Refining safety considerations for intradialytic blood flow restriction exercise. Commentary on “Concerns on the application of blood-flow restriction resistance exercise and thrombosis risk in hemodialysis patients”

Clarkson, Matthew J (2024) Refining safety considerations for intradialytic blood flow restriction exercise. Commentary on “Concerns on the application of blood-flow restriction resistance exercise and thrombosis risk in hemodialysis patients”. Journal of Sport and Health Science. ISSN 2095-2546

HOSTED BY

ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

Journal of Sport and Health Science 00 (2024) 1−2

Commentary

Refining safety considerations for intradialytic blood flow restriction exercise. Commentary on “Concerns on the application of blood-flow restriction resistance exercise and thrombosis risk in hemodialysis patients”

Matthew J. Clarkson *

Institute for Health and Sport, Victoria University, Melbourne, VIC 8001, Australia

Received 26 January 2024; Accepted 10 March 2024

I read with great interest the article “Concerns on the application of blood flow restriction resistance exercise and thrombosis risk in hemodialysis patients” by Corrêa et al.[1] The study presents complementary data from a previous randomized controlled trial,[2] exploring the application of intradialytic blood flow restriction exercise for hemodialysis patients. Importantly, Corrêa et al.[1] further refine our understanding of important safety considerations to screen for when applying blood flow restriction exercise among hemodialysis patients. These include D-dimer thresholds smaller than the current clinically acceptable range (200−400 ng/mL), recent cardiovascular events, hemodialysis time, fasting blood glucose levels, age, and recent comorbidities or concurrent medical interventions (collectively termed “intercurrents”).[1] As intradialytic blood flow restriction exercise has only been explored within the last 5 years,[3] no definitive patient selection criteria exist. To adequately highlight the importance of these findings, it is necessary to consider the compelling need for exercise among hemodialysis patients and the rationale for blood flow restriction exercise specifically.

Chronic kidney disease presentations commonly include comorbidities such as hypertension, diabetes mellitus, cardiovascular disease, and metabolic syndrome.[4] Thus, patients living with chronic kidney disease display a high prevalence of physiological impairments. Hemodialysis patients specifically, display the highest rate of physical inactivity among patients living with chronic kidney disease or renal transplant recipients,[5] worsening with increased hemodialysis vintage. The catabolic state induced by physical inactivity causes impairments to cardiorespiratory fitness, muscle strength and mass, and neuromuscular function.[5] This is further exacerbated by pathology-related uremia, inflammation, and dietary restrictions.[5] Hemodialysis itself further alters protein metabolism, affects circulatory protein concentrations, increases resting energy expenditure, and increases inflammation.[6] The result is that hemodialysis patients display a high prevalence of sarcopenia and/or cachexia, as well as some of the lowest cardiorespiratory fitness among all chronic disease populations (peak oxygen uptake: 18−19 mL/kg/min).[5] This is notable as a peak oxygen uptake of 14−18 mL/kg/min in otherwise healthy older adults is acknowledged as a threshold below which independence is challenged.[7] The muscle mass, strength, and function loss related to sarcopenia and cachexia is a major limiter for performance of activities of daily living.[5]

Despite a clear implication that physical activity can counteract or at least temper the physical decline of hemodialysis patients reported above, several behavioral, pathophysiological, and logistical factors contribute to a degenerative cycle of inactivity and declining physical function.[5] Reported fatigue, low exercise self-efficacy, low motivation, low exertional tolerance, and being time-poor due to time spent on dialysis, attending medical appointments, and extended travel between these engagements are common barriers to physical activity among hemodialysis patients.[5,8] It is for these reasons that intradialytic blood flow restriction exercise was first posited as a novel modality that may be suitably aligned with the needs of hemodialysis patients.[9,10]

Blood flow restricted resistance training such as that in the study by Corrêa et al.[1] involves applying external pressure with an inflatable cuff to the proximal aspect of the active limbs.[11] Compression of the vasculature beneath the cuff partially restricts arterial blood flow to the limb and impedes venous return.[11] The technique achieves greater training adaptations to load-matched non-blood flow restricted resistance training, and similar adaptations to conventional high-load resistance training, despite using only 30%−50% of the training load.[3,11] As such, it imposes less mechanical stress on joint structures,

Peer review under responsibility of Shanghai University of Sport.

* Corresponding author.

E-mail address: matthew.clarkson@vu.edu.au

https://doi.org/10.1016/j.jshs.2024.03.005

similar or reduced metabolic and oxidative stress, and improved autonomic cardiac function compared with conventional resistance training.[3,8] Thus, blood flow restriction exercise poses greater "value" for time spent exercising at a low intensity, appealing to populations contraindicated or unwilling to engage with high-intensity resistance training. Given the reported barriers to exercise for hemodialysis patients,[5] this is a strong rationale for blood flow restriction exercise in this population, providing that patient safety is assured.

