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Review Article

Seasonal variations and the risk of venous thromboembolism: A narrative review article

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Abstract
Different investigations on seasonal variations of the pulmonary thromboembolism and deep vein thrombosis (DVT) incidence have not yielded a definite conclusion. Some papers showed significant increase in incidence of thromboembolism in winter; on the other hand, others neglected that correlation. Some articles have tried to show infrastructure of these variations. Better understanding of the cornerstone of these variations can result in prevention of disease and saving lives of susceptible people. In this narrative review article, we reviewed previous articles according to the region of study and tried to find the factors affecting diverse results among different studies.

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Introduction

Different investigations on seasonal variations of the incidence of pulmonary thromboembolism and deep vein thrombosis (DVT) have not yielded a definite conclusion. Recent investigations try to explain why obtained results are so controversial. Neglected factors, different methodology, and geographic and genetic confounders can explain part of this heterogeneity.[1] A new study showed that in old persons, seasonal variation was an independent risk factor for venous thromboembolism (VTE).[2] Some studies showed that predisposing genetic risk factors were different among Asian and European populations.[3] Also the temperature and humidity are different in Asia and Europe. Hence, we decided to investigate the results of different studies about seasonal variation of VTE in Asian and European countries.

Methods

The ISI Web of Knowledge, PubMed, Scopus, EBSCO, and IranMedex databases were searched for articles with keywords related to season, VTE, pulmonary embolism (PE), and DVT. We included all studies up to October 2019 analyzing seasonal or monthly changes in the incidence of admissions due to thromboembolic events. Then we categorized these studies according to the region of their study and the age of populations studied in these articles.

Seasonal variation of VTE according to the region of study: Western countries: Most articles published about seasonal variations

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of VTE events belong to European countries. Steiner conducted a retrospective study in Czech Republic. Between 1960 and 2005, 628 cases with grossly visible PE autopsies were included in this study. Average incidence of PE death was highest in autumn (18.1%); summer and winter months had intermediate incidence of disease.[4]

Nimako et al. conducted a large retrospective study in the United Kingdom (UK); 640 patients with confirmed PE were included. Statistically lower incidence of PE was seen in spring. Summer, autumn, and winter had highest percentage of event days, respectively.[5]

Masotti et al. conducted a retrospective study in Italy, 457 patients with diagnosis of PE were included in this study. Their study showed a weak seasonal difference in incidence of PE in surgical ward and a strong correlation between mortality of PE and season with a peak of cases in winter in medical and surgical wards.[6]

Gallerani et al. analyzed the database of the Emilia-Romagna Registry in Italy. The total of 19245 patients with PE admitted between January 1998 and December 2005 were included in this study; PE occurred most frequently in winter. The incidence of PE was lowest in spring.[7]

Another retrospective study was conducted in turkey by Oztuna et al., including 206 patients with diagnosis of PE; study was done between 2001 and 2006 and showed PE occurrence most commonly in spring and autumn.[8] Montes Santiago et al. conducted a retrospective study and analyzed registered data of 2831 hospitalizations for PE; they reported more hospitalizations for PE in autumn and winter and higher mortality rate in spring.[9]

Stein et al. studied incidence of PE between 1979 and 1999. They did not find any seasonal difference in PE incidence in United States (US).[10]

Asian countries: Jang et al. conducted a retrospective study in Korea; 1495 patients with VTE were included. They studied admitted cases from 2001 to 2010. They reported that frequency of VTE was highest in the winter and the least frequency was seen in the spring.[11]

In Iran, Hakim et al. reviewed medical records of 120 patients with confirmed massive PE from 2003 to 2007. The study was done in Shahid Madani Hospital in north west of Iran (our clinical center); the maximum PE frequency occurred in the winter.[12] Amiri et al. also could not find any meaningful correlation between PE and season. In their study, 158 patients with diagnosis of PE between 2007 and 2008 were included.[13] The geographic location of this study was the same as 2 previous studies, but they have been done in different time intervals.

103 patients with PE diagnosis were studied by Al Hayali et al. in Iraq from 2002 to 2007; there was no meaningful seasonal variation in incidence of PE in this study.[14]

Lee et al. reported no seasonal variations in incidence of VTE in Taiwan. The total of 2774 patients older than 18 years old with VTE diagnosis were included in this study.[15] Hong et al. studied data from 59626 cases with VTE. They showed that the incidence of new admissions due to VTE increased in winter with higher incidence in January and February; the incidence was lowest in summer.[2]

Salehi et al. showed that cerebral venous sinus thrombosis (CVST) may be absolutely different regarding the incidence according to the seasonal variation. They showed that with increased temperature during summer, the incidence of CVST increased significantly.[16] Table 1 provides a summary of studies discussed.

