Effects of Hemodynamics on Global and Regional Lung Perfusion

A Quantitative Lung Perfusion Study by Magnetic Resonance Imaging

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Background—Cardiac hemodynamics affect pulmonary vascular pressure and flow, but little is known of the effects of hemodynamics on lung perfusion at the tissue level. We sought to investigate the relationship between hemodynamic abnormalities in patients with left heart failure and global and regional lung perfusion using lung perfusion quantification by magnetic resonance imaging.

Methods and Results—Lung perfusion was quantified in 10 normal subjects and 28 patients undergoing clinically indicated left and right heart catheterization and same day research cardiac magnetic resonance imaging. A total of 228 lung slices were evaluated. Global lung perfusion, determined as the average of 6 coronal lung slices through the anterior, mid, and posterior left and right lungs, was significantly lower in patients with reduced cardiac index (<2.5 L/min per m²): 94±30 mL/100 mL per minute versus 132±40 mL/100 mL per minute in those with preserved cardiac index (≥2.5 L/min per m²; P=0.003). The gravitational anterior to posterior perfusion gradient was inversely associated with left ventricular end-diastolic pressure (r=−0.728; P<0.001), resulting in a blunted perfusion gradient in patients with elevated left ventricular end-diastolic pressure, a finding largely attributed to the perfusion reduction in posterior lung regions. In a multivariate regression analysis adjusting for all hemodynamic variables, altered lung perfusion gradient was most closely associated with increased mean pulmonary arterial pressure (P=0.016).

Conclusions—Increased left ventricular filling pressure and the resultant increase in pulmonary arterial pressure are associated with disruption of the normal gravitational lung perfusion gradient. Our findings underscore the complexity of heart-lung interaction in determining pulmonary hemodynamics in left heart failure. (Circ Cardiovasc Imaging. 2012;5:693-699.)

Key Words: hemodynamics ■ lung perfusion ■ left ventricular end-diastolic pressure ■ pulmonary hypertension ■ magnetic resonance imaging

Lung perfusion is decreased in patients with primary and secondary pulmonary hypertension as a result of pulmonary arterial impairment.1,6 The commonest cause of pulmonary hypertension in Western societies is left heart dysfunction, systolic or diastolic.1,4 In patients with left heart failure, pulmonary arterial pressure often arises because of increased pulmonary venous pressure and, in some patients, reactive pulmonary arterial vasoconstriction. However, little is known about lung perfusion at the tissue level in patients with such hemodynamic abnormalities.

Recent advances in lung perfusion quantification1,10,11 can shed new light on the complexity of lung perfusion and perfusion distribution. In healthy human lungs, perfusion is affected by body position and the respiratory cycle.12 They follow a linear gravitational gradient such that perfusion is highest in the posterior lung and lowest in the anterior lung in the supine position.1 It is not clear how the gravitational perfusion gradient responds to increased left ventricular (LV) filling pressure and resultant increases in pulmonary arterial pressure.

In this study, we sought to investigate the relationship between hemodynamic abnormalities in patients with left heart failure and global and regional lung perfusion using lung perfusion quantification by magnetic resonance imaging (MRI) in a patient cohort undergoing clinically indicated right and left heart catheterization and compared the results with those obtained in normal controls.

Methods

Participant Recruitment

The study protocol was approved by the St Francis Hospital Institutional Review Board, and written informed consent was obtained from all participants. The study was conducted on the equip

Received November 23, 2011; accepted September 25, 2012.

From the St. Francis Hospital, Roslyn, NY (J.J.C., Y.W., J.M.L., P.R., N.N., J.C., R.J.G., A.D.B., G.A.P., N.R.); and State University of New York, Stony Brook, NY (J.J.C., Y.W., N.R.).

The online-only Data Supplement is available at http://circimaging.ahajournals.orglookup/doi:10.1161/CIRCIMAGING.112.973206/-/DC1.