A major barrier to the implementation of blood flow restriction exercise among hemodialysis patients is the paucity of research which explore its application. The few studies which have, have largely focused on training adaptations (muscle strength and size, endurance, and physical function), basic hemodynamic responses (blood pressure and heart rate), hemodialysis adequacy (Kt/V), and urea reduction ratio.[9,10,12,13] Assessments of hemodynamic responses among these studies somewhat assuage common safety concerns about a heightened exercise pressor reflex with blood flow restriction exercise.[3,11] However, another significant safety consideration is thrombus formation risk.[11] Notably, thrombogenic factors are present in greater concentrations among hemodialysis patients.[3] Some studies have examined markers of thrombosis risk following blood flow restriction exercise in clinical populations, including older adults[14,15] and ischemic heart disease.[16] These all found that blood flow restriction exercise did adversely increase coagulation factors such as D-dimer, fibrin degradation product, or creatine kinase, but not above clinically acceptable threshold.[14–16] However, Corrêa et al.[1] are the first to explore thrombosis risk with blood flow restriction exercise in hemodialysis patients. They showed elevations in D-dimer post-exercise, which in patients with borderline high D-dimer levels (400–490 ng/mL), elevated patient D-dimer levels above the clinically acceptable range. Subsequently, Corrêa et al.[1] make apt recommendations for future studies exploring blood flow restriction exercise among hemodialysis patients to set a pre-exercise D-dimer level of 400 ng/mL, lower than the commonly accepted cutoff (500 ng/mL). They also identify a need to screen for and take greater caution with patients who have experienced recent cardiovascular events or other intercurrents, patients with longer hemodialysis vintage, high blood glucose levels, patients taking citrate, older patients, and higher inflammatory markers, as these increased risk of elevated D-dimer levels.[1]

In summary, Corrêa et al.[1] adds to a limited body of research exploring the physiological effects of blood flow restriction exercise among hemodialysis patients. This study reinforces that blood flow restriction exercise is safe in this population and provides guidance for future studies to better define patient suitability.[1] However, the evidence in this niche area remains small. Future studies must continue to build upon this progress to affirm the suitability of blood flow restriction exercise as a useful tool for improving hemodialysis patient outcomes.

Competing interests

The author declares that he has no competing interests.

References

1. Corrêa HL, Deus LA, Nascimento DDC, et al. Concerns on the application of blood-flow restriction resistance exercise and thrombosis risk in hemodialysis patients. *J Sport Health Sci*. 2024. doi:10.1016/j.jshs.2024.02.006. [Epub ahead of print].
2. Corrêa HL, Moura SRG, Neves RVP, et al. Resistance training improves sleep quality, redox balance and inflammatory profile in maintenance hemodialysis patients: A randomized controlled trial. *Sci Rep* 2020;**10**:11708. doi:10.1038/s41598-020-68602-1.
3. Rolnick N, de Sousa Neto IV, da Fonseca EF, Neves RVP, Rosa TDS, Nascimento DDC. Potential implications of blood flow restriction exercise on patients with chronic kidney disease: A brief review. *J Exerc Rehabil* 2022;**18**:81–95.
4. Disease Kidney. Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int* 2020;**98**(Suppl. 4): S1–115.
5. Zelle DM, Klaassen G, Van Adrichem E, Bakker SJ, Corpeleijn E, Navis G. Physical inactivity: A risk factor and target for intervention in renal care. *Nat Rev Nephrol* 2017;**13**:152–68.
6. Martins VS, Adragão T, Aguiar L, et al. Can an intradialytic snack model compensate the catabolic impact of hemodialysis? *Clin Nutr ESPEN* 2021;**42**:292–8.
7. Shephard RJ. Maximal oxygen intake and independence in old age. *Br J Sports Med* 2009;**43**:342–6.
8. de Deus LA, Neves RVP, Corrêa HL, et al. Improving the prognosis of renal patients: The effects of blood flow-restricted resistance training on redox balance and cardiac autonomic function. *Exp Physiol* 2021;**106**: 1099–109.
9. Clarkson MJ, Brumby C, Fraser SF, McMahon LP, Bennett PN, Warmington SA. Hemodynamic and perceptual responses to blood flow-restricted exercise among patients undergoing dialysis. *Am J Physiol Renal Physiol* 2020;**318**:F843–50.
10. Cardoso RK, Araujo AM, Del Vechio FB, et al. Intradialytic exercise with blood flow restriction is more effective than conventional exercise in improving walking endurance in hemodialysis patients: A randomized controlled trial. *Clin Rehabil* 2020;**34**:91–8.
11. Patterson SD, Hughes L, Warmington S, et al. Blood flow restriction exercise: considerations of methodology, application, and safety. *Front Physiol* 2019;**10**:533. doi:10.3389/fphys.2019.00533.
12. Dias EC, Orcy R, Antunes MF, et al. Intradialytic exercise with blood flow restriction: Something to add to hemodialysis adequacy? Findings from a crossover study. *Hemodial Int* 2020;**24**:71–8.
13. Nobre R, Cardoso RK, Araujo AM, et al. Is it safe for hemodialysis patients to seek gains with less pain? Acute hemodynamic response to intradialytic blood flow restriction training. *Int J Exerc Sci* 2022;**15**: 434–41.
14. Fry CS, Glynn EL, Drummond MJ, et al. Blood flow restriction exercise stimulates mTORC1 signaling and muscle protein synthesis in older men. *J Appl Physiol (1985)* 2010;**108**:1199–209.
15. Yasuda T, Fukumura K, Uchida Y, et al. Effects of low-load, elastic band resistance training combined with blood flow restriction on muscle size and arterial stiffness in older adults. *J Gerontol A Biol Sci Med Sci* 2015;**70**:950–8.
16. Madarame H, Kurano M, Fukumura K, Fukuda T, Nakajima T. Haemostatic and inflammatory responses to blood flow-restricted exercise in patients with ischaemic heart disease: A pilot study. *Clin Physiol Funct Imaging* 2013;**33**:11–7.

Please cite this article as: Matthew J. Clarkson, Refining safety considerations for intradialytic blood flow restriction exercise. Commentary on "Concerns on the application of blood-flow restriction resistance exercise and thrombosis risk in hemodialysis patients", Journal of Sport and Health Science (2024), https://doi.org/10.1016/j.jshs.2024.03.005