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Relationship between the Incidence of Idiopathic Lower Extremity Deep Vein Thrombosis and the Location of the Thrombus depending on the Changes in Atmospheric Pressure

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Rezumat

Relația dintre incidența trombozei venoase profunde idiopatice de membru inferior și localizarea trombusului în funcție de modificarea presiunii atmosferice

Scop: Studiul a analizat relația dintre incidența trombozei venoase profunde (TVP) idiopatice de membru inferior şi localizarea trombului cu modificările de presiune atmosferică.
Material şi metodă: În cursul perioadei de doi ani între mai 2009 şi aprilie 2011, inclusiv, 124 de pacienți consecutivi au fost diagnosticați ca având TVP idiopatică de membru inferior, la Clinica de Chirurgie Vasculară "Centrul Clinic Niš", Serbia.
Rezultate: Creşterea valorilor medii zilnice ale presiunii atmosferice cu 1 milibar, în ziua în care evenimentul a avut loc şi 7 zile înainte, au fost asociate ($p < 0,05$), cu creşterea riscului total de apariție a TVP idiopatice de membru inferior cu 5,1% (0,7 - 9,8%), precum şi cu apariția TVP idiopatice deasupra genunchilor ($p < 0,05$) cu 5,9% (0,9 - 11,0%) mai frecvent. Creşterea presiunii atmosferice medii cu 1 milibar, în ziua în care evenimentul a avut loc şi 7 zile înainte, în subgrupul de pacienți cu vârsta sub 45 de ani, şi în ziua în care evenimentul a avut loc şi 3 zile înainte de aceasta, în subgrupul de pacienți cu vârsta de 45 şi mai mult, a fost legată de creşterea riscului de apariție a TVP idiopatice de membru inferior.
Concluzie: Creşterea valorilor zilnice ale presiunii atmosferice indică o relație semnificativă cu incidența TVP idiopatice de membru inferior şi cu localizarea trombusului mai sus de genunchi.

Cuvinte cheie: tromboză venoasă profundă idiopatică de membru inferior, localizarea trombusului, presiune atmosferică

Abstract

Aim: The study analysed the relationship between the incidence of idiopathic lower extremity deep vein thrombosis (DVT) and the location of the thrombus with changes in atmospheric pressure.
Material and method: During the two year period between May 2009 and April 2011, inclusively, 124 consecutive patients were diagnosed as having idiopathic lower extremity DVT at the Vascular Surgical clinic "Clinical Center of Niš", Serbia.
Results: The increased average daily values of atmospheric pressure for 1 millibar on the day when the event took place and 7 days before, were associated ($p < 0,05$) with the increase of the total risk of the occurrence of lower extremity idiopathic DVT for 5,1% (0,7 – 9,8%), as well as with the occurrence of idiopathic DVT above the knees ($p < 0,05$) for 5,9% (0,9 – 11,0%). The increase in the average atmospheric pressure by 1 millibar on the day when the event took place and 7 days before this in the subgroup of patients under the age

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of 45 years, and on the day when the event took place and 3 days before it in the subgroup of patients of the age of 45 and above, was related with the increased risk of the occurrence of lower extremity idiopathic DVT.
Conclusion: The increase of daily values of atmospheric pressure shows a significant relationship with the incidences of idiopathic lower extremity DVT and the location of the thrombus above the knee.

Key words: idiopathic lower extremity deep vein thrombosis, location of the thrombus, atmospheric pressure

Introduction

A role of the individual physical environmental factors (temperature, relative humidity, barometric pressure, average and maximum air speed) as risk factors to human health was defined (1).

The seasonal variations and the influence of meteorological parameters in the incidence and morbidity of deep vein thrombosis (DVT) has been investigated in several countries with different climatic conditions and the findings have been inconsistent (2-12). The seasonal variations with the influence of metrological incidence of DVT factors have been demonstrated in several studies (2-9). However, other studies have shown no seasonal variations of DVT (10-12). There is only one study with data about the relationship between the atmospheric pressure and the incidence of DVT (7).

