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Systematic Review

Seasonal Variations of Venous Thromboembolism Incidence: A Systemic Review from Global Trends to Chinese Context

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Abstract

Background: Venous thromboembolism (VTE) is a significant global health concern with seasonal variations in its incidence. Understanding these patterns is crucial for effective prevention and management strategies. **Methods**: Utilizing the PRISMA guidelines, our literature selection process involved systematic screening of both English and Chinese articles. From 21 included studies, involving 98,877 VTE patients, we conducted a meta-analysis examining global and China-specific VTE incidence patterns. Subgroup analyses were performed for pulmonary embolism (PE) and deep vein thrombosis (DVT). **Results**: In the global context, VTE incidence varied across seasons, with significantly lower rates observed in summer compared to winter (relative risk (RR) = 0.90, 95% confidence interval (CI): 0.84–0.98, p = 0.010). PE incidence was lower in summer compared to autumn/winter (RR = 0.93, 95% CI: 0.89–0.97 summer/autumn; RR = 0.90, 95% CI: 0.84–0.98 summer/winter). Conversely, DVT incidence was higher in winter compared to summer (RR = 0.80, 95% CI: 0.66–0.86, p = 0.02). In China, VTE incidence was lower in spring compared to winter (RR = 0.83, 95% CI: 0.72–0.96; p = 0.010), with no significant differences between winter and summer or autumn. **Conclusion**: Our study underscores the importance of considering seasonal and regional factors in understanding VTE incidence. The findings contribute valuable insights for healthcare professionals and policymakers, emphasizing the need for tailored strategies in different geographical areas to address and prevent VTE effectively.

Keywords

venous thromboembolism (VTE); seasonal variations; deep vein thrombosis (DVT); pulmonary embolism (PE); meta-analysis; public health interventions

Introduction

Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), is a significant global health concern associated with considerable morbidity and mortality [1]. VTE significantly impacting patients' quality of life and even leading to fatalities. VTE is a serious medical concern affecting an increasing number of individuals worldwide, becoming a significant economic burden globally. The incidence of VTE in the general population is reported to be 1‰–2‰ [2], with rates in the European population ranging from 1.04‰ to 1.83‰. Although the incidence in the Asian population is slightly lower, recent years have witnessed an upward trend [3], with VTE cases in Hong Kong increasing from 28.1 cases per 100,000 to 48.3 cases per 100,000 between 2004 and 2016. This increase is attributed primarily to an aging population (individuals aged 65 and above) and a rise in malignant tumor cases. While extensive research has focused on traditional risk factors such as surgery, immobilization, and malignancy, emerging evidence suggests potential associations between meteorological factors and the incidence of VTE [4,5]. The impact of seasonal variations on health outcomes has long been a subject of interest in medical research [6,7]. Changes in temperature, humidity, and atmospheric pressure have been linked to various cardiovascular and respiratory conditions [8,9]. However, the influence of meteorological factors on the risk of VTE remains an area that requires thorough investigation. The rationale behind exploring this association lies in the potential interplay between environmental conditions and physiological processes contributing to thrombus formation [10].

Studies indicate that risk factors for VTE include hormone therapy [11], pregnancy [12], hypercoagulable disorders [13], lower limb paralysis [14], cancer [15], and recent surgical history. Meteorological factors, including seasonal variations, atmospheric pressure, and diurnal temperature changes, exert a significant influence on the body's circulatory system, affecting the fibrinolysis system, coagulation system, vascular tone, heart rate, and arterial blood pressure [16,17]. However, the short-term exposure of external climatic conditions to the risk of VTE incidence remains unclear.

Research has confirmed seasonal variations in overall mortality, cardiovascular disease (CVD)-related mortality, and non-CVD/non-cancer-related mortality in 19 countries under different seasonal conditions [18]. In contrast, cancer-related mortality shows no apparent seasonal variation. Although some evidence suggests seasonal variations in the incidence of VTE, existing research conclusions are inconsistent. The impact of atmospheric temperature on pulmonary embolism (PE) is relatively clear, but the relationship between low temperatures and deep vein thrombosis (DVT) is uncertain. While several studies indicate that meteorological elements such as environmental temperature, pressure, and humidity are crucial factors in VTE incidence, there is still controversy regarding the influence of meteorological variables. For instance, some studies argue that the risk of VTE significantly increases in winter [19], while others show peak incidence in spring [20] or autumn [21]. Additionally, a study based in Detroit, USA, suggests a summer peak in VTE incidence [22].

