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Differential effects of contracting muscle mass and relative exercise intensity on arterial plasma potassium concentration during and following incremental arm and leg cycling exercise

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ABSTRACT

Whilst arm cycling is commonly used during clinical testing and rehabilitation, the associated changes in arterial plasma K^+ concentration ($[K^+]_a$) and thus possible risks of associated hyperkalaemia and hypokalaemia are unknown. During exercise, K^+ is released from contracting skeletal muscles and simultaneously taken up by inactive muscles, with $[K^+]_a$ increasing markedly during intense exercise. Hence during exercise $[K^+]_a$ should be influenced by both the contracting muscle mass and the relative exercise intensity. We therefore investigated the effects of incremental one-arm (1ARM) and two-leg (2LEGS) cycling on $[K^+]_a$, and on lactate ($[Lac^-]$), hydrogen ($[H^+]$), adrenaline and noradrenaline. Eight healthy participants performed 1ARM, rested (3.0 ± 0.2 h, mean ± SE) then performed 2LEGS, with radial arterial blood sampled at rest, during common submaximal workrates (25, 50 W), peak workrate and 1–30 min post-exercise. During exercise at 50 W, VO_2, $[K^+]_a$ and $[Lac^-]_a$ were higher during 1ARM than 2LEGS ($P < 0.05$). In contrast, at peak exercise, 2LEGS (272 ± 15 W) elicited higher VO_2, $[K^+]_a$, $[Lac^-]_a$, [adrenaline]$_a$ and [noradrenaline]$_a$ than 1ARM (57 ± 4 W) ($P < 0.05$), with $[H^+]_a$ elevated only in 2LEGS ($P < 0.05$). A curvilinear response for $[K^+]_a$ versus $\%VO_{2peak}$ was similar between modes, until diverging close to VO_{2peak}. The slope of the log$[K^+]_a$ versus $\%VO_{2peak}$ regression was higher in 2LEGS ($P < 0.01$), indicating greater $[K^+]_a$ throughout exercise utilising a larger muscle mass, and similarly for $[Lac^-]_a$. In conclusion, during exercise utilising a smaller contracting muscle mass, $[K^+]_a$ and $[Lac^-]_a$ were greater at the same absolute submaximal work rate compared to utilising a large muscle mass. Whilst responses were similar between modes when expressed against relative exercise intensity, $[K^+]_a$ and $[Lac^-]_a$ were higher during exercise with a large muscle mass. Hence, for submaximal exercise, the relative intensity is more important in determining $[K^+]_a$ and $[Lac^-]_a$, but the size of the contracting muscle mass still exerts a positive effect, whilst during peak exercise, the size of the active muscle mass was more important in determining $[K^+]_a$ and $[Lac^-]_a$. Furthermore, arm cycling did not induce marked disturbances in $[K^+]_a$ during or after exercise, suggesting minimal associated myocardial risks and thus supporting its safe use in clinical and aged populations.

1. Introduction

Arm cycling (arm cranking) is often used in a clinical or rehabilitation setting for testing or aerobic conditioning in a diverse range of patients, including in those afflicted with spinal cord injury,[1–4] stroke,[5] peripheral vascular disease,[6–8] chronic obstructive pulmonary disease,[9] neurological diseases such as Parkinson's disease,[10] as well as in telehealth training[11] and in aged individuals.[12] Physiological responses to arm cycling are mostly well documented, typically showing that arm cycling induces greater increases at low workrates in heart

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rate, pulmonary oxygen consumption (VO_2) and ventilation (V_E), but substantially lesser VO_2 and V_E at peak exercise, compared to leg cycling.[9,12–15] Arm cycling also induced higher blood Lac^- concentration ($[Lac^-]$) at the same submaximal work rates than leg cycling,[16,17] whilst $[Lac^-]$ was similar when expressed relative to the maximal work rate,[18] but with higher $[Lac^-]$ found at maximal exercise during leg than arm cycling.[16,18] Despite these extensive investigations utilising arm cycling, its effects on increases in arterial potassium concentration ($[K^+]_a$) during exercise are not known.

The basis of the increase in $[K^+]_a$ with exercise is cellular excitation.[19] Muscle excitation involves cellular sodium (Na^+) entry and K^+ exit with each action-potential. Repeated contractions can therefore induce large changes in the Na^+ concentration ($[Na^+]$) and $[K^+]$ in muscle intracellular and extracellular (interstitial) spaces, as well as in circulating $[K^+]$.[19,20] Intense contractions in humans can reduce muscle intracellular $[K^+]$ by ~21 mM (range 13–39 mM), increase muscle interstitial $[K^+]$ to ~9–12 mM[19] and depolarise the muscle membrane potential (E_m) by ~16 mv (range −17 to −35 mV, multiple species).[20] Consequently, disturbances in muscle K^+ can play a key role in muscle excitability and fatigue, especially under conditions of cellular metabolic stress, as detailed elsewhere.[20–22] The Na^+,K^+-ATPase (Na^+,K^+-pump, NKA) located in the sarcolemma and transverse-tubules is a key factor regulating the muscle intra- to extra-cellular $[K^+]$ gradient by translocating Na^+ out and K^+ back into the cell.[19] Thus NKA also affects E_m and regulates K^+ release into the circulation, being activated by excitation, catecholamines and insulin.[19] The rise in plasma $[K^+]$ during dynamic contractions will be determined by the balance between excitation-mediated K^+-efflux from and NKA-mediated K^+-uptake within the contracting muscles, as well as K^+ clearance by any other tissues, including inactive muscles.[19]

During exercise, K^+ plays a key role in several physiological processes. Increases in interstitial $[K^+]$ in contracting muscles may potentiate force development during submaximal contractions, as well as depress force during intense contractions.[20,23,24] Hence, the anticipated increase in $[K^+]$ during arm cycling may well be facilitatory during submaximal exercise, whereas at peak exercise may contribute to fatigue. Local release of K^+ from contracting muscle cells may also exert multiple beneficial effects supporting exercise, including contributions to the exercise pressor response, muscle vasodilation, as well as to increased V_E.[21] Intense exercise can induce a large rise in $[K^+]_a$, followed within minutes of cessation of exercise by severe reductions in $[K^+]_a$ and these perturbations can induce considerable ECG changes even in healthy individuals, that may create potential risk of arrhythmias in susceptible individuals.[19,21,25] Hyperkalaemia ($[K^+]_a$ > 5.5 mM) such as occurs during intense exercise, in renal disease and crush injuries,[19] can be associated with T-wave peaking, loss of P waves and to widened QRS complex, creating a potential risk of ventricular fibrillation and death.[26] Hypokalaemia ($[K^+]_a$ < 3.5 mM) such as occurs after K^+ depletion, non-K^+ sparing diuretics, with beta-adrenergic agonists, insulin[27] or after intense exercise,[28] may induce prolongation of the QT interval,[19] with an increased risk of ventricular and atrial fibrillation.[21,23,24,29,30] Given the extensive clinical use of arm cycling, understanding these $[K^+]_a$ perturbations during and after exercise is of considerable interest. The first aim of this study was therefore to determine the magnitude of effects of arm cycling on $[K^+]_a$ during and after maximal incremental exercise.