There is no information about the relationship between changes of atmospheric pressure and the incidence of lower extremity idiopathic DVT and the location of thrombus. Therefore, the aim of the present study was to investigate the relationship between the incidence of idiopathic lower extremity DVT and the location of the thrombus with changes of daily average values of atmospheric pressure.

Methods

During the two year period between May 2009 and April 2011, inclusive, 124 consecutive patients were diagnosed and hospitalised from the territory city of Nis, Serbia, as having idiopathic lower extremity DVT at the Vascular surgery clinic "Clinical center of Niš", Serbia. These were 68 (54.8%) females and 56 (45.2%) males with the average age of 56.87±11.45 years in this retrospective study, identified through hand searching of the prospectively maintained Vascular surgery clinic patient registry.

Out of the total number of patients with idiopathic lower extremity DVT, there were 95 (76,62%) patients with above-knee DVT and 29 (23,38%) patients with below-knee DVT . There were 43 (34,66%) patients with than 45 years and 81 (65,34%) patients with 45 or more years.

The diagnosis of the lower extremity DVT was made according to the anamnestic data, clinical features, biochemical and duplex scanning. The extent of the thrombus was determined by duplex sonography in all the patients.

In the present study only the patients with idiopathic lower extremity DVT were included. The exclusion criteria were the presence of malignancy, biological thrombophilia (e.g. factor V Leiden, deficiency of protein C or protein S, presence of ant phospholipid antibodies), surgery, injury and pregnancy or puerperium.

The patients were divided into subgroups by age and the location of the thrombus. Subgroups in relation with the location of the thrombus were: the above-knee DVT subgroup which included DVT of the thigh and pelvic veins and the below-knee DVT subgroup which included patients with DVT in veins of the lower legs. Subgroups in relation with age were: the subgroup with patiants under the age of 45 years and the subgroup with patients of 45 years or over the age of 45 years

The daily mean atmospheric pressure values for the city of Nis, Serbia, were obtained from the Republic Meteorological Department. The range for the daily average values of barometric pressure was 992,00±6,18 (970,20 to 1009,80) millibars.

Statistical analysis

To investigate the association between the incidence of lower extremity DVT and the atmospheric pressure, we used the negative binomial regression model. This model included the daily DVT counts as the dependent variable and the daily average values of atmospheric pressure as the independent variable. A negative binomial model was used to account for both the over dispersion and the number of days with zero cases. The relationship between the atmospheric pressure and the risk of DVT after lags for 0, 3 and 7 days, as well as the cumulative lags for 0-3 and 0-7 days was examined. The incidence rate of idiopathic lower extremity DVT for 1 millibar (mBar) change in daily average values of barometric pressure was calculated. The analyses were performed using R: A language and environment for statistical computing, version 2.12.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

The incidence rate for DVT and the location of thrombus for 1 mBar change in the daily average values of barometric pressure in all ages patients are shown in *Table 1*.

In all observed patients the increased average daily values of atmospheric pressure for 1 millibar on the day when the event took place and 7 days before was associated ($p < 0,05$) with the increase of total risk of the occurrence of idiopathic DVT of lower extremity for 5,1% (0,7 – 9,8%), as well as with the occurrence of idiopathic DVT above the knees ($p < 0,05$) for 5,9% (0,9 – 11,0%).

