CARDIOVASCULAR AND METABOLIC RESPONSES TO WALKING WITH AND WITHOUT LEG BLOOD FLOW REDUCTION

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ABSTRACT

Low-intensity walking with leg blood flow reduction has been shown to elicit a significant increase in skeletal muscle size and strength, and may also improve cardiovascular fitness. However, the cardiovascular and respiratory response to walking with blood flow reduction has not been explored. The purpose of this study was to examine the cardiovascular and metabolic responses during a graded maximum walking test and low-intensity walking exercise combined with (BFR) and without (CON) blood flow reduction. On two separate days (1 wk apart), 8 young men performed graded maximum walking test in both conditions (CON and BFR) to determine metabolic (VO_{2peak}, etc) and cardiovascular response to exercise. Following 4-6 days; subjects then performed 2 trials of low-intensity treadmill walking with and without BFR (60 minutes between trials). The submaximal exercise trials consisted of walking at 33 m/min with 4% grade for five 2-min bouts, with a 1-min rest between bouts. Impedance echocardiography as well as non-invasive blood pressure monitoring was used to obtain hemodynamic responses. Additionally, 6 young men performed treadmill walking (67 m/min at 0% grade) with and without BFR. During these experiments metabolic and hemodynamic responses were also measured with stroke volume (SV) being measured by ultrasound Doppler echocardiography. *Graded maximum walking test:* Vo_2 and heart rate (HR) during BFR were 11~16% and 16~20% greater, respectively (P<0.05 or P<0.01), compared to CON at all submaximal work, while the Vo_{2peak} during BFR (2.87 l/min, P<0.01) was 18% lower than that of the CON (3.51 l/min). Although there was no difference in systolic arterial pressure (SAP) between two conditions, the W_H (HR x SBP) during BFR was higher (P<0.05) compared to the CON. In the CON, the Vo_2 correlated linearly to the W_H in both individuals and mean values. The 50% of Vo_{2peak} corresponds to a W_H of 17226 in CON. *Low-intensity walking test (Impedance):* During BFR SV was significantly reduced (CON; 83.1±10.3 ml, BFR; 66.6±7.4 ml, p<0.05) throughout exercise, while Vo_2 and W_H were significantly (P<0.05) elevated during the latter half of exercise bout and the 5-exercise bout average compared to CON. The W_H of the 5-exercise bout average was 15652 for BFR and 12556 for CON. *Low-intensity walking test (Doppler):* During BFR SV was significantly reduced (CON; 84.9±19.3 ml, BFR; 70.0±17.3 ml, P<0.05) and Vo_2 and W_H were significantly (P<0.05) elevated during each exercise bout and the 5-exercise bout average compared to CON. The BFR employed impairs exercise SV but cardiac output is maintained by an increased HR during submaximal work, but apparently not at VO_{2peak} which was reduced during BFR. During slow walking with BFR (exercise intensity about 25% the BFR VO_{2peak}), the W_H (HR x SAP) did not reach the exercise intensity level of 50% VO_{2peak} which is recommended for improvement of cardiovascular fitness. To develop cardiovascular fitness by walking with BFR walk, exercise intensity of over 40% BFR VO_{2peak} may be required.

INTRODUCTION

A newly discovered method of muscular blood flow reduction (BFR) during exercise has been shown to elicit significant increases in skeletal muscle size and muscular strength using low-intensity training (20% of one repetition maximum; 3, 13). Perhaps even more astounding and intriguing are the significant improvements in skeletal muscle hypertrophy and muscular strength of knee extensors and flexors following slow walking with BFR in young (1) and elderly (3) subjects. Furthermore, significantly greater oxygen uptake (VO_2, 17%) and heart rate (20%) are observed during the

low-intensity treadmill walking with BFR compared to that of walking without BFR (1). The novelty of BFR training appears to be the unique combination of venous blood volume pooling and reduced arterial blood inflow (5). Takano et al. (12) has shown that after a low-intensity resistance exercise session with BFR, stroke volume (SV) decreased and heart rate (HR) increased without changes in cardiac output (Q). Therefore, BFR walk-induced higher HR observed in our recent study is most likely the consequence of inhibited venous return and subsequent lower SV. Consequently, increases in HR at the same systolic arterial pressure (SAP) during BFR may produce high mechanical stress on the heart, as indicated by a greater work of the heart (HR x SAP). Furthermore, the increased VO_2 observed during BFR walking (1) may be a result of increased arterial and mixed venous blood oxygen difference (a-v O_2 difference) as Q is not different between walking with and without BFR.

