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ORIGINAL RESEARCH

Merino Wool Graduated Compression Stocking Increases Lower Limb Venous Blood Flow: a Randomized Controlled Trial

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ABSTRACT

Introduction: Graduated compression stockings represent a nonpharmacological approach to reduce the risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) due to prolonged immobility through reducing lower limb venous stasis. A novel merino wool, double-layer, below-knee graduated compression stocking has been developed to reduce the risk of air travel-related DVT and PE. ***Methods:*** Twenty healthy adult participants were randomized to wear the novel graduated compression stocking on either the left or right leg. Doppler ultrasound measurements of popliteal venous blood flow were made on both legs over a 120-minute period. The primary outcome was peak systolic velocity in the popliteal vein at 120 minutes. Secondary outcomes included mean flow velocity, total volume flow, vein cross-sectional area, and change in ankle and calf measurements. ***Results:*** The popliteal vein peak systolic velocity was 0.35 cm/s (95% confidence intervals [CI], 0.22 to 0.49, $P<0.001$) higher with stocking use at 120 minutes, a difference of 24%. Mean flow velocity and total volume flow were also significantly higher with stocking use. Ankle and calf circumference were decreased with stocking use, with an overall difference of –6.3 mm (95% CI, –11.3 to –1.2, $P=0.021$) and –7.9 mm (95% CI, –13.3 to –2.4, $P=0.011$), respectively. ***Conclusion:*** The novel merino wool double-layer, below-knee graduated compression stocking increases lower limb venous blood flow during prolonged seated immobility. Its use is likely to reduce the risk of DVT and PE in situations of prolonged seated immobility, such as long-distance air travel. The reduction in lower limb swelling associated with their use suggests that the stockings are likely to

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have utility in the treatment of chronic venous insufficiency and lymphedema.

Keywords: blood flow; compression stockings; Doppler ultrasound; popliteal vein; venous thromboembolism

INTRODUCTION

Prolonged seated immobility is a common and important risk factor for the development of venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE).[1-4] The risk of VTE with prolonged seated immobility may occur in a number of different situations including long-distance air, car, or train travel, work, and recreation.[1-16] The most important mechanism contributing to the risk of DVT is reduced blood flow in the deep veins in the lower limbs.

Graduated compression stockings represent a nonpharmacological approach in reducing the risk of DVT with associated prolonged immobility through reducing venous stasis and enhancing venous blood flow.[17-20] The effectiveness and simplicity of their use have made them popular in preventive care, both in the hospital setting and amongst travelers. In considering new designs of graduated compression products, it is important to determine their physiological effects on venous hemodynamics. In this study, we have investigated the effect on lower limb venous blood flow with a novel merino wool below-knee graduated compression stocking.

METHODS

Participants

Twenty adult (13 female) participants aged between the ages of 18 and 65 years old were recruited into the study from a volunteer database. Exclusion criteria included a history of previous or current DVT, pregnancy (which may alter lower limb venous return from compression at the level of the iliac vein), history of previous or current peripheral vascular disease, or any other lower limb abnormality considered by the study researcher to be inappropriate for wearing a graduated compression stocking.

Eligible participants gave written informed consent, and underwent anthropometric measurements including weight, height, and body mass index, as well as several lower leg measurements which were used to ensure that a correctly sized compression stocking was supplied. Participants were randomized to wear a graduated compression stocking on either their left leg or right leg, by a computer-generated random allocation supplied by a biostatistician.

Participants subsequently attended the ultrasound facility for measurements of popliteal venous blood flow and other outcomes. Participants were requested to refrain from undertaking any strenuous physical exercise, such as running, rowing, or cycling, for 24 hours before the ultrasound examination. Light-to-moderate physical activity, such as walking or swimming, was considered acceptable prior to the appointment. Before testing, participants were rested quietly for 10 minutes. Participants then sat upright on padded chairs, with their feet placed flat on the floor in front of them. The personally sized compression stocking was applied according to the randomization schedule, and the other leg served as the control. An angle of 120 degrees between the femur and the tibia of both legs was achieved using a goniometer, to standardize the degree of flexion between patients. This position also permitted the sonographer enough room in the popliteal fossa to position the ultrasound probe. The feet were elevated until the thigh was horizontal to the floor, in an attempt to limit any venous flow impairment caused by compression exerted by the edge of the seat on the back of the thigh. The participants were instructed not to move their feet and to try to keep their leg muscles relaxed until the conclusion of the study measurements.

