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ORIGINAL ARTICLE

Effect of leg exercises on popliteal venous blood flow during prolonged immobility of seated subjects: implications for prevention of travel-related deep vein thrombosis

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Summary. *Background:* Venous stasis is an important contributing factor in the development of travel-related deep vein thrombosis. This study examined factors affecting popliteal venous blood flow in order to determine the most effective exercise regimen to prevent venous stasis. *Methods:* Twenty-one healthy subjects were randomly assigned to various activities over a 9-week period. Subjects remained seated throughout the investigation and 3660 duplex ultrasound examinations were performed by a single examiner using a SonoSite 180 Plus handheld ultrasound. Baseline popliteal vein blood flow velocity, cross-sectional area and volume flow in subjects sitting motionless were assessed in the first 3 weeks.The remaining 6 weeks involved subjects performing airline-recommended activities, foot exercises, foot exercises against moderate resistance and foot exercises against increased resistance in order to determine the most beneficial method for enhancing popliteal venous flow. Sitting with feet not touching the floor and the effect of sleeping were also assessed. *Results:* The median age of the subjects was 22 years (range: 18–25.5 years), height 171 cm (162.5–180.5 cm) and body mass index 25.3 kg m^{-2} (23.2–26.3 kg m^{-2}). Blood volume flow in the popliteal vein was reduced by almost 40% with immobility of seated subjects and by almost 2-fold when sitting motionless with feet not touching the floor. Foot exercises against increased resistance positively enhanced volume flow ($P < 0.0001$). *Conclusion:* Leg exercise regimens enhanced popliteal venous flow during prolonged immobility of seated subjects, reinforcing the importance of regular leg movement to prevent venous stasis during prolonged sitting, such as in long-distance travel.

Keywords: air travel, deep-vein thrombosis, economy class syndrome, hemodynamics, venous stasis.

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Introduction

Deep-vein thrombosis (DVT) and pulmonary embolism (PE) are manifestations of venous thromboembolism (VTE) and remain important causes of morbidity and mortality. The association between immobility and VTE was initially highlighted in London during World War II when fatal PE occurred in people sleeping in deckchairs in air-raid shelters [1]. In 1954 Homans reported a case of DVT that occurred in a physician after a 14-h flight, thereby associating VTE and long-term immobility from confined seating with air travel [2]. Studies have shown that asymptomatic lower limb DVT may arise in up to 10% of long-distance travelers depending on patient baseline risk of VTE [3,4], and that 4–20% of patients presenting with VTE have traveled within a few weeks prior to the event [5–8].

Venous stasis of the lower limbs because of long-term immobilization and reduced function of the foot and calf muscle pump is thought to increase the risk of VTE. Sitting for up to 1 h decreases venous return from the legs and leads to local hemoconcentration [9], with 12 h of air travel resulting in swelling and fluid retention [10]. Interestingly, 85–100% of VTE cases have been found to occur in passengers in non-aisle seats [4,11]. Factors such as chair position and, in the case of air travel, cabin-related factors such as low humidity, reduced air pressure and relative hypoxia, may be important [12].

Guidelines provided by the Seventh American College of Chest Physician Conference on Antithrombotic and Thrombolytic Therapy recommend frequent calf muscle stretching and the avoidance of constrictive lower extremity clothing and dehydration for long-distance travelers (i.e. flying for >6 h) and in people with additional risk factors. The use of properly fitted graduated compression stockings (GCS) or a single dose of low-molecular-weight heparin (LMWH) prior to departure is suggested if active prophylaxis is considered indicated because of the perceived increased risk of thrombosis. The use of aspirin is not recommended [13].

Preventative DVT measures recommended by airlines include standing, stretching, avoiding constrictive clothing, drinking water and performing leg exercises; however, this fails to account for passengers falling asleep for an extended period and those distracted by other activities.

This study investigated factors affecting popliteal venous blood flow in order to determine the most effective exercise regimen to prevent venous stasis during periods of prolonged sitting.

