Contrast-Enhanced MDCT vs. Time-Resolved MR Angiography vs. Contrast-Enhanced Perfusion MRI: Assessment of Treatment Response by Patients with Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

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Introduction: Chronic thromboembolic pulmonary hypertension (CTEPH) occurs when pulmonary hypertension develops in association with an inciting venous thromboembolic event Although a ventilation/perfusion (V/Q) lung scan is generally performed early in the diagnostic pathway to differentiate patients with CTEPH from those with other forms of pulmonary hypertension, selective digital subtraction angiography (DSA) combined with right heart catheterization is considered the gold standard for evaluating the disease and for assessment of treatment response and other concerns. In addition, it has been suggested that recent progress in non-invasive radiological methods such as cardiac echography (cardiac US), contrast-enhanced multidetector-row CT (CE-MDCT) and phase-contrast magnetic resonance imaging (MRI) have rendered these procedures useful for the above-mentioned purposes in routine clinical practice. In the last several years, dynamic CE-perfusion MRI and four-dimensional (4D) or time-resolved CE-MR angiography have been put forward as new techniques for quantitative and qualitative assessment of pulmonary vascular diseases (1-4). However, there have been no reports on the potential of quantitatively assessed dynamic CE-perfusion MRI and qualitatively evaluated time-resolved CE-MR angiography for assessment of therapeutic effects on CTEPH patients.

We hypothesized that quantitatively assessed pulmonary perfusion by dynamic CE-perfusion MRI has equal to or better potential for therapeutic assessment than CE-MDCT and time-resolved MR angiography in CTEPH patients. The aim of our study was therefore to directly compare the therapeutic effect assessment capability of CE-MDCT, time-resolved CE-MR angiography and quantitatively assessed dynamic CE-perfusion MRI for CTEPH patients.

Materials and Methods: Twenty-four consecutive patients (12 men and 12 women; mean ± standard deviation age, 68.1 ± 8.6 years) treated with conventional therapy underwent pre- and post-therapeutic CE-MDCT, time-resolved CE-MR angiography, dynamic CE-perfusion MRI, 6 minutes walk distance (6-MWD), cardiac US and right heart catheterization. According to therapeutic results evaluated by 6-MWD, cardiac US and right heart catheterization, all patients were divided into response (n=13) and non-response (n=11) groups. CTEPH indexes for CE-MDCT ($CTEPH_{CTA}$) and time-resolved CE-MR angiography ($CTEPH_{MRA}$) were calculated on the basis of embolic burden, and RV/LV diameter ratio was also determined on CE-MDCT in each patient. According to the previously published theories and software (2, 3), pulmonary perfusion parameter maps were generated from all dynamic CE-perfusion MR data, followed by determination of improvements in mean perfusion parameter at ROIs for each patient.

To determine the correlation between improvements of RV/LV diameter ratio, $CTEPH_{CTA}$ index, $CTEPH_{MRA}$ index, PBF, PBV and MTT after treatment and treatment responses (i.e. CI, 6-MWD, mean pulmonary arterial pressure <PAP> and pulmonary vascular resistance <PVR>), all improvements after treatment evaluated by CT, time-resolved MR angiography and dynamic perfusion MRI were compared with those reflected by treatment responses. Then, receiver operating characteristic (ROC) -based positive tests were performed to determine the feasible threshold value for each radiologic index of improvement for distinguishing the responder from the non-responder group. Finally, sensitivities, specificities and accuracies of all parameters for distinguishing the responder from the non-responder group were compared with each other by means of McNemar's test. A p value less than 0.05 was considered significant for all statistical analyses.

Results: Representative case is shown in Figure 1. Results of analysis of correlations between improvement as measured by radiological indexes and treatment responses are shown in Table 1. Improvements of radiological indexes had moderate correlation with treatment response ($p<0.05$). Results of the ROC-based positive test using all radiological indexes for distinguishing the responder from the non-responder group, and diagnostic performances are shown in Table 2. Application of the feasible threshold value of each index resulted in a significantly higher specificity (90.9 <10/11> %) and accuracy (95.8 <23/24> %) for improvement in PBF than for improvements in $CTEPH_{CTA}$ (specificity: 36.4 <4/11> %, $p<0.05$; accuracy: 70.8 <17/24> %, $p<0.05$).

Conclusion: Quantitatively assessed dynamic perfusion MRI has better capability for assessment of therapeutic effect on CTEPH patients than do CE-MDCT or time-resolved MR angiography, and may be able to play a complementary role in the management of CTEPH patients in routine clinical practice.