An experienced sonographer used a Toshiba Aplio XG ultrasound machine with a linear 8 probe (Toshiba America Medical Systems Inc., Tustin, California, USA) to measure popliteal vein blood flow parameters at 0, 30, 60, and 120 minutes after the stocking was applied. The mean of two measurements was used to determine flow at each time point. The Doppler angle of insonance was standardized at 60 degrees to the popliteal vein at the level of the crease in the popliteal fossa. A small Doppler sampling gate of 2.5 mm was used to minimize any interference by arterial pulsations on the tracings. During the measurement process the subjects were asked not to move at all, not to talk, and were encouraged to maintain relaxed, even respiration, to reduce interference with hemodynamics that can be seen with deeper breathing. Due to the length of the stocking and the location of the vein segment scanned, it was not possible to blind the ultrasonographer to which leg had the stocking applied.

The primary outcome variable was the peak systolic velocity in the popliteal vein. Preplanned secondary outcome variables were mean flow velocity, total volume flow, and vein cross-sectional area. After the study started, it was noted that the nonstocking leg of several of the participants was swollen, in comparison with the leg to which the stocking was applied. To further assess this informal observation, the leg circumference was measured at a level just above the lateral and medial malleolus, and at the widest part of the calf, prior to application and after the stocking was removed in the final eight subjects studied.

Figure 1. Encircle Class 1 below-knee graduated two-layer therapy structure and application.

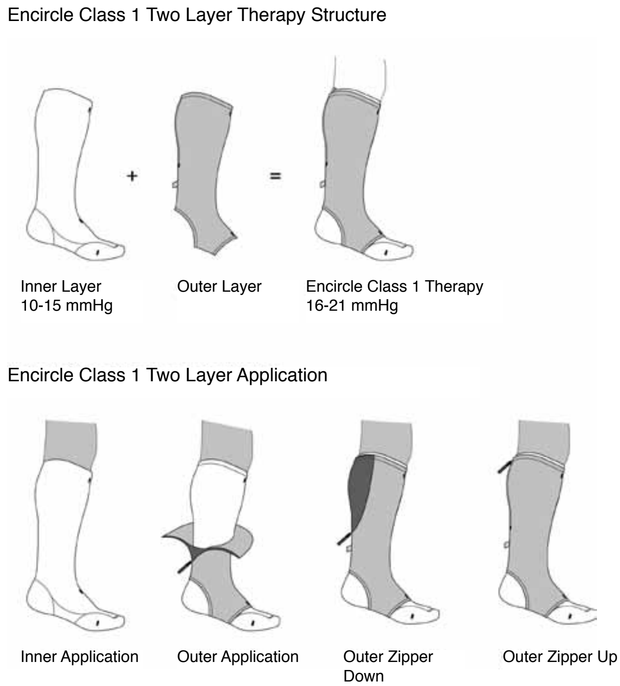
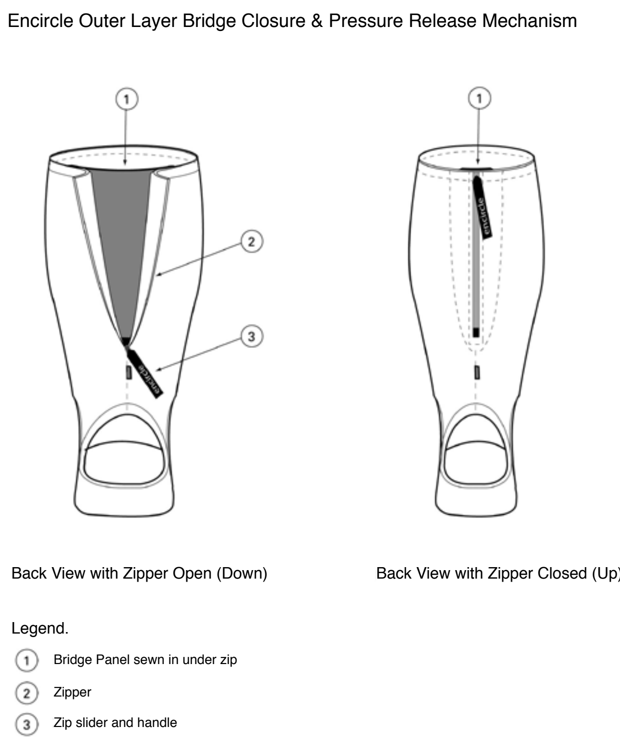


Figure 2. Encircle "bridge" closure and pressure release mechanism. Back view of the outer layer of the compression garment.



