

# Combined Pulmonary Fibrosis and Emphysema: 3D Time-resolved MR Angiographic Evaluation of Pulmonary Arterial Mean Transit Time and Time to Peak Enhancement<sup>1</sup>

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## Purpose:

To correlate conventional invasive pressure indexes of pulmonary circulation with pulmonary first-order arterial mean transit time (MTT) and time to peak enhancement (TTP) measured by means of three-dimensional time-resolved magnetic resonance (MR) angiography in patients with combined pulmonary fibrosis and emphysema (CPFE).

## Materials and Methods:

The study was institutional review board approved. All subjects involved in the study provided written informed consent. Eighteen patients with CPFE were enrolled in this study. Thirteen healthy individuals matched for age and sex served as control subjects. Three-dimensional time-resolved MR angiography was performed by using a 3.0-T MR imager. Regions of interest (ROIs) were drawn manually on first-order pulmonary arteries. Within the ROIs, signal intensity-versus-time curves reflecting the first pass of the contrast agent bolus in the pulmonary vessels were obtained. MTT and TTP were calculated. Pulmonary arterial pressure and pulmonary capillary wedge pressure were measured with a double-lumen, balloon-tipped catheter that was positioned in the pulmonary artery. The mean pulmonary arterial pressure (mPAP) and the pulmonary vascular resistance (PVR) were determined.

## Results:

MTT and TTP values were prolonged significantly in patients with CPFE compared with those in the control subjects ( $P < .001$ ). Mean TTP and mean MTT correlated directly with mPAP and PVR index ( $P < .005$ ). At multiple linear regression analysis, MTT was the only factor independently associated with PVR index and mPAP.

## Conclusion:

Three-dimensional time-resolved MR angiography enables determination of pulmonary hemodynamic parameters that correlate significantly with the pulmonary hemodynamic parameters obtained with invasive methods and may represent a complementary tool for evaluating pulmonary hypertension in patients with CPFE.

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Idiopathic pulmonary fibrosis is the most common among the interstitial lung diseases of unknown cause that are defined according to the 2001 American Thoracic Society/European Respiratory Society international multidisciplinary consensus classification system as idiopathic interstitial pneumonias, which include several disease manifestations (1). Emphysema is a chronic lung condition in which alveoli, or air sacs, are morphologically altered (2). A number of observations have indicated that vascular abnormalities, including pulmonary arterial hypertension, may be important in idiopathic pulmonary fibrosis and emphysema (2). The occurrence of both emphysema and pulmonary fibrosis in the same patient has received increased attention. The syndrome of combined pulmonary fibrosis and emphysema (CPFE) has been characterized as an individual entity that is separate from both idiopathic pulmonary fibrosis and pulmonary emphysema (3). Despite subnormal spirometric results, which may be responsible for the underrecognition of CPFE, this combination syndrome is a severe entity. This entity generally is characterized by emphysema of the upper lung zones and diffuse parenchymal disease with fibrosis of the lower lung zones, mainly in current or previous heavy smokers (4). Although emphysema and fibrosis have been presumed to be two different diseases, data now implicate common cell and molecular activation pathways (5,6). The presence and extent of emphysema have a profound influence on physiologic function in terms of pulmonary functional impairment (7). Thus, the incidence of finding evidence of both emphysema and pulmonary fibrosis in the same patient has received increased attention (7). In patients with CPFE, the pulmonary hemodynamic profile is

the major determinant of the prognosis. The prevalence of pulmonary arterial hypertension is particularly high in patients with CPFE and is higher than that reported with idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, or pulmonary emphysema (3).