Arm cycling utilises a smaller contracting muscle mass than leg cycling and consequently also has a relatively large mass of inactive muscle. Whilst contracting muscle releases K^+ and lactate (Lac^-) into the circulation, non-contracting (i.e. resting) muscle takes up K^+ and Lac^-, indicating that the relative amount of contracting to inactive muscle mass should modulate changes in these ions in plasma or blood (see references in.[19]) The increase in $[K^+]_a$ with exercise is therefore also likely to be dependent on the magnitude of the contracting muscle mass and relative exercise intensity. During dynamic contractions utilising only a small muscle mass, such as handgrip contractions, only a small or even no rise in $[K^+]_a$ occurs, even though venous $[K^+]$ may rise considerably.[19] Surprisingly, the effects of arm cycling on $[K^+]_a$ are not known. Intense exercise utilising a large contracting muscle mass, such as sprint running, cycling, or rowing, sustained for one or several minutes, can elevate $[K^+]_a$ to 7- 8 mM.[28,31–33] However, previous studies were not definitive for assessing the impacts of contracting muscle mass on $[K^+]_a$ as they were conducted in different individuals and exercise conditions. We recently demonstrated during exhaustive exercise in the same individuals, a rise in $[K^+]_a$ of only 0.37 mM with intermittent finger flexion compared to 2.51 mM during two-legged incremental cycling.[34] Whilst this strongly suggests a dependency on the relative size of the contracting muscle mass, the exercise type and protocol differed substantially. Finally, during incremental cycling exercise, $[K^+]_a$ rises progressively with workrate, typically reaching ~6 - 6.5 mM.[31,35,36] The rise in femoral venous $[K^+]$ is also dependent on the exercise duration.[37] These studies collectively suggest that each of the exercise mode, duration, absolute workrate, relative intensity, as well as the size of the contracting muscle mass should all affect $[K^+]_a$ during exercise, but the effects of contracting muscle mass on $[K^+]_a$ remain unclear. We therefore investigated the effect of a small versus large contracting muscle mass on $[K^+]_a$ in healthy participants, comparing one-arm cycling with two-leg cycling, thus utilising a similar contraction mode. We utilised incremental exercise to volitional exhaustion, which enabled comparisons at the same absolute workrate and also to ascertain the effects of relative exercise intensity on $[K^+]_a$. We first hypothesised that incremental arm cycling would induce substantial perturbations in $[K^+]_a$ during and after exercise. We then hypothesised that during leg cycling, using a large muscle mass, $[K^+]_a$ would be greater during exercise at maximal work rates, but similar when expressed against relative exercise intensity, when compared to arm cycling, utilising a small muscle mass.

2. Materials and Methods

2.1. Participants

Eight healthy participants comprising 4 males and 4 females aged 18–34 years volunteered for the study and gave written informed consent, with their physical characteristics presented in Table 1. All of the participants were recreationally active but none were involved in any form of regular physical training. The study was approved by the institutional Human Research Ethics Committee at Victoria University of Technology (VUT HRET 107/94).

2.2. Experimental overview

Participants visited the laboratory on two separate days. On the first visit, each participant underwent basic anthropometric measurements and was familiarised with equipment and exercise testing procedures. They twice performed incremental exercise, initially using one-arm cycling and then after a one hour rest, two-leg cycling, as described below. On the second visit participants underwent arterial cannulation and repeated the two exercise tests.

Table 1
Physical characteristics of participants.

Variable	mean ± SD
Age (yrs)	24.3 ± 6.1
Height (cm)	171.2 ± 7.7
Body mass (kg)	67.0 ± 7.7
Volume of 1 upper arm (l)	1.9 ± 0.4
Volume of 2 thighs (l)	10.3 ± 1.1[#]

Data is n = 8, mean ± SD. Volume of upper arm > 2 thighs, [#] $P < 0.001$.

2.3. Anthropometry

The relative volume of the active musculature in the exercising arm and legs for each participant were estimated from limb volumes determined by water-displacement. Thigh volume was obtained by subtracting the volume of lower leg (at the lateral and medial epicondyles of femur) and foot from the volume of whole leg (up to the gluteal furrow in the horizontal plane). Upper arm volume was obtained by subtracting the volume of the forearm (up to the lateral and medial epicondyles of humerus) and hand from the volume of whole arm (medial wall of the axilla to the tip of the acromion process). The limb segment volume for two legs (thighs) was five-fold greater than for one arm (Table 1). Although no electromyograms were made, additional muscle groups were most likely actively involved during vigorous one-arm cycling, including the pectoralis major, latissimus dorsi and torso stabilisation groups (ie. rectus abdominis, external oblique, internal oblique, transverse abdominis, psoas, quadratus lumborum and the erector spinae). Similarly, additional muscles were most likely actively involved during vigorous two-leg cycling, including the gluteus maximus, gastrocnemius and soleus, as well as the upper body for stabilisation purposes. However, since the size of these additional muscle groups would be difficult to quantify accurately and the extent of their activation during incremental exercise would be less than the primary active muscle groups (see test procedures below), we used volumes of the upper arm and both thigh of each participant to approximate differences in the active musculature during both modes of exercise.

2.4. Experimental protocol

Participants reported to the laboratory in the morning at least two hours after a light breakfast and confirmed that they had not performed strenuous physical activity on the day before, nor taken caffeine or nicotine in the two hours prior to the exercise tests. Heart rate (HR) and rhythm were monitored from a 12 lead-electrocardiogram (Mortara, Boston, USA). After inspection of the auditory canal and removal of wax deposit, a soft micro-thermistor (Phillips, Holland) was inserted, with the tip placed near the tympanum to monitor tympanic temperature. Air currents were prevented by gently placing cotton wool in the ear. Each participant performed incremental one-arm cycling (1ARM) and two-leg cycling (2LEGS) tests on an electrically braked cycle ergometer (Lode, Groningen, The Netherlands). The 1ARM test was performed first in all participants, followed by a 3–4 h recovery interval (3.0 ± 0.2 h) and then by the 2LEGS test. This protocol was chosen to restrict arterial cannulation to once only per participant, with the arm exercise conducted first since this induced the least systemic disturbances, allowing more rapid recovery.

One-arm Cycling Test (1ARM). Participants sat on an elevated secure chair positioned beside the ergometer with their feet off the floor, using a pedal modified for one-arm cycling. Participants cycled with only one arm and the use of shoulder, back and lower extremity muscle groups was discouraged and all other movements restricted by velcro straps fastened around the chest, waist and thigh, without interfering with chest and abdominal movement during breathing. The pedalling cycle axis was adjusted to the participants' mid-sternum level when the arm was positioned 90 degrees from the body, with slight elbow flexion in the extended position. The participant's non-dominant arm was exercised in order to minimise any possible residual training effects. In order to minimise the isometric handgrip contractions that normally accompany arm cranking, the forearm was firmly strapped at the wrist with a bandage to a soft arm rest mounted on the pedal. Participants cycled at 5 W for 1 min with the work rate progressively incremented by 5 W·min^{-1}. The cadence was 70 revs min^{-1} and the test was continued until volitional fatigue, defined as an inability to maintain cadence above 55 revs min^{-1}. The participants were verbally encouraged to maintain cadence and continue working as long as possible.

Two-leg Cycling Test (2LEGS). Participants performed two legged-cycling exercise on the same electrically braked cycle ergometer. Participants commenced pedalling at 25 W for 1 min with the work rate progressively increased by 25 W min^{-1}. The pedal cadence was 70 revs min^{-1} and the test was continued until volitional fatigue, defined as an inability to maintain pedal cadence above 55 revs min^{-1}. The use of a standardised cut-off of 55 rpm for exercise cessation in both trials was based on extensive utilisation during leg cycling in our laboratory[38] and which we also found to be appropriate in arm cycling.