Thus, the benefit of BFR walking may include not only an anabolic response on muscular system (1, 3), but may also involve improvements in cardiovascular fitness. Such benefits of BFR walking on cardiovascular fitness may involve both an increased myocardial work load (SAP x HR) and greater whole body VO_2 (greater a-v O_2 difference at the same Q) at a lower intensity of exercise. However, the cardiovascular and metabolic responses to walking with BFR have not been explored. The purpose of this study was to examine the extent of cardiovascular and metabolic responses to graded maximum walking and submaximal walking exercise (about 20-30% exercise intensity), combined with and without BFR.

METHODS
Subjects.
Eight healthy male (age; 26.4±2.8 yrs, height; 1.73±0.04 m, body weight; 70.9±9.6 kg) volunteered to participate in the study. All subjects led active lives; however none had participated in a regular resistance/endurance training program for at least 1 yr prior to the study. The purpose, procedures, and risks of the study were explained to each subject prior to inclusion and all subjects gave written informed consent to participate in the study. The study was approved by the Ethics Committee for Human Experiments of the University of Tokyo, Japan.

Graded maximum walking test.
At least 4 hr after the meal, on two days about 1 wk apart, the $\dot{V}O_2$, $\dot{V}co_2$, and $\dot{V}_E$ during treadmill walking were measured using an automated metabolic monitor (Aeromonitor AE-300, Minato Medical Science, Tokyo, Japan), combined without (CON) and with BFR. The protocol consisted of warming up for 3 min at 50 m/min (at 0% grade). Then the speed was increased to 60, 80, and 100 m/min every 3 min. Once 100 m/min was reached, the slope was increased gradually every 4 min until exhaustion. The average of the last 1 min for the each stage was considered as steady-state values. The HR (Polar monitor, Kemele, Finland) and blood pressure (Minato, Tokyo) were recorded during steady state for each period. The criteria for reaching Vo_{2peak} test were: respiration exchange ratio (RER) > 1.00, HR > 85% percentile of age predicted maximum. In the maximum walking test with BFR, the subject became fatigued before the above criteria (RER was 0.95-0.98) due to leg muscle fatigue (RPE scale was over 19). Therefore, the highest VO_2 value was considered as VO_{2peak} for BFR trial.

Low-intensity walking exercise test.
Subjects performed treadmill walking with and without BFR on the same day. The exercise consisted of walking at 33 m/min with 4% grade for five 2-min bouts, with a 1-min rest between bouts (1). Order of experiments (CON or BFR) was randomized and there was 60 minutes between experimental trials.

Blood flow reduction (BFR) Technique.
A specially designed elastic belt (50 mm wide) was placed around the most proximal potion of each leg during the walk with BFR. The belt contained a pneumatic bag along its inner surface that was connected to an electronic air pressure control systems that monitored the restriction pressure (Kaatsu-Master, Sato Sports Plaza, Tokyo, Japan). The subjects were seated on a chair, the belt air pressure was set at 140 mmHg for 30 s, and the air pressure was released. The air pressure was increased by 20 mmHg and held for 30 s, and then it was released for 10 s between occlusive stimulations. The process was repeated until a final occlusion pressure for 200 mmHg was reached. This pressure was used for the occlusive stimulus during both low-intensity and maximum walk test.

Cardiovascular Measurements.