Although pulmonary hemodynamic parameters such as pulmonary vascular resistance (PVR) and mean pulmonary arterial pressure (mPAP) can be assessed accurately by means of right-sided heart catheterization (8), a simple, reliable, and noninvasive method to evaluate the pulmonary vascular hemodynamics in patients with CPFE would be preferable. Doppler echocardiography commonly is used to estimate the systolic pulmonary arterial pressure (8). However, echocardiographic findings may be inaccurate and thus lead to considerable overdiagnosis of pulmonary arterial hypertension, and they do not enable direct measurement of PVR (9). The diagnostic usefulness of measuring the size of the main pulmonary arterial diameter within 3 cm of the bifurcation on computed tomographic (CT) scans, which has been proposed as having 84% sensitivity and 75% specificity—albeit without having direct correlation with pulmonary arterial pressure (10)—has not been confirmed in subsequent larger studies (11). Time-resolved magnetic resonance (MR) angiography is a noninvasive technique that enables not only anatomic imaging of the pulmonary vasculature but also evaluation of the hemodynamics (12,13). In particular, analysis of the MR angiographic signal intensity curves of pulmonary vessels could yield two parameters of vascular physiologic relevance: time to peak enhancement (TTP) and mean transit time (MTT) (14). The purpose of the present study was to correlate conventional invasive pressure indexes of

pulmonary circulation with pulmonary first-order arterial MTT and TTP measured by means of three-dimensional (3D) time-resolved MR angiography in patients with CPFE.

## Materials and Methods

### Patients

This study was approved by the institutional review board. All patients and control subjects involved in the study provided written informed consent. Eighteen patients with CPFE (12 men, mean age  $\pm$  standard deviation: 63 years  $\pm$  4; six women, mean age: 62 years  $\pm$  6) were included in the study. Inclusion criteria were emphysema at CT, defined as well-demarcated areas of decreased attenuation (compared with contiguous normal lung) margined by a thin (1-mm) wall or no wall, and/or multiple bullae and diffuse parenchymal lung disease with clinically important pulmonary fibrosis at CT, defined as reticular opacities, honeycombing, architectural distortion, and/or traction bronchiectasis or bronchiolectasis. Exclusion criteria were collagen vascular diseases; cardiac dysfunction, including myocardial infarction; and/or blood cell

### Advance in Knowledge

- Arterial pulmonary mean transit time and time to peak enhancement, as assessed by means of three-dimensional MR angiography, correlate with pulmonary invasive pressure measurements.

### Implication for Patient Care

- MR angiography of arterial pulmonary vessels may facilitate the noninvasive evaluation and monitoring of pulmonary arterial hypertension in patients with combined pulmonary fibrosis and emphysema.

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### Abbreviations:

CPFE = combined pulmonary fibrosis and emphysema  
 mPAP = mean pulmonary arterial pressure  
 MTT = mean transit time  
 PVR = pulmonary vascular resistance  
 PVRI = PVR index  
 ROI = region of interest  
 3D = three-dimensional  
 TTP = time to peak enhancement

### Author contributions:

Guarantors of integrity of entire study, G. Sergiacomi, F.B., M.L.A., F.F., P.R., G.P., F.R., E.M., G. Simonetti; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, all authors; clinical studies, G. Sergiacomi, F.B., M.L.A., F.F., S.C., P.R., G.P., F.R., E.M., G. Simonetti; statistical analysis, G. Sergiacomi, F.B., M.L.A., F.F., S.C., P.R., G.P., F.R., E.M., G. Simonetti; and manuscript editing, all authors

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malignancies. All patients with CPFE underwent right-sided heart catheterization and MR angiography at their initial work-up while breathing room air. Right-sided heart catheterization was performed within 3 days prior to or following MR angiography. At the time of right-sided heart catheterization or MR angiography, none of the patients had a fever, evidence of other infectious diseases or inflammatory disorders, or any malignancy. Thirteen healthy volunteers who matched the enrolled patients in age and sex served as control subjects. No control subjects had a history of smoking; interstitial lung disease such as drug toxicity, environmental exposure-related illness, or collagen vascular disease; cardiac dysfunction; or blood cell malignancies. Estimates of cardiac and pulmonary function based on echocardiographic evaluation were obtained noninvasively in the control subjects.

