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Haemodynamic and Perceptual Responses to Blood Flow Restricted Exercise among Dialysis Patients

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Running Head: Blood Flow Restricted Exercise during Haemodialysis

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Author Contributions

M.J.C., C.A.B., S.A.W., S.F.F., P.N.B. and L.P.M. designed and ensured the feasibility of the study; M.J.C. carried out experiments; M.J.C., C.A.B. and S.A.W. analysed the data; M.J.C. made the figures; M.J.C., C.A.B., S.A.W., S.F.F., P.N.B. and L.P.M. drafted and/or revised the paper; all authors approved the final version of the manuscript.

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Abstract

End stage kidney disease is associated with reduced exercise capacity, muscle atrophy and impaired muscle function. While these may be improved with exercise, single modalities of exercise do not traditionally elicit improvements across all required physiological domains. Blood flow restricted exercise may improve all of these physiological domains with low-intensities traditionally considered insufficient for these adaptions. Investigation of this technique appeals, but is yet to be evaluated in dialysis patients. Using a progressive crossover design, ten satellite haemodialysis patients underwent three exercise conditions over 2 weeks. Condition 1: 2 bouts (10min) of unrestricted cycling during 2 consecutive haemodialysis sessions. Condition 2: 2 bouts of cycling with blood flow restriction while off-haemodialysis on 2 separate days. Condition 3: 2 bouts of cycling with blood flow restriction during 2 haemodialysis sessions. Outcomes included haemodynamic responses (heart rate, blood pressure) throughout all sessions, participant-perceived exertion and discomfort on a Borg scale, and evaluation of ultrafiltration rates and Kt/V obtained *post-hoc*. Haemodynamic responses were consistent regardless of condition. Significant increases in heart rate, systolic blood pressure and mean arterial blood pressure ($P<0.05$) were observed post-exercise, followed by a reduction in blood pressures during the 60 min recovery (12 mmHg, 5 mmHg and 11 mm Hg for systolic, diastolic and mean arterial pressures, respectively). Blood pressures returned to pre-dialysis ranges following the recovery period. Blood flow restriction did not affect ultrafiltration achieved or Kt/V. Haemodynamic safety and tolerability of BFR during aerobic exercise on HD is comparable to standard aerobic exercise.

Introduction

End stage kidney disease (ESKD) is associated with reduced exercise capacity, skeletal muscle atrophy and impaired physical function (22). These deficiencies can be improved with aerobic and/or resistance exercise training performed during haemodialysis (HD) where low- to moderate-intensity exercise is considered safe and well-tolerated (6, 9, 20, 47, 49, 50). However, not all studies using traditional exercise, in particular aerobic exercise alone, result in marked improvements in muscle size, strength, exercise capacity, or physical function, and rarely are improvements observed across all of these physiological domains (18, 50). This is compounded by exercise not being widely adopted among patients with ESKD, with most patients displaying a significant reluctance to exercise (8, 28). Proposed exercise interventions therefore need to be safe, tolerable and at a minimum, similarly efficacious than the current alternatives.

A viable option is blood flow restricted exercise (BFRE), which uses a pressurised tourniquet applied to the active limbs during exercise (14, 33). BFRE is known to enhance skeletal muscle strength and cross-sectional area more than equivalent-intensity non-blood flow restriction exercise, despite typically employing low exercise intensities (1, 15, 30, 34, 39, 46, 54). While aerobic exercise does not typically elicit gains in muscle size and strength, especially at the low volumes used in many exercise and dialysis studies (6, 27, 49, 50), aerobic BFRE continues to confer traditional adaptations of improved aerobic capacity and physical function, especially in deconditioned populations (10, 11, 46). Prominent theories suggest increased and preferential recruitment of type II muscle fibres as a result of localised compression-induced muscle hypoxia combined with greater metabolic stress of type I muscle fibres that are less resistant to hypoxia, as evidenced by examination of heat-shock proteins associated with skeletal muscle damage (12, 31, 55). Combined, this suggests multiple pathways may be responsible for the increased muscle strength and size following BFRE. This positions aerobic BFRE as an interesting prospect for patients with ESKD, as it can potentially elicit significant improvements across multiple physiological domains where traditional exercise generally has not among these patients (9, 18, 50).

The applied cuff pressure during BFRE is typically high enough to occlude venous outflow from the muscles distal to the cuff at rest, but low enough to maintain arterial inflow (32). Capillary blood flow is generally proportional to venous blood flow (35). As venous blood flow is maintained during BFRE via the mechanical pump that occurs during muscular contractions, capillary blood flow is similarly maintained (25, 45, 48). Thus, under the proviso that the cuffs are only inflated during active periods of BFRE among dialysis patients, blood flow to all vascular beds should be largely maintained and not acutely affect dialysis adequacy (Kt/V) or the ultrafiltration rates (UF) of patients.

