

Research article

Metabolic and cardiovascular responses to upright cycle exercise with leg blood flow reduction

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Abstract

The purpose of this study was to examine the metabolic and cardiovascular response to exercise without (CON) or with (BFR) restricted blood flow to the muscles. Ten young men performed upright cycle exercise at 20, 40, and 60% of maximal oxygen uptake, VO_{2max} in both conditions while metabolic and cardiovascular parameters were determined. Pre-exercise VO_2 was not different between CON and BFR. Cardiac output (Q) was similar between the two conditions as a 25% reduction in stroke volume (SV) observed in BFR was associated with a 23% higher heart rate (HR) in BFR compared to CON. As a result rate-pressure product (RPP) was higher in the BFR but there was no difference in mean arterial pressure (MAP) or total peripheral resistance (TPR). During exercise, VO_2 tended to increase with BFR (~10%) at each workload. Q increased in proportion to exercise intensity and there were no differences between conditions. The increase in SV with exercise was impaired during BFR; being ~20% lower in BFR at each workload. Both HR and RPP were significantly greater at each workload with BFR. MAP and TPR were greater with BFR at 40 and 60% VO_{2max} . In conclusion, the BFR employed impairs exercise SV but central cardiovascular function is maintained by an increased HR. BFR appears to result in a greater energy demand during continuous exercise between 20 and 60% of control VO_{2max} ; probably indicated by a higher energy supply and RPP. When incorporating BFR, HR and RPP may not be valid or reliable indicators of exercise intensity.

Key words: Aerobic exercise, doppler echocardiography, apparent exercise intensity, occlusion.

Introduction

Concurrent improvements in muscular strength and aerobic capacity by a single mode of exercise have been achieved after high-intensity, long-duration exercise training. For example, recumbent stepper training (75% of maximal heart rate reserve) improved maximal oxygen uptake (VO_{2max}) and muscle strength in middle-aged adults (Hass et al., 2001). Furthermore, high-intensity (90% of VO_{2max}) interval cycle training increased VO_{2max} and isokinetic knee joint strength (Tabata et al., 1990). While significant improvements in muscular strength were observed in these studies, neither demonstrated significant muscular enlargement, leading to the conclusion that the increased strength was due mainly to neural adaptations. In contrast, low-intensity walk training (50 $m \cdot min^{-1}$) combined with leg blood flow reduction (BFR)

results in both thigh muscle hypertrophy and increased muscular strength in young (Abe et al., 2006) and elderly (Abe et al., 2010) individuals. What remains to understand is if low-intensity walk training with BFR, which elicits muscle enlargement (unlike the studies reviewed), would also impact the metabolic and cardiovascular responses to continuous exercise leading to predictive conclusions about training effects on VO_{2max} .

The novelty of BFR appears to be the unique combination of venous blood volume pooling and restricted arterial blood inflow. While this clearly impacts the active muscle(s), this vascular occlusion and BFR would certainly impact venous return and the cardiovascular response to exercise. Further, the combination of BFR with low-intensity resistance exercise appears to alter muscle activation patterns and increase the apparent intensity of exercise (Yasuda et al., 2008; 2009) such that 20% one-repetition maximal (1-RM) intensity exercise in combination with BFR approximates muscle activation patterns observed during 60-70% 1-RM training without external compression and BFR. We concluded that apparent altered exercise intensity is the basis for the observed adaptations in muscle mass and muscular strength with minimal external loading and which are equivalent to those observed at higher training intensities (e.g. 60-70% 1-RM; Abe et al., 2005; Fujita et al., 2008; Takarada et al., 2000). Hence, the present question includes whether BFR alters the apparent exercise intensity, and therefore the metabolic demand, of continuous exercise (e.g. walking, cycling, etc) as observed with resistance exercise. Indeed in a previous study (Abe et al., 2006) we reported significantly greater VO_2 (14%) and HR (20%) during low-intensity walking with BFR than that observed without BFR which indicate a greater metabolic demand. However, it is unknown whether the relationship between exercise intensity, metabolic demand and cardiovascular response is altered by BFR. Therefore, the purpose of the present study was to examine the metabolic (VO_2) and cardiovascular responses to continuous exercise on a cycle ergometer with BFR at varying intensity of exercise (% VO_{2max}) to ascertain if BFR alter the apparent intensity and metabolic demand of exercise.

