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Chapter

Vein Thrombosis Risk in Women and Travel

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Abstract

Deep vein thrombosis (DVT) of the lower limbs is a serious condition that can lead to pulmonary embolism (PE) in about 15–24% of cases. If it is not diagnosed/treated timely, nearly 15% of these PE are lethal. The relationship between travel and staying in the same position for a long time is well-known since World War II. Generally, it is more frequent in air flights. It is also associated with the economic downturn in airplanes because passengers have limited space and have greater difficulty of moving. It is estimated that approximately 1–6% of long-haul passengers arrive at their destination with a clot in their veins, but most DVT are asymptomatic.

Keywords: thrombosis, travel risk factors

1. Introduction

The real incidence of deep vein thrombosis is not fully known, due to the fact that the studies were depended only on clinical data (the majority of the reported cases had no clinical signs) without confirmation by laboratory and ultrasound findings. A further reason is that the referred studies investigated either DVT or PE and rarely both of the diseases [1, 2]. D-dimers have prognostic value only in 50% of cases of deep vein thrombosis or pulmonary embolism [3, 4]. Most of the published studies indicate that there is an increased risk of venous thrombosis when the travel duration is more than 4 h [3, 4]. Deep vein thrombosis is a serious health issue involving at least half a million Americans each year, and at least 1 in 10 will die suddenly. It depends on the mode of travel either by air flight company or car, bus, and train based fully on all travel-related risks of thrombosis. It is estimated that the risk of such an episode occurring during a long travel is 3–5%, with no reliable international accurate data [5–8]. The reason for the increased risk

of venous thrombosis is an exclusive phenomenon of all travel-related thromboses, which play a role in clot formation. Stasis during the journey, the pressure of the "narrow" seat on the vessels, dehydration, and maybe reduced oxygen saturation are some of the factors that symptoms of venous thrombosis or pulmonary embolism do not always appear immediately. They may occur up to 8 weeks after the travel [9, 10].

Regardless of whether it is a trip by car, train, bus, or plane, travel thrombosis (for flight travel also named "economy class syndrome") will manifest up to 4 weeks after traveling according to the British Committee for Standards in Hematology up to 6 weeks after long-haul flights [9, 10]. It is estimated that 5–15% of all proven venous thromboembolism (VTE) occur in connection with long-haul flights [11, 12]. The risk is highest in the first week and then decreases continuously; the majority (approx. 60–75%) of all travel thrombosis are asymptomatic/low-symptom thrombosis exclusively located in the lower limbs, which is perceived as "unpleasant leg swelling/edema" due to long sitting with the legs hanging down [11, 12].

2. Epidemiology

The clinical relevance of these asymptomatic thromboses is questionable, but they may be the origin for the manifestation of deep vein thrombosis. So far, there is no prospective, controlled study with a sufficient number of cases (adequate statistical power) that proves an evidence-based association between air travel and the risk of venous thromboembolism (VTE). In order to demonstrate a significantly increased risk, a study including around 1 million passengers (+ controls) would be necessary [13].

The risk for VTE mainly depends on the flight duration, the number of flights within 3–4 weeks, and risk factors of each individual predisposing to VTE. According to meta-analyses from case-control studies, long-haul flights increase the risk of VTE by two to four times within the first 4 weeks. For every 2 h of extended flight time, the VTE risk may increase by 26%. The risk of VTE is not increased in healthy passengers without risk factors and a flight duration of less than 3–4 h. It should be taken into account in this context that the basic risk for VTE in healthy women under 35 years without hormone intake is 1–2/10,000/years and increases fourfold after the age of 40 [13–16]. Young women (<30 years) are up to three times more likely to experience VTE than young men. An observational study from France analyzed 116 pulmonary embolisms (PE) over a period of 13 years, which occurred immediately after landing. With approximately the same gender distribution of passengers, 78% of all PE affected women [13–16]. Overall, the incidence of PE was 0.61/1,000,000 female passengers (0.2/1,000,000 male passengers). With a flight distance of more than 10,000 km, this risk rises to 7.2/1,000,000 female passengers. According to another study to 4.8/1,000,000 female passengers with a flight duration over 12 h, the total rate of VTE in healthy women without oral contraceptives is estimated 1/5000 regardless of the flight duration [13–16].

3. Individual risk factors

At least 80% of all passengers (regardless of gender) have at least one identifiable risk factor for VTE (especially PE).