Exercise induces acute changes to haemodynamics, in particular an elevation in systolic blood pressure (SBP) (43). This is sometimes, and more commonly in patients with ESKD, followed by significant post-exercise hypotension (PEH) (19). Both the SBP elevation and PEH are usually, but not exclusively self-resolving and largely asymptomatic (19, 43). This is of concern when programming exercise for patients with ESKD, as their haemodynamics are known to be unstable both during and following HD (17, 53). This instability is further complicated as patients with ESKD exhibit a high incidence of vascular disease (peripheral, cerebral, coronary) and other cardiovascular diseases (3). Symptomatic intradialytic hypotension (IDH) is of particular concern due to the relationship between IDH and vascular access thrombosis, inadequate dialysing, and mortality (17). Thus, while exercise is considered safe to perform intradialytically, it requires vigilant monitoring of the haemodynamic responses and careful patient selection.

The magnitude of the haemodynamic response to BFRE with resistance training is typically greater than for equivalent-intensity non-BFRE (38). However, this response is markedly lower for aerobic BFRE such as cycle ergometer exercise when compared with BFRE with resistance training (36). Notably, this reduced haemodynamic response was also lower than with low-intensity traditional resistance exercise, regarded as safe for patients with ESKD (36, 50, 51). However, BFRE has not been evaluated in patients with moderate to advanced chronic kidney disease or ESKD either intradialytically or off-dialysis.

Therefore, the aim of this study was to evaluate the acute haemodynamic responses (heart rate and blood pressure) as well as the perceived tolerability (required effort and discomfort) to aerobic BFRE under progressively increased haemodynamically unstable environments among patients with ESKD.

Materials and Methods

Study Design

This study utilised a progressive crossover design. Ten participants (Table 1) underwent six supervised cycling exercise sessions over a fifteen-day period aligning with each participant's regular dialysis schedule. The study was conducted according to the Declaration of Helsinki (2013) and ethics approval was granted under a collaborative research agreement by both the Eastern Health Human Research Ethics Committee and the Deakin University Human Research Ethics Committee.

Participants

Participants (n = 7 male; n = 3 female; Table 1) were recruited through promotion in participating dialysis clinics and asked to voluntarily participate in the study. Prospective participants were screened initially by assessing their medical history against the inclusion and exclusion criteria of the study and consulted face-to-face by a member of the research team regarding any personal or undocumented physical limitations. Following this, approval to participate was obtained from the treating physician. Participants were required to provide written, informed consent prior to participation in the study.

Inclusion and Exclusion criteria

Eligible participants were male or female, over 18 years of age, diagnosed with ESKD (stage V chronic kidney disease; glomerular filtration rate <15 $mL.min^{-1}.1.73m^{-2}$), and having undertaking HD for a minimum of 12 weeks. Participants were excluded if they engaged in regular physical activity or sport (>150 $min.wk^{-1}$), or structured resistance training (> 1 $session.wk^{-1}$); if they had persistent uncontrolled blood pressure, clinically significant or symptomatic cardiovascular or peripheral vascular disease, or any musculoskeletal limitations or neurological conditions; if they were current smokers; or if they had required hospitalisation for non-dialysis reasons in the 4 weeks prior to the study. Participants were also deemed unable to exercise during individual sessions if they were over their dialysis base weight by more than 5%, indicating fluid overload, and reduced cardiovascular reserve; if SBP was greater than 180 mmHg or less than 90 mmHg prior to commencing exercise, indicating markedly unstable blood pressure. This did not include the very first blood pressure reading during HD, as this is known to be highly variable (2).

Sample Size Calculation

There was no existing data from which to inform a sample size calculation looking at a difference in SBP response to exercise with blood flow restriction and non-blood flow restriction cycling exercise among patients with ESKD. As such, sample size calculations were made based on previous data showing the change in SBP for standard, non-blood flow restriction cycling exercise among dialysis patients (19, 42). This suggested that 8 participants would provide sufficient power (0.8) to derive significance for a 30% change in SBP immediately following exercise.

Exercise training

Participants were examined under three '*conditions'*, with each comprising exercise sessions on two days, separated by one day (Figure 1). The order of conditions was the same for each participant. Condition 1 was non-BFRE while '*on'* HD (noBFRE-HD), to represent a '*baseline*' response for intradialytic exercise when participants are considered to be at their most haemodynamically unstable while undergoing HD (44). Condition 2 was BFRE while '*off-dialysis*' (BFRE-noHD) to evaluate BFRE, which may cause heightened haemodynamic responses, when participants are more haemodynamically stable, without the influence of HD (38, 44). Condition 3 was BFRE while '*on*' HD (BFRE-HD), which examined the potentially more haemodynamically demanding BFRE while patients were also exposed to greater haemodynamic instability during HD (44). Data were also obtained *post-hoc* from the 4 dialysis runs preceding these exercise sessions to represent a usual care, non-exercising HD control (CON-HD).