Given that most regions in China experience pronounced seasonal variations in a temperate climate, understanding the impact of meteorological factors on VTE incidence patterns can aid in allocating medical resources based on these trends [23–25]. To contribute to this understanding, we conducted a Meta-analysis and systematic review of literature on the relationship between meteorological factors and VTE, exploring seasonal variations in VTE disease. This systematic review aims to explore the relationship between meteorological variables and VTE, providing a comprehensive analysis of existing literature to enhance our understanding of this intriguing intersection between environmental factors and thrombotic events. Our objective is to determine the influence of meteorological elements on VTE incidence. This includes investigating seasonal variations in VTE incidence, the effects of temperatures on different VTE subgroups (PE and DVT), and in China. This research aims to provide insights for health education and offer specific preventive measures for high-risk individuals. By considering nuances in the impact of meteorological factors on specific thrombotic events, we aim to provide a nuanced understanding of this complex relationship. Additionally, focusing on studies conducted in China allows us to explore potential regional variations in the association between meteorological variables and VTE.

Method

Literature Search

This study conducted a comprehensive systematic review to investigate the potential correlation between meteorological factors and VTE. The search covered both English and Chinese literature databases, including MEDLINE (1966-2023.12), Embase (1976-2023.12), China Biology Medicine Literature Database (CBM, 1976-2023.12), and China National Knowledge Infrastructure (CNKI, 1976-2023.12). For the English literature search on the PubMed platform, MeSH terms such as "venous thromboembolism", "pulmonary embolism", "seasons", "chronology as topic", "atmospheric pressure", and "meteorology" were utilized. In the Embase database (Ovid platform), the search included terms like "(embolism or thromboembolism), exp seasonal variation/, exp meteorology/, mortality.mp, and incidence.mp". Chinese literature searches in CBM and CNKI utilized terms such as "venous thromboembolism", "deep vein thrombosis", "pulmonary embolism", and "meteorological factors". Following the database searches, we compiled tables containing article titles and author information. Duplicate articles were meticulously screened out to ensure the inclusion of unique and relevant studies. Additionally, references from the included studies were traced to identify any additional pertinent literature. This systematic review aims to provide a comprehensive synthesis of existing research on the relationship between meteorological factors and VTE, contributing valuable insights to the scientific understanding of this complex association.

Inclusion and Exclusion Criteria

Inclusion criteria were defined to encompass various research types, including observational studies, clinical trials, cohort studies, and case-control studies. Studies meeting the following criteria were considered eligible for inclusion in the systematic review and meta-analysis: studies involving patients diagnosed with VTE; published literature investigating the relationship between meteorological factors and the incidence or mortality rate of VTE. In cases where two articles reported on the same database but one was a follow-up study of the other, both articles were included. The exclusion criteria were as follows: studies focused on non-venous diseases, such as arterial thromboembolism or stroke; literature not in English or Chinese; duplicate reports; and review articles, among others.

Table 1. General Overview of the Included Research.

