

Imaging Protocol of ^{15}O Scans

Briefly, after a 15-min transmission scan was performed, which was used to correct all subsequent emission scans for photon attenuation, 2 dynamic emission scans of 10 min were acquired in 2D acquisition mode, following an intravenous injection of 1.1 GBq $^{15}\text{O}\text{-H}_2\text{O}$ (40 frames) and a bolus inhalation of 7 GBq $^{15}\text{O}\text{-O}_2$ (40 frames), respectively (1). Next, 1 min after the end of a bolus inhalation of 4 GBq $^{15}\text{O}\text{-CO}$, a 6-min ECG-gated static emission scan was acquired.

Analysis of ^{15}O Data

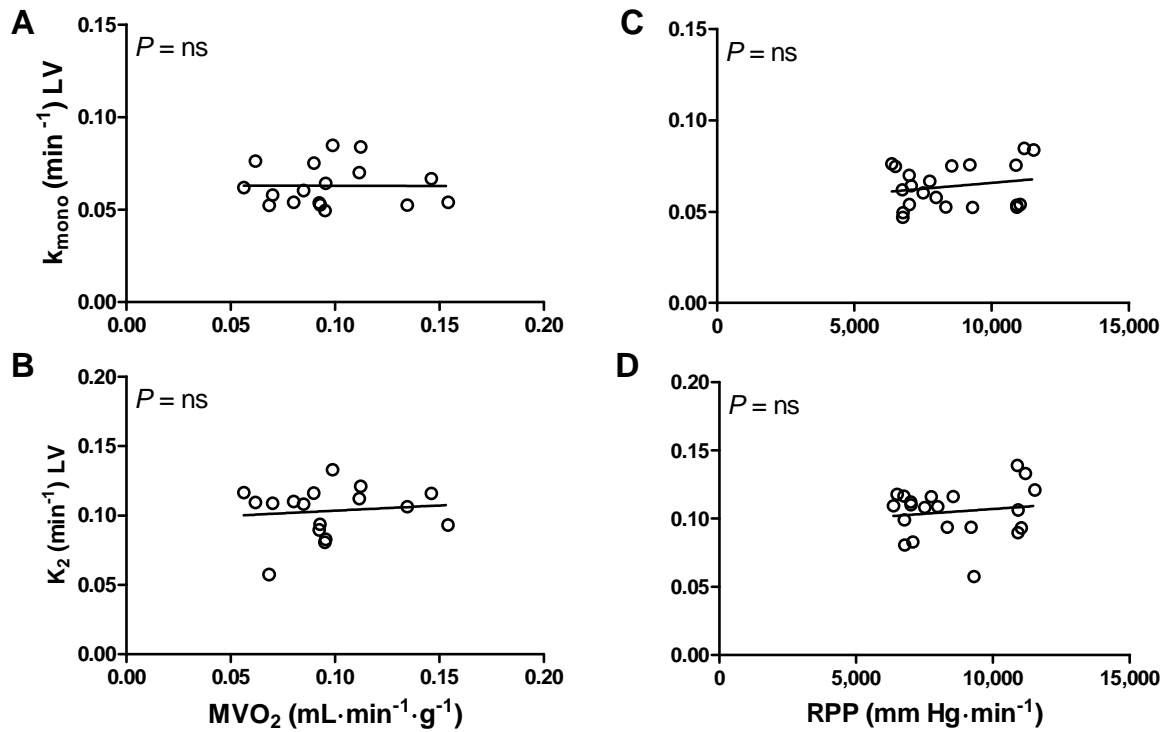
First, an anatomic tissue fraction (ATF) image was generated by subtracting the blood pool image (derived from the $^{15}\text{O}\text{-CO}$ scan) from the transmission image (2). This ATF image was resliced into short-axis images according to the anatomic axes of the left ventricle. The same reslicing parameters were applied to both dynamic $^{15}\text{O}\text{-H}_2\text{O}$ and $^{15}\text{O}\text{-O}_2$ images. Using the ATF image, RV (and left ventricular [LV]) free wall region of interests (ROIs) were defined and projected onto all dynamic $^{15}\text{O}\text{-H}_2\text{O}$ and $^{15}\text{O}\text{-O}_2$ images to generate time–activity curves. Since it is unclear to which ventricle the bulging septum belongs in pulmonary arterial hypertension, the septal regions of interest were not included in the metabolic analysis of the ventricles. Next, RV MBF was determined from $^{15}\text{O}\text{-H}_2\text{O}$ time–activity curves using the standard single-tissue-compartment model, including parameters to account for perfusable tissue fraction and RV spill-over (3). Subsequently, RV OEF was determined from $^{15}\text{O}\text{-O}_2$ time–activity curves using a recent implementation (1) of a model described previously (2), in which RV MBF, perfusable tissue fraction, arterial blood volume, and RV spill-over were fixed to values determined from the fit to the corresponding $^{15}\text{O}\text{-H}_2\text{O}$ data and in which a correction for spill-over from activity in the pulmonary gas volume was applied as described previously (4). Finally, MVO_2 was obtained as the product of RV MBF, OEF, and the oxygen content of arterial blood. Both $^{15}\text{O}\text{-H}_2\text{O}$ and $^{15}\text{O}\text{-O}_2$ arterial input functions were based on a volume of interest drawn in the ascending aorta. $^{15}\text{O}\text{-O}_2$ input functions were corrected for the contribution of recirculating water derived from arterial blood samples. Similar analyses were performed for the LV free wall.