Methods

Subjects

Ten healthy young males volunteered to participate in the

study. All subjects were habitually participating in recreational sports and exercise at the university. The subjects were informed of the procedures, risks, and benefits, and signed an informed consent documents before participation. The study was conducted according to the Declaration of Helsinki and was approved by the Ethics Committee for Human Experiments of the University of Tokyo, Japan.

Table 1. Physical characteristics of the subjects.

Variable	Mean (\pm SD)
Age, yrs	22.6 (1.3)
Height, m	1.74 (.05)
Weight, kg	71.0 (10.5)
BMI, kg·cm ⁻²	23.3 (2.6)
VO _{2max} , l·min ⁻¹	3.44 (.46)
V O _{2max} , ml·kg ⁻¹ ·min ⁻¹	49.2 (7.8)
Maximal heart rate, bpm	192 (6)

BMI, body mass index

Exercise protocol

Two weeks prior to the study VO_{2max} was determined in all subjects. Subjects then participated in two cycle ergometer exercise tests with and without BFR in random order on separate days (one day between trials). The subjects reported to the laboratory in the morning (8:00-9:00 am) after a 12 hr fast. Subjects were instrumented and rested in the seated position. Following 30-min of rest respiratory and cardiovascular data was collected. Immediately following the resting measurements, subjects performed exercise at 20%, 40%, and 60% of VO_{2max}. Exercise was continuously performed in 4-min stages at each workload. Pedal frequency was held at 70 rpm on a cycle ergometer (Monark, model-874E).

VO_{2max} determination

To establish the relationship between steady-state VO₂ and the exercise intensity for each subject, the following pretests were done. VO₂ during 8 min cycling exercise at a constant exercise intensity was determined at 8 or more different intensities below the maximal oxygen uptake (VO_{2max}). The pedal frequency was kept at 70 rpm. The exercise intensity was increased by 13.7-34.3 W. The subjects were allowed to rest for approximately 10 minutes between these exercise bouts. Any subject who did not feel completely recovered to perform at the next higher exercise intensity was allowed more rest.

After a linear relationship between exercise intensity and steady state VO₂ was determined for each subject, VO₂ during several bouts of exercise at higher intensities was measured in order to ensure the leveling-off of the VO₂. In these bouts, since some subjects could not keep the exercise intensity for the entire 8 min, VO₂ was measured every 30 s from the 3rd to 5th minute of exercise to the last. In these cases, the highest VO₂ value was adopted as the VO₂ at that intensity. VO_{2max} was determined by the leveling-off criterion and a leveling-off of VO₂ was observed in all subjects. Then, the exercise intensities corresponding to 20%, 40%, and 60% VO_{2max} were estimated individually by interpolating the linear relationship between VO₂ and the exercise intensity.

Blood flow restriction

Subjects wore pressure belts (KAATSU Master, Sato Sports Plaza, Tokyo, Japan) on both legs during BFR test. Prior to the test, the subjects were seated on a chair and the belt air pressure was repeatedly set (20 s) and then released (10 s) from initial (140 mmHg) to final (200 mmHg) pressure every 20 mmHg. The final belt pressure (testing pressure) was 200 mmHg.

Cardiovascular measurements

Stroke volume (SV) was assessed by the Doppler echocardiographic technique (Rowland and Obert, 2002) using an ultrasound apparatus (Toshiba Model SSH-140A, Tokyo, Japan). A 1.9 MHz continuous wave transducer was directed inferiorly from the suprasternal notch to assess velocity of blood flow in the ascending aorta. The areas beneath highest and clearest velocity curves were traced offline to obtain the average velocity-time integral. The aortic cross-sectional area was calculated from the aortic diameter at the sinotubular junction, recorded at rest, and this value was multiplied by the average velocity-time integral to estimate SV. HR was continuously monitored (Polar HR monitor). Cardiac output (Q) was calculated as the product of SV and HR. All data were averaged over 15 sec and data obtained for the last 15 sec of last minute of the each stage were used for data analysis. Reproducibility of this method in our laboratory was 3%.

Systolic and diastolic arterial pressures (SAP and DAP, respectively) were measured from the upper left arm by using a sphygmomanometer in the last minute of each stage. Mean arterial blood pressure (MAP) was calculated from $MAP = DAP + (SAP - DAP)/3$. Total systemic peripheral resistance (TPR) was calculated by MAP / Q (mmHg·min·L⁻¹). Rate-pressure product (RPP) was calculated by multiplying HR by SAP.

