Formation of Edema and Fluid Shifts During a Long-haul Flight

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Background: More than 1.5 billion passengers travel by aircraft every year. Leg edema, as a sign of venous stasis, is a well-known problem among passengers during and after long-haul flights. Until now, no studies have been done on the development of leg edema and fluid shifts under real flight conditions. The aim of our study was to evaluate edema formation in the leg and to investigate possible fluid shifts to the interstitial space under real flight conditions.

Methods: Twenty participants, 10 without risk and 10 with moderate risk for venous thrombosis, were selected. They flew from Vienna to Washington, flight time 9 h, and returned 2 days later. Investigations were done 48 h before the flight, between the fifth and eighth flight hour on board to Washington and back to Vienna, immediately after arrival in Vienna, and 1 and 3 days after arrival. Plethysmographic measurements were carried out using an optoelectronic scanner system (Perometer). Thickness of the skin was measured at the forehead and in front of the tibia.

Results: There were no differences in all measurements between both groups. The volume of the leg increased from 8242±1420 mL to 8496±1474 mL after the flight ($p < .001$). Volume accumulation was distributed to the lower leg as well as to the thigh. Skin thickness in front of the tibia increased significantly during the flight ($p < .05$), and remained elevated 1 day after arrival.

Conclusion: We have demonstrated that long-haul flights induce significant fluid accumulation in the lower extremity, involving the lower leg and thigh. This increase in tissue thickness was maintained for some days after the flights.

More than 1.5 billion passengers travel by aircraft every year.[1] In the past few years, interest has focused on a possible causal link between deep venous thrombosis (DVT) and long-haul flights.[2–10] The exact incidence of DVT after long flights is at present not clear. Endothelial lesion, stasis and hypercoagulability (Virchow's triad) are the crucial pathophysiologic mechanisms for the development of DVT.[11] It is suggested that sitting in a cramped position, immobility and compression of the popliteal vein result in venous stasis, thus increasing the risk of DVT during long-haul flights. Moreover, aircraft-specific factors, e.g. moderate hypoxia corresponding to a maximum

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altitude of 2,500 m, and low humidity (3% to 15%), have been suggested to be aggravating factors. Recently, we have demonstrated activation of the coagulation system and suppression of fibrinolysis after a long-haul flight.[12] However, there was no evidence of significant intravasal thrombin formation as measured by thrombin–antithrombin (TAT) complexes. Leg edema, as a sign of venous stasis, is a well-known problem among passengers during and after long-haul flights.[13] Landgraf et al. measured leg edema in 12 volunteers who sat for 12 h under simulated aircraft conditions but with normoxia and normal humidity.[13] They found significant fluid accumulation of about 127 mL in the lower leg after the 12 h. Moderate hypoxia may influence fluid balance even in healthy subjects. Gunga et al. observed a significant fluid shift to the interstitial space within several hours after exposure to 2,315 m which was, interestingly, measured in the upper part of the body, namely over the forehead and sternum.[14] Until now, no studies have been done on the development of leg edema and fluid shifts under real flight conditions. The aim of our study was to evaluate edema formation in the leg and to investigate possible fluid shifts to the interstitial space under real flight conditions.

Methods

In summer 2001, we performed the project "economy class syndrome (ECS)-2001". Twenty participants from Innsbruck, Austria were included in the study after laboratory screening. The group was divided into two subgroups according to their risk profiles for the development of DVT as defined in a recent consensus document.[15] The first group comprised those with minor risk (10 healthy subjects, 5 men, 5 women; mean age 29.7 years; mean body mass index (BMI) 23.6) and the second those with moderate risk (4 men, 6 women; mean age 43.5 years; BMI 33.4). The study protocol was approved by the ethics committee of the Leopold Franzens University, Innsbruck. Written informed consent was given by all participants.

