Physiological Mechanisms of Reduced Maximal Aerobic Capacity in Asymptomatic Chronic Kidney Disease Patients

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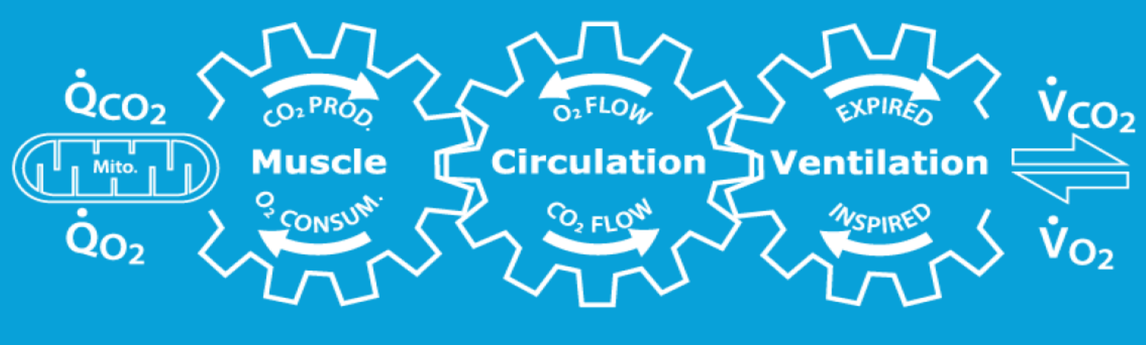

INTRODUCTION

Maximal aerobic capacity [VO_{2max}] has been shown to be impaired in chronic kidney disease (CKD). However, the underlying mechanism of such impairment is not well understood. VO_{2max} is an integrated measure of pulmonary, central cardiac and peripheral skeletal muscle function and we set out to evaluate the differential role of these three components in limiting exercise capacity in CKD.

METHODS

- A cross sectional study of 70 asymptomatic male non-diabetic CKD patients [CKD stages 2-5 (pre dialysis)] without primary cardiac disease.
- The patients were grouped into CKD 2-3a, CKD 3b-4 and CKD 5 for comparison.
- Specialised CPX test with CO_2 rebreathing technique was utilised to measure peak cardiac output (Q_t) non-invasively.
- VO_{2max} was simultaneously measured. Peripheral O_2 extraction [$C(a\text{-}v)O_2$] was derived using Fick's equation, $VO_2 = Q_t \times C(a\text{-}v)O_2$.
- ANOVA, univariate and multivariate analyses were applied. Results are presented as mean±SD. $P<0.05$ is considered as significant.

RESULTS

Parameters of pulmonary function such as minute ventilation (V_E) and ventilatory efficiency (V_E/VCO_2) were within normal limits across the study groups (Table 1) and no patient desaturated during exercise. VO_{2max} increased by 10.49 fold from rest to peak in CKD 2-3a, 8.26 fold in CKD 3b-4 and 8.04 fold in CKD 5 as shown in Fig 1. Also shown are the corresponding increments in its constituents such as heart rate (HR), stroke volume (SV) and $C(a\text{-}v)O_2$. The absolute values of peak exercise parameters are shown in Table 1. On multivariate analysis the strongest independent predictor of VO_2 reserve (VO_{2max}-VO_{2rest}) was $C(a\text{-}v)O_2$ reserve with a standardized beta co-efficient (β) of 0.57 ($P<10^{-6}$). The other independent predictors of VO_2 reserve were heart rate reserve (β, 0.41), stroke volume reserve (β, 0.37) and haemoglobin (β, 0.32), all $P<0.05$.

