) N = 9	P value
sPAP (mm Hg)	84.9 ± 18.3	70.5 ± 35.6	0.206
dPAP (mm Hg)	27.6 ± 6.2	23.5 ± 13.3	0.393
mPAP (mm Hg)	49.4 ± 6.3	42.6 ± 20.6	0.374
PCWP (mm Hg)	7.5 ± 2.6	8.9 ± 2.6	0.212
Cardiac output (L/min)	4.3 ± 0.9	4.2 ± 1.1	0.838
Cardiac index (L/min/m^2)	2.6 ± 0.5	2.8 ± 0.8	0.973
PVR (dyn · s · cm^{-5})	813 ± 204	719 ± 520	0.375
RAP (mm Hg)	4.3 ± 3.5	5.9 ± 6.0	0.731

Discussion. To our knowledge, this is the first study to differentiate PH subjects with RV wall motion asynergy from those without based on 320 slice CT heart images using 2D global longitudinal RV strain measurement.

There were no significant differences between RHC results in subjects with and without RV wall motion asynergy on CT. But there were significant differences between RV volume and RV EF acquired by CT in subjects with and without RV wall motion asynergy. Furthermore the presence of RV wall motion asynergy, confirmed by 320 slice CT in PH subjects could be differentiated using 2D global longitudinal RV strain.

Current speckle-tracking methods using TTE could not accurately separate RV septal from LV septal components, because the septum influences both RV and LV functions.

Therefore, we analyzed the global, longitudinal strain of both whole RV and RV free wall only (not including inter-ventricular septum). There were no significant differences in diagnostic capabilities for

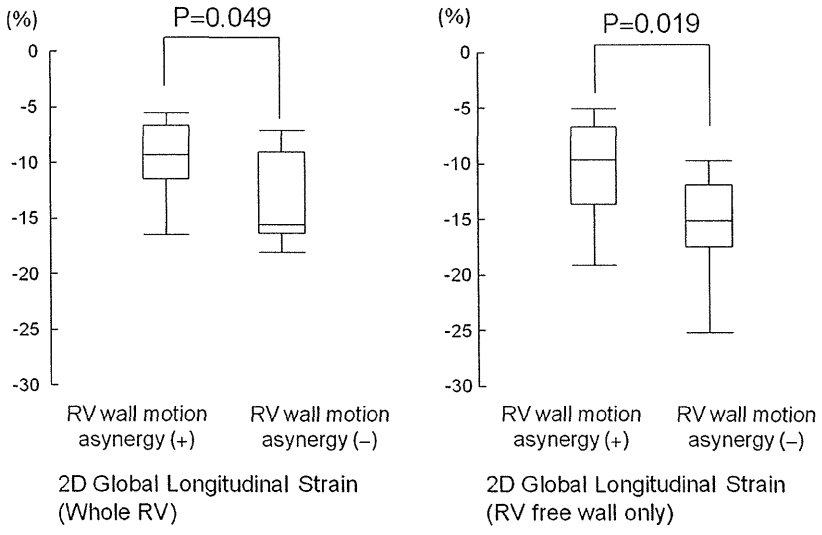

Fig. 4. Comparison of two dimensional (2D) global longitudinal strain of whole right ventricle (RV) and RV free wall only between groups with and without right ventricular (RV) wall motion asynergy on computed tomography. 2D global longitudinal strain of whole RV and RV free wall only were significantly reduced in subjects with RV wall motion asynergy relative to those without (9.8% ± 3.4% vs. 13.3% ± 4.1% for whole RV and 10.4% ± 4.3% and 15.5 ± 4.8% for RV free wall only, both P < 0.05).