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Circ Cardiovasc Imaging is available at http://circimaging.ahajournals.org DOI: 10.1161/CIRCIMAGING.112.973206

693
obtained from all participants. Participants were recruited prospectively in both patient and normal control groups. The patient group consisted of 28 individuals undergoing clinically indicated left and right heart catheterization primarily because of clinically suspected left heart failure who consented to a research MRI study on the same day. Normal controls (n=10) were volunteers who were free of hypertension, diabetes mellitus, smoking history, and cardiovascular disease. Control subjects also underwent echocardiography in addition to cardiac MRI. Exclusions included moderately impaired renal function (glomerular filtration rate <45 mL/min per 1.73 m²), claustrophobia, pacemaker/defibrillator implantation, or other metallic hazards. All participants completed a questionnaire for demographic information, and medical history and clinical charts were reviewed to confirm the cardiovascular history.

**Image Acquisition**

All participants underwent MRI in a 1.5-T Avanto scanner (Siemens, Malvern, PA) with an 8-element phased array surface coil. Cardiac volumes and systolic function were assessed using steady-state free precession cine imaging with retrospective ECG gating. To match pulmonary perfusion images, these images were acquired during breath-holds at end-inspiration. A stack of short-axis views (8 mm thickness with 2 mm gap) and 3 long-axis views (2-, 3-, and 4-chamber views) were obtained with the following parameters: echo time 1.3 ms, repetition time 3.1 ms, flip angle 70°, and average in-plane resolution 1.3×1.3 mm². For lung perfusion assessment, an ECG-gated saturation recovery steady-state free precession sequence was used. Images were acquired every heartbeat up to 100 heartbeats during gadopentetate dimeglumine (0.01 mmol/kg) infusion at a rate of 6 mL/s delivered by power injector (Medrad, Warrendale, PA). A voxel spatial resolution of 4×2.6×15 mm³ was achieved in 3 uniform-thickness with 2 mm gap) and 3 long-axis views (2-, 3-, and 4-chamber views) were obtained with the following parameters: echo time 1.3 ms, repetition time 3.1 ms, flip angle 70°, and average in-plane resolution 1.3×1.3 mm². For lung perfusion assessment, an ECG-gated saturation recovery steady-state free precession sequence was used. Images were acquired every heartbeat up to 100 heartbeats during gadopentetate dimeglumine (0.01 mmol/kg) infusion at a rate of 6 mL/s delivered by power injector (Medrad, Warrendale, PA). A voxel spatial resolution of 4×2.6×15 mm³ was achieved in 3 uniformly spaced parallel coronal planes in anterior, mid, and posterior lung locations. The anterior coronal slice always included the plane of the main pulmonary artery (PA), and the posterior coronal slice was at a level anterior to descending thoracic aorta. The saturation recovery steady-state free precession sequence parameters were as follows: inversion time 90 ms, field of view 500 mm, echo time 0.92 ms, image acquisition window 160 ms per slice, slice thickness 15 mm, and flip angle 50°. Parallel imaging was applied with an acceleration factor of 2. Although low-dose gadopentetate dimeglumine (0.01 mmol/kg) was adequate for perfusion quantification, higher dose (0.025 mmol/kg) was required to generate perfusion parameter maps that were acquired using the same settings used for the low-dose imaging series after at least a 15-minute washout period. A lung perfusion parameter map (Siemens Medical Solution) was used to visualize the relative perfusion distribution (Figures 1 and 2). The perfusion parameter map was constructed using time-intensity relationship of the first-pass perfusion image. A weighted least-square fit was applied to the maximal upslope in pixel-wise time intensity curves, which took into account the T1-weighted signal intensity across all time series and determined relative perfusion from pixel to pixel. The parameter map automatically changed window and level simultaneously in all images in a series when a new display parameter was applied to a single image.

To determine circulation transit time at the left atrium, dynamic images were acquired during lung perfusion imaging in a sagittal plane in which the left atrium was well defined. Cardiac output was assessed using through-plane phase contrast imaging acquired with respective ECG gating during an inspiratory breath-hold in a cross-sectional view of the main PA prescribed based on double oblique reference images. The sequence specifications were as follows: field of view 270 mm×360 mm, echo time 2.8 ms, repetition time 81.7 ms, flip angle 150°, and VENC 150 cm/s for PA with 20 phases per cardiac cycle. Cardiac index was the cardiac output normalized by body surface area.