Author	Publication Date	Region	Research Period	Sample Size	Incidence rate	Subtype	Average age	Female (%)	Coordinates	NOS score	Climate type
Hong J, *et al* [29]	2020	Korea	2009.1–2013.12	59,626	•	PE+DVT	NA	54.2	34–38° N 126–130° E	8	Subtropical monsoon climate/Temperate monsoon climate
Li Y, *et al* [17]	2017	Shenyang, China	2006.1.–2015.12.31	1593	•	DVT	58.2	57.7	41°44’ N 123°27’ E	9	Temperate semi-humid continental climate
Elias S, *et al* [30]	2016	Northern Israel	2009.1–2013.12	1496	•	PE+DVT	63	52	32°49’ N 34°59’ E	8	Mediterranean climate
Shiue I, *et al* [31]	2016	Wiesbaden, Germany	2009.1.1–2011.12.31	1241	•	VTE	NA	NA	50°08’ N 8°24’ E	8	Temperate continental climate
Frappé P, *et al* [32]	2015	France	1996–2012	1395	•	SVT	NA	NA	43°–51° N 5°–9° W	7	Temperate maritime climate
Anar C, *et al* [33]	2015	Izmir, Turkey	2010.1–2012.12	530	•	PE	NA	48.9	38°24’ N 27°09’ E	6	Subtropical Mediterranean climate
Chiu H, *et al* [22]	2013	Detroit, USA	2004–2008	1490	•	VTE	NA	NA	42°23’ N 83°05’ W	8	Temperate climate
Nimako K, *et al* [34]	2012	London, England	2000.1–2008.1	640	•	PE	NA	55.4	39°55’ N 116°23’ W	7	Temperate maritime climate
Jang M, *et al* [35]	2012	Korea	2001.1–2010.12	1495	•	VTE	60	56.8	33–43 ° N 124–131° E	8	Temperate maritime climate
Lee CH, *et al* [23]	2011	Taiwan, China	2002	2774	•	VTE	62.8	53.4	25°05’ N 121°38’ E	9	Subtropical monsoon climate/Tropical monsoon climate
Ma QB, *et al* [25]	2011	Beijing, China	1994.10.1–2010.10.1	727	•	PE	62.7	48	39°55’ N 116°23’ E	6	Temperate monsoon climate
Manfredini R, *et al* [36]	2009	Italy	2002.1–2004.1	2119	•	PE+DVT	59.3	50.2	36°–73° N 5°–39° E	7	Subtropical Mediterranean climate
Oztuna F, *et al* [21]	2008	Trabzon, Turkey	2001.1.1–2006.5.31	206	•	PE+DVT	NA	NA	41°0’ N 39°7’ E	8	Subtropical Mediterranean climate

Table 1. Continued.

Author	Publication Date	Region	Research Period	Sample Size	Incidence rate	Subtype	Average age	Female (%)	Coordinates	NOS score	Climate type
Gallerani M, *et al* [37]	2007	Romagna, Italy	1998.1–2005.12	19,245	•	PE	71.6	57.7	41°52’ N 12°37’ E	8	Mediterranean climate
Tan XY, *et al* [24]	2006	Beijing, China	1974–2005.12	763	•	PE	50.9	41.4	39°55’ N 116°23’ E	7	Temperate monsoon climate
Meral M, *et al* [20]	2005	Erzurum, Turkey	2000.8–2004.9	91	•	PE	NA	NA	39°9’ N 41°3’ E	9	Subtropical Mediterranean climate
Gallerani M, *et al* [38]	2004	Ferrara, Italy	1998.1.1–2002.12.31	1166	•	VTE+DVT	70.8	53	44°8’ N 11°6’ E	7	Subtropical Mediterranean climate
Manfredini R, *et al* [39]	2004	Ferrara, Italy	1998.1.1.–2001.12.31	784	•	PE+DVT	71	53.8	44°8’ N 11°6’ E	8	Subtropical Mediterranean climate
Bilora F, *et al* [40]	2002	Padua, Italy	1997.1–1997.12	44	•	DVT	45	50	45°4’ N 11°9’ E	8	Subtropical Mediterranean climate
Fink AM, *et al* [41]	2002	Austria Vienna	1996–2000	905	•	DVT	64	54	48°2’ N 16°7’ E	8	Marine climate
Ferrari E, *et al* [42]	1997	France	1992.7–1994.12	547	•	VTE	63	51	43°–51° N 5°–9° W	9	Temperate maritime climate

NOS, Newcastle-Ottawa Scale; PE, pulmonary embolism; DVT, deep vein thrombosis; VTE, venous thromboembolism; SVT, superficial vein thrombosis; E, east longitude; N, northern latitude; W, west longitude.

Literature Selection

Upon reviewing article titles and abstracts, obviously ineligible literature was excluded. For articles with potential eligibility or uncertainty, the full text was retrieved for further screening. The full texts were then thoroughly read and analyzed to determine their eligibility, with each piece of literature being meticulously evaluated.