Materials and methods

Study participants

Study subjects included 21 healthy volunteers (21 limbs) from the Redeemer Baptist School, Sydney, Australia. Participants had no history of thrombosis, leg trauma, swelling, surgery, lymphedema, venous reflux or outflow obstruction. The male to female ratio was 1:1 and the median age was 22 years (range: 18–25.5 years), height 171 cm (162.5–180.5 cm), weight 76 kg (63–80 kg) and body mass index 25.3 kg m^{-2} (23.2–26.3 kg m^{-2}). Subjects gave their written informed consent for the investigation to be performed. This study was approved by the institutional review board.

Seating protocol

All examinations and activities were performed with subjects in a seated position with seats placed at a fixed distance apart. Seating pitch was adjusted to 31 inches (78.7 cm) as per Qantas, British Airways and United Airways 'economy' passenger guideline dimensions (http://www.airlinequality.com). Individual seat height was adjusted accordingly and the lumbar region was thoroughly supported using a cushion for each subject. Legs were in a flexed position at a 120º angle with both feet flat, touching the floor, thereby ensuring that identical leg and similar foot pressures were maintained.

Exercise regimens

Baseline popliteal vein blood flow velocity, cross-sectional area and volume flow in subjects sitting motionless were assessed in the first three weeks. The different exercise regimens were randomly assigned to subjects for the remaining 6 weeks with all participants refraining from exercising for at least 2 h prior to activity commencement. Subjects performed airline-recommended exercises, foot exercises, foot exercises against moderate resistance, and foot exercises against increased resistance. Sitting still with feet not touching the floor and the effect of sleeping vs. being awake (in the seated position) was also assessed. Throughout the examination subjects were allowed to read, talk, sew and listen to music.

Qantas and British Airways airline websites and in-flight magazines were reviewed for information on DVT-prevention activities (http://www.qantas.com) (http://www.britishairways.com) [14], with recommended exercises found to be similar for both. Airline-recommended activities were performed by subjects every hour and included ankle rotation (clockwise or anticlockwise), foot exercises (heel-rise and toe-rise foot pumps), knee flexions, forward-back flexion and neck and shoulder roll.

The particular airline activity 'foot exercise' known to produce active contraction of the foot and calf muscle pump was also performed alone. Other activities performed included a foot exercise against moderate resistance (active plantar and dorsiflexion performed against a flat, non-pivoting springboard that the investigators obtained from an armchair), as shown in the Supplementary material (Fig. S1). Foot exercises against increased resistance were performed using an apparatus designed by the investigators consisting of a pivoting pedal connected with an elastic tension band. This allowed subjects to perform active plantar and dorsiflexion exercises as shown in the Supplementary material (Fig. S2) and was considered to provide maximal foot and calf muscle contraction.

Sitting still with feet not touching the floor was also investigated by elevating the chair of seated subjects so that their feet could not touch the surface of the floor. Finally, changes in blood volume flow were compared between sleeping and awake subjects matched by activity performed and time interval of sleeping over a 60-min period.

Duplex scanning

Duplex ultrasound examinations (n = 3660) and measurements were performed by a single examiner (S. Garth) over a 9-week period using a handheld portable ultrasound scanner (SonoSite 180 Plus with L38/10-5 MHz 38-mm linear array transducer, Sonosite Inc., Bothwell, WA, USA). All measurements were performed at the proximal segment of the popliteal vein of the right leg on subjects sitting motionless, with the examiner blinded to the exercise regimen performed. The activities were performed for 30 s every 15–20 min over a 100-min period. Three measurements were obtained per time point and then averaged. The venous hemodynamic parameters studied included: blood flow velocity (cm s^{-1}), popliteal vein cross-sectional area (cm^2) and blood volume flow (ml s^{-1}). The blood flow velocity was obtained by spectral analysis of pulsed Doppler signals insonating the entire lumen of the popliteal vein and was calculated as the time average of the velocity spectra occurring during these intervals. The average blood volume flow was estimated from the average blood flow velocity multiplied by the average cross-sectional area ($\pi \times \text{diameter}^2/4$) of the popliteal vein. All measurements and activities were carried out in a draught-free temperature-controlled room (approximately 21–24°C) and with subjects wearing loose-fitting clothes and no footwear. Baseline parameters (blood flow velocity, cross-sectional area and blood volume flow) were assessed at the popliteal vein, level with the medial femoral condyle on the right leg, during the first 3 weeks, with subjects sitting motionless with feet flat, touching the floor over the 100-min study period.