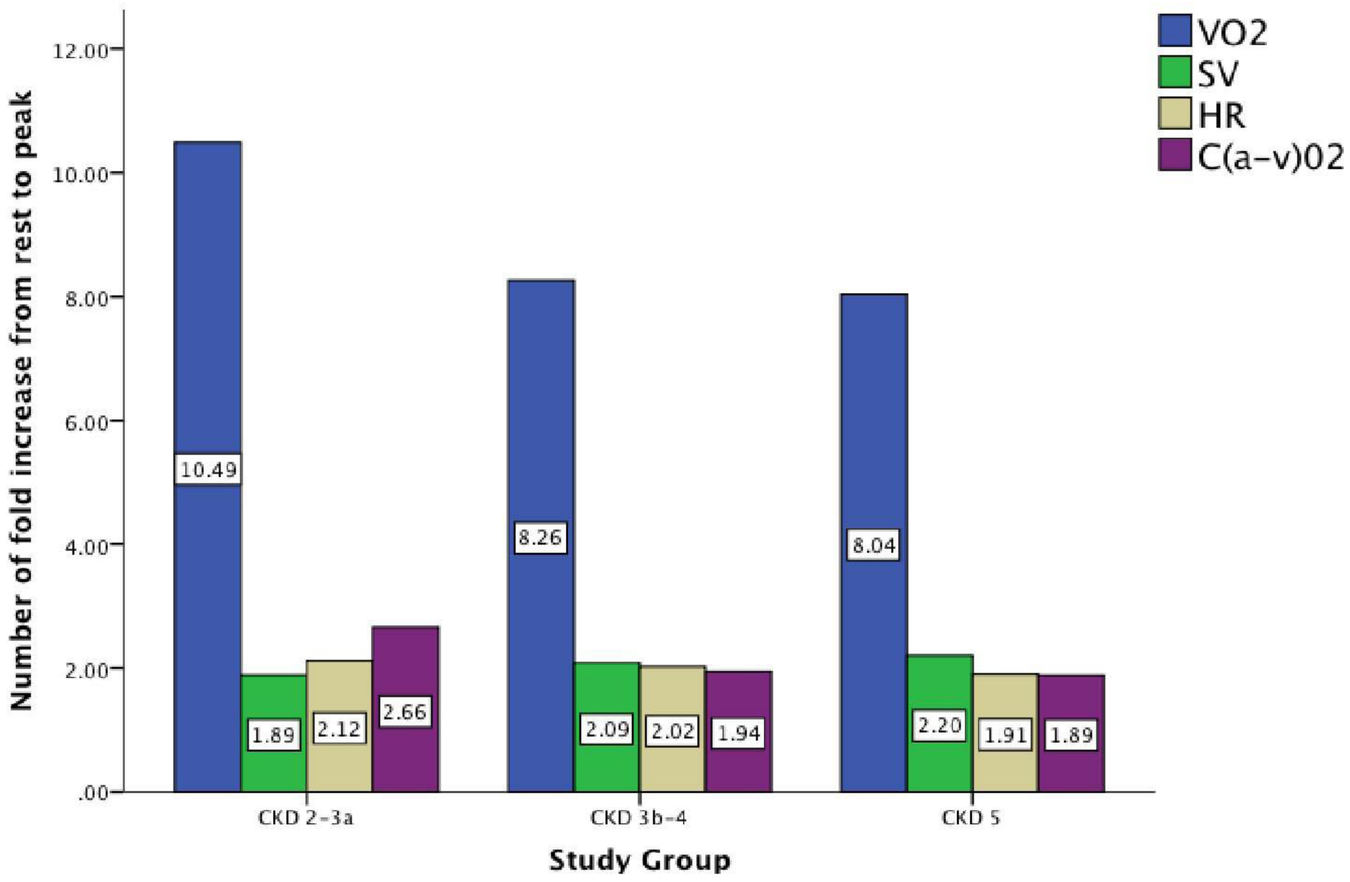

Figure 1: Number of fold increase in VO_2 from rest to peak exercise and the corresponding increments in heart rate (HR), stroke volume (SV) and peripheral O_2 extraction [$C(a\text{-}v)O_2$].

Table 1

	CKD 2-3a (n=21)	CKD 3b-4 (n=27)	CKD 5 (n=22)	ANOVA P value
Age (years)	42.5±11.0	49.4±11.5	52.9±13.6	<0.05
BMI (kg/m²)	27.5±3.8	27.6±4.0	28.4±3.9	NS
Hb (g/dl)	15.0±1.2	13.2±1.5	11.9±1.2	<0.05
eGFR (ml/min)	65.8±13.1	26.5±7.8	12.3±2.3	<0.05
Maximal aerobic capacity				
VO_{2max} (l/min)	2.91±0.46	2.48±0.43	2.17±0.43	<0.05
% VO_{2max} (%)	98.1±16.7	91.3±16.9	84.0±15.2	<0.05
Respiratory parameters				
RER	1.15±0.09	1.15±0.11	1.16±0.06	NS
V_E (l)	97.6±17.3	88.2±17.5	88.4±14.4	NS
V_E/VCO_2 slope	27.6±4.5	29.9±3.9	33.9±4.9	<0.05
Central haemodynamic parameters				
Peak HR (beats/min)	171.3±19.7	158.7±17.9	148.7±24.9	<0.05
Peak SV (ml)	132.4±17.9	128.6±19.9	129.2±24.5	NS
Peripheral O_2 extraction				
Peak $C(a\text{-}v)O_2$ (ml/dl)	14.3±1.9	13.5±2.0	12.9±2.1	<0.05

Hb: haemoglobin, VO_{2max}: peak oxygen consumption, BMI: body mass index, RER: respiratory exchange ratio, HR: heart rate, SV: stroke volume, $C(a\text{-}v)O_2$: peripheral O_2 extraction. P value is for ANOVA across the study groups. $P<0.05$ considered significant

Conclusion: The study for the first time demonstrates that peripheral O_2 extraction by exercising skeletal muscles contribute significantly to the maximal aerobic capacity in CKD. The study also offers insight into the alterations in central haemodynamic function during exercise in CKD. The results have direct implications in the interpretation of VO_{2max} in CKD in settings such as pre-op assessment, exercise rehabilitation and evaluation of cardiac function.

We thank Yorkshire Kidney Research Fund and Sheffield Kidney Research Foundation for supporting the project