Air travel alone increases the risk of VTE by 1.8 (flight time 8–12 h) to 2.8 times (>12 h), factor V Leiden mutation by 13.6 times, and oral contraceptives even up

to 40 times; BMI > 30 kg/m^2 do not significantly increase the risk for air travelers. Already in 2003, Martinelli et al. referred to the increase in VTE risk on long-haul flights (>8 h) in connection with congenital and acquired thrombophilia (risk increase by 16 times) and oral contraceptives (risk increase by 14 times). According to a recent calculation model by Kuipers et al. based on data from a previous cohort study including employees from international companies, the estimated absolute risk for symptomatic VTE in women after long-distance flights (>4 h) and oral contraceptive use was 1/259 flights and with hormone replacement therapy 1/405 flights [2, 8, 17, 19].

The predisposing factors to VTE are mainly:

- Individual or family history of VTE.
- Presence of varicose veins.
- Pregnancy and the first month after giving birth.
- Oral estrogen-containing contraceptives: increased risk of VTE up to 20 times.
- Recent surgery.
- Cancer diseases.

Women with thrombophilia that had surgery or trauma within the last 3 months, taking oral contraceptives or being under hormone replacement therapy.

- Obesity.
- Height >1.90 or <1.60 m increased risk of VTE by 4–5 times [17–19].
- Obese patients with body mass index (BMI) greater than 30 kg/m^2 and risk of VTE increased by 10 times.

3.1 Risk factors in association to flights

Travel participation can expose passengers to a variety of risk factors that may have impact on their health. Health professionals can obtain information from the International Maritime Health Association and Aerospace Medical Association website (www.imha.net and www.asma.org), respectively.

3.2 Factors that may affect passengers traveling by plane

3.2.1 Cabin pressure

At a normal altitude of 36,000–40,000 feet, the cabin pressure equals that of 6000–8000 feet at sea level and is therefore at low levels resulting in a decrease in oxygen supply [20–22]. This is not dangerous for healthy people unless there are cardiopulmonary problems and hematological disorders, for example, sickle cell anemia. These problems are particularly pronounced when the airplane rises (because of the reduction in air pressure in the cabin, outflow from the middle ear and nasal cavities) and also during the cathode of the plane where there is an increase in air pressure in the cabin, inlet air, and the middle ear to balance the pressures. The reduced air humidity in the flight cabin of 10–20% (optimally

40–70%) in conjunction with other factors such as reduced drinking volume, excessive sweating, or increased diuresis due to increased alcohol/coffee consumption can promote the development of dehydration, respiratory diseases, and finally of deep vein thrombosis.

3.2.2 Moisture content

It is low in cabin <20% and can cause skin dryness and eye and nose discomfort. Moisturizing lotion and sunscreen are recommended, whereas contact lenses are contraindicated.

3.2.3 Ozone

It is a form of oxygen with a different structure to its molecule located in the upper layers of the atmosphere and can irritate the upper respiratory system, but eyes and nose are decomposed by heat and eliminated by compressors.

3.2.4 Cosmic radiation

There are no special effects for passengers on board of the flight. The total effective dose from natural radiation exposure in Germany averages 2.1 millisievert (mSv)/year. The International Commission on Radiological Protection recommends exposure of 1 mSv/year and 0.5 mSv/month as a guideline, within which there is no detectable risk of radiation damage. Internationally, radiation exposure during pregnancy of 1 mSv should not be exceeded totally, which is significantly lower than that associated with a potential health hazard (>20 mSv). The radiation exposure during air travel is clearly dependent on the route, altitude, and duration of the flight. The cosmic radiation in an altitude of 9–12 km is about 100 times higher than on the ground.

For short-haul flights (lower flight altitudes), a radiation exposure of on average 0.001–0.003 mSv/h and for long-haul flights (higher altitude, other flight route) of 0.005–0.008 mSv/h have been determined.

3.3 Motion sickness

It does not occur regularly except in case of atmospheric disturbances. If predisposed it is prudent to avoid alcohol and to supply appropriate medicines.

4. Recommendations

Nearly 50% of the passengers with DVT of one or more extremities may be asymptomatic. However, edema of the limb, pain, and signs as red and hot to touch skin are some of the symptoms. Unspecific symptoms of pulmonary embolism may be present, such as unexplained dyspnea, abnormal heart rhythm, chest pain, intolerance that may be aggravated by coughing or deep inhalation, coughing up blood, anxiety, dizziness, or a tendency to faint. Especially, people in high-risk groups should be informed about early recognition of these symptoms in order to seek for medical help. Preventive measures include sufficient hydration, avoidance of alcohol/excessive caffeine intake, and regular walking during the trip.