#### Right-sided Heart Catheterization

Pulmonary arterial pressure and pulmonary capillary wedge pressure were measured with a 7-F double-lumen, balloon-tipped catheter (Swan-Arrow Catheter [Arrow International, Reading, Pa] or Swan-Abbott Catheter [Abbott Critical Care Systems, Mountain View, Calif]) that was positioned in the pulmonary artery. Stroke volume and cardiac output were measured by means of thermodilution. The mPAP (in millimeters of mercury) was determined as follows:  $mPAP = PAP_{dias} + [(PAP_{sys-dias})/3]$ , where  $PAP_{dias}$  is the diastolic pulmonary arterial pressure and  $PAP_{sys-dias}$  is the difference between the systolic and diastolic pulmonary arterial pressure. The PVR (in mm Hg/L/min) was determined as follows:  $PVR = (mPAP - mPCWP)/CO$ , where mPCWP is the mean pulmonary capillary wedge pressure and CO is the cardiac output. Since pressure is independent of the size of the system, the mPAP values of various subjects were compared without the need to take into account potential differences in body size. Conversely, since PVR is proportional to the size of the system, for comparative purposes, the PVR was expressed as a PVR index (PVRI, in mm

Hg/L/min/m<sup>2</sup>), which was calculated as the PVR divided by the body surface area (in square meters).

#### Standard Echocardiography

All control subjects underwent standard echocardiography (Sequoia C256 ultrasonography machine; Acuson, Mountain View, Calif) with a 2.5–3.5-MHz transducer. Echocardiography was performed according to the recommendations of the American Society of Echocardiography (15,16). Images were stored digitally and recalled for analysis by using an offline measuring system (KinetDx; Acuson). Analyses were performed by a single echocardiographer with 8 years of experience in echocardiographic imaging (E.M.).

Right ventricular diameters and left ventricular septal and posterior wall thicknesses were measured from the M mode. Mitral inflow velocity was determined by means of pulsed-wave Doppler imaging. Left ventricular isovolumetric relaxation time was recorded by means of continuous-wave Doppler echocardiography. Left ventricular diastolic and left atrial volume measurements were obtained with two-dimensional measurements by using the modified Simpson rule and were normalized to body surface area. The maximal tricuspid regurgitation velocity was recorded by means of continuous-wave Doppler echocardiography. The estimated pulmonary arterial systolic pressure was equal to the sum of the tricuspid gradient calculated by means of a modified Bernoulli equation from tricuspid regurgitation velocity and an assumed right atrial pressure of 5 mm Hg (17). Right ventricular function was evaluated with the Tei index, which expresses global cardiac function, defined as the sum of the isovolumic contraction time plus the isovolumic relaxation time divided by ejection time (18). Right ventricular eccentricity index, a measure of septal displacement, was measured at both end systole and end diastole by using the method of Ryan et al (19). Cutoff values for echocardiographic measurements were obtained from published echocardiographic reference values (15–19) and are reported in Table 1.

#### MR Imaging

MR imaging was performed with a 3.0-T MR imager (Achieva 3T; Philips Healthcare, Best, the Netherlands). A six-element phased-array thorax coil was used. A 20-gauge cannula was sited in the left antecubital vein and connected to an electronic power injector (MR Spectris; Medrad, Pittsburgh, Pa). After scout images were obtained, 3D time-resolved contrast material-enhanced MR angiography was performed. The first volume was acquired with the patient holding his or her breath before starting the contrast medium injection and was used as the reference for subtraction. Four milliliters of gadopentetate dimeglumine (Magnevist; Bayer HealthCare, Wayne, NJ) was injected at 4 mL/sec and followed by a 20-mL saline flush administered at the same injection rate. Simultaneously with the start of the injection, a continuous fast free-breathing transverse two-dimensional T1-weighted gradient-echo sequence (fluoroscopic MR angiography) across the right ventricle was performed to track the arrival of the bolus of gadolinium-based contrast material in the right ventricle. When the contrast material was visualized at the level of the right ventricle, the breath-hold dynamic 3D time-resolved MR sequence was reenacted and transverse contrast-enhanced dynamic images were acquired. We used a transverse 3D T1-weighted turbo field-echo sequence with the following parameters: 2.6/1.3 (repetition time msec/echo time msec), 10° flip angle, turbo factor of 40, sensitivity-encoding factor of three, field of view of 435 × 326 mm, and reconstruction matrix of 256 × 256. We covered a slab of 150 mm divided in 30 overcontiguous partitions leading to a section thickness of 5 mm. The imaging time for each dynamic sequence was 1.5 seconds. We repeated the sequence 12 times, for a breath-hold imaging time of 18 seconds. The breath-hold sequence was then repeated three times with the subject asked to breathe for 2 seconds after each sequence. Thus, the total examination time was 60 seconds. Breath holding was performed at end expiration.