Data Extraction

Two independent evaluators extracted information from the literature, including publication date, the number of VTE patients included, latitude, *etc*. In cases of disagreement, a third evaluator was consulted to make the final decision. If any data were missing, authors were contacted to provide the necessary information. These rigorous inclusion, exclusion, and selection processes ensure the robustness and reliability of the literature included in our review, maintaining a high standard of scientific scrutiny.

Methodological Quality Assessment

Meta-analysis and systematic review were conducted following the search strategy and methods established by the Cochrane Collaboration [26]. Additionally, this study adhered to the PRISMA [27] guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) that consist of 27 items and 1 flow diagram, as specified by the PRISMA statement. Two evaluators independently completed this assessment, and any differences of opinion were resolved based on the decision of a third evaluator.

Quality Assessment of Studies Using the Newcastle-Ottawa Scale

Two researchers independently assessed the final included studies' quality using the Newcastle-Ottawa Scale (NOS), which assigns scores from 0 to 9 points. Any discrepancies were resolved through discussion with the corresponding author. Since all included studies were cohort studies, the NOS was utilized to evaluate quality across three dimensions: Selection, Comparability, and Outcome. Each criterion in the selection and outcome assessments could receive a score of 1 if met and 0 if not, while comparability could score up to 2, with a minimum of 0. The total NOS score ranged from 0 to 9, with higher scores indicating better quality. Studies with an overall NOS score exceeding 6 points were deemed high quality [28].

Statistical Methods

Binary variables were evaluated using relative risk (RR) to assess the data. The following calculations were performed based on VTE incidence rates for each season: (A) spring *vs*. summer, (B) spring *vs*. autumn, (C) spring *vs*. winter, (D) summer *vs*. autumn, (E) summer *vs*. winter, and (F) autumn *vs*. winter. The RR and 95% confidence interval (95% CI) were calculated for VTE incidence rates. Subgroup analysis was conducted based on VTE classification, the studies were divided into two subgroups: DVT and PE. Similarly, subgroup meta-analysis studies were performed in China. The I^2 test was used to assess heterogeneity: if $I^2 < 50\%$, it indicated homogeneity among the data, and a fixed-effect model was used. If $I^2 > 50\%$, it indicated heterogeneity among the studies, and a random-effect model was used to calculate the RR value and 95% CI. Publication bias was assessed using funnel plots and Egger's regression tests. Review Manager 5.3 version (Cochrane Collaboration, London, UK) and STATA 11.2 version (Stata Corporation, TX, USA) were used for statistical analysis, applying the Metan module for analysis and the Metabias module for publication bias assessment.

Results

Literature Selection Process and Results

Following the guidelines outlined in the PRISMA statement flowchart, we systematically screened both English and Chinese literature retrieved from the search. A total of 21 articles were ultimately included, comprising 20 in English and 1 in Chinese. Among the English literature, 23 articles did not meet the inclusion criteria. Specifically, 4 studies did not provide summarized seasonal data, and 7 reports lacked sufficient data. The detailed literature selection process and inclusion criteria are summarized in Fig. 1. This systematic approach adheres to the PRISMA guidelines (**Supplementary Table 1**), ensuring a transparent and rigorous process in selecting relevant literature for our review.

In the end, 21 literatures meeting the inclusion criteria were included, which involved a total of 98,877 patients with VTE, including PE, lower extremity DVT, and superficial vein thrombosis (SVT). These studies were conducted between 1994 and 2017. Among these studies, 10 were from Europe, 1 was from the United States, and 10 were from Asia (including 4 studies based on the Chinese population). The basic information required for the extraction of the meta-analysis is shown in Table 1 (Ref. [17,20–25,29–42]).