References

1. Lubberink M, Wong YY, Raijmakers PGHM, et al. Myocardial oxygen extraction fraction measured using bolus inhalation of ^{15}O -oxygen gas and dynamic PET. *J Nucl Med*. 2011;52:60–66.
2. Iida H, Rhodes CG, Araujo LI, et al. Noninvasive quantification of regional myocardial metabolic rate for oxygen by use of $^{15}\text{O}_2$ inhalation and positron emission tomography: theory, error analysis, and application in humans. *Circulation*. 1996;94:792–807.
3. Hermansen F, Rosen SD, Fath-Ordoubadi F, et al. Measurement of myocardial blood flow with oxygen-15 labelled water: comparison of different administration protocols. *Eur J Nucl Med*. 1998;25:751–759.
4. Iida H, Rhodes CG, de Silva R, et al. Myocardial tissue fraction—correction for partial volume effects and measure of tissue viability. *J Nucl Med*. 1991;32:2169–2175.

Supplemental Figure 1

Correlations of MVO_2 (A and C; $n = 17$) or LV RPP (product of systolic blood pressure and heart rate) (B and D) with ^{11}C -acetate clearance rates monoexponential rate of clearance of ^{11}C -acetate (K_{mono}) and tissue-to-plasma efflux rate constant of ^{11}C -acetate (k_2) in the left myocardium of IPAH patients. Only 21 of 26 patients were included in B and D. Five patients were excluded either due to lack of systolic pressure data ($n = 3$) or presence of systemic hypertension (systolic BP > 140 mm Hg, $n = 2$). The thick line represents the regression line.



Supplemental Table 1**Rate–Pressure Product and PET-Derived Measures of Left Ventricular Oxygen Consumption**

<i>(n = 26)</i>	<i>Mean ± SD</i>	<i>Range (min–max)</i>
LV RPP (mm Hg·bpm) (<i>n = 23</i>)	8,849 ± 2,036	6,365–12,474
MVO ₂ (mL·min ⁻¹ ·g ⁻¹ left myocardium) (<i>n = 17</i>)	0.10 ± 0.03	0.06–0.15
LV <i>K</i> _{mono} (min ⁻¹)	0.068 ± 0.016	0.047–0.110
LV <i>k</i> ₂ (min ⁻¹)	0.104 ± 0.019	0.057–0.139

*K*_{mono} = monoexponential rate of clearance of ¹¹C-acetate; *k*₂ = tissue-to-plasma efflux rate constant of ¹¹C-acetate; LV = left ventricular; MVO₂ = myocardial oxygen consumption derived from PET and ¹⁵O tracers; RPP = rate–pressure product obtained from systolic blood pressure and heart rate.