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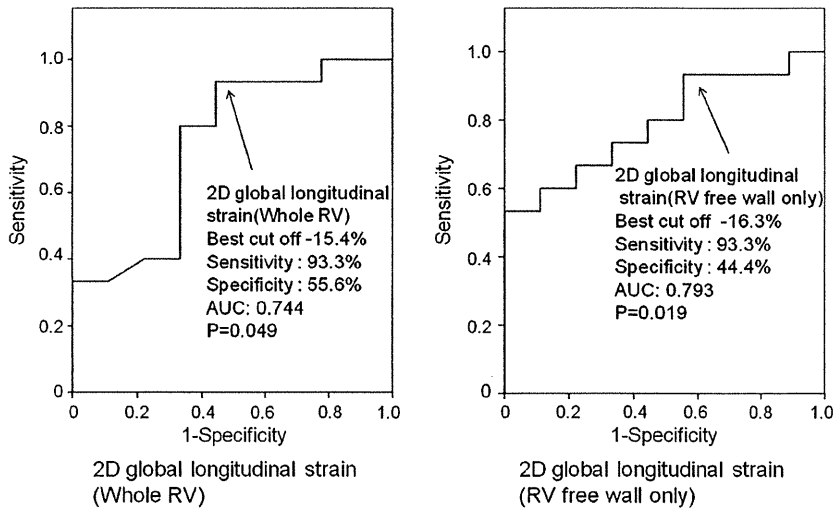

Fig. 5. Receiver operating characteristic (ROC) curves for the presence of right ventricular (RV) wall motion asynergy on computed tomography (CT). ROC curves of two dimensional (2D) global longitudinal strain for whole RV and RV free wall only, to distinguish subjects with and without RV wall motion asynergy on CT, showed areas under the curve (AUC) of 0.744 (P = 0.049) (whole RV) and 0.793 (P = 0.019) (RV free wall only), respectively, and best cutoff points of −15.4% (sensitivity 93.3%, specificity 55.6% for whole RV) and −16.3% (sensitivity 93.3%, specificity 44.4% for RV free wall only), respectively.

detecting RV wall motion asynergy in PH subjects between 2D global longitudinal strain measurement of the whole RV and that of RV free wall only.

Limitations. The 2D speckle tracking TTE method is not a comprehensive quantitative assessment of RV, but a sectional assessment, which is fundamentally different from 320 slice CT due to the limitations of TTE.

Magnetic resonance imaging (MRI) is the gold standard for evaluating RV function [7–9], but some subjects with PAH or CTEPH cannot tolerate long acquisition times in the narrow space of an MRI scanner.

Therefore, in this analysis, we did not evaluate RV morphology and RV wall motion asynergy using MRI in the same PH subjects, and did not compare them using 2D global longitudinal RV strain measured by TTE.

Further prospective study is required using TTE, CT, and MRI in a larger population with evaluation of prognosis versus outcome.

Conclusions. The presence of RV wall motion asynergy, confirmed on 320 slice CT, in PH subjects could not be detected by RHC but could be detected by measuring 2D global longitudinal strain of both the whole RV and the RV free wall only (not including the inter-ventricular septum) by TTE.

Acknowledgement

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

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5. 成人先天性心疾患における肺高血圧

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key words Eisenmenger syndrome, adult congenital heart disease, pulmonary artery hypertension, selective pulmonary dilators, combination therapy, multisystem systematic complications

動　向

成人先天性心疾患にみられる肺高血圧には，高肺血流量を伴う肺高血圧，小欠損孔の先天性心疾患に伴う肺高血圧，心臓手術後の肺高血圧，アイゼンメンゲル症候群，左心系の閉塞性疾患によるものなどが含まれる．アイゼンメンゲル症候群は，その中で肺血管閉塞性病変が最も高度で，全身の系統的合併症を伴う．この分野での最近の最も大きい動きは，肺血管拡張薬の開発，進歩とともにアイゼンメンゲル症候群を含む多くの成人先天性心疾患に伴う肺高血圧で，肺血管拡張薬が広く応用されるようになってきたこととこれら疾患群の罹病率，生命予後が改善される期待が高まっていることである．この期待とともに，肺血管拡張薬の短期中期効果，薬剤選択，併用療法の有効性，手術適応の見直し，予後予測因子の検討と，肺血管拡張薬の投与対象の選別などの研究が広く行われてきている．酸素負荷や肺血管拡張薬で，一定の反応性がみられる場合には，修復術が難しいとされてきた肺血管抵抗値の高い心房中隔欠損，心室中隔欠損でも，欠損孔閉鎖術を行う例がみられている．一方，心臓手術後の肺高血圧，心室中隔欠損小欠損孔での肺高血圧の生命予後についても報告され，アイゼンメンゲル症候群より，予後が悪いと報告されている．肺血管拡張療法は肺血管抵抗値の高い種々の先天性心疾患でも心臓手術直後，術後遠隔期にも用いられている．一方，日本でもアイゼンメンゲル症候群の多施設研究が行われている．避けるべきとされてきたアイゼンメンゲル症候群の妊娠出産の報告も散見される．この稿では，肺血管拡張療法の最近の進歩を中心として，成人先天性心疾患の肺高血圧，特にアイゼンメンゲル症候群のup-datedな問題について検討した．

