

## ORIGINAL ARTICLE

# Intense Triceps Surae Contraction Increases Lower Extremity Venous Blood Flow

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**Objective:** Venous thromboembolism can be prevented by physical prophylaxis, such as active ankle exercise (AAE), in addition to pharmacological treatment. However, the relationship between the intensity of triceps surae (TS) exercise and venous flow is unclear, and physical thromboprophylaxis has not been established for patients with leg cast immobilization. The goals of the current study were to clarify the degree of intensity of TS isotonic contraction required to increase peak blood velocity (PV) in the superficial femoral vein to higher than that at no resistance and to determine if TS isometric contraction can increase PV. **Methods:** A prospective, nonrandomized, controlled trial was performed in 20 healthy young adult men. PVs at rest and during one TS isotonic or isometric contraction were measured using Doppler ultrasonography. Isotonic contraction intensity was defined as no resistance with contraction of maximum effort and 25%, 50%, 75%, and 100% of one repetition maximum (1RM). Isometric contraction intensity was defined as 15–35%, 40–60%, 65–85%, and 90–100% of the maximal voluntary contraction. **Results:** Isotonic contraction at 75% 1RM (51.4 cm/s [95% CI, 40.1–62.6]) and 100% 1RM (54.9 cm/s [95% CI, 43.1–66.7]) significantly increased PV compared to that with no resistance (41.0 cm/s [95% CI, 32.2–49.8]) ( $P=0.005$ ,  $0.001$ , respectively). Isometric contraction increased PV significantly at all intensities (all  $P\leq 0.002$ ). **Conclusions:** Applying resistance at  $\geq 75\%$  1RM increases venous flow and enhances the effect of AAE with TS isotonic contraction. TS isometric contraction may serve as thromboprophylaxis for patients undergoing leg cast immobilization.

**Key Words:** active ankle exercise; muscle pumping; physical prophylaxis; venous thromboembolism; venous velocity

## INTRODUCTION

Venous thromboembolism (VTE) is a series of pathologies ranging from deep vein thrombosis (DVT), which involves formation of a blood clot within a deep vein, commonly in the legs, to pulmonary thromboembolism, which results from blockage of the pulmonary artery caused by a loose blood clot and may result in sudden death.<sup>1–3)</sup> Active ankle exercise (AAE) is a physical prophylactic method for VTE that can be prescribed for patients at high risk of bleeding and avoids the risks associated with pharmacological methods.<sup>4)</sup> AAE

is used in clinical practice and is useful in disaster-stricken areas because of its simplicity and economy. However, clear indications for the use of AAE have not been established. Consequently, care providers are unable to define the most effective AAE for each patient. Moreover, in orthopedics, a VTE prophylactic method for patients with leg cast immobilization is needed because venous stasis can result from fixation of the leg or because of the high risk of thrombosis immediately following trauma. However, there is currently no established method for physical thromboprophylaxis in these patients.

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Virchow described three main factors associated with the formation of blood clots: stasis of blood flow, endothelial injury, and hypercoagulability. Of these factors, physical prophylaxis (including AAE) directly influences stasis of blood flow. The resulting increased blood flow velocity causes shear stress on the endothelium, which activates fibrinolysis against hypercoagulability.<sup>5)</sup> This is the basis of prevention of VTE by physical methods, and AAE has been shown to augment venous blood flow.<sup>6–10)</sup> This enhancement of blood flow by AAE depends on the muscle pumping action of triceps surae (TS) contraction, which increases lower extremity venous blood flow.<sup>11,12)</sup> The relationship between the intensity of TS contraction and the blood flow increase was investigated by Hitos *et al.* who found that AAE against resistance prevented venous stasis more effectively than AAE without resistance.<sup>13)</sup> Moreover, Corley *et al.* showed a significant positive correlation between the plantar flexion force caused by neuromuscular electrical stimulation and the simultaneous peak velocity in the popliteal vein.<sup>14)</sup> However, the intensity of AAE required to increase venous flow to a level higher than that achieved by AAE without resistance is unknown.

This study was conducted to determine the degree of resistance intensity against TS isotonic contraction required to increase the peak velocity (PV) of blood in the superficial femoral vein beyond that achieved with no resistance and to examine whether TS isometric contraction increases PV.