**Table 1**

**Echocardiographic Variables for Control Subjects**

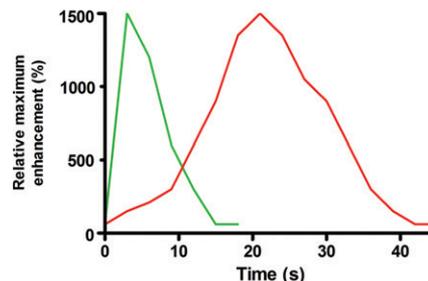
Echocardiographic Measurement	Control Subject Value*	Cutoff Value
<b>Left ventricle</b>		
IVRT (msec) <sup>†</sup>	78 ± 3 (76, 81)	60–90
Mitral E/A <sup>‡</sup>	1.12 ± 0.04 (1.1, 1.2)	<1.5
Septal thickness (cm)	0.76 ± 0.11 (0.68, 0.82)	<1.1
Posterior wall thickness (cm)	0.74 ± 0.09 (0.69, 0.80)	<1.1
Diastolic volume/body surface area (mL/m <sup>2</sup> )	54 ± 12 (46, 72)	<76
Left atrial volume/body surface area (mL/m <sup>2</sup> )	21 ± 3 (19, 24)	<29
Pulmonary artery diameter (cm)	1.76 ± 0.22 (1.6, 1.9)	<2.2
<b>Right ventricle</b>		
Basal diameter (cm)	2.3 ± 0.38 (2.16, 2.63)	<2.9
Middle diameter (cm)	2.9 ± 0.27 (2.79, 3.12)	<3.4
Base-to-apex length (cm)	7.45 ± 0.29 (7.30, 7.66)	<8
Free wall thickness (mm)	3.11 ± 0.36 (2.88, 3.34)	<5
Systolic eccentricity index	1.01 ± 0.01 (1.00, 1.01)	1
Diastolic eccentricity index	1.00 ± 0.01 (1.00, 1.01)	1
Tei index	0.27 ± 0.02 (0.26, 0.28)	<0.3
Tricuspid regurgitation velocity (m/sec)	1.8 ± 0.3 (1.6, 2.0)	<3
Pulmonary arterial systolic pressure (mm Hg)	18 ± 4.3 (15, 21)	<25

\* Data are means ± standard deviations, with 95% confidence intervals in parentheses.

<sup>†</sup> IVRT = isovolumetric relaxation time, defined as the interval between aortic valve closure and mitral valve opening.

<sup>‡</sup> E is the peak early-filling (E-wave) velocity, and A is the late diastolic filling (A-wave) velocity.

**Figure 2**

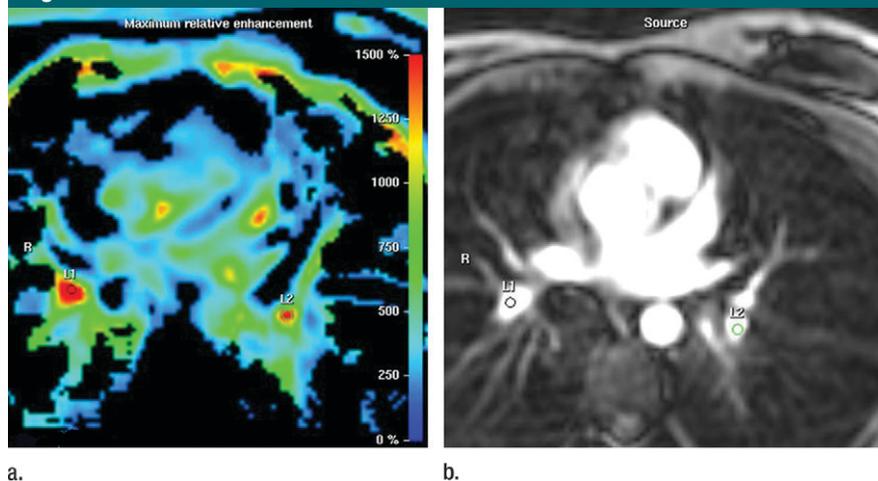


**Figure 2:** Signal intensity-versus-time curves generated throughout one cardiac cycle. Green represents curve for 50-year-old male control subject. Red represents curve for 68-year-old man with CPFE.