A. 成人先天性心疾患における肺高血圧

成人先天性心疾患で認める肺高血圧は，大きく以下の4つに分けられる．1）肺体血流量増加を認める肺高血圧（中隔欠損が中から大欠損で，肺血管抵抗は中等度以上に上昇しており，左右短絡が主体で，チアノーゼがわずかで心房中隔欠損に多く認められる），2）小欠損孔（心室中隔欠損で1cm径以下，心房中隔欠損は2cm径以下で，特発性肺高血圧に近似）に伴う肺高血圧，3）修復術後の肺高血圧（遺残短絡は認めない．術前の

肺高血圧が持続している場合と術後時間の経過とともに肺高血圧が生じる場合がある），4）アイゼンメンゲル症候群[1]．

Manes[2]らは，192例の先天性心疾患に伴う肺高血圧を，上記4群に分け，生命予後を比較した（平均年齢41±18歳）．肺血管拡張療法は78％で使われ，そのうち44％は，併用治療を行っていた．アイゼンメンゲル症候群は，6分間歩行距離は最も短い．15～20年生存率は，修復術後肺高血圧群で36％と最も低く，特発性肺高血圧群と同等であった．小欠損孔群の15年生存率も66％と低い．一方，左右短絡群，アイゼンメンゲル症候群は，それぞれ86％，87％と他群よりも良好であった．アイゼンメンゲル症候群の生存率は，肺血管拡張療法使用以前の5年生存率が60～80％程度[3,4]の報告が多いことと比べると，改善している．この研究結果は，成人先天性心疾患に伴う肺高血圧に対する肺血管拡張療法の適応や手術適応の決定に参考になる[5-7]．

肺体血流量増加群は，肺血管閉塞性病変が，アイゼンメンゲル症候群ほど進行していない状態と考えられる．

小欠損孔に伴う肺高血圧群には，特発性肺高血圧の合併と考えられる例もある．生命予後はアイゼンメンゲル症候群よりも悪く，特発性肺高血圧よりも良好である．このことは，肺高血圧疾患では，欠損孔経由の右左短絡があると，心拍出量の維持ができるため，生存には有利であることを示している．したがって，小欠損孔に伴う肺高血圧群では，比較的早期に肺血管拡張療法の使用を開始する必要があることが示唆される．

修復術後群とアイゼンメンゲル症候群の生命予後に関して，小児を対象とした研究がある．REVEAL研究（the Registry to Evaluate Early And Long-term Pulmonary Arterial Hypertension Disease Management）[8]は，先天性心疾患に伴う肺高血圧での未修復術群と修復術群と比較し，2年生存率は有意差がないとした（86±7 vs 85±5％）．しかし，British PAH registry[9]は，より長い経過観察（5年まで）で，修復術後は，アイゼンメンゲル症候群と比べて明らかに生命予後が悪かった．これは，修復術後の長期経過観察，特に成人期では，修復術後群の予後が悪いことを示唆する．

アイゼンメンゲル症候群は，生直後から継続的に肺高血圧を認め，胎生期の右室肥大（心筋細胞造成を伴う）が持続する．したがって，右室機能は長期間保たれる[10,11]．一方，小欠損孔あるいは修復術後群は，肺高血圧がないか，修復術後に肺高血圧が軽減した時期があり，後天的な右室肥大を生じるため，右心不全の進行が早く，生命予後も悪い．また，右左短絡路が小さいあるいは術後消失していることも予後の悪い大きな要因である．

アイゼンメンゲル症候群以外は，ほとんど新しい研究が行われていない[3,4,12,13]．そこで，この解説では，主にアイゼンメンゲル症候群に関して述べる．また，左心系疾患に伴う肺高血圧には言及しない．