Respiratory measures

Expired gas was collected continuously (in 60-sec periods) by Douglas bag during both rest and exercise to measure oxygen uptake. The O₂ and CO₂ fractions in the expired gas were determined by a paramagnetic O₂ analyzer and an infrared CO₂ analyzer, respectively (Vmax29C, Sormedics Corporation, California, USA). The expired gas volume was measured by a dry gas meter (Shinagawa Seisakusho, Tokyo, Japan). Heart rate (HR) was measured using a portable monitor (Polar, model FS3c). Arterial-venous oxygen (a-v O₂) difference was calculated by VO_2 / Q .

Statistical analysis

Results are expressed as means (SD) for all variables. Statistical analysis was performed by a two-way ANOVA with repeated measures [trial (BFR and CON) x exercise intensity (20%, 40%, and 60% of VO_{2max})]. Post hoc testing was performed by a one-way ANOVA. Differences were considered significant if *P* value was less than 0.05.

Results

Subject characteristics are given in Table 1. Pre-exercise - There were no differences in VO₂ (Table 2), Q (Figure 1),

Table 2. Blood pressure and VO₂ response to upright bicycle exercise combined with (BFR) or without (CON) blood flow reduction. Data are means (±SD).

	Exercise intensity (% VO _{2max})			
	Rest	20%	40%	60%
Mean arterial pressure (MAP, mmHg)				
CON	85 (10)	86 (13)	88 (9)	92 (9)
BFR	91 (10)	96 (8)	106 (11)	118 (8)
Difference	6	10	18 **	26 **
Systolic arterial pressure (SAP, mmHg)				
CON	116 (11)	124 (13)	135 (13)	147 (7)
BFR	121 (9)	142 (15)	163 (17)	189 (17)
Difference	5	18 *	28 **	42 **
Diastolic arterial pressure (DAP, mmHg)				
CON	70 (10)	67 (16)	64 (13)	64 (12)
BFR	76 (11)	73 (7)	78 (11)	83 (8)
Difference	6	6	14	19 *
Rate-pressure product (HR * SAP)				
CON	7532 (1795)	11154 (1531)	15219 (2048)	19767 (2491)
BFR	9684 (2070)	14755 (2551)	22437 (5166)	30510 (5297)
Difference	2152 *	3601 **	7218 **	10743 **
Total systemic peripheral resistance (MAP / Q; mmHg min·L⁻¹)				
CON	19.7 (6.2)	11.4 (2.8)	8.3 (1.4)	7.4 (1.4)
BFR	23.1 (7.7)	14.1 (3.0)	10.6 (2.0)	9.9 (1.9)
Difference	3.4	2.7	2.3 **	2.5 **
VO₂ (ml min⁻¹)				
CON	217 (38)	806 (173)	1421 (197)	2000 (281)
BFR	260 (46)	879 (213)	1546 (224)	2208 (299)
Difference	43	73	125	208
a-v O₂ difference (VO₂ / Q; ml L⁻¹)				
CON	-	107 (26)	136 (32)	163 (40)
BFR	-	129 (40)	155 (42)	186 (46)
Difference	-	22	19	23
Q (L)				
CON	-	7.8 (1.6)	10.8 (2.0)	12.7 (2.4)
BFR	-	7.1 (1.3)	10.4 (2.1)	12.3 (2.4)
Difference	-	.7	.4	.4

a-v O₂ difference, arterial-venous oxygen difference; VO₂, oxygen uptake; Q, cardiac output; HR, heart rate. Significant differences between BFR and CON: * p < 0.05, ** p < 0.01.

MAP or TPR (Table 2) between CON and BFR prior to exercise (Table 1). SV was lower (25%; Figure 1) while HR (23%; Figure 1) and RPP (32-54%; Figure 2) were significantly greater in BFR.