Reproducibility

The intraday reproducibility of the venous hemodynamic parameters examined of blood flow velocity, cross-sectional area and blood volume flow was established by six repeated measurements obtained from the popliteal vein in the right limb by the same examiner (S. Garth) over a period of 3.5 h for all subjects. Table 1 illustrates the reproducibility of this method.

Data analysis

The statistical software package S-PLUS version 6.21 (Statistical Sciences, Inc., Westlake, Seattle, WA, USA) was used for the analysis. Linear mixed-effects models were fitted to the blood flow velocity, cross-sectional area and blood volume flow data. Activity and time interval were fitted as fixed effects, and patient identifier as a random effect. Differences for the percentage change in blood flow velocity, cross-sectional area and blood volume flow from baseline for the different activities were calculated by analyzing the log-transformation of these variables and then back-transforming the parameter estimates and their 95% CI. All tests were two-tailed and *P*-values ≤0.05 were considered to be statistically significant. Reproducibility is expressed as a range of the coefficient of variation (SD/mean) calculated individually for every exercise assessed.

Results

Time course-related hemodynamic changes induced within exercise regimens

Sitting still (feet flat touching the floor) Blood flow velocity significantly decreased at 100 min from baseline (0 min) by 41% (from 0.91 to 0.54 cm s^{-1}; 95% CI −48 to −32%; $P < 0.0001$) and blood volume flow decreased by 42% (from 0.77 to 0.44 ml s^{-1}; 95% CI −51 to −32%; $P < 0.0001$; Fig. 1).

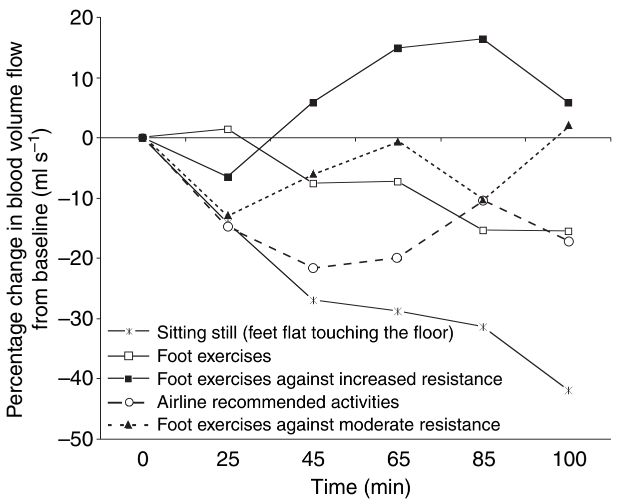

Fig. 1. Percentage change in blood volume flow (ml s^{-1}) in the popliteal vein from baseline in subjects performing all activities.

Airline-recommended activities At 45 min from baseline (before airline-recommended activities), blood flow velocity decreased by 18% (from 0.91 to 0.75 cm s^{-1}; 95% CI −29 to −5%; $P = 0.007$) and blood volume flow decreased by 22% (from 0.77 to 0.60 ml min^{-1}; 95% CI −34 to −8%; $P = 0.0044$). At 85 min from baseline (after airline-recommended activities), the decline in blood flow velocity was 11% less (from 0.91 to 0.81 cm s^{-1}; 95% CI −23 to 1.5%; $P = 0.082$) and blood volume flow was 10% less (from 0.77 to 0.69 ml s^{-1}; 95% CI −24 to 5%; $P = 0.18$; Fig. 1).

Foot exercises At 100 min from baseline, blood flow velocity decreased by 16% (from 0.87 to 0.73 cm s^{-1}; 95% CI −28 to −3%; $P = 0.018$). Similarly, blood volume flow (Fig. 1) also decreased by 16% (from 0.62 to 0.52 ml s^{-1}; 95% CI −29 to 0.5%; $P = 0.057$).