B. アイゼンメンゲル症候群

アイゼンメンゲル症候群は，左右短絡による高肺血流量を伴う先天性心疾患で，二次的に肺血管抵抗値が上昇し，末梢肺動脈に非可逆的な変化を起こし，体肺交通路経由の右左短絡を認める．さらに，右左短絡によるチアノーゼに基づく全身の多臓器症候を特徴とする症候群と定義される．長期にわたる低酸素血症，赤血球増多，特有の血行動態に基づく多臓器症候には，血管拡張，出血凝固異常（出血傾向，血栓形成，奇異性血栓など），腎機能異常，肥厚性骨関節症などの全身の系統的多臓器合併症を伴う．最近，肺血管拡張療法に目が向きがちであるが，多臓器合併症の予防，的確

な治療により本症候群の罹病率が低下し，生命予後も改善してきており，この合併症にも注目する必要がある[14-17]．現在，本症候群は成人先天性心疾患の2～6%と報告されている[18-20]．本症候群の死亡原因の多くは不整脈，肺内出血，肺血栓などの合併症による突然死であり[21,22]，若年での心不全死亡の頻度は低い．妊娠出産は，母児とも死亡率がきわめて高いため，肺血管拡張療法が行われている現在でも避けることが望ましい[23-25]．催奇形性のため，エンドセリン拮抗薬の妊娠中の使用は，禁忌とされるが，ホスホジエステラーゼ5阻害薬（PDE-5阻害薬とくにシルデナフィル）を用い，妊娠出産時の死亡率が低下したとの報告がある[26]．

C. 内科的治療（表1）

近年，肺高血圧に対する肺血管拡張療法が行われ，有効と報告され始めている．現在内科治療は，より根本的治療である肺血管拡張薬治療に移りつつある．日本でも，プロスタサイクリン製剤（エポプロステノール，ベラプロスト[27]），エンドセリン受容体拮抗薬（ボセンタン，アンブリセンタン）[28,29]，PDE-5阻害薬（シルデナフィル，タダラフィル）[30,31]などの使用が認可されている．ここ数年で，これらの薬剤のCHDに対する報告も増加している[32-34]．

最近の日本の多施設研究[19]では，85施設，251症例の検討で，肺血管拡張療法の日本での使用傾向が報告された．肺血管拡張療法は，52（60.5%）施設，124例（49.4%）で行われていた．36/52施設で，併用療法を行っており，エンドセリン受容体拮抗薬45施設，PDE-5阻害薬35施設，ベラプロストは30施設と多かった．

最近の日本と韓国の多施設共同研究では[35]，198人（平均年齢35歳）のアイゼンメンゲル症候群（1998～2007年）で，30例が死亡（突然死は14例）．肺血管拡張療法の臨床的改善効果は54/89例で認めたが，肺血管拡張療法施行例と非施行例とで，生命予後に有意差は認めなかった（87% vs 84%，p＝0.55）．また，欧州を中心に登録システムとして，COMPERA研究が始まっており，今後多数例での研究結果が報告されるものと期待されている[36]．

D. 肺血管拡張薬の最近の報告

1. エンドセリン受容体拮抗薬

a. ボセンタン

ボセンタンは，非選択的エンドセリン受容体拮抗薬であるが，肺血管拡張療法後長期観察を行った報告がなされ[32,37,38]，その有効性は比較的長

表1　現在日本で用いられている肺血管拡張療法とアイゼンメンゲル症候群における使用量

プロスタサイクリン製剤	
エポプロステノール	2～10ng/kg/分（静注）
ベラプロスト	20μg　3回/日
	60μg　1回/日（徐放薬）
エンドセリン受容体拮抗薬	
ボセンタン	62.5mg　2回/日
アンブリセンタン	5mg　1回/日
PDE-5阻害薬	
シルデナフィル	20mg　3回/日
タダラフィル	40mg　1回/日

く保たれるとされている．BREATH-5研究[39]の結果に最近の報告を[40,41]，加味すると，ボセンタンは，肝合併症を除くと，血行動態，運動能，機能分類を改善し，先天性心疾患に合併した肺高血圧に比較的安全に使用でき，有用であると考えられる．

b. アンブリセンタン

アンブリセンタンは，選択的ET_A受容体拮抗薬であり，肝臓機能障害や併用薬との相互作用が起こりにくいことと1日1回投与でよいという利点がある．ARIES-1，ARIES-2研究[42]で，6分間歩行，WHO機能分類を改善したが，先天性心疾患は含まれていない．最近の16人のアイゼンメンゲル症候群を対象とした，単施設研究では，安全で，運動能の改善を認めたとしている[43]．