For exercising conditions conducted on HD, participants underwent exercise during the first 2 hours of HD (21, 41). All sessions were monitored by an accredited exercise physiologist as part of the research team. On each day, cycling was completed on an electronically braked cycle ergometer (LODE Excalibur 911905, Lode B. V., Groningen, The Netherlands) positioned to the side of each participant's dialysis bed allowing them to remain seated on their bed, rotated such that their legs could reach the pedals from behind the cycle ergometer. This was always to the same side as the dialysis machine, to allow participants to have their fistula arm supported and avoid access lines from moving excessively during the active portions of the exercise session.

All cycling sessions followed the same structure (Figure 2). Each session included an unloaded 5-minute cycling warm up and cool down, at a participant-selected cadence. The main component of the exercise session consisted of two 10-minute bouts of cycling separated by a 20-minute rest period. The prescribed volume and intensity reflected a balance between entry-level, multiple bout blood flow restriction protocols and traditional aerobic training components from other HD studies (20, 23, 40). Workload for each 10-minute bout was between 10 W and 30 W, equivalent to a low-to-moderate rating of perceived effort (RPE) (5). RPE was provided by participants during the final 30 seconds of each exercise bout (13, 18, 52). Patient workloads remained constant across all conditions.

Blood Flow Restriction

For conditions that required blood flow restriction, the restriction was applied during each exercise bout only, using an automatic tourniquet system (A.T.S 3000, Zimmer Inc., OH, USA) connected to pneumatically inflated cuffs positioned around the proximal end of the thigh. Measurement of limb occlusion pressure (LOP) was completed prior to each blood flow restriction exercise session. This was done on each lower limb using digital plethysmography (Pulse Sensor, Zimmer ATS 3000, Zimmer

Inc., OH, USA) applied to the second toe. The cuffs were inflated until the plethysmograph no longer detected blood flow (total limb occlusion). This pressure was recorded as LOP. During exercise sessions cuffs were inflated to 50% LOP, typical of training interventions that produce increased skeletal muscle size and strength without the undue neuromuscular or mechanical fatigue often observed with restriction pressures >50% LOP (16, 29, 46). By utilising a restriction pressure individualised to the level of LOP, this accounts for peripheral vascular differences between participants resulting in an equivalent degree of blood flow restriction.

Measurements

Heart Rate and Blood Pressure

For all sessions, haemodynamic measures were taken at baseline, immediately prior to, and immediately following each exercise bout (Figure 2). Haemodynamic measures included HR, SBP, DBP and MAP. In addition, haemodynamic measures were taken at 20-minute intervals until 60 minutes post exercise (Figure 2). HR, SBP, DBP and MAP were measured using the dialysis machines (4008S NG, Fresenius Medical Care Australia Pty Ltd, Milsons Point, New South Wales). These dialysis machines took approximately 30 seconds to take the desired measures, so post-exercise measures (‘End-bout 1’ and ‘End-bout 2’) are within the first 30 seconds following completion of each exercise bout.

In addition, measurements of end-HD SBP and DBP were retrieved *post-hoc* from stored hospital records by a nephrologist from the treating organisation, as these data are collected routinely by renal nurses at the completion of each HD session. Similarly, HR, SBP, DBP and MAP data were retrieved for the 4 sessions preceding the beginning of the trial to act as baseline, non-exercising HD control values for each of these variables (only baseline/pre-dialysis, and hourly thereafter including end-HD). These data were not available for the BFRE-noHD condition.

Ultrafiltration Rate and Dialysis Adequacy

Ultrafiltration rate (UF) and dialysis adequacy (Kt/V) data were obtained *post-hoc* from patient records. This data included both the prescribed UF and actual nett UF achieved, as well as the Kt/V recorded from the dialysis machines. These data were not available for the BFRE-noHD condition.

Perceptual Measures

In the final 30 seconds of each of the main exercise bouts, participants were asked to provide a rating of perceived exertion (RPE) on a Borg scale ranging from 6 (no exertion) to 20 (maximal exertion) (5) and a rating of perceived discomfort (RPD) using a modified Borg scale ranging from 0 (no discomfort) to 10 (maximal discomfort) (4). As a standard precaution, all participants were monitored for, or asked to report, chest pain/discomfort, dyspnoea, lower limb pain, symptoms of severe hyper- or hypotension, and other signs of adverse events.

Statistical Analysis

All statistical analyses were performed using SPSS 25.0 (IBM Corp, Chicago IL, United States of America). Continuous variables were compared using a mixed model analysis of variance (ANOVA) using within factors (time, session), and between factors (condition) for which significance was set at an α level < 0.05.

