Reviewer's report

Title: Oxygen kinetics during 6-minute walk tests in patients with cardiovascular and pulmonary disease.

Version: 1  Date: 2 April 2014

Reviewer: Corey Tomczak

Reviewer's report:

The authors should be praised for recruiting a fairly large sample size for this type of investigation. The reviewer also applauds the authors for their reference of Schalcher’s work (Chest 2003), as it is an often under-recognized study with important findings related to the VO2 MRT and survival.

MAJOR COMPULSORY REVISIONS

1. The introduction would benefit from a description of the physiological meaning of VO2 kinetics parameters such as MRT – what do the time constant mean and what are the physiological factors that can affect this? This may help the reader appreciate to a greater degree the importance of the author’s findings. Indeed, the survival data of this manuscript is very convincing!

The authors have nicely detailed the rationale for their modeling technique. There are some missing details that would benefit their study.

2. First, modeling VO2 kinetics often differentiates phase I (aka: the cardiodynamic phase) and phase II (aka: the fundamental component / metabolic phase) for exercise below the ventilatory (anaerobic) threshold. Modeling both phase together tends to over-estimate a slower tau value. Please address this in the manuscript. One method may be to measure the phase I duration / phase II time delay (TD) and the phase II time constant and add them together to report a MRT (TD + tau = MRT).

3. Second, it is unclear in the end-exercise/steady-state VO2 was above or below the ventilatory threshold (VT). Exercise above VT induces a further phase III exponential increase in VO2. There are techniques previously published that address identifying this (Tomczak et al. Transplantation 2008). This includes modeling data up to the phase III exponential component, or ensuring there is no phase III increase by visual inspection of the data and/or determining the slope of the data from minutes ~2/3 to 6 compared to a reference slope of 0.0 (if not different, then no objective rise in phase III).

4. Third – because so many patients were tested for their VO2 kinetics, was there an opportunity for inter-rater reliability testing of the author’s modeling technique. Is it possible to perform or comment about the author’s “in-house” reliability performing this measure?

5. Figures 3, 4, 5, and 6 contain excellent data. The discussion would benefit
greatly from further elaborating on those presented findings and relaying the findings to the respective literature. For example, Myers et al. (NEJM 2002) has excellent data relating exercise capacity and survival in healthy men and those with CVD.

MINOR ESSENTIAL REVISIONS

6. Elaborate on the statement: “On the other hand, wMRT was no significant prognostic factor for patients with lung disease or PAH”

7. The statement: “In patients with heart failure, exercise may primarily be reduced due to reduced CO secondary to an inability to increase end-diastolic (EDV) and SV via the Frank-Starling mechanism [28]” requires elaboration. Depending on the type of heart failure (preserved or reduced EF), the exercise pathophysiology varies with the degree of ventricular, vascular and skeletal muscle dysfunction ---- I would suggest clarifying the statement.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests