Impaired skeletal muscle oxygen saturation response is associated with self-reported fatigue in CKD: a possible physiological mechanism for fatigue?

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Introduction

- **Chronic Kidney Disease (CKD) =** inability of the kidney/s to adequately filter blood & produce urine. Leading to a ↓ **physical function**[1], **exercise capacity**[1], & ↑ **fatigue**[2]
- Fatigue leads to ↓ **quality of life** [3] & **inability to complete activites of daily living (ADL)**[4]
- Possible physiological mechanisms for fatigue can be categorised
  - **Psychological:** e.g. depression[3]
  - **Physiological:** e.g. anaemia[2,3], inflammation[3], reduced physical activity[5]
- **Poor supply/utilisation of oxygen (O_2) in skeletal muscle (SM)** may contribute to feelings of fatigue [2], particularly during ADL where these SM are used (e.g. leg SM during walking)
- The % of oxyhaemoglobin & oxymyoglobin within SM capillaries (SMO_2%) can be determined by transcutaneous **non-invasive near-infrared spectroscopy (NIRS)**[6]
- **Time to reach minimum SMO_2%** during graded aerobic exercise is a **key outcome**, as it has been **associated with impaired oxidative phosphorylation**[7]
- No studies have investigated changes in O_2 kinetics during exercise in CKD

Aim

To explore changes in **skeletal muscle oxygen saturation (SMO_2%)** during **incremental exercise** & the association with fatigue in **non-anaemic, non-dialysis CKD patients**

Hypothesis

Fatigue is associated with quicker SMO_2% **desaturation** during walking

Participants

- **11 CKD patients** (5♀, age: 55±16 yrs, eGFR: 62±21 ml/min/1.73m², BMI: 27±6 kg/m²) were tested
- **Exclusion criteria:** <18 years, pregnancy, prior kidney transplant within 6 months, visual or hearing impairment, & inability to give informed consent

Methods

- Everyday general **fatigue** was assessed by the validated **Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F)** questionnaire **(higher score = lower fatigue)**
  - Total FACIT-F score **(TFACIT-F)** is scored /160
  - Trial Outcome Index score **(TOI)** is a subscale used to quantify fatigue associated with physical & functional outcomes & scored /108

Fig 1. NIRS device

- Patients wore the NIRS device (**BSXInsight, USA**) on their **dominant leg** (Fig 1)
- NIRS uses infrared light (700-1000nm) to quantify the O_2 saturation of haemoglobin & myoglobin in the vascular bed of SM[7]
- The **gastro-soleus complex** was chosen as this is a large SM group used whilst walking
- **SMO_2% was measured every second.** An average **3 minute baseline recording** was acquired at rest in a seated upright position

- **Walking capacity** was assessed by the **Incremental Shuttle Walk Test (ISWT**). Patients walked a 10m course (Fig.2) at a pace controlled by an audible bleep. There are 12 levels; an increase in level requires an increase in pace (+0.17m/s)

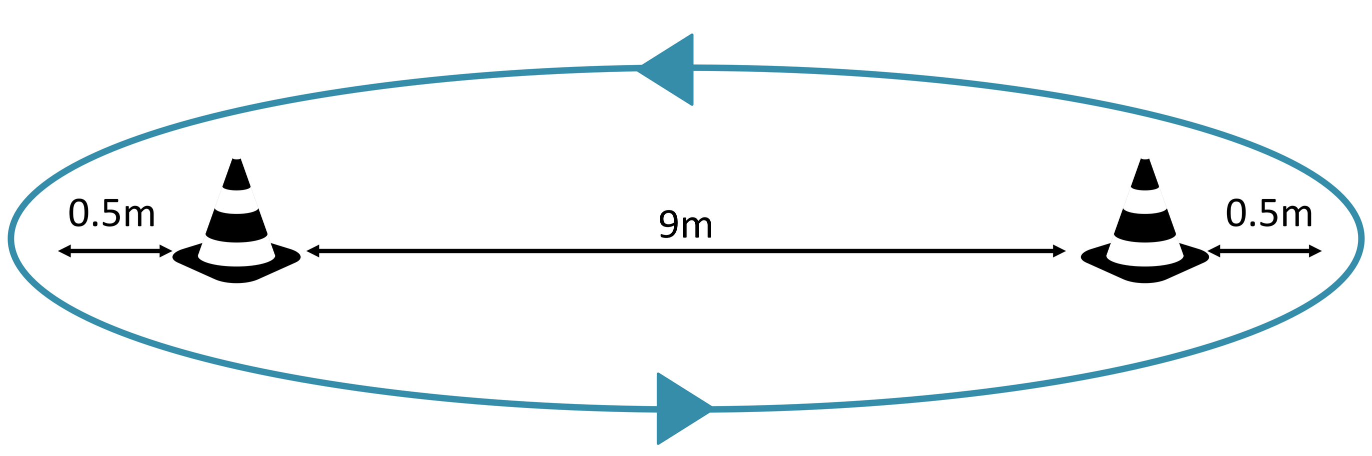

Fig 2. ISWT

All data are expressed as **mean ± standard deviation**. Time to min. SMO_2% & min. SMO_2% were calculated. Statistical analysis was performed by linear regression & Pearson's correlation within SPSS 24 (SPSS Inc.,USA). Significance= $p<0.05$, mean= $\bar{X}$, change=**Δ**

Results

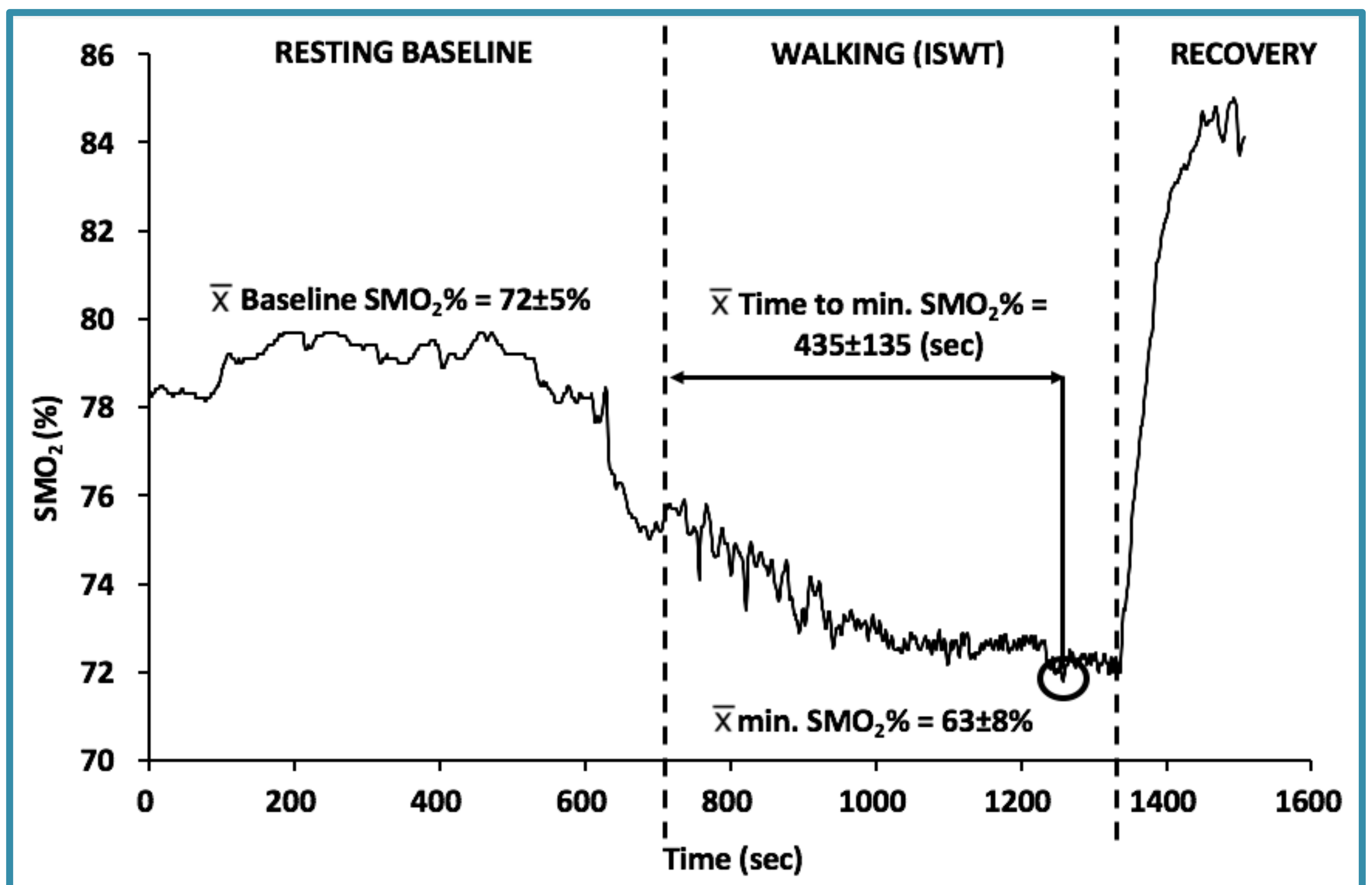

Fig 3. Example of SMO_2 changes during ISWT

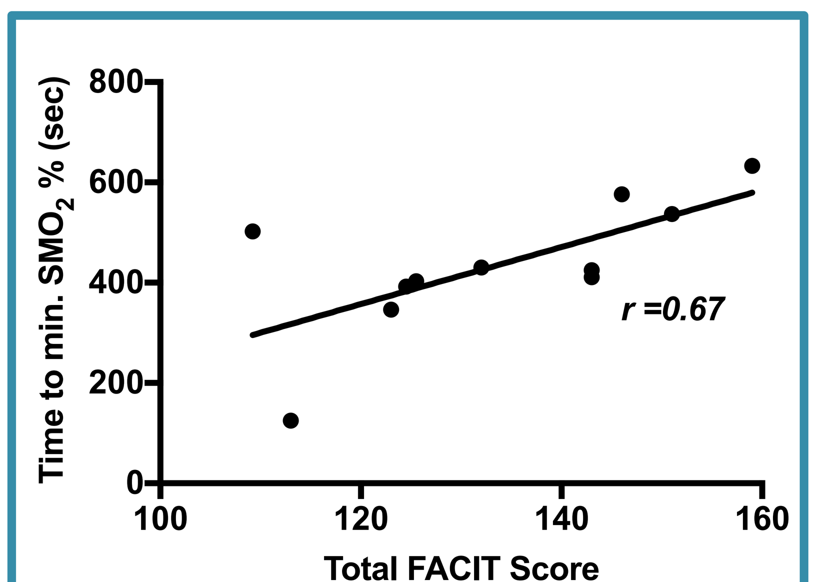

Fig 4. TFACIT score vs time to min.SMO_2%

Patients who experience **increased fatigue** (lower TFACIT-F score) reached a **minimum SMO_2%** quicker during walking (i.e. quicker deoxygenation)

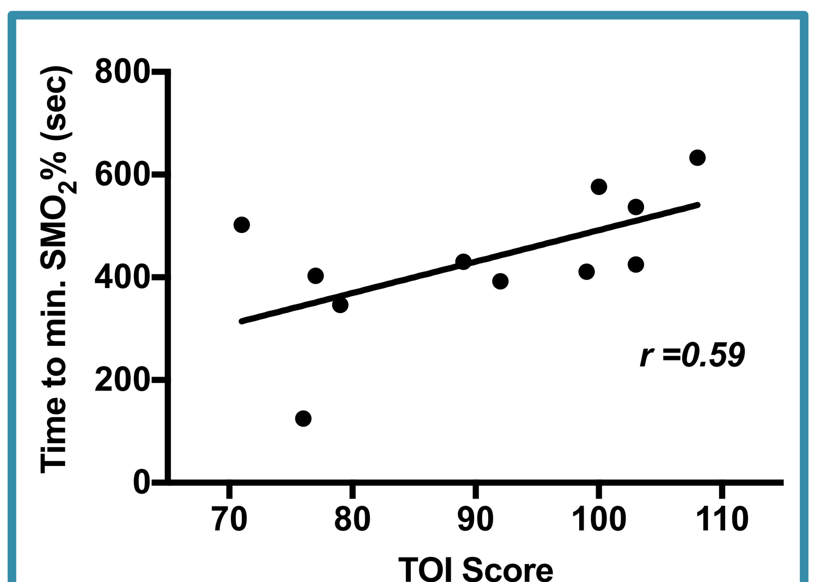

Fig 5. TOI score vs time to min.SMO_2%

A **quicker deoxygenation** (i.e. quicker time to minimum SMO_2%) was also associated with **increased physical & functional fatigue** (lower TOI score)

The **minimum SMO_2%** reached was weakly correlated with **increased fatigue** (lower TFACIT-F score) (r=-0.26)

Discussion

- Patients who experience **greater perceptions of general fatigue** have a more **rapid drop in SMO_2%** during a subsequent walking test. These patients may find **ADL** more **tiring & difficult**
- Mitochondria within SM must efficiently utilise O_2 (via oxidative phosphorylation) to produce energy (adenosine triphosphate) needed for SM contraction[7,8]
- A **reduced number & dysfunction** of the **mitochondria** has been reported **in CKD**[8]
- Mitochondrial dysfunction may cause an **impairment** to **oxidative phosphorylation** & **energy production** resulting in a reduced exercise capacity, walking ability & ADL completion
- Patients may experience this reduced walking capacity as fatigue in everyday life