**Clinical Invasive Hemodynamic Testing**

Right and left heart catheterization were performed under fluoroscopic guidance via a femoral vein and artery, respectively, following standard clinical protocols. Pressure recordings were obtained in the right atrium, main PA, LV and right ventricle (RV), and pulmonary capillary wedge positions. In addition, blood oxygen saturation in the PA and aorta was measured and pulmonary vascular resistance determined. Hemodynamic tracings were recorded and stored electronically. Two experienced cardiologists reviewed tracings, and the values of each hemodynamic measurement were determined by consensus. Inspiratory hemodynamic values were used because MR dynamic imaging was acquired during an inspiratory breath-hold. The average time between invasive catheterization and MRI was 5 hours. There was no hemodynamic instability between studies among the participants.

**Image Analysis**

Left and RV end-diastolic volume, end-systolic volume ejection fraction (EF), and myocardial mass were assessed using QMASS software (Medis, Leiden, the Netherlands). Phase contrast images were

![Figure 1](http://circimaging.ahajournals.org/)

**Figure 1.** Graded increase of relative lung perfusion is shown from anterior (A) to mid (B) and to posterior (C) lung fields depicted on lung perfusion parameter maps as increasing signal intensity of the lung fields in a 54-year-old female patient with normal hemodynamics (left ventricular end-diastolic pressure 11 mm Hg and mean pulmonary arterial pressure 15 mm Hg). The linear regression fit of the average absolute perfusion values of the left and right lungs in anterior, mid, and posterior regions is shown in D.
processed using QFlow software (Medis) to assess cardiac output and index. Dynamic images of lung perfusion were also analyzed using QMASS. The contours of left and right lung parenchymal regions of interest were drawn manually excluding major vessels, and a small circular region of interest was placed in the main PA. The regions of interests were then propagated through the image series and graphs of signal intensity over time constructed. The mean signal intensities in the main PA and the lung parenchyma were transferred to a custom model-independent deconvolution program in Matlab (MathWorks Inc, Natick, MA) to assess absolute pulmonary perfusion. Global lung perfusion was taken as the average of the left and right lung perfusion in anterior, mid, and posterior lung fields.

As described in our prior publication, the model-independent deconvolution program was based on the assumption that the pulmonary circulation is a linear system and the pulmonary signal intensity and blood pool signal intensity can be used to deduce the pulmonary perfusion parameters. The arterial input function \( C_a(t) \) is the signal intensity of the blood pool, and the output function is the pulmonary tissue contrast signal \( C_{pul}(t) \). According to the linear system theorem, the output of a continuous time linear system at certain time \( t \), \( C_{pul}(t) \), is related to the input by the time-varying convolution integral:

\[
C_{pul}(t) = \int_{0}^{t} C_a(\tau) R(t-\tau) d\tau
\]

where the impulse response function \( R(t) \) can be defined as a truncated singular value decomposition function. The truncated singular value decomposition algorithm is a numerical deconvolution regularization technique using less than standard matrix components. Through a process of removing singular values less than a user-defined threshold, a noise filtering effect is achieved as the corresponding linear equation rank decreases.

In the normal control group, RV systolic pressure was assessed using Doppler echocardiography from the tricuspid regurgitation jet velocity and inferior vena cava response to inspiration, LV end-diastolic pressure (LVEDP) in normal controls was estimated from the mean transit time in left atrium as previously reported by our group. The left and RV volumes, EF, and mass were within normal limits (data not shown). Estimated RV systolic pressure by Doppler and estimated LVEDP by MRI were 24±3 mm Hg and 9±2 mm Hg, respectively.

**Statistical Analysis**

Statistical analyses were performed using SPSS 11.0 for Windows (SPSS Inc, Chicago, IL). The Student \( t \) test and \( \chi^2 \) test were used to compare continuous and categorical variables, respectively. The significance of \( t \) test values was determined assuming equal variances if the Levene test for equality of variance was not statistically significant (\( P \geq 0.05 \)). Otherwise, probability values were determined without assuming equal variances.

The relationship of lung perfusion to cardiac output was assessed using Pearson correlation. To test for the difference between normal controls and the patient group, a linear regression model was used, including terms for cardiac index, group, and their interaction term. A linear regression line was applied to fit the anterior, mid, and posterior lung perfusion values. The slope of the regression line was used to characterize the anterior to posterior lung perfusion distribution. Nonparametric tests (Kruskal-Wallis and Mann-Whitney \( U \)) were used to compare the median values of gradient slope in subgroups because the slope was not normally distributed. The logarithmically transformed gradient slope was used in Pearson correlations to assess the univariate associations of the perfusion gradient with LV volumes and EF, cardiac index, and hemodynamic indices. Probability values were further adjusted by Bonferroni correction for multiple testing in Pearson correlations. A multivariate linear regression was performed associating logarithmically transformed lung perfusion slope with all the hemodynamic indices using backward selection with \( P \leq 0.05 \) to remain in the model. Lung perfusion gradient slopes were compared among the subgroups to test for trends by comparing means using polynomial linear comparisons in ANOVA.

**Results**

The 28 patients undergoing invasive hemodynamic testing had a mean age of 60±16 years, and 16 (57%) were men. A prior history of congestive heart failure was present in 12 (43%) patients, whereas 5 (18%) patients had a history of coronary disease (Table 1). Average LVEF was 50%, ranging from 10% to 74% with 10 subjects having LVEF <50%. Among normal controls, mean age was 45±17 years, and 7 (64%) were men. The left and RV volumes, EF, and mass were within normal limits (data not shown). Estimated RV systolic pressure by Doppler and estimated LVEDP by MRI were 24±3 mm Hg and 9±2 mm Hg, respectively.

Reduced global lung perfusion per 100 mL of inspiratory lung volume was significantly associated with reduced cardiac
index ($r=0.657; P<0.001$; Figure 3). There was no significant difference in the relationship of cardiac index to lung perfusion between the patient group and normal controls ($P=0.801$ for interaction term). When analyzed in the entire cohort, global lung perfusion was significantly lower in subjects with reduced cardiac index (<2.5 L/min per m²) compared with subjects with preserved cardiac index ($\geq 2.5$ L/min per m²): 94±30 mL/100 mL per minute versus 132±40 mL/100 mL per minute ($P=0.003$). Reduced global lung perfusion was associated with decreased regional lung perfusion in the anterior, mid, and posterior lung fields (Table 2). Global and regional perfusion differences were consistent between the left and right lungs. There were no significant associations between global lung perfusion and LVEF ($P=0.161$), RVEF ($P=0.196$), or hemodynamic pressure measurements, including pressures in right atrium, RV, PA, and LV (data not shown).

The lung perfusion distribution followed a gravitational gradient. Examples of relative lung perfusion distribution in patients with normal and abnormal hemodynamics are shown in Figures 1 and 2 in lung perfusion parameter maps. The absolute lung perfusion in the corresponding regions is plotted in Figures 1D and 2D, respectively, and the perfusion gradient was highly linear when fitted to a linear regression line ($R^2=0.999$). The median value of perfusion gradient slope in all subjects was 0.31 (interquartile range, 0.24). The perfusion slope was not significantly associated with cardiac index ($r=0.290; P=0.087$). The graded increase in perfusion from anterior to posterior lung fields was present in subjects with both normal and reduced cardiac indices (Table 2). Although a decreased perfusion slope was associated with increased LV end-diastolic volume ($r=−0.389; P=0.019$), increased LV end-systolic volume ($r=−0.516; P=0.001$) and decreased LVEF ($r=0.553; P=0.001$) univariate associations were stronger with hemodynamic abnormalities (Table 3). Among the hemodynamic indices evaluated, the lung perfusion slope had the strongest association with RV systolic pressure ($r=−0.743; P<0.001$), followed closely by LVEDP ($r=−0.728; P<0.001$; Figure 4). When subjects were grouped by LVEDP, there was a significant decrease in the linear perfusion gradient slope (median [interquartile range]) in those with higher LVEDP: 0.35 (0.17) with LVEDP ≤12 mm Hg (n=28), 0.31 (0.10) with LVEDP 13 to 15 mm Hg (n=5), and 0.10 (0.07) with LVEDP ≥16 mm Hg (n=5) ($P=0.001$). There was a trend to suggest that altered perfusion gradient was due largely to the perfusion reduction in the posterior lung slices with posterior perfusion of 158±54 mL/100 mL per minute, 123±28 mL/100