## MATERIALS AND METHODS

A prospective, nonrandomized, controlled trial was conducted with a sample size of 20 subjects. Twenty healthy young adult men (age,  $22.2 \pm 1.3$  years; height,  $171.1 \pm 4.8$  cm; weight,  $63.2 \pm 7.6$  kg; body mass index,  $21.5 \pm 1.9$  kg/m<sup>2</sup>) were enrolled in the study. The exclusion criteria were anamnesis of VTE or lower extremity surgery or paralysis of a lower extremity, heart disease, or respiratory disease. This study was approved by the Kitasato University Allied Health Sciences Research Ethics Committee (2012-G003) and conformed with the Declaration of Helsinki. Verbal and written information to support informed consent was given to all eligible persons. PV as an index of venous blood flow was defined as the primary outcome. Secondary outcomes were flow volume (FV) in the superficial femoral vein, TS muscular activity, and TS muscle force.

### Measurement of Blood Flow

PV and FV were measured in the right limb using Dop-

pler ultrasonography (ProSound SSD-4000, Hitachi Aloka Medical, Ltd., Japan) with a 7.5-MHz linear array transducer. Continuous waveforms were recorded for 8 s using the pulse Doppler method, and PV was extracted using auto-trace mode. First, the probe was placed vertically on the right thigh on the medial surface to display a cross-sectional image of the superficial femoral vein, and the vein was defined using the color Doppler method. Then, the probe was rotated on the surface of the thigh to display a longitudinal sectional image of the vein. The measurement point was defined as 2–3 cm from the bifurcation of the common femoral vein and was marked with tape to allow measurement at the same point for each subject. The angle made by the ultrasonic beam and the lumen wall was set to  $<60^\circ$ . Subjects were instructed to breathe naturally without deep breathing or yawning during measurements because venous return is influenced by respiration.<sup>7,15)</sup> All measurements were performed by the same person.

### Measurement of Muscular Activity

Muscular activity of the medial head of the gastrocnemius was monitored using an electromyogram feedback unit (MyoTrace 400, Noraxon USA Inc., Scottsdale, AZ, USA), so that we and the subject could monitor the activity during isometric contraction.

### Measurement of Muscle Force Exhibited by TS Isometric Contraction

Muscle force in TS isometric contraction was recorded with a hand-held dynamometer ( $\mu$ Tas F-1, Anima Inc., Tokyo, Japan). The dynamometer was positioned between the center of the plantar surface of the metatarsal heads of the right foot and the footplate of a leg press machine (Horizontal Leg Press, SAKAI Medical Co., Ltd., Tokyo, Japan).

### Movement Task

Movement tasks consisted of trials of TS isotonic and isometric contraction. A trial of TS isotonic contraction was defined as one movement of right ankle plantar flexion in a supine position. The ankle starting position was set at a neutral position, and subjects performed ankle movement from the neutral to the plantar-flexed position and back to the neutral position in 2 s. Resistance to the movement was applied using the leg press machine. To prevent the trunk getting out of position as a result of the normal force exerted by the plantar flexion, we fixed the trunk to the leg press machine with a fixing-belt located around the shoulders. The intensity of TS isotonic contraction was defined relative to

the weight of resistance against plantar flexion at one repetition maximum (1RM). Contraction intensity was defined as no resistance and 25%, 50%, 75%, and 100% of 1RM. Ankle movement without resistance was defined as a movement with contraction of maximum effort reaching a maximum range of motion of plantar flexion.

A trial of TS isometric contraction was defined as a 3-s isometric contraction with the ankle in the neutral position and the subject in a supine position. We firmly fixed the right foot on the foot plate of the leg press machine and put a hand-held dynamometer between them to prevent movement of the heel and ankle joint. The trunk was fixed as described above for isotonic contraction. The intensity of TS isometric contraction was defined relative to muscular activity during TS isometric maximal voluntary contraction (MVC). Contraction intensity was defined as 15–35%, 40–60%, 65–85%, and 90–100% of MVC. Subjects were instructed to monitor their muscular activity so that the peak value of the electromyogram waveform would enter the predetermined range of muscular activity during the trial. 1RM and MVC for each subject were measured on different days but under the same conditions as those used for the blood flow measurements.

### Protocol

The subject first rested in a supine position for more than 10 min to allow blood flow to reach a steady state, and the baseline PV was measured. Baseline values were defined as the mean of three values taken when a value was within  $\pm 5\%$  of the previous value. Two trials per condition of the movement task were then performed, as follows. PV and FV during contraction were measured in the first trial for the first condition, after which the subject rested in the same position to eliminate order effects. After confirmation that PV had returned to baseline, PV and FV during contraction were measured in the second trial for the same condition. Subsequent trials were performed similarly. Trials were carried out in order from the lowest resistance intensity to the highest. TS isotonic contraction and TS isometric contraction trials were performed at least one day apart.

