» **Original Article** «

Relationship between Arterial Inflow Rate and Venous Filling Index of the Lower Extremities Assessed by Air Plethysmography in Subjects with or without Axial Reflux in the Great Saphenous Vein

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Objective: To evaluate the relationship between arterial inflow rate (AIR) and venous filling index (VFI) in limbs with or without varicose veins, assessed by air plethysmography (APG).

Materials and Methods: A total of 142 patients (142 limbs) visiting our clinic with leg complaints, but without arterial and venous disease, were defined as the normal group (NG), and 65 patients (65 limbs) with leg varices were defined as the varicose vein group (VG). Both groups underwent duplex ultrasonography and APG to identify venous reflux and measure hemodynamic parameters, respectively. Examinations were performed at the first visit in the NG and before and one month after treatment in the VG.

Results: A strong correlation between resting AIR and VFI was found in the NG ($r = 0.72$) and postoperative VG ($r = 0.71$). Twenty-two and three limbs in the NG and postoperative VG, respectively, had a VFI over 2.0 mL/s because of the high AIR. In the VG, AIR tended to decrease after treatment ($P > 0.01$).

Conclusions: High leg AIR lead to high VFI measured by APG. AIR and VFI should be measured at the same session to assess venous hemodynamic changes after varicose vein treatment when residual venous reflux cannot be diagnosed with duplex ultrasonography.

Keywords: arterial inflow rate, venous filling index, air plethysmography, varicose veins

Introduction

One of the main purposes of varicose vein treatment is to improve of the hemodynamic function of affected limbs. Air plethysmography (APG) has been widely used as a sensitive and reproducible method for quantifying changes in the parameters of arterial and venous function of the lower extremities.^{1–3)} In some studies, APG has been used to obtain hemodynamic information of the leg with chronic venous disease

and compare hemodynamic changes before and after varicose vein treatment.^{4–7)} Several parameters obtained from APG, such as venous filling index (VFI), considered as indicators of venous reflux, should be reduced after a successful operative procedure. The normal range of VFI values is reported to be less than 1.7–2.0 mL/s in the lower limbs.^{4–6)} Although the VFI is surely influenced by the arterial inflow rate (AIR), the relationship between AIR and VFI has not been sufficiently investigated. The purpose of this study is to evaluate the relationship between AIR and VFI in limbs with or without venous reflux using APG.

Materials and Methods

Among 250 ambulatory patients who visited Shirai-shi Cardiovascular Clinic because of leg complaints and underwent physical examination, APG, and duplex

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ultrasonography (DS) from May 2012 to October 2013, 142 patients (142 right limbs) (28 men and 114 women; mean age [range], 63.4 [22–88] years) without arterial or venous disease were selected and defined as the normal group (NG). Arterial disease was ruled out by palpation of the posterior tibial artery and dorsalis pedis artery. The absence of superficial and deep vein incompetence was verified using DS. None of the patients had a history of deep vein thrombosis in the right leg. The mean (range) body mass index (BMI) and body surface area (BSA) was 23.5 (15.4–33.8) kg/m² and 1.56 (1.19–2.12) m², respectively. The selected patients consisted of 32 patients who underwent varicose vein treatment for the left leg, 44 preoperative patients with saphenous type varicose vein in the left leg (no venous reflux in the right leg), 16 patients with orthopedic disease such as osteoarthritis, 25 patients feeling leg dullness during standing work, 2 patients with previous deep vein thrombosis in the left leg, 12 patients with metabolic syndrome, and 11 patients with only telangiectasias in the right leg were also included.

Another 65 patients (24 men and 41 women; mean age [range], 67.0 [36–88] years) having unilateral (13 in the left leg, 52 in the right leg) axial reflux in the great saphenous vein assessed by DS were selected and defined as the varicose vein group (VG). The absence of arterial disease was verified by artery palpation. The mean (range) BMI and BSA were 23.6 (16.7–38.9) kg/m² and 1.6 (1.22–2.36) m², respectively. According to the CEAP classification system, 28 (43.1%), 25 (38.5%), 11 (16.9%), and 1 limb(s) were classified as C2, C3, C4, and C6, respectively.

Patients in the VG were treated by endovenous laser ablation in 27 limbs (41.5%) and by perforated invaginated vein stripping in 38 limbs (58.5%). In seven limbs, popliteal vein incompetence was found both before and after treatment. There were no significant differences in age, BMI, and BSA between the NG and VG.

To evaluate hemodynamic function and anatomical findings of the lower extremities, APG and DS were performed by a well-trained technologist at the first visit to our clinic in the NG and before and one month after treatment in the VG.