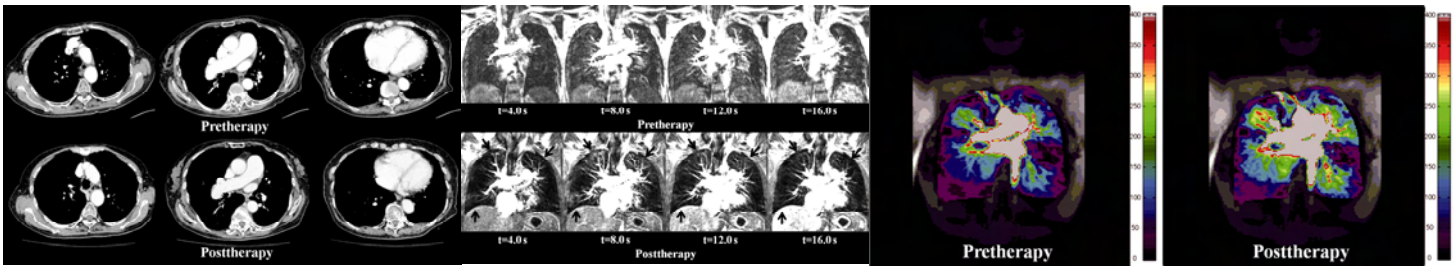

Fig. 1A **Fig. 1B** **Fig. 1C**

Figure 1. 76-year-old male with chronic thromboembolic pulmonary hypertension treated with conservative therapy and assessed as responder

A: Contrast-enhanced MDCT (top to bottom: pretherapeutic MDCT to posttherapeutic MDCT; left to right: cranial to caudal) demonstrates presence of thrombi in subsegmental pulmonary arteries. Although some subsegmental thrombi disappeared, improvement in $CTEPH_{CTA}$ was 0 %, but improvement in the RV/LV diameter ratio was -0.05. This case was identified as true positive on CE-MDCTs. B: Source images of time-resolved contrast-enhanced MR angiography (top to bottom: pretherapeutic time-resolved CE-MR angiography to post-therapeutic time-resolved CE-MR angiography; L to R: ventral to dorsal) shows pulmonary parenchymal enhancement in both lungs, while improvement (arrows) in $CTEPH_{MRA}$ was -13.5 %. This case was identified as true positive on time-resolved CE-MR angiographies. C: Quantitative PBF maps (left to right: pretherapy to posttherapy) demonstrate improvement in PBF in both lungs to 57ml/100ml/min, respectively. This case was identified as true positive on PBF maps.

Table 1 Correlation between improvement in radiological indexes and quantitative treatment responses

	Improvement in CI		Improvement in 6-MWD		Improvement in PAP		Improvement in PVR	
Improvement in:	r	p value	r	p value	r	p value	r	pvale
RV/LV diameter ratio	-0.42	0.04	-0.52	0.0002	0.5	0.0003	0.59	<0.0001
$CTEPH_{CTA}$	-0.42	0.04	-0.5	0.0003	0.5	0.0003	0.56	<0.0001
$CTEPH_{MRA}$	-0.51	0.01	-0.67	<.0001	0.56	<0.0001	0.67	<0.0001
PBF	0.56	0.004	0.71	<.0001	-0.6	<0.0001	-0.7	<0.0001
PBV	0.51	0.01	0.67	<.0001	-0.47	0.0007	-0.64	<0.0001
MTT	-0.42	0.04	-0.41	0.0041	0.42	0.003	0.46	0.0009

Table 2. Capability of each index to differentiate between responders and non-responders among CTEPH patients after conservative therapy

Improvement in:	Feasible threshold value	SE (%)	SP (%)	PPV (%)	NPV (%)	AC (%)
RV/LV diameter ratio	≤0	100 (13/13)	81.8 (9/11)	86.7 (13/15)	100 (9/9)	91.7 (22/24)
$CTEPH_{CTA}$ (%)	≤0	100 (13/13)	36.4 (4/11)	65 (13/20)	100 (4/4)	70.8 (17/24)
$CTEPH_{MRA}$ (%)	≤0	100 (13/13)	54.5 (6/11)	72.2 (13/18)	100 (6/6)	79.1 (19/24)
PBF (ml/100ml/min)	7≤	100 (13/13)	90.9* (10/11)	92.9 (13/14)	100 (10/10)	95.8* (23/24)
PBV (ml/100ml)	0.9<	100 (13/13)	72.7 (8/11)	81.3 (13/16)	100 (8/8)	87.5 (21/24)
MTT (s)	<1	100 (13/13)	72.7 (8/11)	81.3 (13/16)	100 (8/8)	87.5 (21/24)

*: Significant difference with $CTEPH_{CTA}$ ($p<0.05$).

Reference:

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