The risk of VTE is eightfold increased in patients with the factor V Leiden mutation that affects blood clotting. These passengers should be considered for heparin prophylaxis. According to the French Society of Cardiology, the probability

of venous thrombosis during an airline flight is multiplied by 2.81 in a healthy person, regardless of flight time. The risk is then increased by 26% for every 2 h of flight. Before traveling it is prudent to take the following recommendations into consideration:

Wear comfortable clothing, leave space under the front seat to allow mobility of the lower legs, change posture regularly, do exercises for feet regularly, and book aisle seat, if you are predisposed to VTE.

Walk regularly every 60–90 min, and drink a sufficient amount of fluids (at least 150–200 ml every 2 h) which is especially important for people at increased risk of thrombosis. In these passengers well-fitted elastic compression stockings until the knee are recommended and in high-risk passengers additionally the subcutaneous administration of low molecular weight heparin 2–6 h before traveling.

4.1 Pregnancy and travel

It is estimated that there is 1 pregnant woman per 1000 air travelers. Reliable data on the incidence of VTE in pregnant women with long-haul flights are so far not available. Considering an approximately fivefold increased risk of VTE during pregnancy (compared to nonpregnant women), various calculation models by Cannegieter and Rosendaal have shown an estimated incidence of venous thrombosis of 0.03–0.1% after one air travel in pregnancy. According to a cohort study including a small number of cases (26 thrombosis, 3 of them are pregnant women), the OR for DVT with air travel and pregnancy was 14.3 (95% CI, 1.7–121.0), corresponding to an estimated absolute risk of 1/109 flights [2, 23–25].

Overall, the absolute risk of VTE during pregnancy is 1–2/1000 pregnancies. This risk increases by fivefold in the puerperium. 20.4% of VTE manifest in the first, 20.9% in the second, and 58.7% in the third trimester; 95% of all postnatal VTE occur within 6 weeks postpartum. The risk of VTE in the puerperium is 20–80 times higher than that in nonpregnant women. Due to the increased production of coagulation factors and a reduction in fibrinolytic activity, hypercoagulability occurs in physiological pregnancy. Healthy pregnant women compensate this hypercoagulable state by pregnancy-induced hemodilution and the increased perfusion in microcirculation. According to the risk classification for VTE by Andersen and Spencer, pregnancy and the puerperium were considered as moderate risk for VTE (OR between 2 and 9), even in connection with long-haul flights [2, 23–25].

According to RCOG Guideline No. 37a 2015, air travel of more than 4 hours is an independent risk factor for VTE (evidence level III). This risk increases with additional individual risk factors for VTE which have to be considered in the consulting practice (overview at risk factors for VTE associated with air travel). Regardless of pregnancy, the following "thrombogenic" factors were discussed in connection with long-haul flights.

4.2 Immobilization

Long-term immobilization with sitting for hours in a "cramped" posture (especially kinking of the legs and pressure of the edge of the seat on the popliteal veins) may promote venous stasis in the lower extremities. Air travelers over 190 cm and under 160 cm height are particularly at risk. In this context, it should be mentioned that sitting by the window is associated with a twofold higher risk of VTE than sitting at the aisle. In passengers, with a BMI over 30, the risk of VTE is increased even by sixfold. Significant differences regarding the risk of thrombosis (measurement of the D-dimers) between the first/business class and the economy class have not yet been demonstrated; however, related data are limited [26–29].

Other risk factors associated with air travel are dehydration, reduced air pressure and humidity in the aircraft cabin, disruption of circadian rhythm and hypobaric hypoxia and their effects on changes in the coagulation system [30, 31].

4.3 Recommendations for prevention

So far there are no evidence-based recommendations for the prevention of VTE during air travel, but there are some based on expert consensus (mostly grade D) in various international guidelines. Only the RCOG Scientific Impact Paper No. 1 from 2013 and the ACOG Committee Opinion No. 443 of 2009 explicitly address air travel and pregnancy. A decisive prerequisite for adequate prevention (especially for pregnant women) is a careful individual assessment of risk factors by the doctor (gynecologist/family doctor) before starting the flight. This provides the basis for risk-adapted thromboembolism prophylaxis. A total of five guidelines make risk-related recommendations including risk classification for VTE after air travel [26–29].