Baseline investigations (T1) were done within 48 h before departure from Innsbruck. The participants were transported from Innsbruck to Vienna by aircraft (flight time 1 h). After a 2-h stopover, we flew in an Airbus 330, Austrian Airlines, for 8 h 20 min, from Vienna to Washington, US. We stayed there for two nights, and then took the night flight back to Austria, arriving in Vienna at 9 am. In the afternoon, all participants flew back to Innsbruck. Investigations on board were done within the fifth and eighth hours of flying time both to Washington (T2) and to Vienna (T3). Postflight examinations were done immediately after arrival at Vienna airport (T4), on the morning of day 1 (T5), and on day 3 (T6) after returning to Innsbruck.

Plethysmographic measurements were carried out using an optoelectronic scanner system (Perometer).[16–18] The sensor used for measurement is a frame, which is moved over the length of the leg. The frame carries a large number of light emitters, each facing a corresponding detector. They form two arrays of light switches, which are perpendicular to each other. These arrays are interrupted by the limb during movement of the frame. Thus, a computer connected to the system is able to catch pairs of limb diameters spaced only 4.7 mm apart. All diameters and their positions in the frame can be plotted vs. their distance from the sole of the foot (for details, see Figure 1). This results in two silhouette pictures taken from the front and from the side. Furthermore, from each pair of diameters, an elliptic cross-sectional area is determined, which forms the base of a 4.7-mm-thick slice. The leg volume between two given points is integrated from the volumes of all slices between these points. The circumference of each slice plotted vs. the distance of the slice from the sole of the foot establishes the circumference profile of the leg. As data collection for one measurement needs only a few seconds, scans can be repeated more than twice a minute. The measurement system has been comprehensively evaluated. Four scans of both legs of each volunteer were taken on the morning of the day before the flight (T1), and another three scans were taken directly after return from the second flight (T4) at the Vienna airport clinic.

Skin thickness was measured using ultrasonic pulse echo equipment (CL3DL, Krautkraemer and Co., Cologne, Germany) with a 10-MHz probe (methodological details were described earlier).[19,20] Tissue thickness was measured at the forehead (TTF), 20 cm in front of the tibia (TTA), 28 cm in front of the tibia (TTB), and 36 cm (TTC) above the sole of the foot.

Hemoglobin (Hb) concentration and packed cell volume (PCV) were measured at all collection times (T1 to T5), using standard methods with single venepuncture from an antecubital vein.

The subjects were allowed to consume alcoholic beverages (up to a maximum of 0.5 L of beer per flight). In order to get detailed information about the subjects' fluid intake and the time that they did not spend sitting, the volunteers were encouraged to fill out the respective protocols.

Statistical Analysis

A repeated measures ANOVA with gender and group as fixed factors was applied for the assessment of the time dependencies and group differences. In the presence of a significant overall test result, linear contrast was used to assess the significance of changes in parameters of each investigation from baseline. A p-value below 5% was considered to be statistically significant. Since none of the