2.5. Respiratory measurements

Expired gases were analysed for 15 min prior to exercise, during exercise and for 10 min in recovery. Participants breathed through a Hans-Rudolph two way valve with the expired gas passing through low-resistance plastic tubing into a 4-litre mixing chamber. Mixed expired oxygen (O_2) and carbon dioxide (CO_2) concentration were continuously analysed by rapidly responding O_2 and CO_2 analysers (Ametek S-3A/II, Ametek CD-3A, Pittsburgh, USA). Expired volume was determined using a flow transducer (KL Engineering K520, California, USA). Ventilation (V_E) and gas exchange were calculated and displayed (Turbofit, California, USA) every 15 s on an IBM compatible computer. The ventilometer and gas analysers were calibrated before and after each test with a standard 3-l syringe and precision reference gases, respectively.

2.6. Blood sampling and analyses

A catheter (Jelco 20 G or 22 G) was inserted into the radial artery of the non-exercising arm under local anaesthesia (2% lignocaine injection). A miniature pressure transducer (86–434-SN, Surgicare, Melbourne, Australia) was attached to the catheter to continuously monitor intra-arterial blood pressure (Marquette 710, Wisconsin, USA), with the pressure calibration confirmed at the conclusion of each experiment. A slow sterile isotonic saline drip under pressure was used to maintain patency though-out the experiment. Resting blood samples were obtained after the participant had been seated for 12 min on the chair to be used for the arm cycling or on the cycle ergometer for the leg cycling. Samples were drawn during the last 15 s of each minute during incremental exercise, at fatigue and at 1, 2, 5 and 10 min post-exercise, with participants maintaining their seated posture. Subsequent blood samples were obtained at 20 and 30 min after completion of exercise with the participant sitting on an adjacent chair. Additional blood samples were obtained between 2 - 4 h following completion of arm exercise to determine the time at which the participant had fully recovered, as defined by restoration of arterial [K^+], [H^+] and PCO_2 to resting values. Following this, participants commenced the leg cycling exercise test. The total quantity of blood collected in each exercise test was approximately 75 ml. One ml of blood was drawn into a 3 ml blood gas syringe containing lithium-heparin (RapidLyte, MA, USA) for subsequent analysis of plasma acid-base status (pH, HCO_3^-), gas tensions (PCO_2, PO_2) and electrolyte concentrations (Na^+, K^+ and Cl^-) using an automated analyser (Ciba Corning 865, MA, USA). Haemoglobin concentration ([Hb]) and O_2 saturation (SaO_2) were determined spectrophotometrically (Radiometer OSM2, Copenhagen, Denmark). All analysers were calibrated immediately before and during the analyses with precision standards. A further 2.5 ml blood sample was transferred to a tube containing dried lithium heparin (125 IU). About 1.5 ml of blood was placed in an Eppendorf tube, spun at 4000 rpm for 4 min and the plasma separated and aliquotted. The remaining blood was placed in another Eppendorf tube, for triplicate haematocrit (Hct) measures using heparinised micro-haematocrit tubes centrifuged for 4 min at 13,000 rpm (Hettich Zentrifugen D-7200, Germany). Small aliquots (200µl) of blood and plasma were deproteinised in chilled 3 M perchloric acid (600 µl), vortexed vigorously, centrifuged at 4000 rpm for

4 min and the supernatant frozen at − 70 °C for later analyses of [Lac$^-$] using enzymatic methods. Additional blood samples (8 ml) were also taken for analysis of plasma adrenaline ([Adr]) and noradrenaline ([NAdr]) concentrations at each of rest, the work rate corresponding to ~80% VO_2peak (1ARM 77 ± 4%, 2LEGS 87 ± 3%, NS), fatigue and 1 min post-exercise. Blood samples were immediately placed into collection tubes containing lithium heparin (125 IU) and 0.1 M sodium metabisulphite (125 μl), mixed thoroughly, centrifuged at 4000 rpm for 10 min and the plasma stored at − 20 °C in the dark until assayed by high-performance liquid chromatography with electrochemical detection.

Calculations. The decline in plasma volume (ΔPV_a) was calculated during and following exercise from changes in [Hb] and Hct and plasma [ion] were also corrected for ΔPV_a, as previously described.[39] The rise in $[K^+]_a$ from rest to peak exercise ($\Delta[K^+]_a$) was divided by the cumulative work and expressed as the $\Delta[K^+]_a$ work^{-1} ratio.[40] The rate of decline in $[K^+]_a$ from peak exercise to 2 min of recovery was also calculated ($-\Delta[K^+]_a$). Plasma $[H^+]_a$ was derived from measured pH as antilog (-pH). The relationships between $[K^+]_a$ as well as log$[K^+]_a$, with VO_2 and % VO_{2peak} were also determined to allow comparison of slopes of these responses.

2.7. Statistical analyses

Results are expressed as mean ± SE unless otherwise stated. Resting, peak and all recovery data from two modes of exercise were compared by analysis of variance for repeated measures and any differences were further analysed with the Newman-Keuls *post-hoc* test. The responses between the two modes of exercise at the two identical submaximal absolute work rates that were common to the two incremental protocols (25, 50 W) were compared by paired-sample *t*-tests. Comparison of slopes from linear regressions for $[K^+]_a$ as well as log $[K^+]_a$ versus both VO_2 and %VO_{2peak} were determined using paired t-tests. For all analyses, $P < 0.05$ was used to determine statistical significance.

3. Results

3.1. Pre-exercise

All variables were compared between the two trials prior to exercise, to ensure full recovery had occurred. No differences were found between 1ARM and 2LEGS for any of the resting cardiorespiratory values (Table 2), plasma $[K^+]$, [Lac$^-$], $[H^+]$ (Table 3), [Adr] or [NAdr] (Table 4).

3.2. Cardiorespiratory Responses

3.2.1. Exercise at the Same Absolute and Peak Workrates and in Recovery

Responses were contrasted between exercise modes at common absolute submaximal work rates (25 W, 50 W), which because of different incremental protocols were reached after a longer elapsed exercise time during 1ARM than 2LEGS ($P < 0.05$,Table 2). During 1ARM, VO_2 was lower at 25 W, but with VO_2, VCO_2, V_E and HR all lower at 50 W than during 2LEGS ($P < 0.05$). Each of the peak exercise work rate, VO_2, VCO_2, V_E ($P < 0.001$) and HR ($P < 0.05$) were all also markedly lower during 1ARM than 2LEGS, whereas the exercise duration did not differ between exercise modes (Table 2). The peak exercise responses during 1ARM expressed as a percentage of 2LEGS were for work rate (21.0%), VO_2 (44.6%), VCO_2 (46.6%), V_E (56.6%) and HR (87.7%). The peak arterial systolic blood pressure did not differ between exercise modes (1ARM, 225 ± 10 vs 2LEGS, 228 ± 12 mmHg), whilst the peak diastolic blood pressure was higher in 1ARM (1ARM, 106 ± 6 vs 2LEGS, 89 ± 3 mmHg, $P < 0.05$). Tympanic temperature at peak exercise also did not differ between trials (1ARM, 37.0 ± 0.1 vs 2LEGS, 37.1 ± 0.1 °C).

3.2.2. Relative exercise intensities

Responses for each of VO_2, VCO_2, V_E and HR (data not shown) were greater during 2LEGS than 1ARM when expressed relative to the respective VO_{2peak}, consistent with the higher absolute workrates in 2LEGS (Fig. 1).