The effect of age on seasonal variation of VTE: Naess et al. showed that increasing age was a leading cause for VTE.[19] Higher rate of transient infectious diseases (RR = 1-3) plays role in increasing VTE rate.[20]

Elderly is associated with increasing susceptibility to infectious disease.

Ginaldi et al. suggested that hormonal, cellular, and innate immunity malfunction were responsible for this weakness against infection.[21] Because old people are at risk of slipping on ice and consequent bone fractures

Table 1. Summary of articles discussed about seasonal variations of venous thromboembolism (VTE) incidence and their conclusion

Continent	Study	Country	Year of study	Conclusion
Europe	Steiner[4]	Czech Republic	1960-2005	PE incidence was highest in autumn
	Nimako et al.[5]	United Kingdom	2000-2008	Summer, autumn, and winter had the highest PE frequency
	Masotti et al.[6]	Italy	1996-2001	Strong correlation between PE mortality and winter
	Gallerani et al.[7]	Italy	1998-2005	PE occurred most frequently in winter
	Oztuna et al.[8]	Turkey	2001-2006	PE occurrence most commonly in spring and autumn
	Montes Santiago et al.[9]	Spain	1996-2001	More frequent admissions for PE in autumn and winter
	Zoller et al.[17]	Sweden	1964-2010	Peak of VTE admissions during the winter
	Skajaa et al.[18]	Denmark	1977–2016	VTE peaked during winter or fall
Asia	Hong et al.[2]	Korea	2009-2013	Frequency of VTE was highest in the winter
	Jang et al.[11]	Korea	2001-2010	Frequency of VTE was highest in the winter
	Hakim et al.[12]	Iran	2003-2007	Maximum PE frequency occurred in the winter
	Amiri et al.[13]	Iran	2007-2008	No seasonal variation in PE occurrences
	Al Hayali et al.[14]	Iraq	2002-2007	No seasonal variation in PE incidence
	Lee et al.[15]	Taiwan	2001-2003	No seasonal variation in VTE incidence
America	Stein et al.[10]	United States	1979-1999	No seasonal variation in VTE incidence

PE: Pulmonary embolism; VTE: Venous thromboembolism

and also chronic obstructive pulmonary disease (COPD) and ischemic heart disease (IHD) (which are more frequent in elderly) are aggravated in cold weather, old people restrict their activity in winter which may explain higher incidence of VTE in older persons during winter.[22-24]

Hong et al. showed that seasonal variation was seen more prominently in patients older than 60 years, but VTE incidence was not affected in patients aged less than 60 years.[2] Zoller et al. also showed that seasonal variation of VTE incidence was seen more prominently in patients aged 50 years or higher.[17]

Discussion

Although seasonal variation in VTE incidence has been reported in a large number of articles, there is no consensus on the issue. Even in one geographic area, results can be changed during years. Previous studies emphasized the role of age and cold weather on transient infectious diseases which in turn can result in elevated incidence of VTE. Hong et al. showed that patients with > 60 years were more susceptible to developing VTE in winter.[25] This study shows the importance of DVT prophylaxis in this subgroup of patients especially in winter. Our investigation showed that most studies from Middle East region showed no significant VTE seasonal variation. It seems that significant drop in temperature is an important factor for increasing the incidence of VTE and those regions without significant drop in temperature during winter do not have seasonal variation in the incidence of VTE. Higher incidence of acute infection especially upper and lower respiratory tract infections (RTIs) during winter may be a trigger for VTE in non-immobilized patients.[26,27] Genetic variations may also be an important risk factor protecting or predisposing some people to VTE in winter.[28]

Conclusion

It seems that the combination of inflammation, the amount of decreased temperature, genetic factors, age, and acute infections in winter and their interaction are important in predisposing some people to VTE during winter.

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Authors' Contribution

Reza Hajizadeh: Approval of final version of manuscript to be published.

Hanieh Sakha: Preparation of article draft or revising it and study design

Sahar Ghodratizadeh: Considerable contribution to data gathering and analysis and interpretation of data.

Ali Soleimany: Preparation of article draft or revising it and study design.

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Conflict of Interest

Authors have no conflict of interest.

Ethical Approval

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