Oral informed consent was obtained from all patients before they underwent noninvasive evaluations.

Fig. 1 The scattergram demonstrates a strong correlation between VFI and AIR in the normal group. Twenty-two of 142 limbs (15.5%) had a VFI >2 mL/s. VFI: venous filling index; AIR: arterial inflow rate.

Duplex ultrasonography

All subjects were examined for chronic vein insufficiency using DS (HIVISION Avius, Hitachi, Tokyo, Japan). Evaluation of valve competence was performed with the squeezing maneuver. Reflux flow by squeezing the calf, persisting for more than 0.5 s, indicated venous incompetence.⁸⁾

Air plethysmography

Volume changes of the lower limbs were recorded with the APG® (APG-1000, ACI Medical LLC, San Marcos, California, USA). Resting AIR was measured via venous occlusion method. The subjects were asked to rest in the supine position for 10 minutes. Subjects were placed in the supine position with the test leg (right leg in the NG and affected limb in the VG) externally rotated and enclosed from ankle to knee in a 27.5-cm polyurethane sensing cuff, while the foot was elevated 15 cm and rested on a foam block with the knee slightly bent. A 10-cm wide pneumatic tourniquet was placed just proximal to the knee and connected to a rapid inflator Venapulse® (ACI Medical LLC, USA). After calibration, the tourniquet was rapidly inflated to 70 mmHg. Increasing volume tracing was observed and gradually reached a stable plateau. The AIR was calculated from the linear slope of the volume just after tourniquet inflation.⁹⁾ After AIR measurement, an exercise test previously described by Christopoulos, et al.⁵⁾ was performed to measure the VFI.

Fig. 2 A moderate correlation was observed between body mass index (BMI) and arterial inflow rate (AIR) (upper left), body surface area (BSA) and AIR (upper right), BMI and venous filling index (VFI) (lower left), and BSA and VFI (lower right) in the normal group.

Statistical analysis

Paired or unpaired t-test was performed for statistical analysis. A $P < 0.01$ was considered statistically significant.

Results

The results from each normal limb are plotted according to the AIR and VFI as shown in Fig. 1. The mean (range) AIR and VFI were 1.19 (0.20–3.41) mL/s and 1.45 (0.30–3.88) mL/s, respectively. The scattergram demonstrated a strong correlation between AIR and VFI ($r = 0.72$). In 22 out of 142 limbs (15.5%) in the NG, the VFI value was over 2.0 mL/s. A moderate correlation was observed between BMI and AIR ($r = 0.47$), BSA and AIR ($r = 0.33$), BMI and VFI ($r = 0.39$), and BSA and VFI ($r = 0.37$) in the NG (Fig. 2).

The weak correlation ($r = 0.31$) between resting AIR and VFI in the VG before treatment was improved to a strong correlation ($r = 0.71$) at one month after treatment (Fig. 3), similar to the NG. In the VG, among the 19 limbs showing a VFI over 2.0 mL/s after treatment, there were 7 (36.8%), 3 (15.8%), and

3 (15.8%) limbs with popliteal vein incompetence, residual varices in the calf, and an AIR over 2.5 mL/s without residual reflux in the venous system, respectively (Fig. 4).

The preoperative mean resting AIR of the VG was significantly greater than that of the NG (1.46 vs. 1.18 mL/s). According to the CEAP classification, preoperative AIR tended to be greater in the severe VG; however, the difference did not reach statistical significance (C2–3: 1.34 ± 0.58 vs. C4–6: 1.96 ± 1.21 , $P = 0.05$). When preoperative and postoperative mean AIR values were compared, there was a tendency toward a reduction, but the difference was not statistically significant (1.46 vs. 1.31 mL/s, $P = 0.02$), whereas VFI was significantly reduced (5.41 vs. 1.74 mL/s, $P < 0.001$) (Fig. 5). The comparison of preoperative and postoperative AIR (mean $\pm$ standard deviation) demonstrated no significant reduction according to the CEAP classification (C2–3: 1.34 ± 0.58 vs. 1.19 ± 0.63 mL/s, $P = 0.03$; C4–6: 1.96 ± 1.21 vs. 1.71 ± 1.15 mL/s, $P = 0.05$). However, regarding the case classified as C6, the AIR was markedly reduced from 1.13 to 0.69 mL/s after vein

Fig. 3 The relationship between VFI and AIR in the varicose vein group before (left) and after (right) treatment shows that the correlation coefficient after treatment was almost the same as that in the normal group. VFI: venous filling index; AIR: arterial inflow rate.