3.3. Plasma $[K^+]$, [Lac$^-$], $[H^+]$ and ΔPV_a

3.3.1. Exercise at the Same Absolute and Peak Workrates and in Recovery

Plasma $[K^+]_a$ was higher during 1ARM at 50 W ($P < 0.05$), but lower at peak exercise than 2LEGS ($P < 0.001$,Table 3, Fig. 2). The peak exercise $[K^+]_a$ during 1ARM was 85.9% of that during 2LEGS. Thus the $\Delta[K^+]_a$ during 1ARM was less than 2LEGS (1.34 ± 0.08 vs 2.25 ± 0.13 mmol l^{-1}, respectively, $P < 0.001$). With an ~80% lower peak work rate, the $\Delta[K^+]_a$ work^{-1} ratio was ~3-fold higher during 1ARM than 2LEGS (70.40 ± 10.96 vs 24.70 ± 3.27 μmol·l^{-1}·J^{-1}, respectively, $P < 0.001$). After exercise, $[K^+]_a$ fell rapidly, reaching similar pre-exercise levels by 2 min after both exercise modes (Fig. 2), but the $-\Delta[K^+]_a$ was 49% less after 1ARM than 2LEGS (0.52 ± 0.07 vs 1.02 ± 0.07 mmol·l^{-1}·min^{-1}, respectively, $P < 0.005$). The lowest $[K^+]_a$ was evident at 5 min post-exercise, being 4.11 ± 0.08 mM after 1ARM, similar to 3.91 ± 0.04 mM after 2LEGS.

Plasma [Lac$^-$]$_a$ during 1ARM was higher at common submaximal work rates, but lower at peak exercise versus 2LEGS (Table 3,Fig. 2, $P < 0.01$), with peak values during 1ARM only 51.3% of that during

Table 2
Exercise characteristics and cardiopulmonary measures at rest, during incremental exercise at the same absolute workrate and at peak workrates, for one-arm cycling compared to two-leg cycling.

Variable	Mode	Rest	Submaximal exercise 25 W	Submaximal exercise 50 W	Peak exercise
Work rate (W)	1ARM				57 ± 4
	2LEGS				272 ± 15$^{\#}$
Elapsed exercise time (min)	1ARM		5	10	11.4 ± 0.7
	2LEGS		1	2	10.9 ± 0.6
VO_2 (l min^{-1})	1ARM	0.24 ± 0.03	0.63 ± 0.03	1.12 ± 0.06	1.31 ± 0.07
	2LEGS	0.31 ± 0.05	0.84 ± 0.06 *	0.94 ± 0.05 *	2.94 ± 0.16$^{\#}$
VCO_2 (l min^{-1})	1ARM	0.20 ± 0.02	0.66 ± 0.04	1.41 ± 0.14	1.79 ± 0.10
	2LEGS	0.26 ± 0.03	0.66 ± 0.05	0.73 ± 0.05 *	3.84 ± 0.25$^{\#}$
V_E (l min^{-1})	1ARM	8.5 ± 1.2	23.0 ± 2.1	52.7 ± 7.3	79.2 ± 12.5
	2LEGS	9.9 ± 1.0	21.8 ± 1.9	22.1 ± 1.8 *	140.0 ± 15.4$^{\#}$
HR (beat min^{-1})	1ARM	70 ± 5	108 ± 8	133 ± 6	159 ± 4
	2LEGS	77 ± 5	95 ± 6	97 ± 5 *	181 ± 3 *

1ARM, one-arm cycling; 2LEGS, two-leg cycling. Data is shown as mean ± SE and n = 8, except during 50 W exercise where n = 6. 1ARM vs 2LEGS, * $P < 0.05$, $^{\#}$ $P < 0.001$

Table 3
1ARM, one-arm cycling; 2LEGS, two-leg cycling. Data is shown as mean ± SE and n = 8, except during 50 W exercise where n = 6 and peak exercise [Lac$^-$] where n=7, mean+/-SE. 1ARM vs 2LEGS, *$P < 0.05$ **$P < 0.01$ ***$P < 0.005$, #$P < 0.001$.

Variable	Mode	Rest	Submaximal exercise 25 W	Submaximal exercise 50 W	Peak exercise
A. Raw data					
ΔPV	1ARM		-4.31 ± 1.07	-10.74 ± 1.78	-14.5 ± 1.0
	2LEGS		-2.36 ± 0.80 *	-4.02 ± 0.98 *	-12.1 ± 0.7
$[K^+]$ (mmol l^{-1})	1ARM	4.01 ± 0.08	4.48 ± 0.12	5.01 ± 0.23	5.35 ± 0.12
	2LEGS	3.99 ± 0.04	4.27 ± 0.06	4.35 ± 0.45 *	6.23 ± 0.14#
$[Lac^-]$ (mmol l^{-1})	1ARM	0.98 ± 0.16	2.11 ± 0.40	5.15 ± 0.81	7.31 ± 0.97
	2LEGS	0.76 ± 0.15	0.97 ± 0.14 **	1.09 ± 0.08 ***	14.25 ± 1.2 ***
$[H^+]$ (nmol l^{-1})	1ARM	39.1 ± 0.4	38.6 ± 0.9	38.3 ± 1.5	38.0 ± 1.5
	2LEGS	38.2 ± 0.4	38.5 ± 0.4	39.7 ± 0.5	51.6 ± 1.4#
B. Corrected for fluid shifts from rest (ΔPV)					
$[K^+]_{corr}$ (mmol l^{-1})	1ARM		4.28 ± 0.08	4.46 ± 0.14	4.60 ± 0.08
	2LEGS		4.24 ± 0.07	4.27 ± 0.08	5.45 ± 0.11#
$[Lac^-]_{corr}$ (mmol l^{-1})	1ARM		1.99 ± 0.36	4.56 ± 0.61	6.25 ± 0.78
	2LEGS		0.91 ± 0.11 *	1.05 ± 0.07 **	11.8 ± 1.67 ***

Table 4
Comparison between 1ARM and 2LEGS of slopes of linear regressions of $[K^+]_a$ or $\log[K^+]_a$ versus VO_2 or $\%VO_{2peak}$.

Variable	Mode	Slope Mean	± SD	P (slope)	Intercept Mean	± SD	P (intercept)	R^2
$[K^+]_a$ (mmol l^{-1}) vs VO_2 (l min^{-1})	1ARM	1.2916	± 0.3156	P < 0.0005	3.6368	± 0.3271	NS	0.9009
	2LEGS	0.7545	± 0.1451		3.5495	± 0.1412		0.8690
$[K^+]_a$ (mmol l^{-1}) vs $\%VO_{2peak}$ (%)	1ARM	0.0168	± 0.0037	P < 0.01	3.6368	± 0.3271	NS	0.9009
	2LEGS	0.0224	± 0.0037		0.0224	± 0.0037		0.8690
$\log[K^+]_a$ vs VO_2 (l min^{-1})	1ARM	0.1196	± 0.0299	P < 0.001	0.5717	± 0.0351	NS	0.9039
	2LEGS	0.0644	± 0.0101		0.5719	± 0.0148		0.8967
$\log[K^+]_a$ vs $\%VO_{2peak}$ (%)	1ARM	0.0016	± 0.0003	P < 0.05	0.5717	± 0.0351	NS	0.9034
	2LEGS	0.0019	± 0.0003		0.5719	± 0.0148		0.8968

1ARM, one-arm cycling; 2LEGS, two-leg cycling. Data is shown as mean ± SD and n = 8.

2LEGS. The highest $[Lac^-]_a$ occurred at 1 min post-exercise and was also lower for 1ARM compared to 2LEGS (8.48 ± 1.08 vs 16.30 ± 1.83 mmol l^{-1}, respectively, $P < 0.005$), reaching only 52.0% of that after 2LEGS and also at 30 min post-exercise (1ARM 2.21 ± 0.36 vs 2LEGS 5.09 ± 0.73 mmol l^{-1}, $P < 0.05$,Fig. 2).