relative to the background signal intensity (phase before administration of contrast material) and is expressed by the following formula:  $E_k = I_k(R) - [I_0(R)/I_0(R)] \cdot 100 \cdot k \cdot \epsilon$  (1, n series), where  $I_k$  is the examined image,  $k$  is the series index,  $I_0$  is the corresponding precontrast image, and  $R$  is the user-selected ROI (20). The corresponding relative maximal signal intensity projection color-coded maps were generated by using an automated process at the workstation according to this formula. The relative maximal signal intensity values are coded according to color (blue, green, yellow, and red). The increase in signal intensity (relative maximal signal intensity values) is reflected in the color. The bottom and top values on the color-coded scale were 0% (blue) and 1500% (red), respectively.

Two radiologists (G. Sergiacomi and F.B., with 7 and 4 years, respectively, of experience in MR angiography) who were blinded to the patients' clinical data manually drew the ROIs (typically 3 pixels) over the arterial first-order pulmonary vessels within the hot spots (red) on the color-coded maps in consensus. ROIs were then superimposed electronically over the anatomic contrast-enhanced images, and the signal intensity-versus-time curves were generated throughout one cardiac cycle (first bolus pass) (Fig 2). Subsequently, the TTP and MTT were calculated automatically. Since the number of hot spots varied from patient to patient, the number of ROIs varied accordingly. Thus, a mean of 15 ROIs

**Figure 1**



**Figure 1:** Transverse MR images in 58-year-old woman with CPFE show ROI positioning. (a) ROIs were drawn manually on the color-coded maps over the areas of the pulmonary vessels showing the highest relative maximal signal intensity projection values (red). (b) ROIs were then superimposed electronically over the anatomic contrast-enhanced images. L1 and L2 are the manually drawn ROIs. R = right.

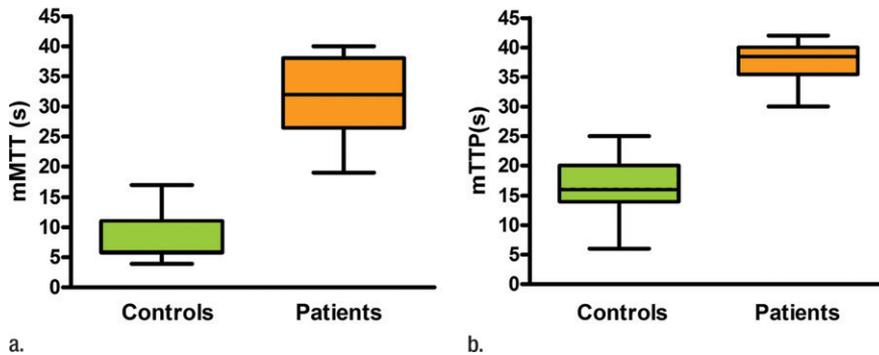
**Data Processing**

Data were processed at a workstation (ViewForum; Philips Healthcare). The relative maximal signal intensity color-coded maps were used for guidance together with the anatomic contrast-

enhanced images for region-of-interest (ROI) placement (Fig 1).

The relative maximal signal intensity projection value ( $E_k$ ) represents the percentage increase in signal intensity (contrast agent concentration)

Figure 3



**Figure 3:** Comparisons of MR angiography–derived (a) mean MTT (*mMTT*) and (b) mean TTP (*mTTP*) for first-order pulmonary arteries between patients with CPFE and control subjects. Median, range, and interquartile range values are shown. Significant differences ( $P < .001$ ) in mean MTT and mean TTP were observed. The line inside each box represents the median value. The ends of the vertical lines represent minimal and maximal data values. The upper hinge of each box represents the 75th percentile of the data set. The lower hinge of each box indicates the 25th percentile.

(range, 10 to 25) were drawn manually for each patient.