![Figure 3. Reduced average lung perfusion in subjects with decreased cardiac index (CI) ($r=1.033x+1.292$), with Pearson correlation coefficient of 0.657 and $P<0.001$.](http://circimaging.ahajournals.org/)

### Table 1. Patient Cohort Data (n=28)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean±SD or n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>60±16</td>
</tr>
<tr>
<td>Men, %</td>
<td>16 (57)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29±5</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.98±0.26</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>69±13</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>129±16</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>73±14</td>
</tr>
<tr>
<td>Medical history, %</td>
<td></td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>13 (46)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>13 (46)</td>
</tr>
<tr>
<td>Ever smoking</td>
<td>20 (71)</td>
</tr>
<tr>
<td>History of coronary artery disease</td>
<td>5 (18)</td>
</tr>
<tr>
<td>History of congestive heart failure</td>
<td>12 (43)</td>
</tr>
</tbody>
</table>

### Table 2. Regional Lung Perfusion (mL/100 mL per Minute) in Subjects With Normal and Reduced CI (L/min per m²)

<table>
<thead>
<tr>
<th></th>
<th>Left Lung</th>
<th>Right Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI ≥2.5</td>
<td>CI &lt;2.5</td>
<td></td>
</tr>
<tr>
<td>Anterior lung</td>
<td>97±42</td>
<td>65±29</td>
</tr>
<tr>
<td>Mid lung</td>
<td>134±43</td>
<td>98±38</td>
</tr>
<tr>
<td>Posterior lung</td>
<td>167±50</td>
<td>114±36</td>
</tr>
<tr>
<td>Average lung perfusion</td>
<td>133±42</td>
<td>92±32</td>
</tr>
</tbody>
</table>

CMR indicates cardiovascular magnetic resonance; LVEDV, left ventricular end diastolic volume; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume; LVEF, left ventricular ejection fraction; RVEDV, right ventricular end diastolic volume; RVESV, right ventricular end systolic volume; RVEF, right ventricular ejection fraction; and LA, left atrium.
Table 3. Pearson Correlation of Lung Perfusion Gradient Slope With Invasive Hemodynamic Measurements

<table>
<thead>
<tr>
<th>Hemodynamic Variables</th>
<th>Correlation Coefficient</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular end-diastolic pressure</td>
<td>−0.728</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Right ventricular systolic pressure</td>
<td>−0.743</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Pulmonary artery systolic pressure</td>
<td>−0.649</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean pulmonary artery pressure</td>
<td>−0.635</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Right ventricular end-diastolic pressure</td>
<td>−0.616</td>
<td>0.001*</td>
</tr>
<tr>
<td>Pulmonary vascular resistance</td>
<td>−0.581</td>
<td>0.002*</td>
</tr>
<tr>
<td>Mean right atrial pressure</td>
<td>−0.484</td>
<td>0.011</td>
</tr>
<tr>
<td>Mean pulmonary capillary wedge pressure</td>
<td>−0.444</td>
<td>0.020</td>
</tr>
<tr>
<td>Systemic vascular resistance</td>
<td>−0.446</td>
<td>0.026</td>
</tr>
<tr>
<td>Pulmonary artery oxygen saturation</td>
<td>0.693</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Arterial oxygen saturation</td>
<td>0.486</td>
<td>0.010</td>
</tr>
</tbody>
</table>

*p<0.05 after Bonferroni correction for multiple testing in Pearson correlations.

Figure 4. Inverse relationship of lung perfusion gradient from anterior to posterior lung fields with left ventricular end-diastolic pressure (LVEDP).

Discussion

Using lung perfusion quantification by MRI, we have demonstrated the complex association of lung perfusion with cardiac output and hemodynamics. Although absolute global and regional lung perfusion are determined mainly by cardiac output, regional perfusion distribution is affected by hemodynamic abnormalities, predominantly elevated LVEDP and resultant increases in mPAP. Among those with significantly elevated LVEDP, there is near equalization of lung perfusion from anterior to posterior lung fields in the supine position, abolishing the normal gravitational lung perfusion gradient. Multivariate regression analysis suggests that mPAP is the most important determinant of altered perfusion distribution among all the hemodynamic indices, underscoring the importance of the pulmonary arterial response to LVEDP and not simply LVEDP alone in the pathophysiology of left heart failure.