Meta-Analysis Results

VTE Incidence in the Global Context: Among the 21 studies included, a comprehensive analysis of seasonal VTE incidence was conducted. The occurrence rates were as follows: 24.3% in spring, 24.3% in summer, 24.8% in autumn, and 26.5% in winter (refer to Fig. 2). Notably, the meta-analysis revealed a significantly lower incidence of VTE during summer compared to winter (RR = 0.90, 95% CI: 0.84–0.98, p = 0.010) (Fig. 3). However, no sta-

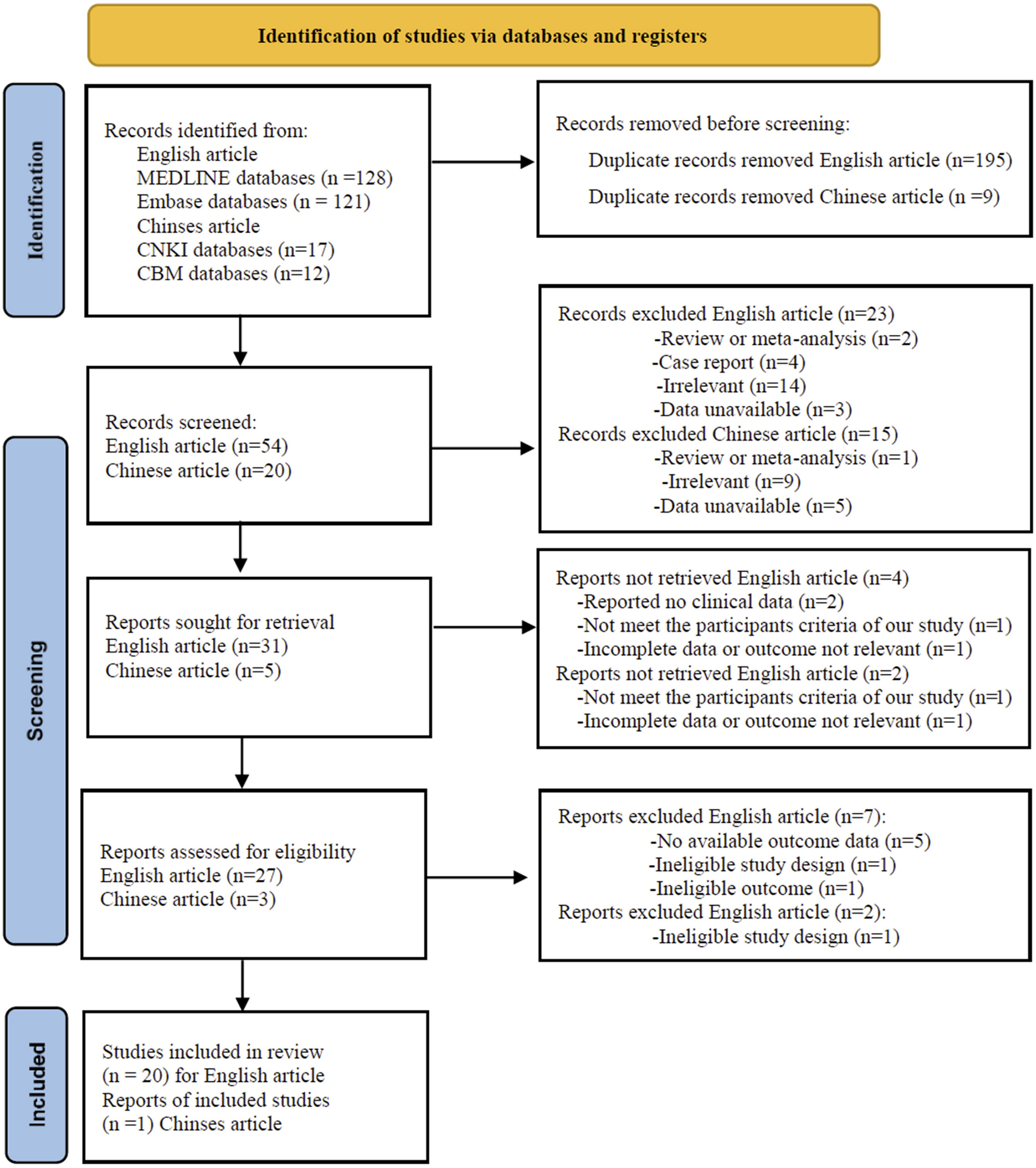

Fig. 1. PRISMA flow diagram for literature selection.

tistically significant differences were observed in VTE incidence among the other seasonal comparisons. Rigorous evaluation, including funnel plot analysis and Egger's test, demonstrated no evidence of publication bias, affirming the reliability of the meta-analysis results.