To have a single noninvasive hemodynamic parameter value reflecting changes in whole first-order pulmonary arterial segments to be compared with the single values obtained with the invasive pressure measurements (mPAP and PVRI), we averaged the MTT and TTP values calculated for each ROI to obtain a single mean first-order pulmonary arterial hemodynamic value (mean MTT, mean TTP) for each subject. MTT was defined as the interval between the wash-in time and the washout time (14). The wash-in time was defined as the point where the tangent to the signal intensity–versus–time curve between the arrival time of the contrast material and the maximal signal intensity time had the maximal slope (14–21). The washout time was defined as the point where the tangent to the signal intensity–versus–time curve between the maximal signal intensity time and the end had the minimal slope (21). TTP was defined as the time between the arrival of the contrast medium and the maximal signal intensity (14–21).

#### Statistical Analyses

Patients with CPFE were compared with healthy control subjects with respect to MTT and TTP by using the nonparametric Mann-Whitney test. Correlations of mean MTT and mean TTP

with mPAP and PVRI values were evaluated with the Spearman nonparametric test. To assess the independent value of MTT and TTP with respect to mPAP and PVRI, we performed a multiple linear regression analysis.  $P < .05$  was considered to indicate statistical significance. Data were expressed as means  $\pm$  standard deviations. Statistical analysis was performed with commercially available software (InStat, version 3.01, and Prism, version 4.7; GraphPad, San Diego, Calif).

#### Results

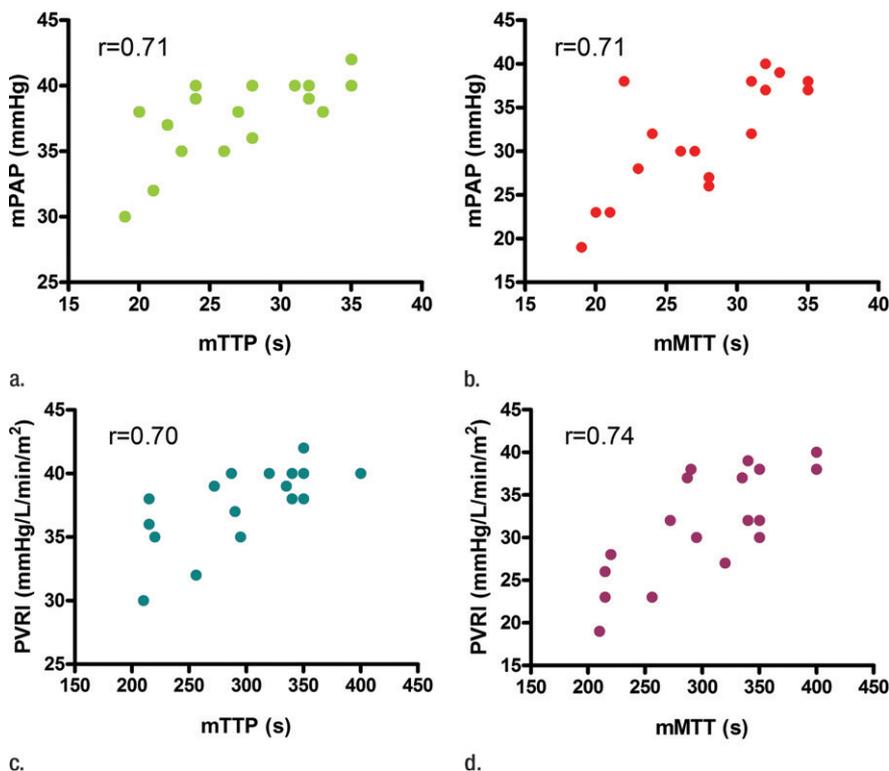
Cardiac catheterization was performed successfully in all patients with CPFE. The mPAP was 27 mm Hg  $\pm$  5 (range, 19–35 mm Hg); the mean PVRI was 302  $\pm$  61 (range, 210–400). Echocardiograms in control subjects were of adequate technical quality for the evaluation of cardiac and pulmonary function. Maximal tricuspid regurgitant jet velocity was measurable in all 13 control subjects. No control subjects showed signs of cardiac impairment or pulmonary systolic hypertension according to the echocardiographic measurements (Table 1). Dynamic MR angiograms of the pulmonary vasculature were obtained successfully in all of the study participants. Mean MTT and TTP values were prolonged significantly ( $P < .001$ ) in the patients with CPFE (mean MTT, 32 seconds  $\pm$  6; 95%