If there was no statistical difference between the two sessions within each condition (noBFRE-HD, BFRE-noHD, BFRE-HD, CON-HD), the mean data for each condition was subsequently analysed, allowing for a direct comparison of conditions. To achieve this, comparisons between each condition for all continuous variables was made with a mixed model ANOVA using within factors (time), and between factors (condition). Mauchly's test for sphericity was used to assess equality of variance, and if violated a Greenhouse-Geisser correction was applied. A significant α level of less than 0.05 was adopted for all statistical tests. All outcome data are presented as means ± SEM unless stated. The differences between prescribed UF and nett UF achieved, as well as the dialysis machine Kt/V were assessed using one-way ANOVAs using a between factor (condition) with a significant α level < 0.05.

Results

Haemodynamic Measures

There was a main effect for time for HR ($F_{8, 216}$ = 76.09, P < 0.001), SBP ($F_{8, 216}$ = 52.81, P < 0.001), DBP ($F_{8, 216}$ = 17.44, P < 0.001), and MAP ($F_{8, 216}$ = 37.47, P < 0.001), such that they increased with exercise and returned to baseline following the 60-minute recovery period (Figure 3). In addition, there was a mild post-exercise hypotension evident for all conditions over the first 60 min of recovery when compared with baseline (P < 0.001). The lowest recovery measures for SBP, DBP and MAP were 12 (3) mmHg, 5 (1) mmHg, and 11 (2) mmHg lower than baseline, respectively (P < 0.001). There was no main effect for condition or interaction between time and condition in any of the haemodynamic measures. Similarly, there were no significant differences between any exercising groups and CON-HD for any haemodynamic measures immediately before HD or at the completion of HD.

Ultrafiltration Rate and Dialysis Adequacy

Results for both UF and dialysis adequacy are presented in Table 2. There was no significant difference between the prescribed UF for any of the dialysis conditions, including non-exercising dialysis sessions for which data was obtained *post-hoc* ($F_{2,27}$ = 0.15, P = 0.86). Similarly, there was no significant difference between any of the dialysis conditions for the difference between prescribed UF and nett UF achieved ($F_{2,27}$ = 0.58, P = 0.57). The dialysis machine-based Kt/V was also not different for any of the dialysis conditions ($F_{2,24}$ = 0.63, P = 0.54).

Perceptual Measures

There was a main effect for exercise bout for RPE ($F_{1,27}$ = 21, P < 0.001) and RPD ($F_{1,27}$ = 11.88, P = 0.002), as well as a main effect for condition for RPE ($F_{2,27}$ = 3.43, P = 0.047) and RPD ($F_{2,27}$ = 33.33, P < 0.001) (Figure 4). However, there was no interaction for bout and condition for either RPE ($F_{2,27}$ = 0.859, ns), or RPD ($F_{2,27}$ = 2.14, P = 0.14). Specifically, RPE was significantly higher following exercise bout 2 [16 (0)] than following exercise bout 1 [14 (0)] (P < 0.001). RPE was also significantly lower for noBFRE-HD [13 (1)] than for both BFRE-noHD [16 (1)] (P = 0.027) and BFRE-HD [16 (1)] (P = 0.01), with no significant difference between BFRE-noHD and BFRE-HD. RPD was significantly higher following exercise bout 2 [13 (0)] than following exercise bout 1 [12 (0)] (P = 0.002). RPD was also significantly lower for noBFRE-HD [9 (1)] than for both BFRE-noHD [15 (1)] and BFRE-HD [15 (1)] (P < 0.001), with no significant difference between BFRE-noHD and BFRE-HD.

Adverse Events

One case of exercise-related syncope occurred with BFRE-HD (blood pressure 88/68). Ultrafiltration was stopped, and a saline bolus administered. No prolonged effects of the adverse event occurred, and the participant chose to remain enrolled in the study. One additional instance of a participant feeling '*light-headed*' in recovery was reported (blood pressure 85/56), during which ultrafiltration was stopped briefly. However, this was self-resolving, and ultrafiltration resumed within five minutes.

Despite both of these instances of symptomatic IDH occurring following BFRE-HD, which may imply a temporal association with that condition, both participants also presented with fluid overload and subsequent abnormally high prescribed UFs on these days relative to each patients norm. However, the excess pre-dialysis weight was not outside the limits defined in the exclusion criteria for this study, so exercise proceeded. Each of these patients also completed another BFRE-HD session without issue. Regardless, a tighter limit for how much fluid overload prior to an HD session precludes participation in exercise may be useful in future research (for example 3% above base-weight). Additionally, constant monitoring of haemodynamic variables is necessary to ensure that these adverse events are captured.

One participant also suffered mid-fistula bruising when repositioning themselves on their dialysis chair following an exercise session. This was not a result of the exercise intervention itself but occurred during a session and warranted reporting.