Impedance echocardiography as well as non-invasive blood pressure monitoring was used to obtain hemodynamic responses during low-intensity walk test (Task Force Monitor, CNSystem Medizintechnick, Graz, Austria). The impedance signal, electrocardiograph (ECG), and beat-to-beat blood pressure were sampled at 1000 Hz. These data were then used to determine all hemodynamic parameters including HR, mean (MAP), systolic (SAP) and diastolic (DAP) arterial pressure, SV, Q, and total peripheral resistance (TPR). In both experiments, the calculation of Q, work of the heart (W_H), MAP, and TPR were calculated as follows:
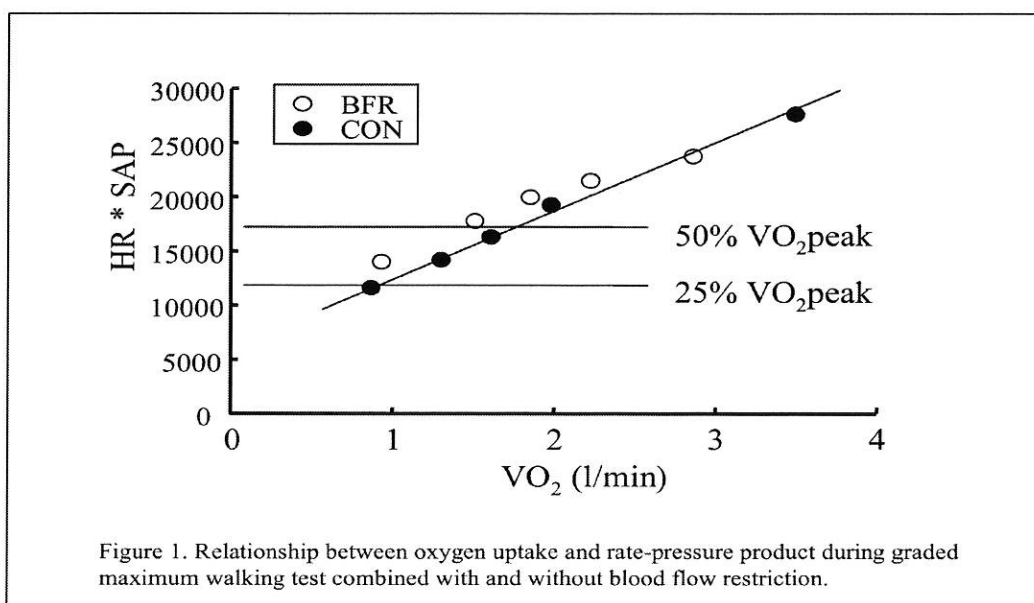
$$\dot{Q} = SV * HR$$
$$MAP = DAP + [0.333 * (SAP - DAP)]$$
$$TPR = MAP * 80/Q$$
$$W_H = SAP * HR$$

Additional cardiovascular test during walking.

Six young men (age; 21.8±1.2 yrs, height; 1.75±0.04 m, body weight; 67.8±8.3 kg) were habitually participating in exercise training at the university. The subjects performed treadmill walking with and without BFR on the same day. The exercise consisted of walking at 67 m/min at 0% grade for five 2-min bouts, with a 1-min rest between bouts (total time, 14 min). Order of experiments (CON or BFR) was randomized and there was 60 minutes between experimental trials. Cardiovascular responses were assessed by ultrasound Doppler echocardiography (Aloka SSD-5500, Tokyo, Japan). To measure SV, a 1.9 MHz continuous wave transducer was directed inferiorly from the suprasternal notch to assess velocity of blood flow in the ascending aorta (10). The areas beneath highest and clearest 2-3 velocity curves were traced off line to obtain the average velocity-time integral (VTI). 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 VTI to estimate SV. All data were averaged over 15 sec and data obtained for the last 15 sec of every minute were used for data analysis. Systolic and diastolic blood pressure was obtained auscultation using a sphygmomanometer. Expired gas was collected continuously every 60s by Douglas bag during both rest and exercise to determine VO_2, Vco_2, and V_E. The O_2 and CO_2 fractions in the expired gas were determined by mass spectrometry (Perkin-Elmer MGA 1100, Norway. CT). The expired gas volume was measured by a gasometer (Shinagawa Seisakusho, Tokyo, Japan).

Data analysis.

Results are expressed as means (SD) for all variables. All data were averaged over each minute and analyzed for differences. Thus, data are reported for each exercise bout by two 1 min values and as an

Figure 1. Relationship between oxygen uptake and rate-pressure product during graded maximum walking test combined with and without blood flow restriction.