The incidence rate of DVT and the location of the thrombus for 1 millibar change in daily average values of

Table 1. *Incidence rate ratios (95% confidence interval) of DVT and location of thrombus for 1 millibar change in daily average values of barometric pressure in all ages patients*

Barometric pressure	Location of thrombus		
(1mBar)	All locations	Above-knee	Below-knee
Lag 0	1,019 (0,988-1,052)	1,015 (0,980-1,052)	1,026 (0,965-1,091)
Lag 3	1,025 (0,993-1,058)	1,032 (0,996-1,070)	0,998 (0,940-1,059)
Lag 7	1,011 (0,980-1,043)	1,013 (0,978-1,050)	1,001 (0,943-1,063)
Lag 0-3	1,033 (0,996-1,072)	1,036 (0,994-1,079)	1,017 (0,948-1,091)
Lag 0-7	1,051 (1,007-1,098)*	1,059 (1,009-1,110)*	1,016 (0,936-1,103)

*p < 0,05

Table 2. *Incidence rate ratios (95% confidence interval) of DVT and location of thrombus for 1 millibar change in daily average values of barometric pressure in patients under the age of 45 years*

Barometric pressure	Location of thrombus		
(1mBar)	All locations	Above-knee	Below-knee
Lag 0	1,036 (0,987-1,087)	1,038 (0,986-1,092)	1,020 (0,894-1,163)
Lag 3	1,038 (0,990-1,089)	1,041 (0,989-1,095)	1,019 (0,894-1,162)
Lag 7	1,070 (1,018-1,124)**	1,073 (1,018-1,130)**	1,043 (0,913-1,190)
Lag 0-3	1,077 (1,019-1,139)**	1,076 (1,014-1,141)*	1,079 (0,926-1,257)
Lag 0-7	1,120 (1,049-1,196)**	1,114 (1,040-1,194)**	1,141 (0,954-1,365)

*p < 0,05 **p < 0,01

Table 3. *Incidence rate ratios (95% confidence interval) of DVT and location of thrombus for 1 millibar change in daily average values of barometric pressure in patients of 45 years or over the age of 45 years*

Barometric pressure	Location of thrombus		
(1mBar)	All locations	Above-knee	Below-knee
Lag 0	1,006 (0,967-1,045)	0,995 (0,951-1,042)	1,028 (0,960-1,100)
Lag 3	1,012 (0,974-1,052)	1,021 (0,975-1,069)	0,992 (0,928-1,061)
Lag 7	0,974 (0,937-1,012)	0,968 (0,926-1,012)	0,991 (0,927-1,059)
Lag 0-3	1,055 (1,008-1,098)*	1,049 (1,007-1,089)*	1,001 (0,926-1,083)
Lag 0-7	1,000 (0,949-1,054)	1,007 (0,946-1,072)	0,985 (0,898-1,080)

*p < 0,05

barometric pressure in patients under the age of 45 years are shown in *Table 2*.

In the subgroup of patients under the age of 45 years, the increase of the average atmospheric pressure for 1 millibar on the day when the event took place and 7 days before it (Lag 0-7) was associated with the increase of the risk of the occurrence of lower extremity idiopathic DVT ($p < 0,01$) for 12,0% (4,9 – 19,6%), as well as of the occurrence of idiopathic DVT above the knees ($p < 0,01$) for 11,4% (4,00 – 19,4%).

The incidence rate of DVT and the location of the thrombus for 1 millibar change in the daily average values of barometric pressure in patients of 45 years or over the age of 45 years are shown in *Table 3*.

In the subgroup of patients of the age of 45 and over, the increase of the average atmospheric for 1 millibar on the day when the event took place and 3 days before it (Lag 0 – 3) was related to the increase of the total risk of the occurrence of lower extremity idiopathic DVT ($p < 0,05$) for 5,5% (0,8 – 9,8%), as well as to the occurrence of idiopathic DVT above the knees ($p < 0,05$) for 4,9% (0,7 – 8,9).

Discussion

The presented study shows that the increased average daily values of atmospheric pressure on the day when the event took place and 7 days before it was associated with the increase of total risk of the occurrence of lower extremity idiopathic DVT in the entire observed population.

At sea level the atmospheric pressure is 101 kPa and oxygen makes up 21% of inspired air (13). It is estimated that 60-75% of the blood in the body is to be found in veins. Although arterial pressures are generated by muscular contractions of the heart, the pressure in the venous system is

largely determined by gravity (14).