Discussion

This present study demonstrates the novel application of blood flow restriction aerobic exercise for patients with ESKD on dialysis. The major finding was that haemodynamic responses (HR, SBP, DBP, and MAP) are not significantly different immediately following intradialytic aerobic BFRE (BFRE-HD) compared with either aerobic BFRE off-dialysis (BFRE-noHD), or to intradialytic aerobic non-BFRE (noBFRE-HD). Following exercise all blood pressure measures (SBP, DBP, MAP) were significantly lower compared with pre-exercise levels across all conditions, which continued through the first 60-minutes of recovery. This is similar to post-exercise blood pressure reductions observed previously among studies examining time-course changes in blood pressure with intradialytic aerobic exercise (19, 26, 43). However, in the present study the haemodynamic responses were not significantly different between exercising conditions, nor when compared to a usual care HD session (CON-HD). Therefore, responses to BFRE can be considered similar to what would typically be expected from traditional intradialytic aerobic exercise, and not devoid from usual care HD. It is important to note that the present study was powered to assess changes in SBP in response to exercise and, due to the lack of prior data examining BFRE among dialysis patients, the study may not be powered to detect the differences between conditions.

The US National Kidney Foundation's Kidney Disease Outcomes Quality Initiative guidelines define IDH as a decrease in SBP $\geq$ 20 mmHg or MAP $\geq$ 10 mmHg with accompanying symptoms (17). However, the potency of various IDH definitions suggest that absolute thresholds of SBP < 90 mmHg for those with pre-HD SBP < 160 mmHg, and SBP < 100 for those with pre-HD SBP > 160 mmHg display more robust associations with mortality (17). In the present study there were only two occasions where such readings were accompanied by symptoms of hypotension, both of which we report as adverse events, and each specifically aligned with abnormally high relative prescribed UF for each patient. However, the overall mean data from the present study indicates that neither the fall in systolic blood pressure or mean arterial pressure, nor the lowest absolute mean values for blood pressure measurements were representative of IDH. In addition, blood pressure data collected *post-hoc* from dialysis records suggested that all blood pressure measures returned to pre-exercise levels after the recovery period and prior to the conclusion of HD (Figure 3). When comparing the time-course changes in blood pressure measures across the HD sessions including exercise with the usual care HD data retrieved *post-hoc*, it appears that the mild overall reduction in blood pressure across the duration of HD was commonplace. Thus, the observed down-trend in blood pressure of HD sessions may be attributable to fluid removal during the treatment itself. Indeed, the instances of symptomatic IDH were similar in the present study between exercising HD runs and usual care HD runs, with 2 episodes of IDH occurring among 40 intradialytic exercise sessions and 3 episodes of IDH occurring among the data from 40 usual care HD sessions collected *post-hoc*.

Alongside haemodynamic responses to BFRE, it is equally important to ensure that BFRE does not impact the efficacy of the HD treatment itself. In the present study the differential between prescribed UF and nett UF achieved was no different following any of the intradialytic exercise conditions compared with the same patients' usual care HD sessions. This was also true for the dialysis machine Kt/V values, which were no different during exercising HD sessions compared with usual care HD sessions, and all also exceeded recommended UF targets of 1.4 per HD session (24). This suggests that blood flow is sufficiently maintained during BFRE to ensure that the process of ultrafiltration was maintained, likely mediated by the mechanical pump facilitated by repeated muscular contractions during exercise (i.e. skeletal muscle pump).

The absence of any main effects for condition across all haemodynamic measures in the present study suggests that neither the application of blood flow restriction to the exercise, nor whether exercise was completed '*on*' or '*off*' HD significantly affected the response. Similarly, that none of the exercising conditions required modifications to UF nor affected dialysis adequacy (Kt/V), is a positive indicator that utilising BFRE intradialytically does not impede the treatment fundamentally required by patients undergoing HD. Therefore, it does not appear that aerobic BFRE should be considered any less suitable from a haemodynamic perspective compared with traditional exercise regimens recommended for patients with ESKD. Undertaken chronically, BFRE may in fact be preferable if it can provide greater enhancement to muscle size, strength and physical function among patients with ESKD, although this requires further research.

The perceptual responses during both BFRE conditions were significantly higher than the non-BFRE condition. However, both perceived effort and perceived discomfort were still lower than common perceptual responses to moderate-to-high intensity non-BFRE with resistance training, which is considered a safe mode of exercise in this population (7, 37, 50). Furthermore, previous studies have highlighted that perception of effort and discomfort with BFRE subsides with repeated use of the technique, approaching that of equivalent non-BFRE (10, 36). With such a reduction in perceptual responses following repeated use of BFRE, it seems unlikely that BFRE would dissuade participation in a training program or adversely affect exercise adherence beyond what is already seen among patients with ESKD.

Recommendations and Clinical Implications

Future studies utilising this exercise modality would benefit from a simpler, and more practical exercise equipment set up, whereby participants can remain in their normal seated position during HD. This may involve the use of commercial pedal sets which are able to be fitted to the dialysis chair, or customised cycle ergometers that can be positioned in front of the dialysis chair more easily. This may also reduce some patient discomfort caused by a lack of postural support in the present study.