"Encircle" Graduated Compression Stocking

The study intervention was the "Encircle" product - a novel, two-layered, Class 1, below-knee graduated compression stocking, with a composition of up to 45% merino wool, 40% elastane, and 15% polymide, manufactured by The Merino Company (Levin, New Zealand). The Encircle compression system is comprised of an inner layer together with an outer layer, which incorporates a novel zipper with an elasticized "bridge" closure mechanism (Figures 1 and 2). This mechanism facilitates the application of the outer layer over the inner layer, and protects the user from potential pressure caused by the zip. The inner layer exerts 10-15 mmHg of pressure; upon zipping the outer layer of the garment closed over the inner layer, a total compression of 16-21 mmHg (Class 1) is achieved.

In contrast to the synthetic fabrics used in the majority of compression hosiery available, merino wool is a natural protein fiber with hygroscopic properties, which helps to provide a healthy skin environment underneath the stocking.[21-23] Merino wool fibers have a smaller diameter than most other types of wool, so help to minimize skin irritation. Stockings were worn straight out of the packet without any prewashing.

Statistical Methods

Paired t-tests compared the outcome variables (the mean of two readings) for the stocking use, compared to no use, at each time point separately, and also for the change from baseline. The primary outcome was popliteal peak systolic velocity at 120 minutes. A mixed linear model was used to estimate the overall difference between wearing stockings or not, the effect of time, and whether there was an interaction between wearing stockings and the effect of time. Paired t-tests compared the circumference of the ankle and calf before and after 120 minutes for the stocking and nonstocking leg, and then for the difference between before and after, for stocking use versus no use.

Power Calculation

A pilot study demonstrated a standard deviation for paired differences in popliteal peak systolic velocity of 1.3 cm/s, and the mean peak systolic velocity in the seated position was around 3.5 cm/s.[24] A difference of 20% was considered to represent a significant difference in blood flow. A sample size of 20 participants had 80% power to detect a difference of 0.9 cm/s of peak systolic velocity, using a paired t-test.

RESULTS

Out of the 20 participants who completed the study, one subject withdrew due to fainting after seeing the initial ultrasound image on the monitor. A total of 63.2% of the participants were female (*n*=12; male participants, *n*=7). The characteristics of the participants are shown in Table 1.

Table 1. Characteristics of participants.

Variable	Mean (SD)	Median (IQR)	Min to max
Age (years)	37.9 (9.7)	35 (30 to 43)	26 to 61
Height (m)	1.73 (11.6)	1.74 (1.65 to 1.80)	1.52 to 1.98
Weight (kg)	71.4 (11.6)	70 (61 to 82)	57 to 99
BMI (kg/m^2)	24.1 (4.7)	22.7 (21.3 to 25.0)	19.9 to 39.7

BMI= body mass index; IQR=interquartile range; SD=standard deviation.

Table 2. Popliteal vein measurements according to stocking and no stocking treatments during the 120 minutes of seated immobility. Data presented as mean (SD).

	Time (minutes)			
Variable	**0**	**30**	**60**	**120**
Peak systolic velocity (cm/s)				
Stocking	2.4 (1.0)	2.2 (0.64)	2.3 (0.74)	2.1 (0.50)
No stocking	2.1 (0.57)	1.9 (0.47)	1.9 (0.37)	1.7 (0.45)
Mean flow velocity (cm/s)				
Stocking	1.6 (0.62)	1.4 (0.36)	1.4 (0.44)	1.3 (0.30)
No stocking	1.4 (0.46)	1.3 (0.27)	1.2 (0.27)	1.1 (0.33)
Total volume flow (L/min)				
Stocking	0.09 (0.036)	0.08 (0.029)	0.09 (0.035)	0.08 (0.025)
No stocking	0.08 (0.026)	0.07 (0.029)	0.07 (0.025)	0.07 (0.020)
Vein area (mm²)				
Stocking	64.0 (19.0)	62.4 (17.5)	63.7 (20.6)	60.0 (17.6)
No stocking	62.4 (15.5)	63.3 (16.9)	64.5 (17.8)	65.1 (16.8)

SD=standard deviation.