According to the AWMF guideline 003/001 (S3), long air flights or bus trips do not require any special prophylaxis measures apart from general basic measures; in individual cases when there are risk factors, calf-length compression stockings should be considered.

If the risk is low, general measures are enough. With intermediate risk, e.g., pregnancy/puerperium, in addition to the general measures from a flight duration of 4 h, the wearing of graduated compression stockings up to the knee is recommended. The importance of compression stockings for thrombosis prophylaxis on long-haul flights (>4 h) also emerges from a 2006 Cochrane analysis (revised 2010) including 10 randomized trials [26–33].

The scientific studies (n = 2856) with moderate quality and different risk profiles for VTE were considered. The primary outcome criterion of this analysis was the rate of symptomatic and asymptomatic (diagnosed by sonography or phlebography) deep vein thrombosis. Wearing well-fitted compression stockings has shown to reduce the rate of asymptomatic deep vein thrombosis from 3.6 to 0.2% (OR 0.10; 95% CI 0.04–0.25; $p < 0.00001$); in addition, the frequency of leg edema was also significantly shown to be significantly decreased as reported by the LONFLIT-4 study [26–35].

If there is a high risk of VTE, in addition to compression stockings, the prophylactic subcutaneous administration of low-molecular heparin (LMH) after individual risk assessment should be considered; aspirin is not indicated in these cases [26–33].

5. General contraindications for air travel of pregnant women

Severe anemia <7.5 g/dl; otitis media and sinusitis; severe heart and lung diseases; recent gastrointestinal surgery, including laparoscopic surgery; bone fractures; risk of leg swelling, especially in the first few days after wearing one plaster cast; referred fear of flying are contraindications for air traveling [26–35].

5.1 Absolute and relative obstetric contraindications

It goes without saying that unclear symptoms such as bleeding, abdomen pain, gastrointestinal symptoms, or clinical signs of preeclampsia or thrombosis must be clarified before traveling, especially since most airlines issues demand a medical certificate about the safety air of travel. The 2nd trimester, especially the interval between the 18th and 24th week of gestation, is considered the safest time to travel because the risk of obstetric complications (e.g., premature labor) is lowest at this

time. In the third trimester, pregnancy risks, such as preeclampsia, intrauterine growth restriction, antenatal bleeding due to placenta previa, severe anemia, and the increased risk of premature birth (previous preterm birth, recurrent premature labor, and cervical insufficiency), should be excluded prior to the flight. Most airlines allow pregnant women with uncomplicated single pregnancy to travel up to (and including) 36th week of pregnancy and women with uncomplicated multiple-child pregnancy up to 32nd week of pregnancy, which is in accordance with the regulations of the International Air Travel Association. As shown in previous studies, there are still no uniform regulations for the transportation of pregnant passengers in civil aviation. It is therefore advisable to check the relevant conditions of carriage of the different airlines on their website before each flight; this also applies to the certification obligations. In addition, information about the destination/place of residence should be obtained before starting the flight, in particular about the climate, altitude, humidity, risk of infection, etc., and about the medical/obstetric (emergency) care on site [26–35].

5.1.1 Absolute contraindications

"Premature placental abruption" due to manifestation of contractions.
"Cervical insufficiency" premature labor, premature bladder jump.
"Suspected ectopic pregnancy".
"Vaginal bleeding".
"Impending abortion".
"Preeclampsia" (previous/current pregnancy).

5.1.2 Relative contraindications

"Abnormal child growth".
"Previous abortions/ectopic pregnancy".
"Maternal age <15 or >35 years".
"Multiple pregnancy".
"Placenta previa, placental disorders" [26–35].

6. Discussion

6.1 General effects of travel in pregnant women's health

The association between air travel and pregnancy outcome concerning early or late pregnancy loss, incidence of malformations placenta abruption, etc. is very limited. The average altitude for commercial long-haul flights is 10,000–12,500 m. The air pressure drops from 760 mmHg (at sea level) to 560 mmHg at flight level. This drop-in air pressure is largely compensated for by the cabin pressure in the aircraft (equivalence to an altitude of 1524–2438 m above sea level) so that an altitude of about 12,200 m is tolerated by the passengers without hypoxic stress. The partial pressure of oxygen in the arterial blood depends on the lung function (cave: chronic obstructive pulmonary diseases); in healthy passengers it drops from 95 mmHg to 53–78 mmHg in the airplane, and the arterial oxygen saturation decreases from 97 to 99% to 90–94% [36–41].