Foot exercises against moderate resistance At 100 min from baseline, the reduction in blood flow velocity was 6.9% (from 0.97 to 0.90 cm s^{-1}; 95% CI −21 to 10%; $P = 0.40$). During the same period, blood volume flow (Fig. 1) increased slightly above baseline by 2.2% (from 0.59 to 0.60 ml s^{-1}; 95% CI −16 to 25%; $P = 0.83$).

Table 1 Intraday reproducibility of venous hemodynamic parameters of blood flow velocity, popliteal vein cross-sectional area and blood volume flow measured in this study. The reproducibility is expressed as a range of the coefficient of variation (SD/mean) calculated individually for every exercise regimen assessed and was established by six repeated measurements obtained by the same examiner (S. Garth) from the popliteal vein in 21 healthy subjects over a time period of 3.5 h

Exercise regimen	Blood flow velocity	Popliteal vein cross-sectional area	Blood volume flow
Sitting still (feet flat touching the floor)	7.9–23.4	3.7–8.3	12.7–25.2
Sitting still (feet not touching the floor)	5.8–15.6	1.3–3.5	6.6–16.3
Airline-recommended activities	9.8–19.4	2.4–5.5	10.4–20.5
Foot exercises	9.5–20.2	2.6–7.2	8.8–19.8
Foot exercises against moderate resistance	7.3–13.4	2.2–9.1	7.7–17.9
Foot exercises against increased resistance	10.1–18.1	2.0–7.6	11.3–21.5

Foot exercises against increased resistance Blood flow velocity at 85 min from baseline increased by 15% (from 0.90 to 1.03 cm s^{-1}; 95% CI 0.90 to 31%; $P = 0.036$). Blood volume flow also rose, corresponding to a 16% increase (from 0.71 to 0.82 ml s^{-1}; 95% CI −0.1 to 35%; $P = 0.050$; Fig. 1).

Changes in blood volume flow at 100 min from baseline: sitting still (feet flat touching the floor) vs. foot exercises, foot exercises against moderate resistance, and foot exercises against increased resistance

At 100 min from baseline (Fig. 1), blood volume flow was reduced by 17% for airline-recommended activities (from 0.77 to 0.64 ml s^{-1}; 95% CI −30 to −2.6%) and by 16% for foot exercises (from 0.62 to 0.52 ml s^{-1}; 95% CI −29 to 0.49%). This was significantly less (both $P = 0.0024$) than the reduction of 42% (from 0.77 to 0.44 ml s^{-1}) for subjects sitting still (feet flat touching the floor). Foot exercises against moderate resistance demonstrated a slight but significant increase ($P < 0.0001$) above baseline of 2.2% (from 0.59 to 0.60 ml s^{-1}; 95% CI −16 to 25%) compared with the 42% decrease below baseline in subjects sitting still (feet flat touching the floor). The greatest increase above baseline of 5.8% (95% CI −16 to 33%) was seen for foot exercises against increased resistance (from 0.71 to 0.75 ml s^{-1}). This was significantly higher ($P < 0.0001$) than that found in subjects sitting still (feet flat touching the floor).

Differences in the popliteal vein cross-sectional area for sitting still (feet flat touching the floor) vs. foot exercises, foot exercises against moderate resistance and foot exercises against increased resistance, for the duration of the study

As shown in Fig. 2, the popliteal vein cross-sectional area for subjects sitting still (feet flat touching the floor) decreased by 14% compared with foot exercises (from 0.83 to 0.71 cm^2; 95% CI −17 to 11%) and decreased by 25% compared with foot exercises against moderate resistance (from 0.83 to 0.62 cm^2; 95% CI −28 to −22%), which was significant (both $P < 0.0001$).Compared with sitting still (feet flat touching the floor), the reduction of 5.9% in the cross-sectional area for foot exercises against increased resistance (from 0.83 to 0.78 cm^2; 95% CI −9.4 to −2.4%) was significant ($P = 0.0014$).

Sitting still, feet flat touching the floor vs. sitting still, feet not touching the floor

Blood volume flow for subjects sitting still, feet not touching the floor decreased by 48% (from 0.70 to 0.36 ml s^{-1}; 95% CI −63 to −28%; $P = 0.015$) at 65 min from baseline, representing a decline of almost 2-fold compared with the 29% decrease for subjects sitting still with feet flat touching the floor during the same period (Fig. 3).