Table 3. Differences in popliteal vein measurements between stocking and no stocking treatment during the 120 minutes of seated immobility.

	Time (minutes)			
Variable	**0**	**30**	**60**	**120**
Peak systolic velocity (cm/s)				
Mean (SD)	0.31 (0.75)	0.29 (0.51)	0.47 (0.67)	0.34 (0.47)
95% CI	−0.05 to 0.67	0.05 to 0.53	0.15 to 0.80	0.12 to 0.56
P value	0.084	0.022	0.007	0.004
Mean flow velocity (cm/s)				
Mean (SD)	0.14 (0.40)	0.12 (0.30)	0.25 (0.38)	0.20 (0.27)
95% CI	−0.05 to 0.33	−0.03 to 0.26	0.07 to 0.43	0.07 to 0.32
P value	0.150	0.110	0.011	0.005
Total volume flow (L/min)				
Mean (SD)	0.010 (0.030)	0.007 (0.017)	0.017 (0.029)	0.007 (0.024)
95% CI	−0.003 to 0.026	0.000 to 0.015	0.004 to 0.031	−0.004 to 0.019
P value	0.110	0.070	0.017	0.210
Vein area (mm²)				
Mean (SD)	1.6 (15.9)	−0.9 (16.6)	−0.8 (17.6)	−5.1 (19.1)
95% CI	−6.1 to 9.3	−8.9 to 7.1	−9.3 to 7.7	−14.4 to 4.1
P value	0.67	0.81	0.84	0.26

CI=confidence intervals; SD=standard deviation.

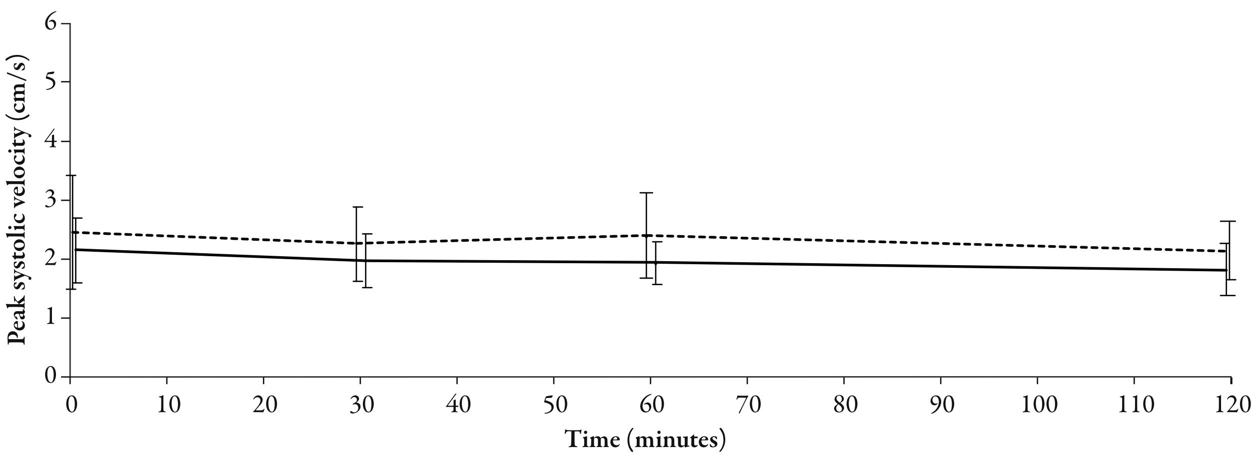
The summary statistics for the outcome variables are shown in Tables 2 and 3. At 120 minutes, the peak systolic velocity was 24% higher with the stocking treatment, with a mean difference of 0.34 cm/s (95% CI, 0.12 to 0.56, P=0.004). The peak systolic velocity was also significantly greater with stocking use, compared with no stocking use, at 30 and 60 minutes. The mean flow velocity and total volume flow were greater at 60 and 120 minutes with stocking use,

Table 4. Differences in popliteal vein measurements between stocking and no stocking treatment analyzed by mixed linear model.