Exercise - VO₂ increased linearly with exercise intensity in both groups but tended to be greater in BFR (60%VO_{2max}; 10% [p=0.12]; Table 2). Although linear, the relationship between VO₂ and exercise intensity were not parallel between BFR and CON (Figure 3). Consequently VO₂ during BFR at 40 and 60% of VO_{2max} corresponded to about 45 and 70% of VO_{2max} of CON. Q increased linearly with exercise intensity and was similar in BFR and CON (Figure 1). During exercise SV increased linearly from pre-exercise values and peaked at 40% VO₂ in CON (Figure 1). BFR resulted in a similar pattern of change in SV peaking at 40% VO₂; however, pre-exercise differences were maintained during exercise as the values were 20% less than that observed during CON. HR (Figure 1), SAP (Table 2), and RPP (Figure 2) increased linearly with exercise intensity but were significantly greater at each workload with BFR. The relationship between RPP and exercise intensity for BFR and CON are not parallel (Figure 2); e.g. RPP at approximately 40% VO_{2max} in BFR correspond to ~80% VO_{2max} in CON (Figure 2). DAP was significantly greater only at 60% VO_{2max}

with BFR (Table 2). Thus, MAP and TPR were similar at 20% VO_{2max}, but significantly greater at 40 and 60% VO_{2max} in BFR (Table 2).

Discussion

The major finding of the present study was that VO₂ during submaximal BFR exercise on a cycle ergometer is tended to elevate (~10%) compared to CON exercise. This result is consistent with previous observations that mean VO₂ was significantly greater (14%) during low-intensity walking with BFR compared to during walking without BFR (Abe et al. 2006). In the previous study the walking speed was set at 50 m min⁻¹ and the metabolic demand was slightly greater in BFR (20% of VO_{2max}) than in CON (17% of VO_{2max}). The significance of this observation is that the typical response to reduced muscle blood flow would be premature fatigue and reduced VO₂ (Brechue et al., 1995; Kaijser et al., 1990; Lundgren et al., 1988; Timmons et al., 1996). Further, BFR appears to alter the relationship between exercise intensity and VO₂. While the relationship between exercise intensity and VO₂ was linear in both BFR and CON, it was not parallel between the groups. The difference in VO₂ between BFR and CON during very low intensity walking (~3%; Abe et

al. 2006) or cycling (~3%; Figure 3) is small. At 40% of $\dot{V}O_{2max}$ the differences are still minimal but are increased (~6%), whereas at 60% of $\dot{V}O_{2max}$ the differences are ~10% (Figure 3).

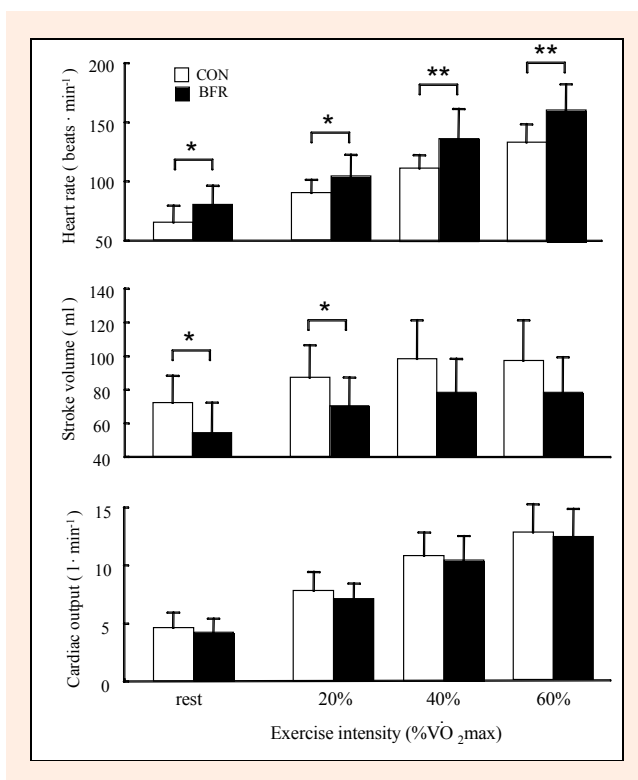


Figure 1. Cardiovascular response to upright bicycle exercise combined with (BFR) or without (CON) blood flow reduction. Significant differences between BFR and CON. * $p < 0.05$, ** $p < 0.01$.