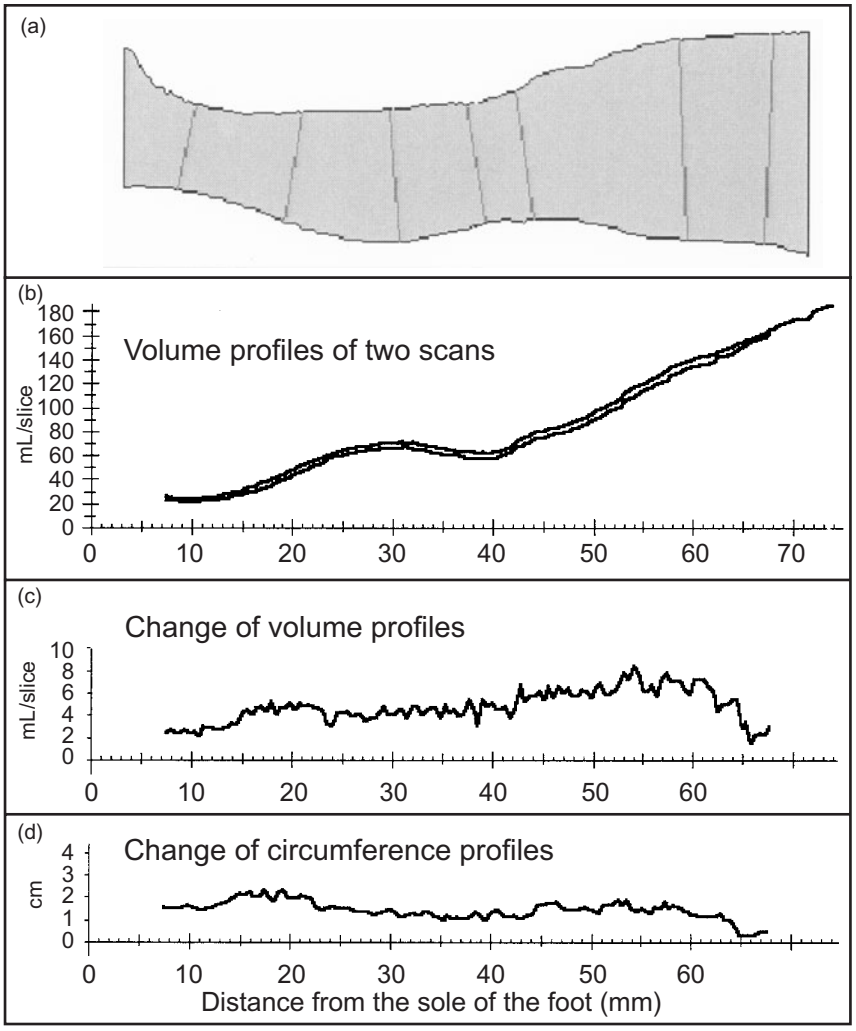

Figure 1 LED scanner method (Perometer) for measuring leg volume changes. (a) Typical side view of the leg before the flights as displayed by the Perometer computer. (b) Volume profile of the leg taken from a scan before flight (lower curve) and after flight (upper curve). (c) Differences between the two volume profiles in an extended scale taken from (b). (d) Differences between the circumference profiles taken from the two scans.

measured parameters showed differences between both groups, the data were pooled. Data in text and the table are given as mean values plus the range (minimum/maximum).

Results

DVT

No volunteer participating in our project showed signs of DVT as measured by compression Duplex sonography.

Perometer Measurements

The volume of the leg increased by +254 mL (–130/577; mean values of both legs) at T4 as compared to T1. Volume accumulation was distributed in the lower leg as well as in the thigh. The volume of the lower leg showed a significant increase of +120 mL (–19.7/273.5) after the flight (T4; $p < .001$). Thigh volume increased by +134 mL (–110.3/303.9) at T4 ($p < .001$). For the separate volumes of the left and the right legs, see the table.

Skin Thickness

The tissue thickness of the tibia (TTA, TTB, TTC) increased significantly during the flight (T2, T3; $p < .05$). It remained elevated (TTA, TTB) 1 day after arrival (T5). Three days after return (T6), tissue thickness returned to preflight levels (T1; Figure 2a,b,c). Tissue thickness at the forehead (TTF) remained unchanged at T2, but showed a significant increase from 4.75±0.92 mm at T1 to

Table Volume of the Leg (Thigh and Calf) Before Flight (T1) and After Arrival at Vienna Airport (T4) as Measured with the Perometer. Values are Means (Minimum/Maximum)

Side	*Thigh/ Lower Leg*	*T1*	*T4*	*p-value (T1 vs. T4)*
Right	Thigh (mL)	5,637 (3,421/7,460)	5,761 (3,474/7,638)	p<.001
Right	Lower leg (mL)	2,544 (1,615/3,824)	2,651 (1,699/3,916)	p<.001
Left	Thigh (mL)	5,747 (3,869/8,075)	5,890 (3,798/8,189)	p<.001
Left	Lower leg (mL)	2,556 (1,589/3,830)	2,688 (1,694/3,977)	p<.001

5.1±0.71 mm at T3 (p<.05). At T6, tissue thickness significantly decreased to 4.23±0.91 mm as compared to baseline measurements (p<.05; Figure 2d).