average of the 5-bout average (average of all ten 1 min values). Statistical analysis were performed by a two-way ANOVA with repeated measures by group (BFR and CON) * time (pre-exercise and exercise periods). Post hoc testing was performed by a one-way ANOVA. Differences were considered significant if P value was less than 0.05.
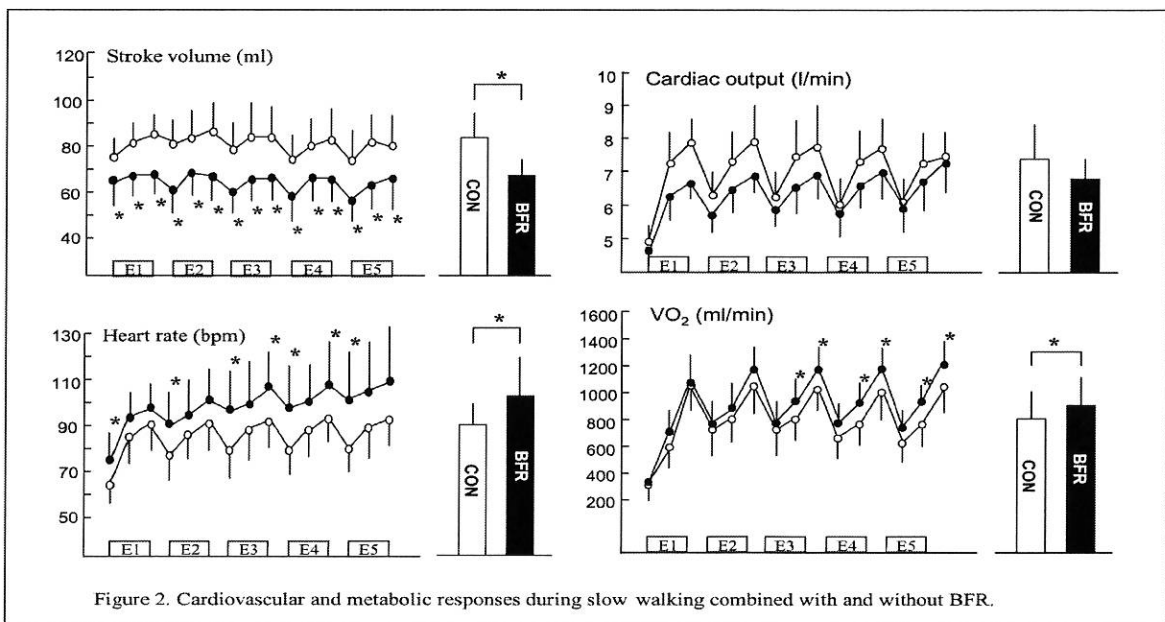
RESULTS

Graded maximum walking test.

VO_2 during BFR walking was 11~16% (P<0.05 or P<0.01) greater compared to during CON walking at any given work rate, while the VO_{2peak} during BFR (2.87 l/min, P<0.01) was 18% lower than that of the CON (3.51 l/min). HR was 16~20% greater during BFR than during CON at all submaximum work rate. There was no significant difference in peak HR between BFR and CON. Although SAP was similar between two trials, the W_H (HR*SAP) during BFR was higher (P<0.05) compared to the CON. The RPE was higher (P<0.01) in BFR than the CON, excluding at the peak exercise. In the walking without BFR, the VO_2 correlated linearly to the W_H in both individuals and mean (Fig. 1) values. The 50% of VO_{2peak} is corresponding to 17226 of the W_H in the CON.

Low-intensity walking exercise test.

VO_2 during BFR was significantly (P<0.05) greater than CON from the third bout of exercise and beyond as was the 5-bout average VO_2. Q was significantly (p<0.05) lower during BFR than CON at first and second exercise bouts, but the latter half of exercise bout and the 5-bout average were similar between BFR and CON (P=0.06). VO_2/Q (index of a-v O_2 difference) was significantly greater during BFR than CON (P<0.05). There was no significant difference in SAP and DAP (P=0.07-0.15) between BFR and CON. SV was significantly (CON; 84.9±19.3 ml, BFR; 70.0±17.3 ml, P<0.05) reduced throughout exercise, while HR (p<0.05) and W_H (p<0.05) were significantly elevated during the latter half of exercise bout and the 5-bout average during BFR as compared to CON (Fig. 2). The W_H of the 5-bout average was 15652 for BFR and 12556 for CON. TPR (P<0.05) was significantly greater during BFR than CON during the first half of exercise bout and the 5-bout average. V_E during the latter half of exercise bout and the 5-bout average was significantly greater during BFR (P<0.05). Vco_2, V_E/Vco_2, and V_E/VO_2 were similar between BFR and CON throughout exercise.

Figure 2. Cardiovascular and metabolic responses during slow walking combined with and without BFR.

Additional study for cardiovascular response during walking.