	Stockings minus no stockings (95% CI)	**Change per minute (95% CI)**	***P* value for stockings time interaction**
Peak systolic velocity (cm/s)	0.35 (0.22 to 0.49) $P<0.001$	−0.0024 (−0.0044 to −0.0005) $P=0.019$	0.77
Mean flow velocity (cm/s)	0.17 (0.10 to 0.25) $P<0.001$	−0.0022 (−0.0035 to −0.0009) $P=0.003$	0.46
Total volume flow (L/min)	0.011 (0.0054 to 0.017) $P<0.001$	−0.001 (−0.0016 to −0.0003) $P=0.003$	0.76
Vein area (mm^2)	1.2 (−2.2 to 4.5) $P=0.49$	−0.004 (−0.042 to 0.034) $P=0.83$	0.17

CI=confidence intervals.

Figure 3. The time course of peak systolic velocity in popliteal vein for stocking (dotted line) and no stocking (continuous line) treatments.



but there was no statistically significant difference in vein cross-sectional area (Tables 2 and 3). Mixed linear models confirmed these findings, with the peak systolic velocity, mean flow velocity, and total volume flow all significantly greater with the use of stockings (Table 4). For both the legs with the stocking and without the stocking there was a gradual decline in these variables with time, but the rate of decline was independent of whether or not stockings were used (Figure 3). The peak systolic velocity was 0.35 cm/s (95% CI, 0.22 to 0.49, $P<0.001$) higher with stocking use, using the mixed linear model estimate.

There was a significant increase in the ankle circumference by the end of the 120-minute study period in the nonstocking leg of the subgroup; the reduction in ankle circumference in the stocking leg was not significant. The overall difference in the baseline to 120-minute endpoint measurement of ankle circumference

Table 5. Differences in "after versus before" measurements of ankle and calf circumference (mm) accordance to stocking and no stocking treatments.

Variable (*n*=8 for all)	Mean (SD)
Ankle	
Nonstocking leg before	220.6 (13.0)
Nonstocking leg after	225.0 (15.9)
Nonstocking leg after minus before	4.4 (3.2)
Estimate (95% CI)	4.4 (1.7 to 7.1)
P value	*P*=0.006
Stocking leg before	222.3 (13.2)
Stocking leg after	220.4 (14.6)
Stocking leg after minus before	−1.9 (4.3)
Estimate (95% CI)	−1.9 (−5.4 to 1.7)
P value	*P*=0.25
Stocking leg after minus before, minus nonstocking leg after minus before	−6.3 (6.0)
Estimate (95% CI)	−6.3 (−11.3 to −1.2)
P value	*P*=0.021
Calf	
Nonstocking leg before	384.8 (28.0)
Nonstocking leg after	397.3 (33.1)
Nonstocking leg after minus before	12.5 (6.9)
Estimate (95% CI)	12.5 (6.8 to 18.2)
P value	*P*=0.001
Stocking leg before	383.9 (24.6)
Stocking leg after	388.5 (32.8)
Stocking leg after minus before	4.6 (10.7)
Estimate (95% CI)	4.6 (−4.3 to 13.6)
P value	*P*=0.26
Stocking leg after minus before, minus nonstocking leg after minus before	−7.9 (6.5)
Estimate (95% CI)	−7.9 (−13.3 to −2.4)
P value	*P*=0.011

CI=confidence intervals; SD=standard deviation.

between the stocking leg and nonstocking leg was –6.3 mm (95% CI, –11.3 to –1.2, *P*=0.021) (Table 5). There was a significant increase in the calf circumference during the 120-minute period in the nonstocking leg; the increase in calf circumference in the stocking leg was not significant. The overall difference in the baseline to 120-minute measurement in calf circumference between the stocking leg and nonstocking leg was –7.9 mm (95% CI, –13.3 to –2.4, *P*=0.011) (Table 5).

DISCUSSION

This study has demonstrated that the novel, merino wool, below-knee graduated compression stocking increases lower limb venous blood flow during prolonged seated immobility. The magnitude of the increase in popliteal vein peak systolic velocity was similar to that observed with other Class 1 and 2 graduated compression stockings.[18] A wide range of Class 1 and 2 below-knee graduated compression stockings have been shown to reduce the risk of VTE associated with long-distance travel.[25] As a result, it is reasonable to conclude that the novel stockings may be effective in reducing the risk of VTE associated with prolonged seated immobility, due to long-distance travel. The stocking was also associated with a reduction in the swelling of the leg at both the ankle and calf, which suggests potential utility in lower limb edema, secondary to chronic venous insufficiency and lymphedema.