There is very little data about the pathophysiological mechanism of the influence of the changes in values of atmospheric pressure on the occurrence of DVT. Experimental research of LaCroix et al. (15) studied hemostatic response to acute exercise and increased atmospheric pressure in 20 healthy male subjects exercised to volitional exhaustion on a cycle ergometer in a hyperbaric chamber at 3 atmospheres absolute (ATA). The findings of their study demonstrate that increasing atmospheric pressure from 1 ATA to 3 ATA does not alter the exercise-induced changes in hemostasis.

In the experimental study of Bowser-Riley and Kidd (16) the reduced systolic blood pressure and the increase sensitivity of the baroreflex heart rate response by exposure to increase atmosphere pressure were reported. Therefore, the correlation between the increase of the daily values of atmospheric pressure and the occurrence of lower extremity idiopathic DVT can be hypothetically explained by the observation that the increase of sensitivity of the baroreflex heart rate causes hypotension and slowing down the blood flow through the veins of lower limbs, which can be a reason for the occurrence of lower extremity DVT.

The results of the presented study differ from the results of the study of Brown et al. (7) results. Their study shows that every decrease of pressure for 10 millibar is associated with the increase of incidence for the occurrence of DVT for 2.1%. This difference in results can be explained by the fact that Brown et al. analyzed the influence of changes in atmospheric pressure on the occurrence of DVT generally, and not only in a group of patients with lower extremity idiopathic DVT.

The mechanism which affects the location of the thrombus in the leg is still not understood. The presented study shows the correlation of a change in atmosphere pressure with the occurrence of idiopathic DVT in a group of patients with idiopathic DVT above the knees, while such correlation is not present in a group of patients with idiopathic DVT above the knees. Fink et al. (6) showed that distal DVT of the leg was found to be more frequent during the winter halves of the year while proximal DVT was diagnosed more often during summer halves. They hypothesized that the veins of the lower leg are more susceptible to low temperatures than veins of the thigh or abdomen, which are better protected by muscles and fat, so the vasoconstrictory effect resulting from the low external temperatures may therefore be more pronounced in veins of the lower leg. Dentali et al. (8,9) reported that seasonal variability in the incidence of DVT was independent with the location of the thrombus.

In both age groups of patients with DVT, the influence of the increase of atmosphere pressure on the incidence of lower extremity idiopathic DVT was presented as well as the correlation with the location of the thrombus above the knees. In the patients under the age of 45 most significant confirmed correlation was with the increased average daily values of atmospheric pressure on the day when the event took place and 7 days before it, while in the subgroup of patients of the age of 45 and over the most significant confirmed correlation was with the pressure on the day when the event took place and 3 days before it. In the group of patients with the age of 45 or older, it took shorter time for the occurrence of lower extremity DVT related to the increase of atmospheric pressure. Aging, which can be related to numerous disorders in artery (17) and vein systems (18), can be the reason that contributes to faster manifestation of the effects of increased atmospheric pressure on the occurrence of DVT of lower limbs in the older group of patients.

The major limitation of our study is the fact that it is retrospective. However, it should be noted that all data was registered prospectively. Also, a certian number of patients with peroneal DVT can pass without major clinical sings of the existence of disease wich may affect the number of the diagnosed patient with below-knee DVT.

The strengths of this study is the fact that this is the first study evaluating the relationship between incidence of lower extremity DVT and location of the thrombus with changes of daily average values of atmospheric pressure. Further researches should be directed to revealing the accurate pathophysiological mechanism and additional factors that influence the occurrence of lower extremity idiopathic DVT and location of thrombus related to the increase of atmospheric pressure.

Conclusion

According to the results of this study, one can conclude that the increase of daily values of atmospheric pressure shows a significant relationship with incidences of idiopathic lower extremity DVT. Also, the increase of daily values of atmospheric pressure shows a significant relationship with the location of the thrombus above the knee. These findings could help investigators and clinicians understand the pathophysio-logy of idiopathic lower extremity DVT.