Additionally, although diabetes is the most frequent underlying comorbidity among ESKD, only two participants in the present study had diabetes. As there is potential for blood flow restriction to elicit a metabolic response, future studies utilising BFRE among dialysis patients could provide additional insight by examining blood glucose and lactate responses.

Given the established capabilities for chronic BFRE training to increase muscle size, strength and physical function over a non-blood flow restriction equivalent among other populations (10, 46), it has the potential to be a valuable adjunct to essential medical treatment among populations such as patients with ESKD who are contraindicated to or unlikely to participate in exercise of sufficient intensity to achieve these beneficial musculoskeletal adaptations.

Conclusion

The present study supports the notion that blood flow restriction aerobic exercise is a tolerable and viable alternative mode of exercise for patients with ESKD. While perceived to be more challenging, the haemodynamic response to blood flow restriction aerobic exercise suggests that there is no greater cardiovascular stress than equivalent aerobic exercise without blood flow restriction. Similarly, the technique did not appear to have any detrimental effect on the adequacy of the HD treatment itself. Therefore, our demonstration of the haemodynamic response and tolerability of blood flow restriction exercise as a technique is a meaningful step towards improving the physical outcomes for ESKD patients.

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Disclosures

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Table 1. Participant characteristics.

Age (years)	61 ± 13
HD Vintage (years)	5.6 ± 3.7
Base weight (kg)	68.23 ± 15.51
Resting brachial SBP (mmHg)	137 ± 14
Limb Occlusion Pressure (mmHg)	223 ± 17
BFRE cuff pressure (mmHg)	112 ± 9
Comorbidities (*n*):	
• Diabetes	2
• Hypertension	4
• Glomerulonephritis	3
• Pancreatitis	1
• Hyperlipidemia	1
• Previous Stroke	1
• Duodenitis	1
• Gout	1
• Osteoarthritis	1
• Polycystic Kidney Disease	1
• Asthma	1
• Obstructive Sleep Apnoea	1
Pathology data:	
• Haemoglobin (g/L)	111.2 ± 10.9
• Potassium ()	5.2 ± 0.6
• URR (%)	75.2 ± 5.5
• Phosphate (mmol/L)	1.9 ± 0.6
• Albumin (g/L)	33.4 ± 4.5
• Parathyroid Hormone (pmol/L)	64.2 ± 35.0
Exercise load (W)	21 ± 6

Data are mean ± SD; **Abbreviations:** HD – Haemodialysis; SBP - Systolic blood pressure; BFRE – Blood flow restricted exercise.

Table 2. Mean values by condition (during haemodialysis only) for the prescribed ultrafiltration rate, nett ultrafiltration rate achieved, the difference between the prescribed and the nett achieved ultrafiltration rate, and dialysis adequacy.

Condition	Prescribed UF ($ml \cdot kg^{-1} \cdot h^{-1}$)	Nett UF achieved ($ml \cdot kg^{-1} \cdot h^{-1}$)	Δ UF (prescribed – nett) ($ml \cdot kg^{-1} \cdot h^{-1}$)	Kt/V
CON-HD	6.18 ± 0.81	5.53 ± 0.84	0.65 ± 0.34	1.6 ± 0.06
noBFRE-HD	5.53 ± 0.84	5.27 ± 0.79	0.26 ± 0.18	1.53 ± 0.08
BFRE-HD	6.02 ± 0.93	5.6 ± 0.86	0.42 ± 0.22	1.51 ± 0.06

Data are mean ± SD; **Abbreviations:** UF – Ultrafiltration rate; Kt/V – value for dialysis adequacy; CON-HD – non-exercising usual care haemodialysis; noBFRE-HD – non-blood flow restricted exercise performed during haemodialysis; BFRE-HD – blood flow restricted exercise performed during dialysis.

Figure Legends

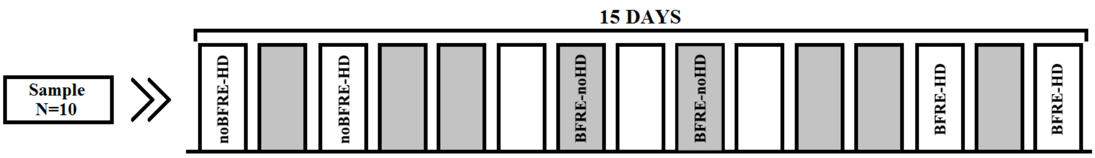

Figure 1: Study design. Timing of exercise sessions. *Abbreviations: noBFRE-HD – Non-blood flow restriction intradialytic cycling; BFRE-noHD – Blood flow restriction cycling off-haemodialysis; BFRE-HD – Blood flow restriction intradialytic cycling; Shaded blocks indicate non-dialysis day.*