For healthy pregnant women who have sufficient oxygen saturation, this "relative" hypoxia in the plane poses no significant risk even for a healthy fetus. No influence on the fetal heart rate during short-haul flights was observed [30, 31, 42]. Due to the approximately 50% higher hemoglobin concentration compared to the

mother, the 20–30% higher oxygen affinity of fetal hemoglobin and the Bohr effect which guarantees a preferred oxygen release on the placental level, and negative effects on the fetuses are not to be feared. There is no need to fear mild hypoxia associated with air travel. However, this does not apply to pregnant women with reduced oxygen saturation due to underlying diseases (e.g., severe anemia, chronic obstructive pulmonary diseases) [41–48].

In general, a general attest must be introduced for the transportation of all pregnant passengers from the child's extrauterine viability, i.e., from the 25th week of pregnancy. The certificate should be issued in the period from approximately 1 week to 2 days before departure in order to guarantee that it is up to date to some extent. In addition to the exact gestational age, risks must also be specified which should be related to the health risk for both the mother and the child, and a distinction between single and multiple pregnancies should be documented. Concerning multiple pregnancies, long-haul flights up to the 28th week of pregnancy or short-haul flights up to the 32nd week of pregnancy in these cases are recommended to prevent premature birth. Short-haul flights are those routes on which an airport can be reached within 1 hour. Considering the average duration of pregnancy and birth in the case of single pregnancies, transport on long-haul flights up to the 36th week of pregnancy and on short-haul flights up to the 37th week of pregnancy is possible [41–48].

6.2 People's health problems and thrombosis

For all traveling people, the risk of VTE is slightly increased. It is significantly increased in passengers who have particular risk factors such as advanced age, taking estrogen-containing oral contraceptives or are at hormonal replacement therapy, obesity, and the presence of factor V Leiden mutation, at most high or very low body height [49–52].

The underlying mechanism responsible for travel-related thrombosis is not fully understood. But the fact that risk has been found for all modes of travel suggests that immobility and associated venous stasis may be a key factor in generating the disease. The reduction of oxygen levels may be an additional reason for the initiation of thrombus formation during long air travel in groups of people with specific risk factors.

Additional abovementioned thrombogenic risk factors increase the risk of VTE significantly.

Low air pressure and reduced blood oxygenation increase the risk of deep vein thrombosis in susceptible air passengers.

To date, deep vein thrombosis in air passengers has been mainly associated with the fact that they have been stationary for long periods of time as is usually the case in air travel.

Deep vein thrombosis occurs in the lower limbs when there are long periods of inactivity or sedentary activity.

The risk is that the clot can move through the bloodstream to the heart, lungs, and brain. This can happen hours, days, or weeks later after the initial formation of thrombosis. It is the cause of a heart attack or stroke.

Studies have shown that the risk of deep vein thrombosis of the lower limbs increases by two to four times after an air trip [49–52].

They believe that the main culprit is the hypoxia of blood resulting from low cabin pressure and reduced oxygen levels of passengers compared to what is happening on the ground. The decrease in oxygen concentration in the blood seems to activate the coagulation system leading to the formation of clots.

In addition, this research provides us with important information about who is at greater risk than others.

These include people carrying the Leiden-type factor V mutant of the blood coagulation system, women taking birth control pills, patients recently undergoing surgery, and some groups of cancer patients.

High-risk patients may be prescribed anticoagulant medicines such as aspirin, heparin, dipyridamole, clopidogrel (Plavix®), and others after medical evaluation and advice.

In addition, alcohol should be avoided in the flight, and passengers should be able to stretch their legs and do as much exercise and walking as possible. They can also wear special socks. These measures improve blood circulation and help prevent thrombosis and its consequences.

6.3 Air travel, pulmonary embolism, and thrombosis

Air travel can cause clots of the deep veins of the thigh and feet [49–52].

This thrombosis can in turn cause a pulmonary embolism which is a very serious condition which can cause death.

Thrombosis in the lower limbs (thighs, ankles, legs) is due to thickening phenomena that occur in the deep long veins due to the many hours that passengers remain seated.

Lack of physical movement, dehydration observed in passengers, and alcohol consumption in flight are considered to be among the factors contributing to the occurrence of dangerous thrombotic conditions and pulmonary embolism.