References

1. Rahmanov RS, Gadzhiibragimov DA, Medzhikova MA, Kudriavtseva OA. Assessment of the significance of climato-geographic conditions as health risk factors. Gig Sanit. 2010;(2):44-6. [Article in Russian]
2. Manfredini R, Imberti D, Gallerani M, Verso M, Pistelli R, Ageno W, et al. Seasonal variation in the occurrence of venous thromboembolism: data from the MASTER Registry. Clin Appl Thromb Hemost. 2009;15(3):309-15. Epub 2008 Jun 10.
3. Stein PD, Kayali F, Olson RE. Analysis of occurrence of venous thromboembolic disease in the four seasons. Am J Cardiol. 2004;93(4):511-3.
4. Boulay F, Berthier F, Schoukroun G, Raybaut C, Gendreike Y, Blaive B. Seasonal variations in hospital admission for deep vein thrombosis and pulmonary embolism: analysis of discharge data. BMJ. 2001;323(7313):601- 2.
5. Montes Santiago J, Rey Garcia G, Mediero Dominguez A. Seasonal changes in morbimortality caused by pulmonary thromboembolism in Galicia. An Med Interna. 2003;20(9):457-60.

6. Astrid M. Fink, Wolfgang Mayer, Andreas Steiner. Seasonal variations of deep vein thrombosis and its influence on the location of the thrombus. Thrombosis Research. 2002;106(2): 97-100.
7. Brown HK, Simpson AJ, Murchison JT. The influence of meteorological variables on the development of deep venous thrombosis. Thromb Haemost. 2009;102(4):676-82.
8. Dentali F, Ageno W, Rancan E, Donati AV, Galli L, Squizzato A, et al. Seasonal and monthly variability in the incidence of venous thromboembolism. A systematic review and a meta-analysis of the literature. Throm Haemost. 2011;106(3):439-47.
9. Dentali F, Manfredini R, Ageno W. Seasonal variability of venous thromboembolism. Curr Opin Pulm Med. 2009;15(5): 403-7
10. Galle C, Wautrecht JC, Motte S, Le Minh T, Dehon P, Ferreira J, et al. The role of season in the incidence of deep vein thrombosis. Mal Vasc. 1998;23(2):99-101.
11. Bounameaux H, Hicklin L, Desmarais S. Seasonal variation in deep vein thrombosis. BMJ. 1996;312(7026):284-5.
12. Lee CH, Cheng CL, Lin LJ, Tsai LM, Yang YH. Epidemiology and predictors of short-term mortality in symptomatic venous thromboembolism. Circ J. 2011;75(8): 1998-2004.
13. J.H. Comroe, P.Walker. Normal human arterial oxygen saturation determined by equilibration with 100 per centO2 in vivo and by the oxymeter. Am J Physiol. 1948;152(2):365–71.
14. Somjen GM. Anatomy of the superficial venous system. Dermatol Surg. 1995;21(1):35-45.
15. LaCroix KA, Davis GL, Schneider DA, Lavoie P, Kintzing E, Waterfield DA. The effects of acute exercise and increased atmospheric pressure on the hemostatic mechanism and plasma catecholamine levels. Thromb Res. 1990;57(5):717-28.
16. Bowser-Riley F, Kidd C. Hydrostatic pressure enhances baroreceptor reflexes in the rat. O J Exper Physiol. 1988;73(5):785-8.
17. Tekin N, Baskan M, Yesilkayali T, Karabay O. Prevalence of peripheral arterial disease and related risk factors in Turkish elders. BMC Fam Pract. 2011 Sep 19;12:96.
18. Nüllen H, Noppeney T. Diagnosis and treatment of varicose veins. Part 1: definition, epidemiology, etiology, classification, clinical aspects, diagnostic and indications. Chirurg. 2010;81(11): 1035-44; quiz 1045. [Article in German]