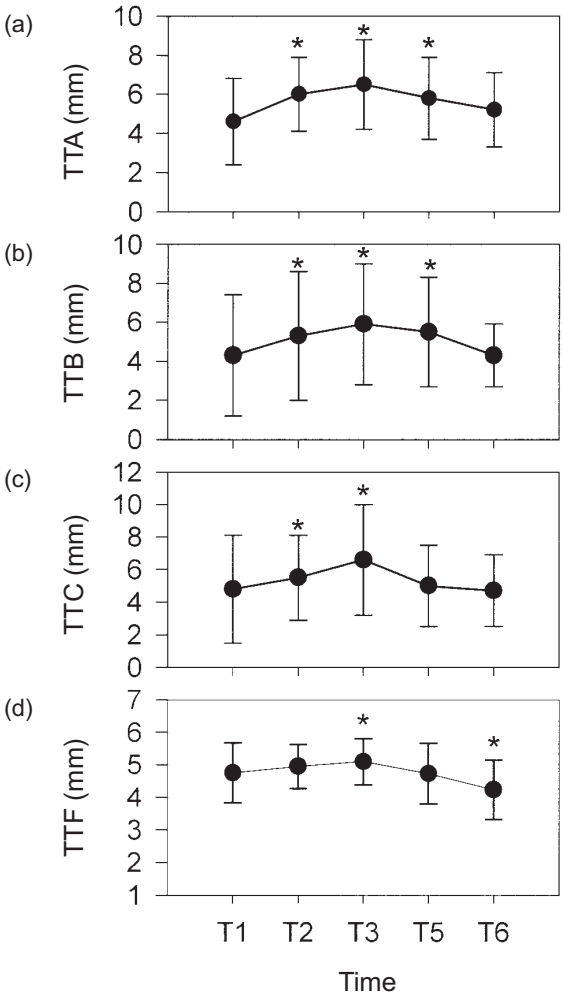

Figure 2 Tissue thickness at different time points (T1, before flight; T2, during the first; T3, during the second flight; T5, 1 day after arrival; T6, 3 days after arrival): (a) 20 cm in front of the tibia (TTA), (b) 28 cm in front of the tibia (TTB), (c) 36 cm above the sole of the foot (TTC) and (d) at the forehead (TTF). Values are means±SD; *= p<.05 compared to T1.

Hemoglobin, Packed Cell Volume

Hb was significantly reduced after return when compared to baseline (mean value and the range at T1—148.5 g/L, 137 g/L to 155 g/L; mean value and the range at T3—145 g/L, 125 g/L to 148 g/L; p<.001). PCV showed a similar time course (mean value and the range at T1—44.5%, 41% to 47%; mean value and the range at T3—43.5%, 37% to 45%; p<.01).

Fluid Intake

Fluid intake was 1.75 L (range 1.15 L to 2.50 L) during the flight to Washington, and 1.61 L (range 0.57 L to 2.85 L) on the flight back to Vienna (p>.05, flight to Washington vs. flight back to Vienna). The time not spent in a sitting position in the aircraft was 34 min (20 min/53 min) and 38 min (20 min/56 min; p>.05, flight to Washington vs. flight back to Vienna).

Discussion

The Perometer method revealed increases in total leg volume (thigh and calf) of 231 mL for the right leg and 275 mL for the left leg after the long-haul flight, or a mean value of ~250 mL per leg.

The measurement of the skin thickness allowed us to localize and to quantify these changes at the calf area more specifically. According to data given in the literature, one-third of the superficial tissue layer consists of exchangeable water. The average surface area of the subjects can be assumed to be 19,400 cm^2.[21] The surface area for one calf represents 6.5% of this total body surface area or 1,261 cm^2 or 2,522 cm^2 for both legs. In the present study, the mean skin thickness of the subjects' calf was determined to be 4.2 mm. This gives, for one calf, a superficial tissue thickness volume of 530 mL for one leg (both legs 1,060 mL). Since the mean tissue thickness during the long-haul flight increased by about 1.5 mm at the tibia at T3, this increase in tissue thickness represents an additional fluid accumulation for each leg of about 189 mL. This is less than the fluid accumulation determined by the Perometer method of about ~250 mL (see above). The difference between the Perometer and the tissue thickness measurements is not surprising, because the Perometer measurements include volume

accumulations of the thigh, knee and a part of the foot, whereas the tissue thickness data are limited to changes from the knuckle up to the knee.