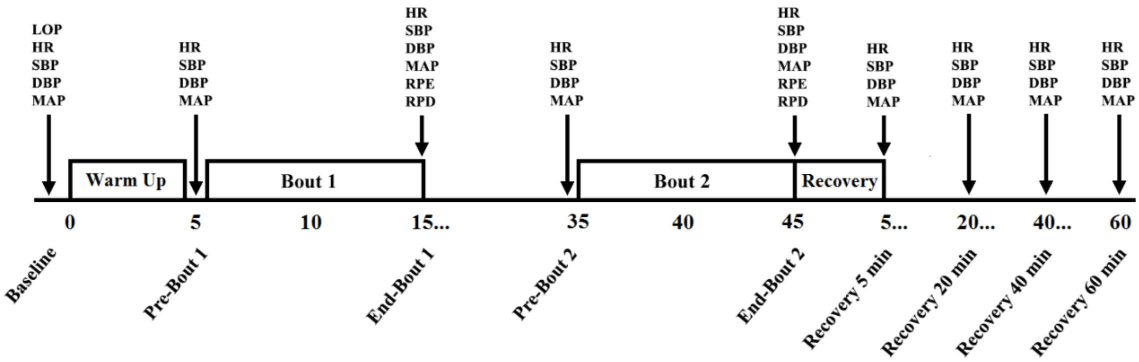

Figure 2: Single session timeline. Timing of measures indicated on the single session timeline. *Abbreviations: LOP – Limb occlusion pressure; HR – Heart rate; SBP – Systolic Blood pressure; DBP – Diastolic Blood pressure; MAP – Mean arterial pressure; RPE – rating of perceived exertion; RPD – rating of perceived discomfort.*

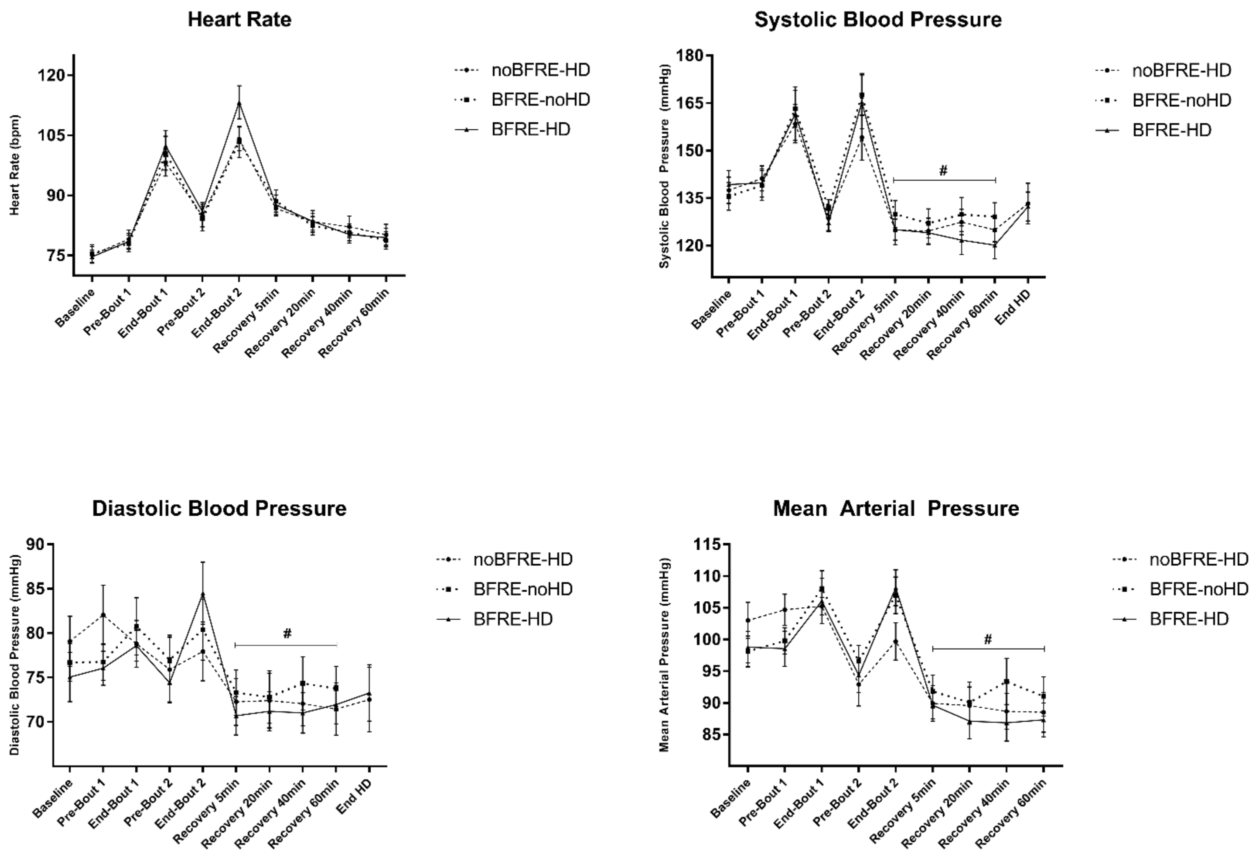

Figure 3: Haemodynamic responses to both blood flow restriction, and non-blood flow restriction exercise among patients on dialysis. Figures representative of changes in a) Heart rate, b) Systolic blood pressure, c) Diastolic blood pressure, and d) Mean arterial pressure. # = *significantly different to baseline (P < 0.001).*