- Further research is needed to explore other potential mechanisms

Clinical implications

- We have shown that NIRS can be used to evaluate SMO_2 kinetics & walking performance in CKD. This may be a **possible physiological mechanism of fatigue**
- **This non-invasive technique** could be **used** to explore SMO_2 kinetics **in other conditions** with increased perception of fatigue
- In the future, the effects of **exercise rehabilitation programmes** on fatigue & SMO_2%, should be **assessed using NIRS**

References

[1] Padilla, J. et al. 2008, *Journal of nephrology*, *21*(4), pp.550-559; [2] Macdonald, J.H. et al. 2012, *American Journal of Kidney Diseases*, *60*(6), pp.930-939; [3]Jhamb, M et al. 2008, *American Journal of Kidney Diseases*, *52*(2), pp.353-365 [4] Bonner, A et al. 2010, *Journal of Clinical Nursing*, *19*(21-22), pp.3006-3015; [5] Brunier, G.M. and Graydon, J., 1993, *ANNA Journal/American Nephrology Nurses' Association*, *20*(4), p.457; [6] Boushel, R et al. 2001, *Scandinavian Journal of Medicine & Science in Sports*, *11*(4), pp.213-222; [7] Grassi, B. and Quaresima, V., 2016, *Journal of Biomedical Optics*, *21*(9), pp.091313-091313; [8] Yazdi, P.G et al. 2013, *International Journal of Clinical and Experimental Medicine*, *6*(7)

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CKD - Clinical epidemiology II

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