The higher $\dot{V}O_2$ at a given workload, disproportionate increase in $\dot{V}O_2$ with increasing workload, and the RPP response (Figure 2; see discussion below) suggests that the energy demand and apparent exercise intensity is greater with BFR as compared to normal blood flow, especially greater than 40% $\dot{V}O_{2max}$. This is in agreement with previous work showing that exercise intensity during resistance exercise is apparently increased with BFR (Takarada et al. 2000; Yasuda et al. 2008; 2009). Muscle activation patterns (integrated EMG) during 20% one-repetition maximal 1-RM resistance exercise in combination with BFR approximate muscle activation patterns observed during 60-70% 1-RM training without external compression and BFR. Increased muscle activation during BFR is a consistent finding and may be related to maintenance of muscle force output (Bigland-Ritchie et al., 1986; Moritani et al., 1986; 1992), coordinated and integrated muscle chemoreflex (Takarada et al., 2000; Yasuda et al., 2008) and/or altered sensory feedback (Leonard et al., 1994). From these studies it is suggested that this apparent increase in exercise intensity during exercise with BFR may associate with the observed higher $\dot{V}O_2$ at a given workload in the BFR.

The apparent increase in exercise intensity and energy demand is being met by an increase in energy supply ($\dot{V}O_2$) despite the BFR. Since Q was equivalent at each exercise intensity and muscle blood flow is reduced (Iida

et al., 2007) the oxygen demand is being met by an increased a-v O_2 difference during BFR (15-20%, Table 2). Reduced blood supply is compensated by increased oxygen extraction to maintain $\dot{V}O_2$ (Strandell and Shepherd, 1967) or in the present case increased $\dot{V}O_2$ as long as the tissue oxygen levels remain above zero. This appears to be the case with BFR as venous PO_2 and oxygen saturation have been shown to be significantly reduced, compared to CON (venous PO_2 ~26 mmHg; Yasuda et al. 2010). These minimum values are consistent with previous studies (21 mmHg; Soller et al., 2007; 15-25 mmHg; Stringer et al., 1994) utilizing BFR during exercise, but are certainly still within the range of compensation for the reduced muscle blood flow.

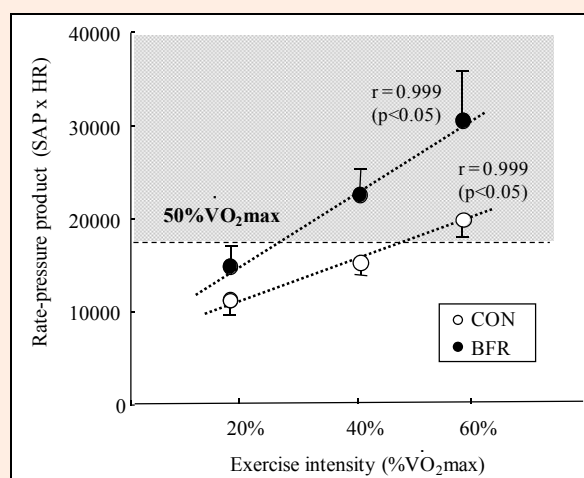


Figure 2. Relationships between exercise intensity and rate-pressure product (SAP x HR) in the control (CON) and blood flow reduction (BFR) conditions. Dashed line indicates the rate-pressure product at 50% of control $\dot{V}O_{2max}$.

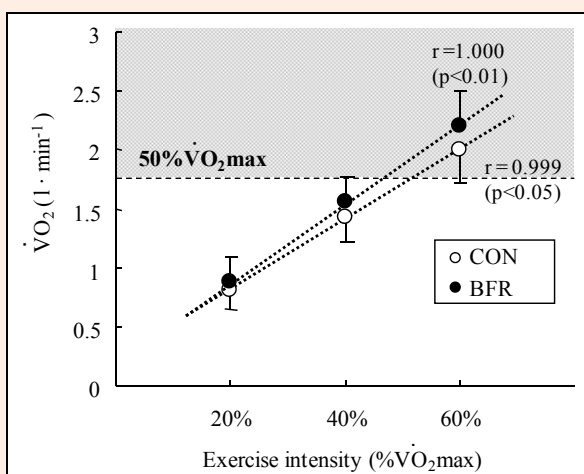


Figure 3. Relationships between exercise intensity and oxygen uptake ($\dot{V}O_2$) in the control (CON) and blood flow reduction (BFR) conditions. Dashed line indicates the $\dot{V}O_2$ at 50% of control $\dot{V}O_{2max}$.