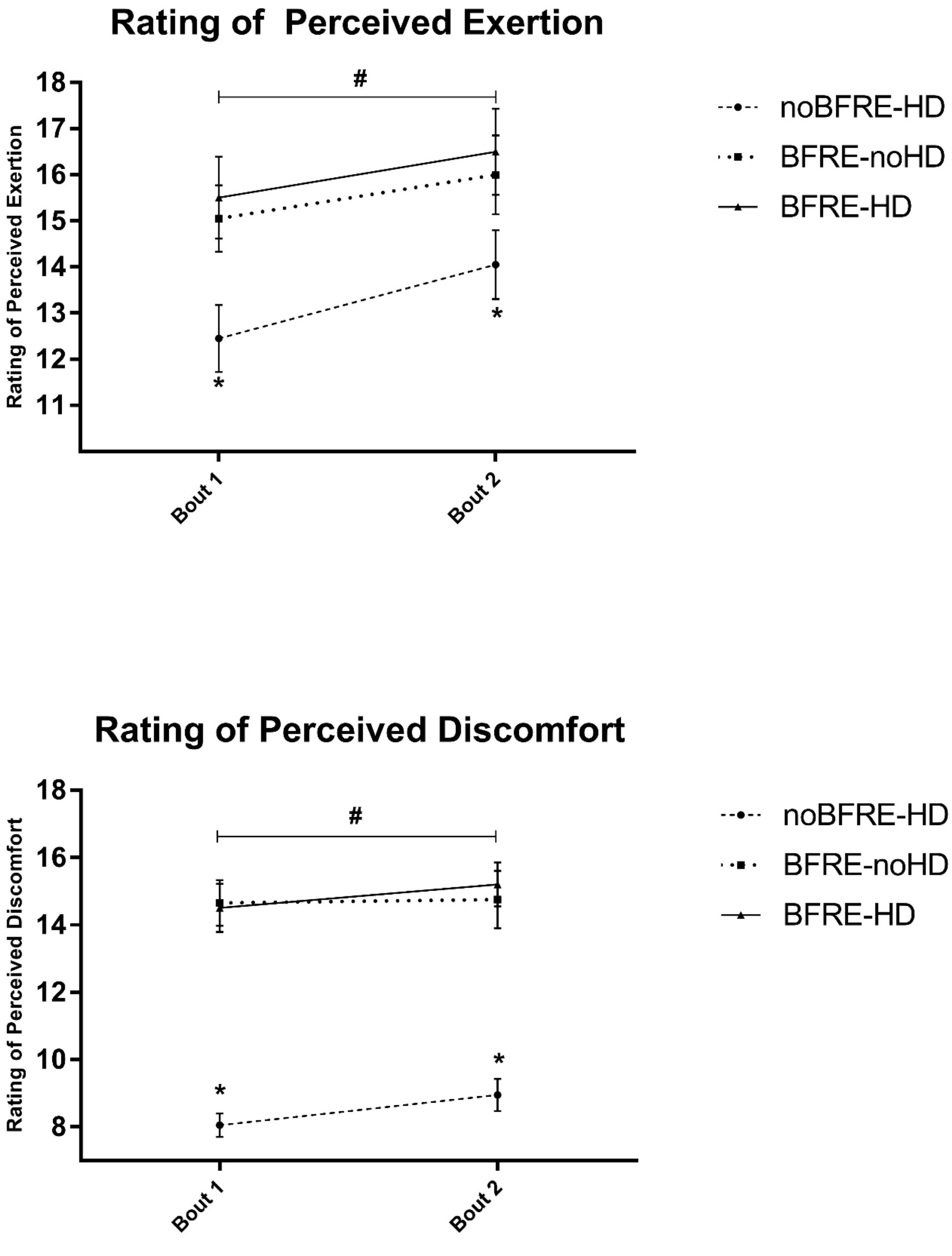

Figure 4: Perceptual responses to both blood flow restriction, and non-blood flow restriction exercise among patients on dialysis. Figures representative of a) rating of perceived exertion, and b) rating of perceived discomfort immediately following each exercise bout within a session. # = *Exercise bout 2 significantly different from bout 1 (P < 0.001).*