Fig. 4 Relationship between VFI and AIR after operation including 19 limbs with VFI > 2 mL/s. The closed square represents limbs with popliteal vein incompetence, and the double circle represents limbs with significant residual varices in the calf postoperatively. VFI: venous filling index; AIR: arterial inflow rate.

stripping; this patient presented a completely healed ulcer in the affected limb.

Discussion

APG has been used as a standard device for assessing hemodynamic venous function of the lower limb. Several studies that investigated the hemodynamic improvement after varicose vein treatment assessed by APG have been published.^{6,7,10} In the absence of venous valvular reflux, arterial volume flow should be the main source of venous filling. Although it is important to understand the relationship between AIR and

Fig. 5 Comparison of AIR (closed column) and VFI (open column) in three groups. There are significant differences in the means of both parameters between (*: $P < 0.01$, **: $P < 0.001$) the normal group and the varicose vein group before treatment. Although the VFI in the varicose vein group was significantly reduced (***: $P < 0.001$), the AIR was not statistically significantly reduced (Δ : $P = 0.02$) after treatment. Brackets represent standard error of the mean. NG: normal group; VG: varicose vein group; VFI: venous filling index; AIR: arterial inflow rate.

VFI in subjects with or without venous reflux, to the best of our knowledge, no studies regarding this subject have been reported to date. Christopoulos, et al. reported that the normal VFI should be less than 1.7–2.0 mL/s;^{4–6} however, in the present study, a VFI greater than 2 mL/s without the presence of venous reflux was found in some of the subjects in the NG. Although Nicolaides, et al. reported a resting AIR of 50–120 mL/min, depending on the size of the leg, in

20 normal limbs;¹¹⁾ however, not enough data regarding the size of the investigated legs were reported. In the normal 142 limbs in the present study, the AIR at rest was found to range from 0.20 to 3.41 mL/s (12.0–204.6 mL/min), depending on the BMI and BSA. Both BMI and BSA had moderate correlations with AIR and VFI. A strong correlation ($r = 0.72$) between AIR and VFI was found in normal subjects including 11 limbs with AIR over 2.0 mL/s and 22 limbs with VFI over 2.0 mL/s. This result suggests that a high VFI without venous reflux is mainly caused by a high AIR depending on the physique (BMI and BSA).

Some investigators indicated that AIR is higher in limbs with incompetent veins than in normal limbs.¹²⁾ Although Christopoulos, et al. demonstrated increased arterial inflow in patients with venous disease with increasing clinical severity,⁵⁾ Paoloni, et al. reported no correlation between the CEAP classification and arterial inflow at rest.¹²⁾ When compared with the entire group, we also found an increasing AIR in the VG; there was a greater tendency of preoperative AIR in the VG according to the CEAP classification, but the difference between the groups was not statistically significant. This result suggests that inflammation, microangiopathy, and arteriovenous fistulae in the preoperative VG may lead to increasing AIR.

Christopoulos, et al.⁶⁾ showed that correction of the source of primary venous insufficiency causing venous hypertension does not result in a return to normal resting arterial inflow. In the present study, when preoperative and postoperative AIR values were compared, there was a tendency toward a reduction, but the difference was not significant. However, in the present study, a markedly reduced and normalized AIR (from 1.39 to 0.58 mL/s) was found in the case classified as C6 after healing of the leg ulcer by vein stripping. This phenomenon suggests that the reduction in AIR was possibly due to the resolution of inflammation, microangiopathy, and arteriovenous fistulae in the cutaneous and subcutaneous tissues.

We also found three limbs with high postoperative VFI that was only caused by a high AIR of >2.5 mL/s. A possible explanation for the persistently increased arterial inflow is the existence of dilated capillaries in the lower limb, which act as micro arteriovenous fistulae.^{6,9,12)}

Limitations

Although there are differences in arterial inflow of the lower extremities between the supine position and standing position,¹³⁾ we assumed that there was no major difference in AIR between the supine and standing positions in the present study.

Conclusion

The relationship between resting AIR and VFI assessed by APG in the limbs with or without varicose veins was investigated. There was strong correlation between resting AIR and VFI in normal and postoperative varicose vein legs. VFI over 2 mL/s was found in 15.5% of normal limbs owing to increased BMI and BSA. Although resting AIR in limbs with varicose veins was significantly higher than that of normal limbs, it was not significantly reduced after treatment. Some limbs after treatment showed persistently high VFI without residual reflux due to high AIR. These results suggest that it is important to measure AIR and VFI in the same session to interpret high VFI values in case of ultrasonographic absence of venous reflux.

Disclosure Statement

The author has no financial or related disclosures and conflict of interest.

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