Subgroup Analysis of VTE (PE/DVT) in the Global Context: A detailed subgroup analysis was conducted on the two subtypes of VTE, namely PE and DVT. The incidence rate of PE during summer was significantly lower than in autumn/winter (RR = 0.93, 95% CI: 0.89–0.97 summer/autumn; RR = 0.90, 95% CI: 0.84–0.98 summer/winter), with statistically significant differences (Table 2). Additionally, meta-analysis results indicated a significantly higher incidence rate of DVT in winter compared to summer (RR = 0.80, 95% CI: 0.66–0.86, $p = 0.02$, Fig. 4).

VTE Incidence in China: In the context of China, five studies addressing seasonal VTE were identified. Two studies originated from Beijing, one from Shenyang, Liaoning Province, and one each from Taiwan Province and Hong Kong Special Administrative Region. Of the four studies focusing on the incidence rate of seasonal VTE, one specifically investigated the relationship between PE mortality

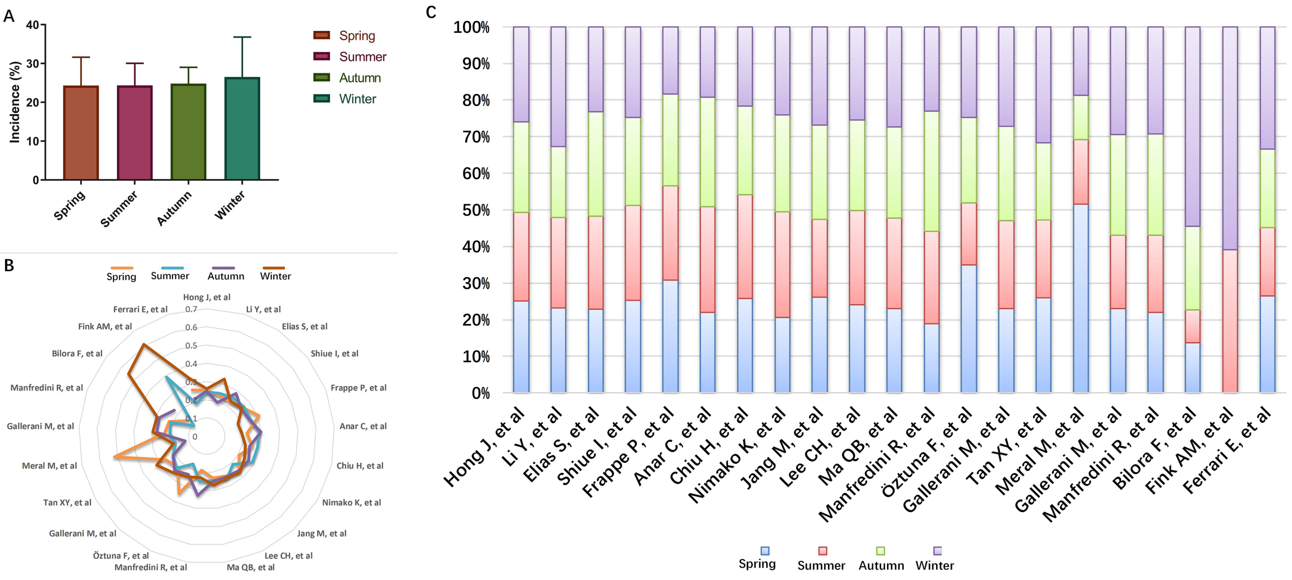

Fig. 2. Seasonal variation characteristics of global VTE incidence. Graphical representation of seasonal VTE incidence (A); Radar chart depicting seasonal variation characteristics in the included 21 studies (B); Seasonal incidence rates in each study of the included 21 studies (C).