In addition, some people may have inherited diseases with an increased risk of thrombosis and thus be at greater risk than air travel.

To date, 100 cases of pulmonary embolism due to venous thrombosis of the lower limbs have been described. A significant number of cases have died due to this condition. A case of lower limb amputation due to thrombosis has recently been described.

Research shows that clotting problems occur in the lower limbs and in up to 10% of long-haul passengers.

In fact, this syndrome is called by some people the "financial position" syndrome because passengers in these places do not have enough space in front of them to move their legs and remain motionless for many hours.

Researchers believe the incidence of pulmonary embolism after a long plane trip is higher.

The reason they are not detected is because the passengers are not immediately aware of what is happening or because the clinical signs are manifesting themselves severely a few hours after disembarkation. Even sudden deaths on flights or on landings may be due to a pulmonary embolism.

Some even argue that the problem is even greater and that the incidents detected constitute a very small percentage of those occurring.

6.4 Precaution that must be taken into account during traveling

Passengers should drink plenty of water to eliminate the risk of dehydration.

Avoid drinking alcohol and excessive caffeine intake.

Passengers should be able to get up, walk, do small exercises, or even stretch or move their lower limbs. It is also not good to cross legs.

Patients with a personal or family history of thrombosis should consult their physicians prior to an air trip [5, 52–54].

Some researchers recommend that passengers wear special high-pressure socks to improve blood circulation to the lower limbs. This is especially true for people at increased risk for thrombosis.

For some passengers, taking low doses of aspirin before a long flight can be beneficial. The World Health Organization recommends [5, 52–55] the following:

- Do not leave space under the front seat to allow for freedom of movement for the lower extremities.
- Exercises for feet.
- Often stop by car to walk, or get up regularly for a bit of unwinding and walking on an airplane, train, or boat.
- Do not drink too much water and avoid drinking alcohol.
- For persons at high risk of thrombosis, elastic compression with special socks and sometimes administration of low molecular weight heparin are recommended (2–6 h before travel). The aspirin intake is controversial.

The mechanisms that have been implicated to date for this phenomenon are venous posture due to prolonged sitting posture, pressure exerted on the large vein behind the knee, blood buildup due to reduced intake and increased fluid loss, abnormalities in the system, and blood coagulation created in the subarctic and hypoxic environment.

Air travel or road trips, for many hours, run the risk of vein thrombosis in the legs and even more severe, pulmonary embolism. Posttraumatic thrombosis accounts for about 10% of all thromboses that occur.

According to the American College of Chest Physicians (ACCP) (2012) British Committee for Standards in Hematology (BCSH) (2011), British Thoracic Society (BTS) (2011) Traveler's thrombosis: International Consensus Statement (Wien 2008) [21, 57–59], low-risk, medium-risk, and high-risk factors for VTE after air travel are as follows:

Low risk

- No individual risk factors other than long-haul flights (ACCP, >6 h; BCSH, >6 h; BTS, >8 h/several flights in a short time (approx. 4 weeks)).

Medium risk

- Previous provoked VTE.
- Thrombophilia.
- BMI >30 kg/m^2.
- Positive family history for VTE.
- Pronounced varicose.
- Combined oral contraceptives.
- Hormone replacement therapy.

- Pregnancy.
- Puerperium: within 2 weeks (BTS) orup to 6 weeks (BCSH) postpartum.
- Height >190 cm/<160 cm (BTS).

High risk

- Previous idiopathic VTE.
- Cancer.
- Major surgery/trauma within.
- The last 4–6 weeks.
- Severe underlying diseases.
- Immobilization (e.g., plaster cast).
- Homozygous or combined congenital thrombophilia.
- ≥2 risk factors under B.

Recommendations for the prevention of deep leg vein thrombosis on long-haul flights are as follows:

Low risk

General measures:

- Physical activity: regular walking around in the corridor every 2–3 h.
- Movement of the legs (calf muscles, e.g., "foot rocker") at the seat.
- All 30 min, isometric exercises.
- Sitting in the aisle (freedom of movement):
- Feet should reach the floor.
- Cave: bending the popliteal veins.
- Avoid dehydration:
- Regular liquid intake (at least 250 ml every 2 h).
- No excessive alcohol/coffee enjoyment.
- Do not take tranquilizers/sleeping pills:
- Cave: prolonged sleep in a cramped posture.