VO_2 during BFR was significantly greater than CON (P<0.05) at the first and second exercise bouts, and the 5-bout average (P<0.05). Q was not different between groups, but VO_2/Q (a-v O_2 difference) was significantly greater during BFR than CON (P<0.05) during the first half of exercise bout and the

5-bout average. TPR (P>0.05) was not different between groups, but the 5-bout average was significantly greater during BFR (P<0.05). MAP, SAP (P<0.05) and SAP (P<0.05) were similar between BFR and CON throughout exercise. SV (p<0.05) was significantly reduced and HR (P<0.05) and W_H (P<0.05) were significantly elevated during each exercise bout and the 5-bout average during BFR as compared to CON. V_E tended to be greater during first half of exercise bout (P=0.08), but the latter half of exercise bout and the 5-bout average was similar between BFR and CON. Vco_2, V_E/Vco_2, and V_E/VO_2 were similar between BFR and CON throughout exercise.

DISCUSSION

Critique of Method.

In the present study, two special measurements were applied to ensure the effect of BFR on hemodynamic parameters. These two methods are now considered to be major indirect (noninvasive) methods to evaluate changes in hemodynamic parameters, and there are differences in data collection, via impedance signals (Task Force Monitor, TFM) and ultrasound (Doppler method). Since we found that visualized biosignals converted into analogue digital (AD) had fluctuations especially during walking on a treadmill, necessity of evaluation by other method was raised to obtain convincing data. In the present study, the data obtained by TFM have been smoothed out and data have been averaged over every 1-min, while data collection was carried out in every 15 second by Doppler. This double estimation enabled us to confirm BFR-induced reduction in SV and increase in HR. Though disparity between statistical significance was observed in other parameters, similar alterations in these parameters in different measurement may be indicating the characteristic of effects of BFR on hemodynamic parameters.

BFR-induced reduction in SV during walk.

A previous study reported that at rest with supine posture, BFR-induced (restriction pressure 200 mmHg) venous blood pooling in both legs and inhibition of venous return resulted in 27% reduction in SV as well as Q, and slight increase in HR (6). The BFR-induced decrease in SV with supine posture is similar to the only other study which has examined an effect of BFR exercise on hemodynamic parameters; a higher level of HR and BP were observed in exhaustive knee extension exercise with BFR compared to those in exercise without BFR, while SV decreased. Consequently Q increased significantly and similarly in response to exercise with and without BFR, no difference was found in Q between exercises with and without BFR (12). Thus, changes in these parameters are thought to be compensatory response to the BFR-induced venous blood pooling and decreased venous return to satisfy blood flow for increasing Q demand during exercise.

Increase in VO₂ with BFR.

A previous study (1) has demonstrated that that BFR-walk required higher $\dot{V}O_2$ uptake during one bout of exercise as well as resulted in significant hypertrophy after 3wk training using the same walking protocol as in the present study. In the present study, a considerable effect of BFR on metabolic function was demonstrated and leads to the suggestion that BFR has a potent impact in increasing exercise intensity inducing greater cardiovascular responses, even though exercise intensity is low. As with previous study (1), significant increases in VO_2 were observed during both walking experiments with BFR in the present study. According to the Fick equation, VO_2 is obtained by multiplying a-v O_2 difference and Q. In the present study, the increase in VO_2 during BFR walk should be related to increasing a-v O_2 difference, because Q was not different during BFR and CON submaximal walk. Further, arterial blood oxygen content is typically maintained throughout the high-intensity exercise in healthy subjects. Therefore, the increased a-v O_2 difference during BFR walk is most likely due to significant reductions in mixed venous blood oxygen content of the working muscles.

Increase in Work of the Heart with BFR.