Plasma $[H^+]_a$ was unchanged from rest during 1ARM exercise, did not differ between 1ARM and 2LEGS at common submaximal work rates, but was increased at peak exercise during 2LEGS (Table 3, $P < 0.001$), with peak values during 1ARM being 73.6% of that during 2LEGS. The peak $[H^+]_a$ occurred at 5 min post-exercise and was lower in 1ARM than 2LEGS (47.0 ± 0.6 vs 63.3 ± 2.2 nmol l^{-1}, respectively, $P < 0.001$), being 52.0% after 1ARM versus after 2LEGS. $[H^+]_a$ returned to pre-exercise levels after 20 min in 1ARM, but remained elevated at 30 min post-exercise for 2LEGS ($P < 0.05$, data not shown).

The ΔPV_a became more became more negative with increased exercise intensity for both trials (Fig. 2), being more negative for 1ARM than 2LEGS at the common submaximal work rates of 25 W and 50 W ($P < 0.05$), but did not differ between modes at peak exercise (Table 3). The ΔPV_a gradually recovered post-exercise but remained negative after 30 min and did not differ between trials (Fig. 2). The difference in $[K^+]_a$ between modes at 50 W were not seen after correction for ΔPV_a, whereas these at submaximal workrates remained greater for $[Lac^-]_a$ in 1ARM, whilst greater $[K^+]_a$ and $[Lac^-]_a$ at peak exercise remained after correction for ΔPV_a (Table 3).

3.4. Relative exercise intensities

When $[K^+]_a$ was plotted against relative exercise intensity, responses were similar between exercise modes at submaximal intensities, with a rise in $[K^+]_a$ against $\%VO_{2peak}$, only appearing to diverge between modes for the final two exercise workrates, where higher values in 2LEGS were seen (Fig. 2). Linear regressions of individual data were performed for $[K^+]_a$ versus both VO_2 and $\%VO_{2peak}$. As these relationships between $[K^+]_a$ were curvilinear, a linear regression was then undertaken for $\log[K^+]_a$ versus VO_2 and $\%VO_{2peak}$, with comparisons between 1ARM and 2LEGS (Table 4). The regression equation slope of the $[K^+]_a$ vs VO_2 relationship was 71% higher in 1ARM than 2LEGS ($P < 0.0005$), but the reverse was evident for $[K^+]_a$ vs $\%VO_{2peak}$, with the slope being 33% higher in 2LEGS than 1ARM ($P < 0.01$). These differences between modes persisted when the regression was determined for $\log[K^+]_a$ versus VO_2 and $\%VO_{2peak}$ (Table 4), indicating a greater slope occurred for 2LEGS even when expressed versus $\%VO_{2peak}$.

Similar responses were seen for plasma $[Lac^-]_a$ plotted against relative exercise intensity, between exercise modes at submaximal intensities, with a curvilinear rise for $[Lac^-]_a$, diverging for the final two exercise workrates (including peak) with higher values in 2LEGS (Fig. 3). Regression equations for $[Lac^-]_a$ versus relative exercise intensity data were for ARM, $[Lac^-]_a = 0.0916 \times (\%VO_{2peak}) - 2.2809$ ($R^2 = 0.9660$) and for 2LEGS, $[Lac^-]_a = 0.142 \times (\%VO_{2peak}) - 4.6644$ ($R^2 = 0.7718$), whilst for $\log([Lac^-]_a)$ versus relative exercise intensity, were for ARM, $\log[Lac^-]_a = 0.0123 \times (\%VO_{2peak}) - 0.319$ ($R^2 = 0.9629$) and for 2LEGS, $\log[Lac^-]_a = 0.0153 \times (\%VO_{2peak}) - 0.4794$ ($R^2 = 0.9819$). The ΔPV_a was also similar between 1ARM and 2LEGS when expressed relative to the respective mode VO_2 peak (Fig. 3). Regression equations for ΔPV_a versus relative exercise intensity data were for ARM, $\Delta PV_a = -0.1817 \times (\%VO_{2peak}) + 3.7897$ ($R^2 = 0.9769$) and for 2LEGS, $\Delta PV_a = -0.1268 \times (\%VO_{2peak}) + 1.7195$ ($R^2 = 0.9454$). For plasma $[H^+]_a$, no rise occurred for 1ARM but a small linear increase was seen for 2LEGS (data not shown), with respective regression equations being for 1ARM, $[H^+]_a = 0.0235 \times (\%VO_{2peak}) + 37.443$ ($R^2 = 0.4935$) and 2LEGS, $[H^+]_a = 0.0986 \times (\%VO_{2peak}) + 35.032$ ($R^2 = 0.983$).

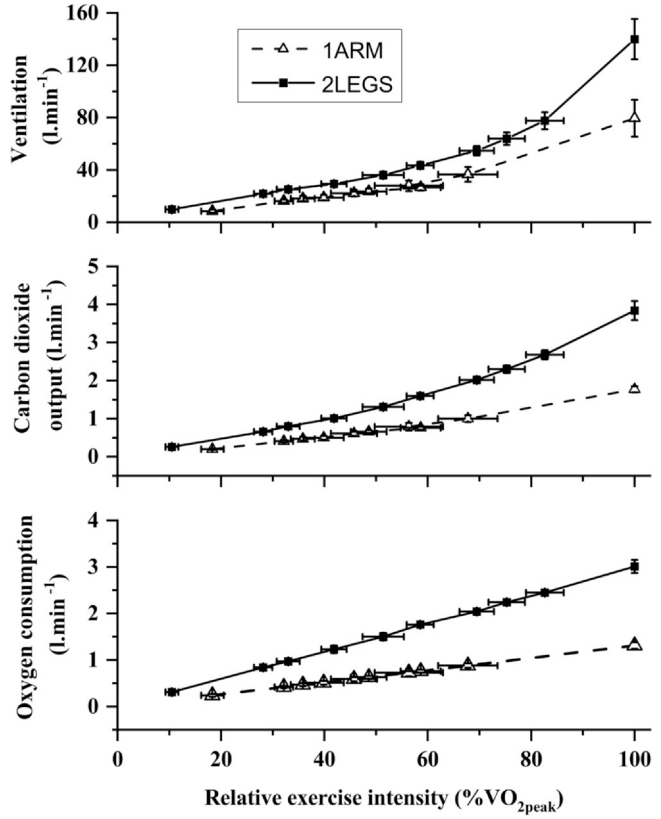

Fig. 1. Pulmonary oxygen consumption, carbon dioxide output and ventilation plotted against the relative exercise intensity, expressed as $\%VO_{2peak}$, during incremental one-arm cycling (1ARM, Δ - - Δ) and two-leg cycling (2LEGS, ■–■). Data is mean ± SE, $n = 8$. Each absolute workrate was expressed as $\%VO_{2peak}$, with the horizontal error bars indicating the SE for all individuals at that workrate.