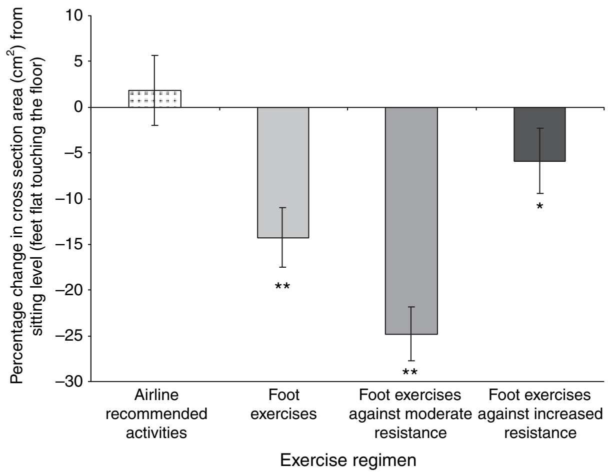

Fig. 2. Comparison of percentage change and 95% CI in the popliteal vein cross-sectional area (cm^2) for subjects sitting still (feet flat touching the floor) vs. subjects performing airline-recommended activities, foot exercises, foot exercises against moderate resistance and foot exercises against increased resistance over the 100-min study period. *$P = 0.0014$, **$P < 0.0001$ when compared with sitting still (feet flat touching the floor).

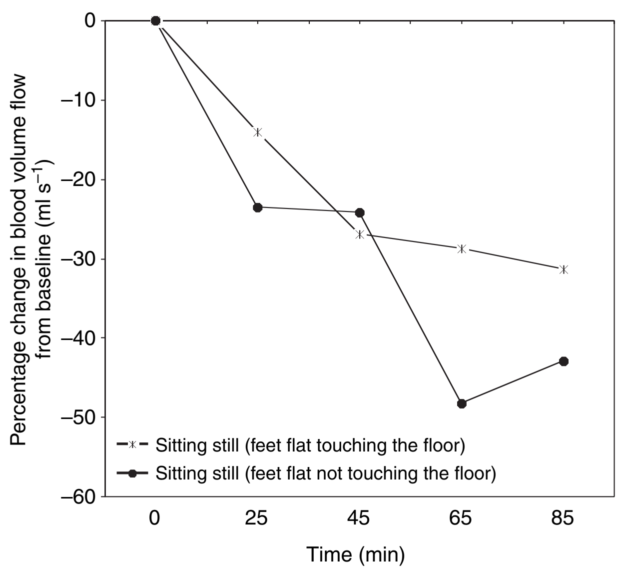

Fig. 3. Percentage change in blood volume flow (ml s^{-1}) in the popliteal vein in subjects sitting still, feet flat touching the floor and subjects sitting still, feet not touching the floor.

Change in blood volume flow for sleeping subjects vs. awake subjects

Over a period of 1 h, sleeping subjects in the sitting position had a decreased blood volume flow of 0.08 ml s^{-1}, reflecting a reduction of 4.4% (95% CI −20 to 11%). In contrast, awake subjects had an increase in volume flow of 0.06 ml s^{-1}, representing a rise of 18% (95% CI −2.1 to 38%). A 22% difference in blood volume flow was demonstrated between sleeping subjects vs. subjects who had been awake for > 1 h ($P = 0.033$).

Discussion

It is well-appreciated that inactivation of the natural calf and foot muscle pumps in subjects sitting motionless results in attenuated blood flow (Figs 1 and 3) that may lead to stagnation and ultimately thrombogenesis [15–17]. Our study showed that this reduction in volume flow may be further compounded when sleeping. Commencing recommended airline activities showed a rise in blood volume flow (Fig. 1). However, initiating the activities earlier and continuing these more regularly may have improved volume flow sooner. Vigorous activities such as foot exercises and foot exercises against moderate resistance proved to be essential in order to provide a positive increase in blood volume flow. The most beneficial positive increase above baseline was demonstrated in subjects performing foot exercises against increased resistance (Fig. 1).