2. PDE-5阻害薬

a. シルデナフィル

最近報告された84例のシルデナフィルを使用した，アイゼンメンゲル症候群の前方視的な多施設研究（経過観察年数1年）[44]では，運動能の改善と血行動態の改善を認めたとしている．現在までのデータからは，シルデナフィルも，先天性心疾患に伴う高度肺高血圧症に対して安全であり，臨床症状，運動能，血行動態指標を改善する[30,45]．シルデナフィルの投与量は20mg×3/日とされるが，さらに高用量の投与も有効と推測されている[46]．しかし，小児では，高用量では，低用量と比べて，生命予後が劣るとの報告があり，使用上の注意が必要である[8]．

b. タダラフィル

少数のアイゼンメンゲル症候群の観察研究によると，12週間の使用で，酸素飽和度，機能分類の改善を認めたとの報告がある[47]．肺高血圧症に対して安全で有効と考えられ，1日1回投与で良い点が有利であるが，今後の多数例での検討が必要である．

3. プロスタサイクリン製剤

a. エポプロステノール

静注薬である，エポプロステノールは，初期から用いられ，先天性心疾患に伴う肺高血圧で，血行動態やQOLを改善させるとされた[48]．しかし，脳梗塞，感染など合併症は少なくない．したがって，現在，エポプロステノールは，経口薬が有効でない場合，重度の状態である場合，さらにWHO機能分類IVの場合に用いられている[5,33]．

b. ベラプロスト

経口薬で唯一認められている薬剤で，おもに日本で使用されている．今まで2つの無作為化二重盲検試験がある[49,50]．それぞれ12週間，1年間の経過観察を行い，特発性肺高血圧では運動能の改善効果が得られたが，それ以外は，血行動態，WHO機能分類の改善は認められなかった．さらに，6カ月までは，病態の進行抑制効果があったが，1年後は，対照群と比べ，有意差は認めなかった．最近の日本と韓国の研究では，アイゼンメンゲル症候群63/199例に用いられていた[35]．最近，徐放薬も用いられており，今後，その有効性が検討される必要がある[51]．

E. 併用療法(combination therapy)

異なる系統の薬剤の併用療法は，重度の有症状例，単一薬剤で効果を認めない例で行われ始めている[52,53]．特発性肺高血圧では，up-front治療として，肺血管拡張療法の開始初期から用いられることも少なくない．アイゼンメンゲル症候群は病状の進行が遅いことと予後が特発性肺高血圧と比べ良好なため，初期から行われることは少なく，単一薬剤無効例に加えることが殆どである．最近，アイゼンメンゲル症候群の併用療法に関する研究が行われている[34,54,55]．Iversonら[32]は，ボセ

ンタンにシルデナフィルを加えるという無作為対照二重盲検クロスオーバーデザインの研究を行ったが，有効性は見出せなかった．D'Altoら[54]は，観察研究ではあるが，ボセンタンが有効でない患者を対象としシルデナフィルを加え，臨床症候，運動能，血行動態の改善を認めた．Dillerら[37]は，本症候群の患者の20%程度では，2剤ないし3剤の併用療法を行う傾向にあり，一定の有効性を認めるとした．日本でも，併用療法は単一薬剤使用より広く行われている（36施設 vs 16施設）[19]．しかし，いずれも多数例での検討はなく，有効性を評価するには時期尚早である．

F. 生命予後予測因子と肺血管拡張療法

肺血管拡張療法の適応と開始時期に関しては，確立したガイドラインがないが，生命予後予測因子の有無は参考になる．以前から，生命予後予測因子には，様々な報告があるが，最近でも，酸素飽和度，運動能の低下[56]，トロポニン値[57]，心エコーでのパラメーター[58]，脳性ナトリウム利尿ペプチド値[59,60]，右室機能低下[61]など多くの指標が予後予測に有用と報告されている．これらは，肺血管閉塞性病変の進行，右室機能の低下を反映する指標が多い．しかし，本症候群は突然死が多いため，その予測は難しい場合が少なくない[19,35,62]．