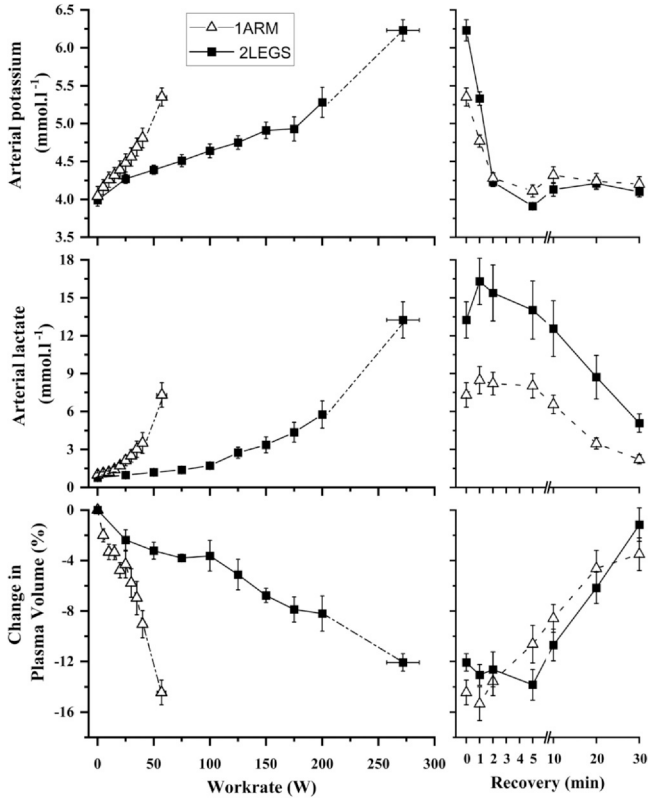

Fig. 2. Arterial plasma potassium concentration, lactate concentration and the decline in plasma volume (ΔPV), at rest, during and for 30 min following incremental one-arm cycling (1ARM, Δ - - Δ) and two-legged cycling (2LEGS, ■—■). Data is mean ± SE, $n = 8$. Horizontal error bars indicate the SE for peak workrate. Post-exercise values are plotted commencing from end-exercise as time 0 min.

3.5. Catecholamines

Plasma [Adr] and [NAdr] increased during both exercise modes ($P < 0.001$), each being ~2-fold and ~4-fold higher in 2LEGS than 1ARM during exercise at ~80% VO_{2peak} ($P < 0.05$) and at peak work rates, respectively ($P < 0.005$, Table 5). Both [Adr] and [NAdr] remained elevated at 1 min post-exercise and were lower in 1ARM than 2LEGS ($P < 0.05$).

4. Discussion

4.1. Major findings

We documented the magnitude of fluctuations in $[K^+]_a$ during and after incremental one-arm cycling exercise, finding that $[K^+]_a$ at peak exercise was considerably lower than leg cycling exercise, but with similar post-exercise values. These indicate that one-arm cycling exercise does not pose undue hyperkalaemia–, or hypokalaemia-related risks in healthy individuals, and also suggest a similar conclusion in clinical or aged populations. Furthermore, both the size of the contracting muscle mass and the relative exercise intensity exerted important effects on $[K^+]_a$ during incremental exercise, but these had differing importance during submaximal and at near-maximal exercise. The relative exercise intensity was most influential in determining $[K^+]_a$ during submaximal exercise, but a small effect of the greater muscle mass on $[K^+]_a$ was still apparent. The contracting muscle mass exerted dominant effects during very heavy exercise, including just below and at the peak incremental workrate. The higher $[K^+]_a$ found during 1ARM at identical workrates than 2LEGS could be explained by occurring at a higher relative exercise intensity. A similar relationship between the contracting muscle mass and the relative exercise intensity was seen for $[Lac^-]_a$, whilst $[H^+]_a$ was dominated by the size of the contracting muscle mass, with no rise in $[H^+]_a$ occurring during 1ARM.

4.2. Modest $[K^+]_a$ changes during and after arm cycling

We determined the perturbations in $[K^+]_a$ during and after incremental arm cycling exercise for the first time. During one arm cycling, $[K^+]_a$ rose only to ~5.3 mM at peak exercise, whilst the lowest post-exercise $[K^+]_a$ was only ~4 mM at 2 min after exercise. Thus, one arm cycling did not induce either hyperkalaemia or subsequent hypokalaemia, which strongly suggests that this exercise does not pose undue myocardial risks for healthy individuals. Although somewhat larger changes in $[K^+]_a$ would be expected with two arm cycling, which is typically used clinically (see Introduction), it is highly unlikely that the magnitude of changes in $[K^+]_a$ would be greater than and indeed quite likely to be less than with two-legged cycling. Furthermore, during one arm cycling at peak exercise, the increase in $[Lac^-]_a$ was small, $[H^+]_a$ did not differ from rest, the rise in blood pressure was not greater than with leg cycling and whilst pulmonary oxygen uptake rose considerably, this was only to ~45% of that during two legged cycling. Hence, one arm cycling exercise should impose relatively low cardiac risk when applied in healthy, clinical, or aged populations. In addition, as this exercise mode does not require standing or locomotion, it is thus also advantageous for many clinical populations.

4.3. Efficacy of the contracting muscle mass comparisons

The higher peak exercise work rate and cardiopulmonary responses during 2LEGS than 1ARM exercise were as expected[9,12–15,41–43] and

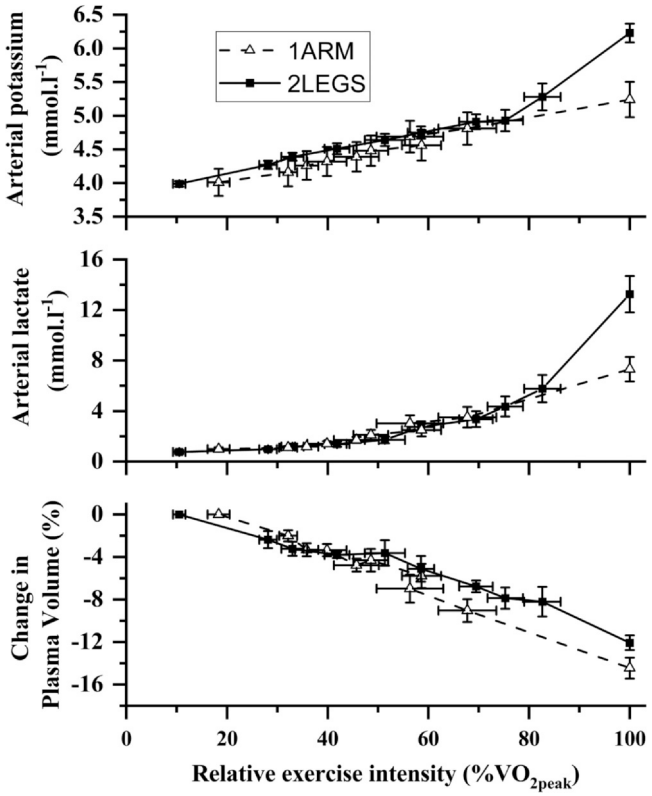

Fig. 3. Arterial plasma potassium concentration, lactate concentration and decline in plasma volume plotted against the relative exercise intensity, expressed as $\%VO_{2peak}$, during incremental one-arm cycling (1ARM, Δ - - Δ) and two-leg cycling (2LEGS, ■–■). Data is mean ± SE, $n = 8$. Each absolute workrate was expressed as $\%VO_{2peak}$, with the horizontal error bars indicating the SE for all individuals at that workrate.