confidence interval [CI]: 29 seconds, 35 seconds; mean TTP, 38 seconds  $\pm$  3; 95% CI: 36 seconds, 39 seconds) compared with those in the control subjects (mean MTT, 8.38 seconds  $\pm$  4; 95% CI: 6 seconds, 11 seconds; mean TTP, 16 seconds  $\pm$  5; 95% CI: 13 seconds, 19 seconds) (Fig 3). Significant correlations were observed between mPAP and both mean TTP and mean MTT (mean TTP:  $r = 0.71$ ; 95% CI: 0.33, 0.88;  $P < .005$ ; mean MTT:  $r = 0.71$ ; 95% CI: 0.34, 0.88;  $P = .001$ ). Significant correlations between PVRI and both mean TTP and mean MTT also were observed (mean TTP:  $r = 0.70$ ; 95% CI: 0.34, 0.88;  $P = .001$ ; mean MTT:  $r = 0.74$ ; 95% CI: 0.40, 0.90;  $P < .001$ ) (Fig 4). We performed multiple linear regression analysis to assess which, between MTT and TTP, correlated independently with PVRI and mPAP. As shown in Table 2, MTT was the only variable that correlated independently with PVRI and mPAP ( $P < .050$ ).

#### Discussion

In this study, we measured the first-order pulmonary arterial MTT and TTP in patients with CPFE by using 3D time-resolved MR angiography. MTT and TTP were prolonged significantly in the patients with CPFE compared with those in the control subjects and correlated directly with mPAP and PVRI. Pulmonary vascular resistance is a useful parameter for assessing potential small-vessel disease (8). Pulmonary hypertension in patients with CPFE may reflect the increased PVR due to hypoxia and the reduction of the capillary bed secondary to both emphysema and fibrosis. The PVR may be fixed and/or potentially reversible: Arterial obliteration and remodeling are responsible for the fixed component, whereas active increases in vascular tone are responsible for the reversible component, which can be treated pharmacologically (8). In patients with CPFE, increased PVRI may reflect both the presence of hypoxia and the reduction of the capillary bed secondary to emphysema and fibrosis (8). Morphologic changes in the vessel wall, decreased segmental arterial compliance, and changes in compliance

**Figure 4**



**Figure 4:** Plots show Spearman correlations: (a) mPAP versus mean TTP (*mTTP*), (b) mPAP versus mean MTT (*mMTT*), (c) PVRI versus mean TTP, and (d) PVRI versus mean MTT.

**Table 2**

**Multiple Linear Regression Analysis Results**

Variable*	Coefficient $\beta$	Standard Error	T Value	P Value
With respect to mPAP				
MTT	0.42	0.18	2.3	.04
TTP	0.57	0.38	1.5	.15
With respect to PVRI				
MTT	5.23	2.20	2.4	.03
TTP	6.06	4.50	1.4	.20

\* The overall  $R^2$  for the model was 0.62. The T value is the coefficient  $\beta$  divided by its standard error.

in response to vasodilators have been demonstrated in patients with pulmonary hypertensive disease (22). The progressive increase in MTT and TTP values measured with the increasing PVRI observed in our study may reflect these morphologic changes. However, multiple linear regression analysis showed that MTT is the only variable independently correlated with mPAP and PVRI.