### Sample Size Calculation

A sample size calculation was performed using G\*Power 3.1.9.2.<sup>16)</sup> A preliminary examination was conducted to compute the required sample size with sufficient power to show significance in one-way repeated measures analysis of variance within six factors to compare the main effects of TS isotonic contraction on PV. PVs during contractions were measured without and with resistance in three healthy young

adult men, as described above. Using the measured values, the effect size  $f$  and the correlation among repeated measures were calculated as 1.02 and  $-0.25$ , respectively. The  $\alpha$  error probability was set as 0.05, the power as 0.95, and the nonsphericity correction  $\epsilon$  as 0.2. Based on these values, the required sample size was estimated to be 16. With reference to this power calculation and previous studies,<sup>6,7)</sup> we determined the required sample size in this study to be 20.

### Statistical Analysis

The means of two PV (cm/s) and two FV (ml/min) values from each measurement and the percentage increases of PV and FV were used in analyses. One-way repeated measures analysis of variance was performed using the Greenhouse–Geisser correction to adjust for sphericity with Bonferroni adjustment to compare the main effects on PV and FV of the different conditions of TS isotonic and isometric contraction. Similar analyses were performed for comparison between exhibited muscle forces (kgf) under the different conditions of TS isometric contraction. Correlations between the weight of resistance (kg) and the percentage increase of PV with TS isotonic contraction and between muscle force and the percentage increase of PV with TS isometric contraction were evaluated using Pearson product-moment correlation coefficients. All analyses except for power analysis were performed using IBM SPSS Statistics for Windows, ver. 22.0 (IBM Corp., Armonk, NY, USA).  $P < 0.05$  was considered to indicate significance. All tests of significance were two-tailed.

## RESULTS

Analyses of PV, FV, and muscle force were performed in all 20 subjects. Values for muscular activities with TS isotonic contraction in only 10 subjects were used for analysis because of noise in measurements for the other 10 subjects.

Changes of PV and FV with TS isotonic contraction are shown in **table 1**. The PVs at 75% and 100% 1RM were significantly higher than those without resistance. The percentage increase of PV at 75% and 100% 1RM were significantly higher than that at 50% 1RM or lower resistance. FVs at 50% 1RM or more were significantly higher than those without resistance. The percentage increase of FV at 50% 1RM or more was significantly higher than that at 25% 1RM or lower. There was a moderate positive correlation between the weight of resistance of TS isotonic contraction and the percentage increase of PV ( $r=0.42$ ,  $P=0.003$ ).

Changes of PV and FV with TS isometric contraction are

shown in **table 2**. PV increased significantly under all TS isometric contraction conditions, and stronger contraction resulted in significantly greater PV. TS isometric contraction also increased FV, with significant increases in FV from 15–35% to 40–60% MVC and from 65–85% to 90–100% MVC. The percentage increase of FV showed a similar tendency. There was a strong positive correlation between muscle force and the percentage increase of PV ( $r=0.61$ ,  $P<0.001$ ). The muscle forces were 19.4 kgf [95% CI, 15.0–23.8] at 15–35% MVC, 41.3 kgf [95% CI, 35.2–47.4] at 40–60% MVC, 55.3 kgf [95% CI, 48.3–62.2] at 65–85% MVC, and 72.8 kgf [95% CI, 63.8–81.7] at 90–100% MVC. The muscle forces increased significantly with augmentation of relative muscular activity (all  $P<0.001$ ).

## DISCUSSION

AAE is a simple method to reduce venous stasis and achieve thromboprophylaxis. Recent clinical studies have shown its efficacy for the prevention of DVT,<sup>17,18</sup> following many reports showing that AAE without resistance enhances venous velocity as a surrogate outcome of DVT.<sup>6–10</sup> However, current thromboprophylaxis does not lower the incidence of VTE to zero, even with the use of anticoagulants. AAE that achieves high venous velocities would likely have a greater thromboprophylactic effect because the use of VenaFlow (Aircast Inc.), an intermittent pneumatic compression (IPC) device, produced a larger increase of venous velocity than did a sequential compression device (SCD) (Kendall Company).<sup>9</sup> The VenaFlow device significantly lowered the VTE incidence compared to the use of SCDs.<sup>19</sup> In the current study, we examined whether TS contraction with heightened intensity increased venous flow to a higher level than that achieved without resistance (which is commonly used in clinical practice) and whether TS isometric contraction can increase venous flow.