demonstrate the efficacy of our model requiring large differences in the amount of contracting versus inactive musculature. Whilst we did not measure the exact muscle mass in the two exercise modes, limb volume measures indicated a 5-fold greater volume for the 2LEGS than 1ARM. This volume includes muscle, bone and fat, so provides only a relative indicator for contracting muscle mass. Also the exact mass of contracting muscle would be difficult to determine given the likely recruitment of additional muscles for both modes during heavy exercise. Nonetheless, a major difference in the contracting muscle mass was also evidenced by the 2-fold greater VO_{2peak} during 2LEGS than 1ARM. This difference was less than that for limb volume, which probably also reflected a disproportionate rise in VO_2 for a given work rate during 1ARM, most likely due to a small rise in the postural component of the work during 1ARM at high relative exercise intensity, due to additional muscle recruitment for stabilisation of the shoulder and trunk. Whilst arm cycling and two-legged cycling use different muscle groups, the type and frequency of muscular contraction were similar, thereby also enabling an appropriate comparison between the metabolic and ionic responses to exercise. Muscle fibre composition may vary between muscles within an individual and also for a given muscle between individuals, but is typically similar with ~40–60% Type I fibres in muscles involved in upper limb and lower limb exercise, apart from higher Type II fibres in triceps brachii,[44] so seems unlikely to differentially affect these findings. However, in rats, muscle K^+ release per action potential was ~6-fold greater from stimulated fast-twitch extensor digitorum longus than slow-twitch soleus muscles.[45] This suggests a possible effect of fibre type difference on muscle K^+ release could similarly occur in humans, albeit smaller due to the mixed fibre composition in human muscles. Future determination of muscle K^+ release during 1ARM compared to 2LEGS cycling, along with muscle fibre composition analyses, is however required to investigate this.

4.4. Muscle mass and relative exercise intensity effects on arterial plasma $[K^+]$

A small rise in $[K^+]_a$ during 1ARM is consistent with other studies that utilised repeated handgrip contractions or finger flexion exercise (see references in.[19]) In contrast, intense exercise utilising a large contracting muscle mass, such as sprint running or cycling, or rowing, sustained for one or several minutes, can elevate $[K^+]_a$ to 7- 8 mM and the mean peak exercise $[K^+]_a$ of 6.2 mM seen here during 2LEGS was consistent with findings in other incremental cycling or knee extension studies (see references in.[19]) These studies were conducted in different individuals, exercise conditions and/or studies and therefore are not definitive for assessing the impacts of contracting muscle mass on $[K^+]_a$. In a study contrasting responses in the same individuals, $[K^+]_a$ during intermittent finger flexion exercise was increased by only 0.37 mM, substantially less than the rise of 2.51 mM found during two-legged cycling to exhaustion at $90\%VO_{2peak}$.[34] Here we show that whilst $[K^+]_a$ increased substantially above rest during both modes of exercise, greater increases were found at a given submaximal workrate for 1ARM than 2LEGS, with the opposite at peak exercise, with a 71% higher slope of the $[K^+]_a$ versus VO_2 regression. The $[K^+]_a$ during submaximal arm and leg exercise were similar when $[K^+]_a$ was plotted against the relative exercise intensity ($\%VO_{2peak}$), whereas during peak exercise, $[K^+]_a$ reflected the size of active skeletal muscle mass. A muscle mass effect was seen during exercise, however, evidenced by the greater slope of the $\log[K^+]_a$ versus $\%VO_{2peak}$ regression during 2LEGS than 1ARM. This indicates that the absolute and relative exercise intensity, as well as the size of the contracting muscle mass all exerted important effects on $[K^+]_a$. Whilst $[K^+]_a$ during exercise at a given absolute workrate could largely be explained by the relative exercise intensity for submaximal exercise, the size of the contracting muscle mass also had a small additional effect on $[K^+]_a$, with $[K^+]_a$ at peak exercise during arm exercise only ~85% of that attained during 2LEGS. The size of the contracting muscle mass exerted dominant effects on $[K^+]_a$ at very heavy-to-peak exercise workrates, which may also reflect a further increase in K^+ release from additional muscle recruitment, consistent with the elevated VO_2 at these workrates.

The ΔPV_a became progressively more negative with exercise intensity in both exercise modes, consistent with earlier reports of a ΔPV during incremental exercise measured in venous blood of

Table 5
Arterial plasma adrenaline and noradrenaline concentrations at rest, during and after incremental exercise, for one-arm cycling and two-leg cycling. Exercise data is at the submaximal workrate corresponding to ~80% VO_{2peak}, at peak workrates and at 1 min post-exercise.

Variable	Mode	Rest	Submaximal exercise at ~80%VO_{2peak}	Peak exercise	Post-exercise (1 min)
Adrenaline (nmol l^{-1})	1ARM	0.48 ± 0.10	0.82 ± 0.22	2.03 ± 0.38	1.09 ± 0.20
	2LEGS	0.51 ± 0.11	1.87 ± 0.56 *	8.07 ± 1.55 *	4.01 ± 0.79 *
Noradrenaline (nmol l^{-1})	1ARM	2.21 ± 0.62	2.74 ± 0.66	4.88 ± 0.65	3.60 ± 0.13
	2LEGS	2.28 ± 0.64	6.18 ± 0.83 *	21.95 ± 2.78 *	16.09 ± 2.04*

1ARM, one-arm cycling; 2LEGS, two-leg cycling. Data is shown as mean ± SE and is n = 7, except for post-exercise Noradrenaline during 1ARM, where n = 6. 1ARM vs 2LEGS, $*P < 0.05$

~14-16%[46,47] and of ~18% in arterialised capillary blood.[48] Whilst a greater ΔPV_a was seen in 1ARM than 2LEGS at submaximal workrates, the decline at peak exercise did not differ significantly and the responses were similar between exercise modes when expressed relative to the respective VO_2 peak. This is consistent with earlier findings in arterialised capillary blood of a greater ΔPV during arm cranking than leg cycling, but with an identical response when compared as a $\%VO_{2peak}$.[48] In that study the ΔPV was related to the mean arterial pressure and the lack of difference here between modes is also consistent with the similar systolic and diastolic pressures observed. Thus, these responses in ΔPV between 1ARM and 2 LEGS are qualitatively similar to those of $[K^+]_a$ during exercise and hence correction of $[K^+]_a$ for the ΔPV_a during exercise did not alter these findings.

The rise in $[K^+]_a$ for both 1ARM and 2LEGS is consistent with a net K^+ release from contracting muscles into the circulation, with an overall net gain of K^+ persisting after correction for fluid shifts out of plasma. This is consistent with many previous studies, as reviewed elsewhere.[19,21,22,37] The K^+ released from contracting muscles is due to K^+ efflux with action potentials and is thus expected to be proportional to the frequency of muscle action potentials and exercise intensity.[31,49] The higher peak $[K^+]_a$ in 2LEGS than 1ARM is consistent with the greater mass of active muscle involved and is most likely due to greater total K^+ release. In addition, inactive muscle has long been demonstrated to remove K^+ from the circulation (see references in.[19]) Thus with a higher contracting musculature in 2LEGS, the inactive muscle mass available to remove K^+ from arterial plasma would be less, also potentially contributing to the higher $[K^+]_a$ found at peak exercise. The higher $[K^+]_a$ and $\Delta[K^+]$ work^{-1} ratio during 1ARM at identical submaximal work rates, could be explained by greater K^+ release from a small active muscle mass that was contracting at greater relative exercise intensity. This conclusion is consistent with the greater rate of K^+ efflux during knee extension vs leg cycling exercise, albeit in different participants, participating in separate studies.[49] Possible differences in muscle blood flow between 1ARM and 2LEGS are not known but could affect K^+ release from the contracting muscles. A lesser arm blood flow at matched submaximal exercise workrates was reported during two-arm than two-legged cycling,[50] which would be inconsistent with a greater flow-mediated K^+ release accounting for the higher submaximal exercise $[K^+]_a$ in 1ARM. Further studies are required to determine possible differences in blood flow and muscle K^+ release.