The BFR technique produces a combination of venous blood volume pooling and restricted arterial blood inflow (~50% reduction; Iida et al., 2007). While this clearly impacts the active muscle(s), this vascular occlu-

sion appears to reduce venous return as the increase in SV with exercise and increasing intensity of exercise is impaired with BFR (Figure 1). This is consistent with a previously reported reduction in SV (~13%) when measured after a bout of resistance exercise (Takano et al., 2005). In contrast, however, our results show that SV was able to increase with exercise but to much lower levels than CON. Perhaps venous return is slightly augmented by the muscle pumping action during continuous cycle exercise, as compared to resistance exercise, allowing some venous return and a slight increment in SV observed with exercise. In the present case the impact of the impaired increase in SV on Q was minimal as an increase in HR at each workload fully compensated for the lower SV and Q was similar between BFR and CON (Figure 1). Importantly, the increase in HR (although disproportionate with intensity; see discussion below) is still well below maximal HR and thus, can compensate for the level of SV impairment observed up to 60% of VO_{2max} . Thus up to 60% of VO_2 max is a reasonable workload for training with BFR, however, the feasibility and applicability of workloads beyond 60% VO_{2max} with BFR remains to be determined.

During treadmill walking, HR and Q increase with a concomitant decrease in systemic total peripheral resistance so that there is only a small elevation in MAP or no measurable change (Bogaard et al., 1997). In the present study, MAP during CON exercise was similar between pre-exercise and low- and moderate-intensity exercise. Although Q was similar between groups, MAP was elevated during BFR, due mainly to increase in TPR. Undoubtedly the external compression cuff used to institute BFR is playing a role in the increased TPR. Further, serum noradrenaline concentration has been shown to increase significantly with BFR, compared to CON, during rest in the supine position (Iida et al., 2007) and slow walking (Abe et al., 2006). Thus, noradrenaline-induced vasoconstrictor responses likely play a role in the greater TPR (Watson et al., 1979).

Implications for training

Our results indicate that at an exercise intensity of 40% of VO_{2max} intensity exercise in the BFR condition corresponds to at 45% of VO_{2max} intensity in the normal flow condition. In the present scenario this corresponds to the minimum training stimulus necessary to evoke a change in VO_{2max} (Gaesser and Rich, 1984; Wenger and Bell, 1986). However, the typical training range is 60-80% VO_{2max} (American College of Sports Medicine, 1998), thus, an intensity of 55% VO_{2max} with BFR would appear to provide a more appropriate training stimulus approximating 65% of VO_{2max} . For improvement of aerobic capacity concurrently using BFR walk training, it may be predicted that brisk and/or uphill walk are needed as exercise intensity to stimulate the necessary training stimulus as 50 m min^{-1} slow walk only generated a 20% VO_{2max} exercise load.

Both HR and SAP, and consequently RPP, were greater at each workload with BFR. As was seen with VO_2 the increase in RPP with exercise intensity was linear in both BFR and CON, however, the relationships were not parallel. There was a much greater increment in

RPP with exercise intensity in BFR. When evaluating apparent exercise intensity by rate-pressure product (RPP), our result shows that the RPP at about 40% of VO_{2max} during BFR exercise corresponds to the RPP approximating 80% of VO_{2max} (Figure 2) during normal flow condition. Using only HR results in about a 20% overestimation of exercise intensity (Figure 1). Neither estimate of exercise intensity is supported by VO_2 data observed. Thus, HR and RPP may not be valid or reliable indicators of exercise intensity when incorporating BFR. More work concerning the relationship between exercise intensity and HR response or RPP during continuous exercise is needed.

Conclusion

In conclusion, the BFR technique employed impairs exercise SV but central cardiovascular function (Q) is maintained by an increased HR. BFR appears to result in a greater energy demand during continuous exercise between 20 and 60% of control VO_{2max} ; probably indicated by a higher energy supply (VO_2) and RPP. Adjustments in the peripheral metabolic (a-v O_2 difference) and central cardiovascular (HR) response to exercise permit the necessary oxygen and metabolite supply to meet the demand during BFR exercise at the exercise intensities investigated.

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Key points

- Blood flow reduction (BFR) employed impairs stroke volume (SV) during exercise, but central cardiovascular function is maintained by an increased heart rate (HR).
- BFR appears to result in a greater energy demand during continuous exercise between 20 and 60% of control VO_{2max}.
- Probably indicated by a higher energy supply (VO₂) and rate-pressure product (HR x systolic blood pressure).

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