Despite extensive knowledge about the pulmonary pressure and flow response to LVEDP, little has been known of the lung perfusion response to increased LVEDP, caused by abnormalities in systolic function, diastolic function, and loading conditions. Limited reports suggest that the gravitational lung perfusion gradient is regulated by intrathoracic hydrostatic pressure and possibly by the local pressure gradient between pulmonary arterial and venous pressure. Despite the strong correlation with LVEDP in univariate analysis, lung perfusion gradient was most significantly associated with mPAP in multivariate analysis, suggesting that lung perfusion distribution is likely regulated by pulmonary vascular response to LVEDP. The fact that reduced PA oxygen saturation, a potent stimulus for pulmonary vasoconstriction, was also significantly associated with perfusion gradient abnormality further supports the relationship of perfusion redistribution to pulmonary arterial constriction and suggests that accentuated local pulmonary arterial vasoconstriction impairs regional perfusion in dependent lung regions. Thus, reactive pulmonary arterial vasoconstriction in patients with elevated LVEDP may not be uniform throughout the lung. Rather it may vary from region to region following the gradient of venous pressure. A full explanation of this feature of the perfusion pattern is yet to emerge.

We speculate that in the anterior regions, pulmonary arteriolar vasodilation is fully compensatory for the reduced arterial-venous pressure gradient, whereas in the more posterior regions with further reduction in the arterial-venous pressure
gradient, reduced flow may induce pulmonary arteriolar constriction, thereby causing altered lung perfusion distribution. In healthy subjects, lung perfusion distribution is complex, varying with body posture and respiratory cycle. The complexity is compounded in patients with compromised hemodynamics. Global and regional perfusion are reduced in response to decreased cardiac output. But the gravitational lung perfusion gradient may be maintained when LVEDP is not elevated. Advances in MRI quantification of lung perfusion make it possible to study heart-lung interaction with high spatial and temporal resolution. In recent years, several publications have demonstrated the value of quantitative lung perfusion by MRI in primary pulmonary hypertension and in patients with chronic obstructive pulmonary disease. This approach can now be extended to patients with left heart failure. Despite differences in perfusion sequences and quantification algorithms, MRI lung perfusion measurements in normal subjects have been similar among published reports, demonstrating that MRI is a reliable modality for lung perfusion imaging. When combined with well-established quantitative cardiac MRI imaging methods for structure, function, and myocardial tissue characterization, MRI is a promising modality for exploration of heart-lung interaction. However, challenges remain. As a result of the large variation in lung perfusion during the respiratory cycle, suspension of respiration is essential in MRI perfusion quantification but is difficult for patients with advanced heart failure. Furthermore, breathing also has an effect on hemodynamics, which in turn can affect lung perfusion distribution. Future research will focus on developing free breathing MRI methods, possibly with imaging guided by navigator techniques.

We acknowledge several study limitations. The lung perfusion distribution heterogeneity demonstrated in this study is primarily in the gravitational direction. There may also be variations within a given gravitational plane. We examined only the effects of cardiac and circulatory abnormalities on global and regional lung perfusion. However, two-thirds of the participants also had smoking histories and 1 patient had clinical history of chronic obstructive pulmonary disease, but their pulmonary function testing was not performed. Therefore, potential underlying pulmonary and pulmonary arterial disease may have been overlooked. However, confounding effects of pulmonary disease would likely have served to lessen the association between the regional perfusion gradient and left heart hemodynamics, if present. Nonetheless, it is essential for future studies to systematically assess the role of intrinsic pulmonary disease. Breath-hold variability can also contribute to variability of lung perfusion quantification in light of the changes in lung perfusion per unit of tissue during respiratory cycle, although gravitational perfusion gradient remains constant in end-inspiration and end-expiration in normal subjects. Furthermore, lung perfusion analysis using 2-dimensional MRI image acquisitions has limited spatial coverage as opposed to 3-dimensional approaches and may introduce errors in assessment of global lung perfusion if there is marked perfusion heterogeneity. Greater spatial coverage is undoubtedly desirable and can be achieved with improved temporal resolution using advanced coil technologies and parallel imaging. On the other hand, use of a 2-dimensional steady-state free precession perfusion sequence provides a superior signal-to-noise ratio, thereby allowing us to use very small amounts of gadolinium contrast (1–2 mL) for quantitative perfusion assessment compared with that required for analogous gradient-echo sequences commonly used in 3-dimensional acquisition. We also recognize that potential background phase offsets can lead to flow measurement errors when using phase contrast imaging for PA flow assessment. The potential phase error is reported to be ±5%, which is relatively small and, we think, acceptable in the present context. Our study population is also small, and larger studies with more diverse patient populations are needed to confirm and extend our findings. In particular, studies including patients with advanced pulmonary and pulmonary vascular disease will be needed to further elucidate the relative contribution of all relevant variables to abnormal pulmonary perfusion. Finally, we acknowledge that this cross-sectional study does not establish causality. Hence, we view our study as hypothesis generating rather than hypothesis testing with regard to mechanisms. Future study, most suitably animal work, should further examine mechanisms.