The current study has limitations, such as the definition of the number of contractions as one per trial to compare the change of blood flow accompanied by a change of contraction intensity, including at 100% 1RM or 90–100% MVC, which, by definition, cannot be repeated. Thus, the study does not reveal the TS contraction intensity required to increase venous flow in repeated AAEs. The duration of increased venous velocity after the contraction has finished is also an issue to be examined for risk reduction of VTE. Second, we measured blood flow only in the superficial femoral vein, whereas DVT occurs in crural veins such as the soleal vein and peroneal vein more often than it does in the femoral

vein.<sup>20</sup> Some crural thrombi extend to the proximal veins as free-floating thrombi that can lead to fatal pulmonary thromboembolism.<sup>21</sup> Therefore, the blood flow change produced by physical prophylaxis also needs to be measured in the crural veins. Third, the subjects were all healthy young adult men, whereas patients undergoing operations with increased VTE risk, such as artificial joint replacement or hip fracture surgery, are usually older.<sup>22–25</sup> Muscle has quantitative and qualitative differences between young adults and elderly people, and women have a higher risk of osteoporosis, which contributes to fracture.<sup>26,27</sup> Moreover, reduction of venous flow occurs in patients after total hip arthroplasty.<sup>28</sup> Thus, venous flow during resistance-applied ankle movement postoperatively may not show changes that correspond to the results of the present study.

TS isotonic contraction without resistance increased PV by 43.2%. This value is a little higher than the increase of 33% in plantar flexion found by Sochart and Hardinge.<sup>6</sup> This may be because we measured blood flow at the first TS contraction, whereas Sochart and Hardinge made measurements avoiding the initial phases of exercise. In our study, we applied resistance to plantar flexion. Contractions at 75% or 100% 1RM increased PV to a higher level than that without resistance, whereas contractions at 25% or 50% 1RM did not produce an increase. Contractions at 50% 1RM or higher also increased FV beyond that without resistance. These results suggest that applying resistance of at least 50% 1RM will increase venous flow more effectively than applying no resistance, but that contraction at less than 50% 1RM may not do so.

TS isotonic contraction without resistance was performed with maximum effort, but PV with contraction without resistance did not exceed that at 25% 1RM, which was the lightest of the four resistance conditions. The reason for this result is thought to be that the TS is difficult to contract strongly without resistance because the muscle does not fit compactly between the knee and heel.<sup>29</sup> Therefore, applying resistance, rather than making a great effort without resistance, would be more efficient at strongly contracting the TS and thereby enhance venous flow. In addition, some subjects stated that it was easier to apply strength in contraction at 25% 1RM than without resistance. In clinical practice, the lack of clarity relating to adherence to AAE without resistance (that is, whether patients actually perform the method as instructed by a care provider) is a concern. Therefore, applying resistance to AAE using equipment such as an exercise band may improve adherence, although the use of resistance is possible only for patients not undergoing cast immobilization.

**Table 1.** Changes of peak velocity and flow volume of blood in the right superficial femoral vein with TS isotonic contraction (n=20)

Weight of resistance	Peak velocity (cm/s)	Percentage increase of peak velocity (%)	Flow volume (mL/min)	Percentage increase of flow volume (%)
Rest	29.0 [22.9–35.1]	-	187.4 [139.0–235.9]	-
No resistance	41.0 [32.2–49.8] **	+43.2 [31.2–55.1]	295.5 [198.7–392.2] *	+57.0 [37.8–76.2]
25% 1RM	40.6 [31.4–49.7] **	+45.9 [32.5–59.3]	303.8 [224.7–382.9] **	+69.4 [46.7–92.1]
50% 1RM	46.4 [34.3–58.5] **	+65.5 [43.9–87.2]	380.3 [282.7–478.0] **†	+117.3 [78.7–155.8] ††
75% 1RM	51.4 [40.1–62.6] **†††	+81.5 [61.0–102.0] †††§§	407.2 [312.4–502.0] **†††	+139.7 [89.6–189.7] ††
100% 1RM	54.9 [43.1–66.7] **††††	+96.2 [71.1–121.3] †††§§§	491.9 [381.2–602.6] **††††§§	+195.7 [134.3–257.0] ††††§§

Values are means and 95% confidence intervals. \* P <0.05 vs. rest; \*\* P <0.01 vs. rest; † P <0.05 vs. no resistance; †† P <0.01 vs. no resistance; ††† P <0.01 vs. 25% 1RM; †††† P <0.01 vs. 25% 1RM; § P <0.05 vs. 50% 1RM; §§ P <0.01 vs. 50% 1RM; || P <0.05 vs. 75% 1RM (Bonferroni).