Takano et al., (12) have examined the effect of exhaustive knee extension exercise with BFR on hemodynamic parameters. The measurement immediately after cessation of the exercise due to fatigue in legs, demonstrated changes in HR, SV, Q, mBP and TPR similar to our present observations. Our study reports that BFR-walk induced increase or decrease in these parameters was kept through consecutive BFR-walk including resting periods between exercise sets. In addition, BFR-walk induced alterations in hemodynamic parameters during resting period before starting exercise was found. This

reflex response to BFR may be due to partly activation of mechanoreceptor which monitors pressure load within muscles. Supposedly, an application of BFR belt may activates mechanoreceptor and afferent impulses from the receptor provide rapid feedback (14). Previous studies are demonstrating (4, 7, 11) this feedback modifies either parasympathetic or sympathetic outflow to bring about appropriate cardiovascular responses to various intensities of physical activity. In addition, pressure-sensitive baroreceptor which is located in the aortic arch and carotid sinus and responds to changes in pressure load, may be partly playing a role in presser response of mBP and consequently increase in TPR and HR in response to BFR. As Prakosh et al., (9) clearly stated about the arterial baroreflex mechanism, decrease in venous return results in decrease in SV and Q and then BP falls and this fall in BP is detected by carotid barorecptors and the response consists of an immediate increase in HR followed by an increase in TPR. Therefore, BFR-induced increases in MBP, TPR and HR might be introduced by the same process in response to BFR-induced blood pooling inducing decrease in venous return. After onset of the BFR-walk, arise in chemoreseptor and/or metaboreceptor, chemically sensitive afferents within muscle or within the interstitium of muscles may also contribute partly in regulation of cardiovascular responses besides mechanoreflex and baroreflex regulation.

CONCLUSION

The BFR employed impairs exercise SV but cardiac output is maintained by an increased HR during submaximal work, but apparently not at VO_{2peak} which was reduced during BFR. During slow walking with BFR (exercise intensity about 25% the BFR VO_{2peak}), the W_H (HR x SBP) did not reach the exercise intensity level of 50% VO_{2peak} which is recommended for improvement of cardiovascular fitness. To develop cardiovascular fitness by walking with BFR walk, exercise intensity of over 40% BFR VO_{2peak} may be required.

References

1. Abe T, Kearns CF, and Sato Y. Muscle size and strength are increased following walk training with restricted venous blood flow from the leg muscle, Kaatsu-walk training. J Appl Physiol 2006; 100(5):1460-66.
2. Abe T, Sakamaki M, Fujita S, et al. Effects of low-intensity walk training with restricted leg blood flow on muscle strength and aerobic capacity in elderly subjects. J Geriatr Phys Ther 2009; (in press).
3. Abe T, Yasuda T, Midorikawa T, et al. Skeletal muscle size and circulating IGF-1 are increased after two weeks of twice daily "KAATSU" resistance training. Int J KAATSU Training Res 2005; 1(1): 6-12.
4. Adreani CM, Kaufman MC. Effect of arterial occlusion on responses of group III and IV afferents to dynamic exercise. J Appl Physiol 1998; 84:1827-33.
5. Iida H, Kurano M, Takano H, et al. Hemodynamic and neurohumoral responses to the restriction of femoral blood flow by KAATSU in healthy subjects. Eur J Appl Physiol 2007; 100(3): 275-85.
6. Iida H, Takano H, Meguro K, et al. Hemodynamic and autonomic nervous responses to the restriction of femoral blood flow by KAATSU. Int J KAATSU Training Res 2005; 1(2):57-64.
7. Herr MD, Imadojemu V, Kunselman AR, et al. Characteristic of the muscle mechanoreflex during quadriceps contractions in humans. J Appl Physiol 1999; 86:767-72.
8. Hisdal J, Toska K, Walloe L. Beat-by-beat cardiovascular responses to rapid, low-level LBNP in humans. Am J Physiol 2001; 281:R213-21.
9. Prakash ES, Pal M, Pal GK. What is the ultimate goal in neural regulation of cardiovascular function? Adv Physiol Educ 2004; 28: 100-1.
10. Rowland T, Obert P. Doppler echocardiography for the estimation of cardiac output with exercise. Sports Med 2002; 32(15):973-86.
11. Stebbins CL, Brown B, Levin D, et al. Reflex effect of skeletal muscle mechanoreceptor stimulation on the cardiovascular system. J Appl Physiol 1988; 65:1539-47.
12. Takano H, Morita T, Iida H, et al. Hemodynamic and hormonal responses to a short-term low-intensity resistance exercise with the reduction of muscle blood flow. Eur J Appl Physiol 2005; 95:65-73.
13. Takarada Y, Sato Y, Ishii N. Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. Eur J Appl Physiol 2002; 86:308-14.
14. Yasuda T, Brechue WF, Fujita T, et al. Muscle activation during low-intensity muscle contractions with restricted blood flow. J Sports Sci 2009; 27(5):479-89.