G. 合併症の治療

肺血管拡張療法の発達は著しいが，本症候群の基本的な治療は，全身療法と合併症の予防である．特に新しい進歩は認められていないが，系統的全身合併症の予防と治療は重要で，肺血管拡張療法とともにこれらの合併症の治療，予防を的確に行う（たとえば，非心臓手術の管理，妊娠出産の制限，抗凝固薬，抗血小板薬の使用の制限など）ことにより罹病率は減少して予後は改善する[6,33]．

H. 外科手術

本症候群は肺血管抵抗値が高く，肺血管病変が非可逆的であるため，修復手術は禁忌である．しかし，酸素，NO，あるいは，エポプロステノール静注などに反応性があり，肺血管抵抗が6単位以下に低下するあるいは肺体血流量比が2.0単位をこえる，いわゆるグレーゾーンにある肺高血圧は，外科的な修復術が可能な例がある[6,7,63]．本症候群を含む高度肺高血圧群に対する肺血管拡張療法の使用経験は限られており，中長期予後の持続効果は明らかではない．また，肺血管組織のリモデリングが生じているかどうか明らかではない．このため，修復術後も肺血管拡張療法を継続する必要があると考えられている．

アイゼンメンゲル症候群では，肺血管拡張療法の開発と内科的な経過観察での生存率が，肺移植後の生存率より良いことが多く，心肺移植の適応となることは少ない．

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特集2　慢性血栓塞栓性肺高血圧症（CTEPH）

5．CTEPHに対するバルーン肺動脈形成術の適応とその効果

大郷　剛*

慢性血栓塞栓性肺高血圧症（chronic thromboembolic pulmonary hypertension：CTEPH）は，肺動脈の慢性血栓塞栓により肺血管抵抗（PVR）が上昇し，肺高血圧となり右心不全へ至る予後不良の疾患である。CTEPHの治療として，肺動脈血栓内膜摘除術（pulmonary endarterectomy：PEA）が確立され，現時点で最も推奨される治療であるが，手術適応外と判断された場合の問題は解決されていない。近年，手術適応外のCTEPHに対する治療として，バルーン肺動脈形成術（balloon pulmonary angioplasty：BPA）の成績が報告されている。国立循環器病研究センター病院では血管外科，肺循環科，放射線科でのカンファレンスにてPEA適応外の患者に精度の高いCT（computed tomography）を用いて末梢病変を評価し，BPAを施行したところ，著明な血行動態や臨床データの改善が得られ，重篤な合併症は認めていない。施設によりBPAのアプローチは異なるが，今後さまざまなBPAのデータが報告され，治療の効果や安全性も改善されていくことが予想される。

1．はじめに

慢性血栓塞栓性肺高血圧症（chronic thromboembolic pulmonary hypertension：CTEPH）は肺動脈の慢性血栓塞栓により肺血管抵抗（PVR）が上昇し，肺高血圧となり右心不全へ至る予後不良の疾患である[1]。CTEPHの治療はSan Diegoのグループが外科的治療法である肺動脈血栓内膜摘除術（pulmonary endarterectomy：PEA）を確立し，以後その治療結果に関して報告が数多くなされている[2]。手術可能なCTEPHにおけるPEAの効果は明らかであり，エビデンスも豊富であることより現時点で最も推奨される治療である。しかしCTEPH患者全員がPEAによる恩恵を受けられる訳ではなく，国際的なレジストリーにおいて約1/3以上の患者が手術困難と判断されると報告されている[3]。手術適応外と判断された患者へは抗凝固療法，在宅酸素療法等の保存的治療を行うが，重症肺高血圧症の場合，予後は不良である[4][5]。これらの手術適応外と判断されたCTEPHの治療は，解決されていない問題である。近年，手術適応外のCTEPHに対する治療として，バルーン肺動脈形成術（balloon pulmonary angioplasty：BPA）の成績がいくつか報告されている。2001年にはFeinsteinらが18名の患者へBPAを施行したところ，血行動態の改善を認めたものの，11人の患者は肺水腫を合併（61%）し，1人の患者は周術期に死亡している[6]。その後，合併症および効果の問題により，世界的に確立された治療としては認識されていない。しかし，治療適応外の患者において，主に日本およびノルウェーでBPAは行われており，初期成績が報告されてきて