To our knowledge, this study is the first in which MR angiography-derived

vascular MTT and TTP were correlated with invasive pulmonary arterial pressure measurements. Previous contrast-enhanced MR studies on pulmonary hypertension have focused on parenchymal perfusion alterations. Several authors have found a correlation between perfusion parameters and invasive pulmonary pressure measurements (23–26). To our knowledge, Ohno et al (24) were the first to show that 3D dynamic contrast-enhanced perfusion MR imag-

ing may enable quantitative assessment of regional pulmonary perfusion abnormalities and disease severity identified according to PVR and mPAP. However, investigators in most pulmonary perfusion studies have evaluated primary pulmonary hypertension or secondary pulmonary hypertension due to either chronic pulmonary thromboembolism or chronic obstructive pulmonary disease. In these groups of patients, parenchymal perfusion evaluation seems to be valuable, since the pulmonary parenchymal architecture is not substantially altered, and the eventual signal loss recorded may indicate peripheral small-vessel alterations, thus providing valuable information about pulmonary circulation, including regional blood volume, regional blood flow, and MTT (23–26). On the contrary, in patients with CPFE, the diffuse destruction of lung parenchyma (emphysema) or the increase in parenchymal density (fibrosis), either of which is more prominent than that in patients with chronic obstructive pulmonary disease, may be responsible for the signal loss or gain and can confound measurement of perfusion. Despite severe architectural distortion due to fibrosis and emphysema, only 47% of patients with CPFE develop pulmonary hypertension (3).

The angiographic technique described in this study yields time-resolved images of the pulmonary circulation, from which physiologic information can be derived. In patients with CPFE, the MTT for first-order pulmonary arteries provides insight into the functional status of the pulmonary circulation and becomes a tool for identifying patients with CPFE who have pulmonary hypertension. An advantage of the MR angiographic technique is the minimal contrast material requirement. In accordance with a previous study (14), we used only a 4-mL dose of gadopentetate dimeglumine, which can be injected within 1 second, greatly improving the shape of the input function compared with that yielded in protocols that require input across several seconds. Phase-contrast MR imaging is a well-established and validated technique for measuring blood flow (27). Results of

several studies have shown the potential use of a variety of phase-contrast MR imaging-derived parameters in the evaluation of pulmonary hypertension (28,29). A combined MR protocol, which might include pulmonary flow information derived from phase-contrast imaging in addition to perfusion and angiographic information provided by contrast-enhanced techniques, may be helpful for assessing the global pulmonary circulation status in patients with different types of pulmonary hypertension.

Contrast-enhanced high-temporal-resolution MR angiography of the pulmonary circulation at 3.0 T has been described previously, with results revealing that time-resolved contrast-enhanced MR angiography at 3.0 T can depict the pulmonary vasculature in encouraging detail (14). Several technical approaches for acquiring time-resolved MR angiograms have been described (30,31). In our study, to increase the data acquisition speed, we used the sensitivity-encoding technique (32). Although sensitivity encoding can improve temporal and spatial resolution, the reduction in the signal-to-noise ratio may become a limiting factor, depending on the degree of k-space undersampling (33). The main advantage of MR imaging at 3.0 T is the signal-to-noise ratio gain that scales approximately linearly with field strength. Willinek et al (34) and Campeau et al (35) showed that a higher signal-to-noise ratio at 3.0 T is an important element for increasing the spatial resolution and is likely to improve visualization of small-blood-vessel segments.

Our study had limitations. The enhancement curves generated by using ROI methods are prone to partial volume errors and are sensitive to ROI selection and placement (36). We did not assess the noise level in any ROI. Image noise at MR imaging generally is characterized by the noise level measured in regions outside of the object of interest on the image. However, in our study, noise measured in one region on the image did not correspond to the noise elsewhere, since the parallel imaging technique that we used causes a

spatial variation in noise described by a geometric factor known as the g factor (37). Moreover, MR angiography was performed with breath holding, the phase of which may influence bolus kinetics and prolong circulation times (38). To minimize this possible bias, we instructed all study participants, in a standardized fashion, to hold their breath at end expiration.

We did not evaluate the inter- and intraobserver agreement of the method described, although this would be necessary before using the method for clinical follow-up in individual patients. Similarly, technique reproducibility was not evaluated. Additional studies with larger cohorts of patients are required to further establish the interobserver variability and assess the intraobserver variability and reproducibility of the method. In conclusion, 3D time-resolved MR angiography enables determination of the pulmonary hemodynamic parameters that significantly correlate with the pulmonary hemodynamic parameters obtained with invasive methods and may represent a complementary tool for evaluating pulmonary hypertension in patients with CPFE.

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