Medium risk

Pregnancy, puerperium.

- Customized, graduated compression stockings to the knee (15–30 mmHg compression in ankle).

High risk

Previous VTE, symptomatic thrombophilia.
Additional (grade 2C/2D):

- Low molecular weight heparin (e.g., 5000 IU dalteparin s.c.) 6–12 h before the flight and 1–3 days after the flight (individual decision).

- No aspirin.

6.5 What causes vein thrombosis and pulmonary embolism?

Clots can be formed at various points, in the legs and in the thighs, with similar problems. All veins have valves every 10–12 cm, and some of them can form clots.

If the clot stays there, then the member has swelling and pain. Small fever may occur, and the member may be warmer. The most serious complication, however, is pulmonary embolism (PE), which occurs in 25% of cases with thrombosis. If the clot is detached, it is transported through the veins and eventually clamped to the lung. The condition can appear immediately or even 2 weeks after the long journey. The most common symptoms to suspect pulmonary embolism are sudden chest pain, dyspnea, dizziness, fever, hemoptysis, etc. Symptoms depend on the size of the plunger and the size of the vessel, the age of the person, if he or she is suffering from other diseases, etc. Immediate admission to the hospital is required for diagnosis and special treatment. In rare cases, a part of the clot can cause embolism in other organs, such as the brain.

People predisposed to thrombosis, as well as patients with previously mentioned illnesses, should be consulted by their physician prior to long journeys. In these individuals, it is recommended to inject antithrombotic (heparin) once 24 h before flight. It is also recommended to take aspirin before takeoff, except for pregnant women who are not allowed [5, 53–56].

6.6 Practical and useful tips

- Wear comfortable clothing.

- Leave space under the front seat to allow freedom of movement for the lower legs.

- Change your posture regularly and do exercises for your feet.

- Take regular breaks to walk.

- Drink plenty of liquids.

- For persons at high risk of thrombosis, elastic compression with special socks is recommended and sometimes administration of low molecular weight heparin (2–6 h before travel).

People suffering from diseases that increase the risk of venous thromboembolism should follow the guidelines above, and the possibility of administering low molecular weight heparin (2–4 h before or earlier before flying) may also be considered.

In patients receiving anticoagulants, the dose should be reassessed.

Overall, however, there is insufficient data on pregnancy complications after air travel.

Occasional air travel, especially in the second trimester, is safe for healthy pregnant women and their child, according to the current state of knowledge, and has no negative effects on the course of pregnancy. Before starting the flight, the gynecologist should carefully ascertain the patient's own (pre-existing illnesses) and obstetric history, as well as individually check the previous course of pregnancy (pregnancy-related risks) to identify pregnant women with risk factors who are advised against traveling by air. In any case, it is advisable to consider the different conditions of carriage of the airlines (including mandatory certification) and to obtain information about the destination of the flight. A drop-in air pressure, a reduction in partial oxygen pressure, and air humidity are generally not a problem for healthy pregnant women and their children. Dehydration during long-haul flights should be avoided. A radiation dose of 1 mSV should not be exceeded during pregnancy; pregnant women with frequent long-haul flights near the pole (e.g., Europe-North America) should take care of this. Most people believe that commercial air travel does not increase the risk of pregnancy complications (e.g., premature birth) in healthy pregnant women [5, 53–57, 60].

The estimated radiation dose for infants/toddlers should be 0.05 μSV/scan, which for the fetuses are negligible [61].

7. Conclusion

Travel thrombosis in connection with long-haul flights (>4 h flight time) are rare (about 1/4500 passengers) and mostly affect the deep veins of the calf muscles. The proportion of pulmonary embolisms is significantly higher for female passengers than for male passengers (flight duration > 12 h: 4.8–7.2/1 million). The risk of venous thromboembolism depends primarily on the duration of the flight, the number of flights within 4 weeks, and individual thrombogenic risk factors. As a result of hypercoagulability and venous stasis, the risk for pregnant women is increased, and it is estimated at 0.03–0.1%. Long-term immobilization is the most important predisposing factor; the importance of hypobaric hypoxia and dehydration is controversial.

Before starting the flight, especially pregnant women are advised to carefully assess their risks. To reduce risk, in addition to general measures (e.g., physical activity), wearing graded, well-fitting compression stockings is recommended and if there is a high individual risk (e.g., previous VTE), prophylaxis administration of low molecular weight heparin before and immediately after the flight.

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