There are a number of methodological issues relevant to the interpretation of the study findings. We studied healthy participants without previous DVT or PE to ensure that our results were generalizable to the working public. Doppler ultrasound was employed as a highly sensitive, specific, and reproducible noninvasive method of measuring lower-limb deep-vein hemodynamics.[26,27] The peak systolic velocity was chosen as the primary outcome variable, as it represents the most consistent nonartefactual wave form detected by ultrasound. Participants were instructed not to move their legs in each position to provide a stable baseline measurement, and to ensure that the findings related to seated immobility. Although it has been demonstrated that the right and left legs have similar venous hemodynamics and vein diameters,[18,28] our participants were randomized to the application of the stocking to either the right and/or left leg, to avoid any potential difference. As popliteal vein blood flow decreases progressively over time,[29] the measurements were made over a 120-minute time period. This also had the advantage of replicating the situation of prolonged seated immobility. It is known that small changes in a person's seating position can affect lower limb hemodynamics, and for standardization, measurements were made with the leg flexed to 120 degrees.

A limitation of the study is that it was conducted in a research setting under controlled conditions in healthy participants. As a result, our findings may not be generalizable to participants with venous or arterial disease, or different body habitus. A further limitation was that it was not possible to blind the sonographer from the intervention allocation, due to the requirement to undertake the ultrasound examination of popliteal vein close to the upper end of the stocking, and this may have biased the results.

We note the lack of concordance in the available literature of the magnitude of popliteal peak systolic velocity reported when participants are seated at rest. We observed a peak systolic velocity of 2.1 cm/s without any compression therapy, which contrasts with the findings reported by Kalodiki et al.[30] and Delis et al.,[31] who reported peak systolic velocity values of 8.4 cm/s and about 6 cm/s, respectively. The differences in peak systolic velocity values are most likely explained by our strict requirement that the participants kept their legs very still and relaxed for the duration of the testing period. However, we cannot rule out other relevant variables that were technician dependent such as ultrasonography measurement settings, probe placement, orientation, and pressure, or protocol related variables such as chair design and material, clothing worn, participant hydration, or environmental variables such as ambient temperature.

The main finding was that wearing the graduated compression stocking increased lower limb venous hemodynamics, determined by measurements of peak systolic velocity, mean flow volume, and total volume flow in the popliteal vein. The magnitude of the increase in peak systolic flow was 24%, similar to the 26% increase previously reported with a comparable Grade 1 below-knee graduated compression stocking.[18] In contrast, there was no reduction in vein cross-sectional area, which had been noted previously.[18]

After the study started, we observed that some participants developed swelling in the leg without the stocking. To investigate this further, we undertook a supplementary investigation in a subgroup of participants who attended later in the study, in whom ankle and calf measurements were made before and immediately after the stocking had been worn for 120 minutes. This showed that there was a reduction in swelling at both the ankle and calf in the legs with the use of the stocking. Although the interpretation of this observation was limited by the possibility of bias, as the comparisons were based on nonblinded measurements, it does suggest that the stockings may have utility in reducing lower limb edema associated with lymphedema and chronic venous insufficiency, including varicose veins and venous ulcers. Our findings are consistent with previous observations that below-knee compression stockings with a pressure range of between 11 and 22 mmHg are able to reduce or totally prevent edema developing during the working day.[32]

Prolonged seated immobility during either work or travel is now the most common risk factor for DVT and PE in the New Zealand population.[3,4] As venous stasis is the most important factor contributing to the risk of DVT and/or PE with prolonged seated immobility, the increase in lower limb venous blood flow with this compression stocking would suggest that its use may reduce the risk of DVT and/or PE in this situation. In support of this view, it has been shown in clinical trials that similar below-knee graduated compression stockings reduce the risk of DVT with long-distance air travel by about 90%.[25]

CONCLUSION

In view of these findings, it would be reasonable to recommend the use of the novel merino wool, Grade 1, below-knee graduated compression stockings to reduce the risk of VTE in situations of prolonged seated immobility, such as long-distance travel. Their use can also be recommended to reduce VTE risk in other situations associated with immobility, such as in the hospital setting with a medical illness, or following surgery.[20] The study findings also suggest that this stocking can be used to reduce lower limb edema secondary to chronic venous insufficiency and lymphedema.

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Thomas Charles is the named guarantor author responsible for the integrity of the work.

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