In conclusion, although global lung perfusion is determined by cardiac output, perfusion distribution is affected mainly by the pulmonary arterial response to increased LVEDP, resulting in perfusion reduction that is maximal in the posterior lung fields in supine position and disrupts the normal gravitational lung perfusion gradient. Our findings underscore the complexity of cardiopulmonary interactions in determining pulmonary hemodynamics in left heart failure and demonstrate the use of quantitative MRI methods in their exploration.

Sources of Funding

The study was partly funded by American Heart Association grant-in-aid 10GRNT4580000 (J.J.C.).

Disclosures

None.

References

findings underscore the complexity of heart-lung interactions in determining pulmonary hemodynamics in left heart failure. Our among all the hemodynamic indices, underscoring the importance of the pulmonary arterial response to left ventricular end-diastolic pressure, mean pulmonary artery pressure was the most important determinant of altered perfusion distribution in the lung fields in the supine position, abolishing the normal gravitational lung perfusion gradient. Multivariate regression analysis demonstrated that, although absolute global and regional lung perfusion were determined mainly by cardiac output, regional perfusion distribution was affected by hemodynamic abnormalities, predominantly elevated left ventricular end-diastolic pressure, there was near equalization of lung perfusion from anterior to posterior lung fields in the supine position, abolishing the normal gravitational lung perfusion gradient. Multivariate regression analysis suggested that mean pulmonary artery pressure was the most important determinant of altered perfusion distribution among all the hemodynamic indices, underscoring the importance of the pulmonary arterial response to left ventricular end-diastolic pressure and not simply left ventricular end-diastolic pressure alone in the pathophysiology of left heart failure. Our findings underscore the complexity of lung-lung interactions in determining pulmonary hemodynamics in left heart failure.

**CLINICAL PERSPECTIVE**

Using lung perfusion quantification by magnetic resonance imaging, we demonstrated the complex association of lung perfusion with cardiac output and hemodynamics. Although absolute global and regional lung perfusion were determined mainly by cardiac output, regional perfusion distribution was affected by hemodynamic abnormalities, predominantly elevated left ventricular end-diastolic pressure and resultant increases in mean pulmonary artery pressure. Among those with significantly elevated left ventricular end-diastolic pressure, there was near equalization of lung perfusion from anterior to posterior lung fields in the supine position, abolishing the normal gravitational lung perfusion gradient. Multivariate regression analysis suggested that mean pulmonary artery pressure was the most important determinant of altered perfusion distribution among all the hemodynamic indices, underscoring the importance of the pulmonary arterial response to left ventricular end-diastolic pressure and not simply left ventricular end-diastolic pressure alone in the pathophysiology of left heart failure. Our findings underscore the complexity of heart-lung interactions in determining pulmonary hemodynamics in left heart failure.
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Circ Cardiovasc Imaging. 2012;5:693-699; originally published online October 17, 2012; doi: 10.1161/CIRCIMAGING.112.973206
Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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Supplemental Material

Cao et al
Supplemental Figure I. Inter-observer variability of lung perfusion slope in 10 randomly selected subjects.
Supplemental Figure II. Correlation of cardiac output (L/min) assessed by phase contrast of cardiac magnetic resonance imaging (MRI) and Fick method of invasive cardiac catheterization excluding patients with severe mitral or aortic insufficiency

\[ y = 0.9605x + 1.1516 \]
\[ R^2 = 0.6567 \]