The 2-fold reduction in blood volume flow in subjects sitting still with feet not touching the floor compared with feet flat touching the floor reinforces the evidence that seat height and subject leg-length are significant factors that should be considered when traveling for extended periods. Studies on popliteal venous blood flow in short people have been limited. Our results provide additional confirmatory evidence for the MEGA study, a large, population-based, case–control study [18], validating that short-legged individuals have an increased DVT risk when traveling seated for long periods. The MEGA study showed that, compared with people of average height, the DVT risk was almost 5-fold for tall (more than 1.90 m) individuals for road journeys and 7-fold for air travel. The risk of air travel in short people (less than 1.60 m) was almost 5-fold. The MEGA results should, however, be interpreted with caution because of the small within-strata sample sizes [18]. Furthermore, our study suggests that possible popliteal vein compression in short-legged individuals may be an important contributing factor to precipitating venous stasis, leading to a higher risk of DVT in air travel compared with traveling by car, where the seating position is adjustable.

Blood flow is important for preserving hemostatic equilibrium, with vascular endothelium playing an important antithrombotic role. A positive increase in blood volume flow, i.e. when subjects performed vigorous activities, is likely to enhance fibrinolytic activity. Comerota *et al.* showed that the predominant mechanism of fibrinolytic enhancement by intermittent pneumatic compression devices, in which the antithrombotic effect is thought to be the result of increased venous blood flow, was a decrease of plasminogen activator inhibitor-1, leading to an increase in activity of tissue-type plasminogen activator (t-PA), although t-PA is probably not the only cause [19]. Giddings *et al.* demonstrated a significant association between t-PA and fibrinolytic activity; however, the increased fibrinolysis was not directly proportional to the rise in t-PA and urokinase plasminogen activator. This study revealed a significant fall in factor VIIa associated with increased levels of tissue factor pathway inhibitor [20]. Throughout our study no DVTs were detected and there were no complaints of either edema or leg swelling.

Compression stockings have been shown to decrease the incidence of DVT by almost nineteenfold in extended flights in high-risk subjects and all DVTs were observed in subjects sitting in a window or central seats [4]. In-flight stockings providing 20–30 mmHg graduated pressure have been shown to prevent edema and swelling [21]. When correctly fitted, they significantly reduce vessel diameter and are associated with an expected increase in linear velocity of venous outflow, preventing stasis and venous distension by enhancing the emptying of valvular cusps [22–24]. Recommended DVT preventative measures for high-risk long-distance travelers include correctly fitted below-knee GCS (15–30 mmHg graduated pressure) or prophylaxis with single dose of LMWH prior to departure [4,11,13]. The use of aspirin is not recommended [13].

Our study limitations include generally an older traveling population with possible risk factors for thrombosis compared with our participants. Additionally, the duration of the examination, 1.5 h, may not have been sufficient to observe leg swelling and edema, a problem when traveling for ≥2 h with the risk rising exponentially with increasing time of travel [21]. Blood flow in the popliteal vein varies between individuals and differs in a single person [25] over time because of body position, breathing and the cardiac cycle [26]; therefore, reproducibility of velocity results will not be precise [17]. Reports have shown that a coefficient of variation of < 20% is acceptable [27].

Although it is possible that reduced venous blood flow may lead to extended contact time of activated platelets and clotting factors within the vein wall thereby permitting thrombus formation, stasis alone cannot be causally related to DVT. Current 'flow' models examining how the processes of coagulation and thrombosis come together are limited, and investigating the dynamic 'flow' environment continues to remain a challenge [28].

With the increasing number of air travelers each year, our findings of popliteal venous blood flow being decreased by being motionless, reduced more in people with feet not touching the floor and enhanced by more vigorous foot exercises, have implications for the risk of DVT associated with prolonged travel.

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Disclosure of Conflict of Interests

The authors state that they have no conflict of interest.

Supplementary material

The following supplementary material is available for this article:

Fig. S1. In the foot exercise against moderate resistance, active plantar and dorsiflexion foot exercises were performed on a flat, non-pivoting springboard obtained from an armchair.

Fig. S2. In the foot exercise against increased resistance, an apparatus was designed that consisted of a pivoting pedal connected with an elastic tension band. This allowed subjects to perform active plantar and dorsiflexion exercises requiring increased muscle exertion.

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