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いる[7~10]。しかし，これらの近年の報告においても，死亡例や肺水腫，肺出血等の合併症がまだ問題となっている。国立循環器病研究センター病院（以下，当院）では，日本で最も古くからPEAを行っていた。だが，末梢病変のため手術適応外とされている患者も多く存在し，これらの患者を対象に2010年よりBPAを開始した。当院では手術適応に関しては血管外科，肺循環科，放射線科でのカンファレンスにて決定し，手術治療適応外の患者へはBPAの説明を行い，同意が得られた場合にBPAを施行している。今後さまざまなBPAの効果や安全性も改善されていくことが予想されるが，今回現時点での当院におけるBPAの治療データを元に，効果と安全性に関する初期成績をまとめ，問題点を考察したい。

2．当院のBPA手技

刺入部位は右頸部もしくは右鼠蹊部とした。シース挿入後ヘパリン5000単位を投与しballoon wedge catheterを挿入し，治療直前の血行動態の評価を行い，0.035 inch wire（Radifocus® guide wire〔0.035inch〕；TERUMO, Tokyo, Japan）にて6Fr long sheath（Bright Tip SHEATH introducer®；Cordis/Johnson&Johnson, New Brunswick, NJ）を挿入した肺血管形状にshapingした6Fr multipurpose guideing catheter（Mach1 Peripheral MP' R；Boston Scientific, Natick, MA）を挿入した。治療目標血管に対してテストショット造影を行い，0.014 inch guide wire（Cruise；Asahi Intec, Tokyo, Japan）を挿入し2.0～4.0mmまでのバルーン（IKAZUCHI PAD, Kaneka, Osaka, Japan）を使用し，治療を行った。当初の治療目標としては，平均肺動脈圧（mPAP）を30mmHg以下とした。BPA施行時（右A8b）の画像所見を示す。（図1）。肺動脈（A8b）は分岐部を中心としたwebで血流は極めて悪いが（A），2.0mmのバルーンで拡張し（B），肺動脈血流はやや末梢まで改善しているが，拡張不良である。（C）。その後4.0mmのバルーンで拡張し，血管径も拡大し肺動脈の血流と静脈還流も良好となっている。（D）。

3．当院のBPAの初期治療成績

1）BPAを施行したCTEPH症例の臨床像

2010～2013年に当院においてBPAを最終まで施行した22人のCTEPH患者を対象にした。CTEPHの診断は肺高血圧症ガイドラインに基づきcomputed tomography（CT），perfusion lung scintigraphyとpulmonary angiography, right heart catheterizationで行った。手術適応は当院の肺高血圧症専門家，放射線科医，PEAを施行する外科医によるチームによって判断した。PEAの適応がないと判断された患者に対しBPAの説明を行い，同意が得られた患者においてBPAを行った。PEAの適応外とされた理由としては，19人（86%）が末梢病変のためであり，2人（9%）がPEA術後残存肺高血圧，残りの1人（5%）は重篤な併存症（抗生剤でコントロールできない感染症，敗血症，重篤な肝不全）であった。（表1）。BPAのターゲットとなる病変はCone-beam CT，もしくはMulti-detector CTにおいて行い，治療バルーン径の決定もCTによる病変部の血管径に応じて行った。

今回の検討はBPAを終了している患者とした。検討項目としてBPA前後および3カ月後での自覚症状，6MWT（6分間歩行テスト），BNP（脳性ナトリウム利尿ペプチド），右心カテーテル検査による血行動態，治療回数，周術期合併症（死亡者数，ショック例，重症肺障害数）とした。BPA後の重症肺水腫は人工呼吸器の使用もしくは3日以上のNPPV（非侵襲的陽圧換気）の使用が必要であった場合と定義した。BPAを行った22人の臨床的背景を示す。（表2）。女性が多く，平均年齢は63±13歳，WHO-FC（World Health Organization functional class）はⅠ：0人，Ⅱ：0人，Ⅲ：18人，Ⅳ：4人であった。右心カテーテル