The prolonged increase of skin thickness shows that the redistribution of interstitial fluid after a long-haul flight takes several days. This fluid shift into the tissue is associated with an increase of the hematocrit in the leg veins,[22] which may promote thrombosis. Interestingly, there was no difference in fluid accumulation and edema formation between passengers without and passengers with moderate risk for DVT.

To our knowledge, comparative studies analyzing tissue thickness changes during a real long-haul flight are not available in the literature. Landgraf et al.[13] investigated the influence of sitting for 12 h in a Boeing 747 passenger cabin mockup but with normoxia and normal humidity. They found a significant increase in the lower leg volume that was more pronounced at night (mean increase 127±53 mL) than during the day (83±59 mL). An average of 1,150 ml of fluid retention was calculated. These findings are in very good agreement with our own results.

Peripheral edemas of the head, arms and legs at moderate and, especially, high altitudes have frequently been described by different authors.[23–25] A possible underlying pathophysiologic mechanism for these fluid shifts might be the hypobaric–hypoxic environment inside the aircraft, which affects the Starling forces in the peripheral vascular bed, leading to increased outward filtration from the intravascular bed into the interstitial space. In a large field study with 29 male subjects at 2,315 m under terrestrial conditions (Alpine region), we were able to show that extravasation into the superficial tissues occurred.[14] This earlier study revealed that the fluid shifts in the subjects were accompanied by a loss of total protein and a concomitant drop in the intravascular colloid osmotic pressure 48 h after arrival at this altitude. In contrast, in the present study—in a shorter time frame—the total protein and the colloid osmotic pressure remained unchanged between T1 and T5. Nevertheless, the data from the long-haul flight show that the fluid shifts also have a very rapid component, starting a few hours after exposure to a hypobaric–hypoxic environment. We are aware that, besides the hypobaric–hypoxic environment inside the aircraft, additional factors might contribute to fluid accumulation in the superficial tissues, such as an uncomfortable, cramped sitting position, the ambient temperature in the vicinity of the seat, and the permanent vibration of the underlying surface of the aircraft. Studies underway in our own laboratory (unpublished data) have revealed that human exposure to a vibration with frequencies between 30 and 50 Hz leads to rapid and remarkable edema formation in the leg. Since the degree of fluid accumulation in the leg was similar in the subjects of Landgraf's study, [13] even under normobaric normoxic conditions as in our volunteers, the contribution of hypobaric hypoxia to edema formation has to be clarified in further studies. Rheologic changes in the blood have been reported even after sitting in a quiet position for 2 h.[22] These changes, i.e. increases in viscosity and PCV, were much more pronounced in blood from veins in the dorsum of the foot than in arm veins. Similar results were reported by Iwama et al.,[26] who measured increased PCV and lactate concentrations in the leg venous blood after 2 h of sitting; this was prevented by the wearing of graduated compression thigh-length stockings. We could not detect increases of Hb and PCV in our passengers, but have actually found decreases in these parameters, which may result from adequate fluid intake during the flights.

Conclusions

In conclusion, these data give good support to the argument that travelers should wear individual adjusted pressure stockings during long-haul flights. This seems to be an important outcome of the present study; wear stockings during the flight and especially after the flight, because, as this study has shown by the tissue thickness measurements, outward filtration continues to rise *after* long-distance flights. Since the outward filtration diminishes the intravascular volume, such a vascular volume reduction might propagate venostasis and a thromboembolic event. This is especially likely for those subjects who have additional hemostatic risk factors for clot formation. An increased risk of DVT is evident in long-haul travelers if additional risk factors are present.[27] These pathophysiologic mechanisms are supported by field studies showing that below-knee stockings are beneficial in reducing the incidence of DVT,[7,28] and leg edema formation[29] after long-haul flights.

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