**Table 2.** Changes of peak velocity and flow volume of blood in the right superficial femoral vein with TS isometric contraction (n=20)

Relative muscular activity	Peak velocity (cm/s)	Percentage increase of peak velocity (%)	Flow volume (mL/min)	Percentage increase of flow volume (%)
Rest	27.7 [21.3–34.1]	-	239.8 [171.2–308.3]	-
15–35%MVC	32.0 [25.0–39.0] **	+18.6 [11.6–25.6]	292.6 [214.7–370.6] *	+30.4 [9.4–51.4]
40–60%MVC	37.9 [30.1–45.6] **††	+42.4 [31.0–53.8] ††	418.8 [326.7–510.8] **††	+100.4 [61.0–139.7] ††
65–85%MVC	42.3 [33.7–50.9] **†††	+58.2 [45.5–71.0] †††	485.8 [366.0–605.5] **†††	+125.9 [81.5–170.3] ††
90–100%MVC	46.4 [37.4–55.4] **††††	+76.3 [61.6–90.9] †††§§	582.7 [459.6–705.7] **††††§§	+184.8 [122.9–246.8] †††§§

Values are means and 95% confidence intervals. \* P <0.05 vs. rest; \*\* P <0.01 vs. rest; †† P <0.01 vs. 15–35%MVC; ††† P <0.01 vs. 40–60%MVC; §§ P <0.01 vs. 65–85%MVC

TS isometric contraction with greater intensity increased PV and FV significantly. The percentage increase of PV with isometric contraction at 40–60% MVC was comparable to that with isotonic contraction without resistance, and isometric contraction at more than 65% MVC achieved an increase in PV equivalent to that with a mobile IPC device, e.g., WizAir DVT (Medical Compression Systems DBN-Ltd, Or Aqiva, Israel). This device reportedly increases PV by 66%,<sup>30)</sup> which we regard as the minimum required increase of PV to prevent VTE. This is because this level of PV increase prevented VTE noninferiorly to commonly used anticoagulants<sup>31)</sup> and is referred to in the 9th ACCP Evidence-Based Clinical Practice Guidelines.<sup>32)</sup> These results indicate that isometric contraction at more than 40% MVC enhances venous flow to a similar extent to that in methods used commonly at present.

Thus, TS isometric contraction can be effective as a VTE prophylactic method, especially for leg fracture patients with cast immobilization. Such patients have a high risk for VTE because they possess the conditions described by Virchow for the formation of a blood clot. Fracture increases coagulability, and the endothelium is injured by the fracture itself and by manipulations performed to reduce the fracture.<sup>33)</sup> Patients with a cast on their leg cannot use an IPC device or move their feet. This leads to stasis of venous flow, in addition to hypercoagulability and endothelial injury caused by the fracture itself, and results in VTE at a rate of 4.3–40% in patients with leg cast immobilization without thromboprophylaxis.<sup>34–37)</sup> TS isometric contraction can be performed during cast immobilization to prevent venous stasis and to activate fibrinolysis, as achieved by IPC devices,<sup>38)</sup> but a method is required to prevent breakage of the cast by strong muscle contraction.

PV tended to increase in proportion to the contraction intensity in both TS isotonic and isometric contractions. We suggest that a strong muscle contraction with a low frequency is a more effective thromboprophylactic method than a frequent contraction because the low frequency allows the soleal vein to refill with blood before the next contraction. Also, heightening the intensity of plantar flexion enables TS contraction intensity during AAE to approach that during ambulation, which is effective for VTE prophylaxis in the early stage.<sup>32,39–42)</sup> Exercises in a standing position, such as ambulation and calf raising, generate resistance to plantar flexion under the patient's own weight. An increase of venous velocity during such exercises is likely, although making accurate measurements of a moving extremity by ultrasonography is difficult.

Further studies are required to define the appropriate conditions, such as the frequency and interval, for clinical application of AAE with increased TS contraction. There is also a need to examine the duration of the increased venous velocity resulting from AAE, changes of venous flow with increased TS contraction intensity in elderly women or patients at high risk for VTE, and follow-up of the effect of AAE with resistance on the rate of VTE.

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## CONFLICT OF INTEREST

We have no conflicts of interest to declare.

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