CTEPH：chronic thromboembolic pulmonary hypertension（慢性血栓塞栓性肺高血圧症）
PVR：肺血管抵抗，PEA：pulmonary endarterectomy（肺動脈血栓内膜摘除術）
BPA：balloon pulmonary angioplasty（バルーン肺動脈形成術），mPAP：平均肺動脈圧
6MWT：6分間歩行テスト，BNP：脳性ナトリウム利尿ペプチド

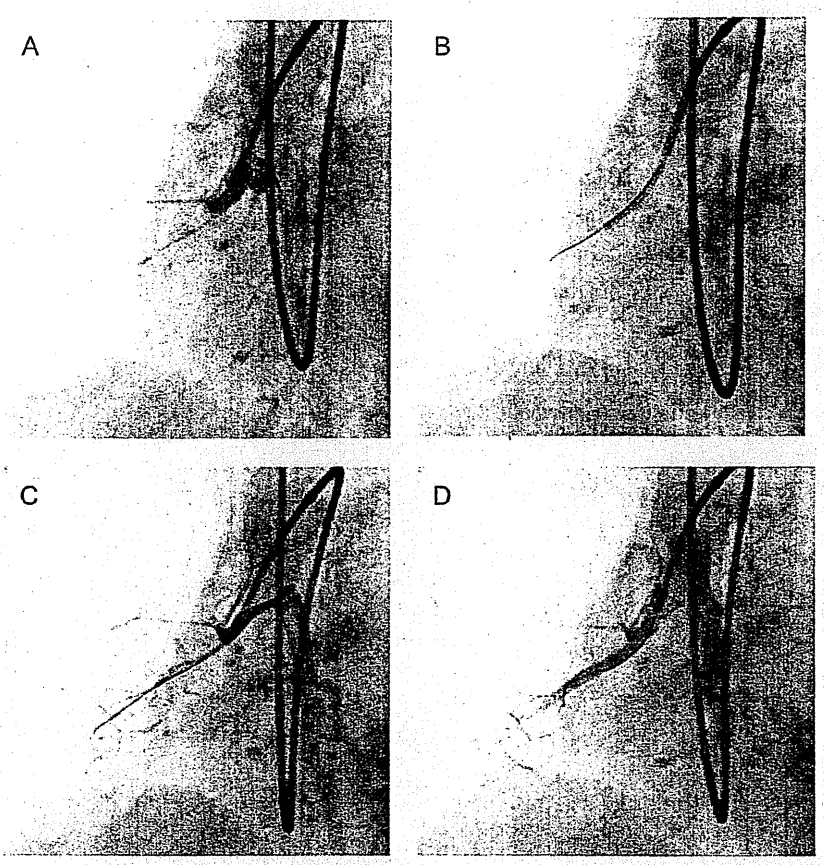

図1　BPA 施行時（右 A8b）の画像所見

A：肺動脈（A8b）は分岐部を中心とした web で血流は極めて悪い．
B：2.0mm のバルーンで拡張．
C：肺動脈血流はやや末梢まで改善しているが，拡張不良である．
D：4.0mm のバルーンで拡張した後の造影所見，血管径も拡大し肺動脈の血流と静脈還流も良好となっている．
BPA：バルーン肺動脈形成術

（筆者提供）

による mPAP は 44.5±10mmHg，心係数は 2.2±0.8L/分/m^2 であった。

2）BPA 前後の血行動態における短期効果

患者1人につき平均 3.2±1.0 回の BPA を施行した。BPA 施行前および3カ月後の右心カテーテル検査における血行動態の変化を示す。（**図2，表3**）。mPAP は 44.5±10mmHg より 26±6.5 mmHg へと有意に減少し，PVR も 12.7±6.3 wood units より 5.9±2.5 wood units へと著明に低下していた。心係数は今回の検討においては上昇傾向にあったが，有意差は認めなかった。

3）BPA 後の短期的臨床経過

BPA 施行前および3カ月後での WHO-FC，6

表1　PEA 適応外の理由

今回バルーン肺動脈形成術を行った 22 人中 19 人が末梢病変のため PEA 適応外とされた．

理由	患者数
末梢病変	19 人（86%）
PEA 術後残存肺高血圧	2 人（9%）
重篤な併存症	1 人（5%）

PEA：肺動脈血栓内膜摘除術

（筆者作成）