NKA-mediated K^+ uptake occurs in both contracting and non-contracting muscles[19,31,36,39,51] and is regulated by membrane electrical activity, increased intracellular $[Na^+]$, increased catecholamines and insulin.[19,36,52] It is not possible with the methods used here to directly determine K^+ release and/or uptake rates in the two exercise modes. Interestingly, the ~2–4-fold higher plasma catecholamines at peak exercise, the ~2-fold greater post-exercise -$\Delta[K^+]$ and the larger active muscle mass during 2LEGS are all consistent with a greater stimulation of NKA, which would potentially both reduce K^+ release from active muscles and increase K^+ uptake in resting muscles compared to 1ARM, thus lowering $[K^+]_a$. This may then have attenuated the impacts of a large active muscle mass elevating $[K^+]_a$ at peak exercise and thus protect against excessive hyperkalaemia with intense exercise. Conversely, this might also be expected to result in a lower post-exercise $[K^+]_a$, but this did not occur, as hypokalaemia (i.e. $[K^+]_a < 3.5$ mM) was not found. Studies that demonstrated post-exercise arterial hypokalaemia typically utilised both a very large contracting muscle mass and very high intensity, such as treadmill sprinting bout(s) or all-out rowing, or repeated 45 s cycling bouts at 130% VO_{2max}.[19,28,32,53,54] Whilst two-legged cycling typically lowers post-exercise $[K^+]_a$ below resting values, usually $[K^+]_a$ remains above 3.5 mM, after exercise at 90–110%VO_{2max}[31,34] or repeated 30 s bouts of maximal cycling exercise.[55,56] The higher $[K^+]$ during submaximal exercise in 1ARM may reflect both greater K^+ rate of efflux due to an increased action potential frequency due to the higher relative exercise intensity, as well as lesser NKA-mediated K^+-reuptake resulting from lower adrenergic stimulation. During intense contractions the peak gradient between $[K^+]_a$ and muscle interstitial $[K^+]$ can reach 6.5 mM in *m. gastrocnemius medialis*[57] and ~4.3 mM in the *m. vastus lateralis*.[58] If a similar gradient occurred here, the muscle interstitial $[K^+]$ may have reached ~10–11 mM at peak exercise during 1ARM and 2LEGS. Increases in interstitial $[K^+]$ with exercise have important implications for muscle function, with increases to values seen during submaximal exercise likely potentiating muscle force and thus supporting exercise performance.[20,23,24,59] Increases in interstitial $[K^+]$ at peak exercise may either facilitate or impair exercise performance depending on the magnitude of rise and also several other factors directly influencing an intracellular metabolic stress (reduced ATP availability), including activation of K_{ATP} and opening of ClC-1 channels, which would exacerbate the depressive effects of high interstitial $[K^+]$.[20] The rise in $[K^+]_a$ to 5–6 mM at peak exercise would not suggest a muscle interstitial $[K^+]$ exceeding 12 mM and thus contributing to fatigue. Furthermore, increased [Lac] was shown to protect against the inhibitory effects of high extracellular $[K^+]$ on muscle force in isolated rat muscles.[60] However, the elevated $[Lac^-]_a$ in both exercise modes and especially with 2LEGS, raises that the possibility also of an intracellular metabolic stress, such that the elevation in interstitial $[K^+]$ may still be compatible with a possible role in fatigue of the active muscles.[20]

4.5. Muscle mass and relative exercise intensity effects on plasma $[Lac^-]$ and $[H^+]$

During 1ARM, $[Lac^-]_a$ was higher at common submaximal work rates but substantially less during peak work rates than 2LEGS, in agreement with earlier studies.[16,18] Furthermore, $[Lac^-]_a$ was closely related to the relative exercise intensity for both exercise modes, similar to one previous study,[18] but contrary to another in which $[Lac^-]$ was higher during arm cranking than leg cycling matched at the same relative intensity.[17] In the present study we minimised the isometric component of muscle contraction during arm cycling, which may have affected the Lac^- released from contracting arm muscles. Further, we used a fast incremental work rate protocol (increases each 1 min), whereas slow intervals (10 min) were used during arm cranking elsewhere.[17] It is likely that our non-steady state exercise protocol resulted in lower $[Lac^-]_a$ responses compared to steady-state arm cycling .[17] The mechanisms for the higher $[Lac^-]$ reported during 1ARM most likely reflect greater muscle Lac^- production and release from contracting arm muscles.[17] The increase in $[Lac^-]_a$ was greater during 2LEGS than 1ARM exercise, with the peak exercise and post-exercise $[Lac^-]_a$ responses with 1ARM being only ~51–52% that of 2LEGS. This large difference in peak $[Lac^-]_a$ between exercise modes was likely because only one arm was contracting, whereas earlier studies typically used two arm cycling.[16,18] The higher slope of the $[Lac^-]_a$ versus $\%VO_{2peak}$ regression further suggested an important effect of muscle mass persisted throughout exercise. Whilst hemoconcentration had a small impact on $[Lac^-]_a$ there was a net gain of Lac^- for both 1ARM and 2LEGS, consistent with previous reports for leg exercise.[39,61,62] Finally, $[H^+]_a$ was unchanged from rest throughout 1ARM, whereas a 25% increase occurred during 2LEGS, followed by increases during the first 5 min post-exercise in both modes of exercise, where further increases in $[Lac^-]_a$ also occurred. The highest peak exercise and post-exercise $[H^+]_a$ in 1ARM were only ~73–74% that of 2LEGS, consistent with a clear dependence of $[H^+]_a$ on the magnitude of the active muscle mass. Our findings differ to a previous study in which no difference in $[H^+]_a$ was found at peak exercise between arm and leg cycling,[18] likely because we utilised only one arm and thus the muscle mass difference was greater.

4.6. Conclusions

In conclusion, arterial plasma $[K^+]$ was greater at the same absolute submaximal work rate but lower at peak exercise when utilising a small (one arm cranking) compared to large contracting

muscle mass (two-legged cycling). However, these differences between exercise modes during submaximal exercise were small when $[K^+]_a$ was plotted against $\%VO_{2peak}$, indicating that the relative exercise intensity is more important than the size of the exercising muscle mass in determining $[K^+]_a$. However, a muscle mass effect existed throughout exercise as the slope of the $\log[K^+]_a$ versus $\%VO_{2peak}$ regression was higher in 2LEGS than 1ARM. A clear difference was seen during intense exercise close to, or at VO_{2peak}, where the size of the contracting muscle mass had an additional effect, further elevating $[K^+]_a$ during two-legged cycling. Similar responses occurred and conclusions were drawn for $[Lac^-]_a$. Hence, sports utilising a large active muscle mass contracting at high intensity such as rowing or cross country ski sprint events would be anticipated to induce large changes in $[K^+]_a$. Importantly, neither hyperkalaemia or subsequent hypokalaemia were induced by one arm cycling, suggesting that this exercise mode does not pose undue $[K^+]_a$-related risks of arrhythmia and is safe for use in healthy as well as clinical and aged populations.

CRediT authorship contribution statement

Conceptualization and methodology: Michael J. McKenna, Termboon Sangkabutra, Sandford L. Skinner; **Data acquisition and analysis:** Termboon Sangkabutra, Claudia Schneider, Steve F. Fraser, Simon Sostaric, Sandford L. Skinner, Michael J. McKenna; **Funding acquisi- tion:** Not applicable; **First draft:** Termboon Sangkabutra and Michael J. McKenna; **Review, editing and acceptance of the manuscript:** all authors, excluding review of the final manuscript by Sandford L. Skinner (deceased), who did comment on earlier drafts.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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