Quantitative measurement of whole body oxygen consumption using magnetic resonance imaging: a volunteer study

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Introduction:

Heart failure is the final pathway for many cardiovascular diseases such as coronary artery disease and has become a major public health problem, with an incidence approaching 1% among persons older than 65 years old (1). In clinical practice, exercise capacity testing with expired gas analysis is an established technique for assessing patients with heart failure and known coronary artery disease; in this test the peak oxygen consumption measurement is considered the most valuable prognostic factor (2,3). Magnetic resonance imaging (MRI) techniques to quantify the oxidative metabolism have been applied to the brain and heart (4,5). In this study, we investigated the feasibility of an integrated MRI technique for the quantitative measurement of whole body oxygen consumption (VO2) in healthy volunteers at resting state as the first step in obtaining peak VO2 value.

Materials and Methods:

Our institutional research board had approved this study and every volunteer participated with informed consent. Five healthy male volunteers with ages of 42.9 ± 11.5 (Mean ± SD) years old underwent the study in a GE 1.5T Excite system using peripheral gating and using an eight-channel cardiac coil (4 subjects) or a five-inch surface coil (1 subject). The MRI protocol was similar to that of our previous work in myocardial oxygen consumption measurement in which the following three parts were included (5): 1). *In vitro* blood T2-%O2 calibration: 20 ml blood was collected from each volunteer in which 15 ml was manipulated to various oxygen saturations in five 3-ml tubes for blood T2 measurements, as per the methods described by Wright et al (6). Another 5 ml blood was used for hemoglobin (Hb) measurement. 2). T2 measurement in the main pulmonary artery (MPA): A 3-plane localizer or Fiesta pulse sequence for MPA localization followed by a motion-insensitive multi-echo T2 prep pulse sequence with the Diminishing Variance Algorithm applied for respiratory motion compensation (TR=2R-R interval, refocusing pulse interval= 12 ms, spatial resolution ~1.36mm) (5, 7). Considering the orientation of MPA from anterior-inferior to posterior-superior direction and trying to get the true short axis section of MPA, we placed the imaging slice perpendicular to the long-axis of mid-MPA as shown in Fig.1 a-c. 3). MPA flow measurement (Fig.1 d): free-breathing 2D cine phase contrast (PC) was used to obtain the flow volume at the same position as MPA T2 measurement. The maximum velocity encoded was 150 cm/s, TR ~30 ms, TE 4-6 ms, flip angle 30º, Matrix 256*128, cardiac phases=20. MPA flow volume was calculated using the CV Flow software 3.1(MEDIS, Netherlands). 2D Fiesta short-axis oblique (SAO) images were obtained for calculating stroke volume and cardiac output to verify the MPA flow volume measurement in four cases using MASS plus software 5.1(MEDIS).

Based on Fick's principle, VO2={Q*(98%-MPA_%O2)*[Hb]*Cm/BW} where the parameters are defined as follows: Q (ml/min): MPA flow volume; Oxygen saturation in the aorta was assumed as 98%; MPA_%O2: oxygen saturation in MPA based on MPA T2 and *in vitro* blood T2-%O2 calibration; [Hb] (g/ml) obtained from hematology test; Cm (maximal oxygen carrying capacity, ml of oxygen per gram Hb): a constant of 1.36 in normal physiological situations. The final unit of VO2 value was expressed as ml/min per kg body weight (BW).

Results:

The results demonstrated that whole body VO2 measurement using MRI was feasible in all five volunteers. The measured resting VO2 values were 3.75 ± 0.68 ml * min $^{-1}$ * Kg^{-1} (mean ± SD), which was comparable to 3.5 ml * min $^{-1}$ * Kg $^{-1}$ as reported in literature (3,8). The results demonstrated that MPA flow volume measured with 2D cine PC (7.04 ± 1.53 L/min) and cardiac output measured with 2D Fiesta (7.05 ± 1.58 L/min) were statistically indistinguishable (P=0.83 using a paired t-test).

Discussion:

By combining MPA oximetry, cine PC MR technique and *in vitro* blood T2-%O2 calibration, we successfully obtained the whole body resting VO2 values in healthy volunteers as the first step to obtain peak VO2 that is considered as the gold standard for assessing patients with heart failure (2). The measured resting VO2 value was quite comparable to the predicted value as reported in literature (3,8). Although it is relatively easy to obtain peak VO2 using an exercise capacity test, its inclusion in an MRI examination is more challenging. Ideally, the stressing mechanism induces a stable and elevated cardiovascular response to ensure cine and T2 image quality and to increase the validity of Fick's approach. Dobutamine is preferred by clinicians, being relative safe and well tolerated while providing a high level of control of dose (9). Isometric exercise may provide a useful alternative for stressing difficult subjects. With this, one could quickly get a peak VO2 measurement as part of a comprehensive cardiac MR exam.

Conclusion:

Based on Fick's principle, whole body oxygen consumption measurement could be realized using an integrated MRI technique of cine phase contrast, T2 measurement of main pulmonary artery and *in vitro* blood T2-%O2 calibration. Further validation of this MR technique is needed.

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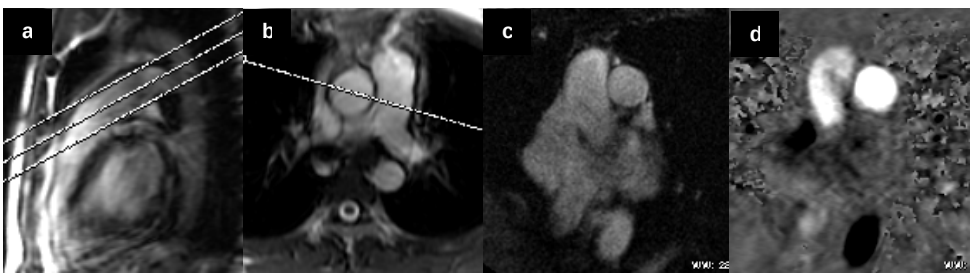

Fig 1. An example of MRI resting VO2 measurement. Male, 42 yrs **a-b.** MPA localization. **c.** Mutiple-echo T2 prep images (only the 1st echo image shown here). **d.** MPA PC image. BW=65.8 kg, Q=5197.19 ml/min, MPA %O2=81%, [Hb]=0.16 g/ml, Cm=1.36 ml per g Hb.

Resting VO2 =2.9 ml * min $^{-1}$ * kg^{-1}