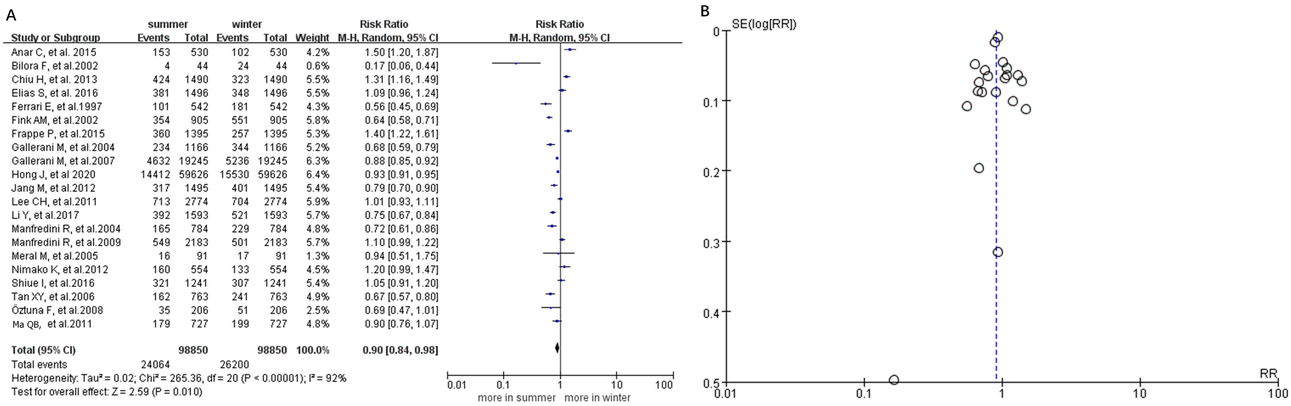

Fig. 3. Forest plot comparing global VTE incidence rates between summer and winter. The forest plots (A) and funnel plot (B).

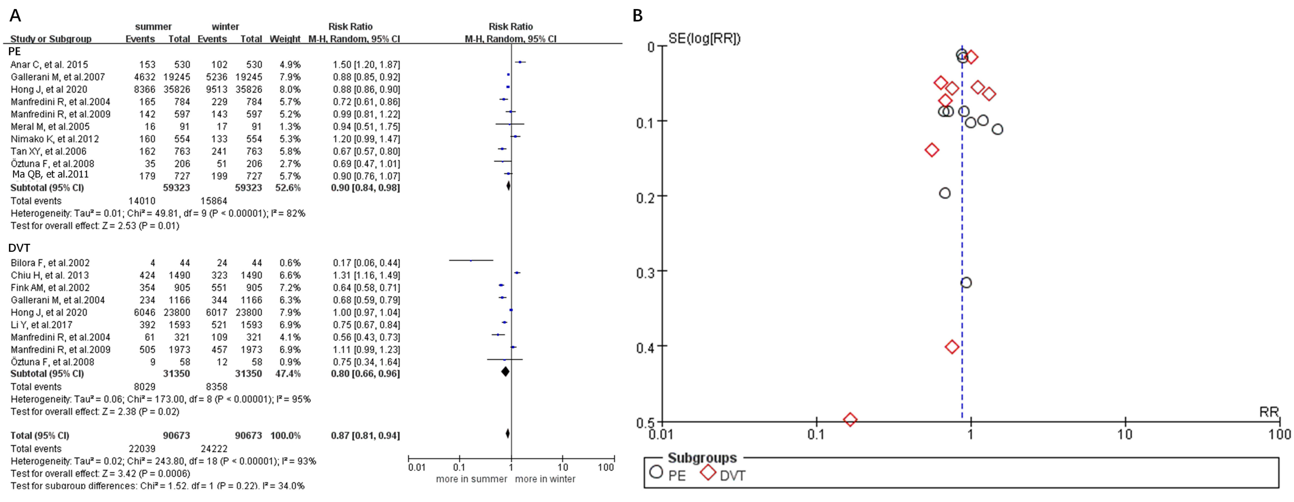

Fig. 4. Forest plot of PE and DVT incidence rates between summer and winter. The forest plots (A) and funnel plot (B).

Table 2. Seasonal Incidence Rates of PE and DVT.

PE	References	Number of included literatures	RR	95% CI	Model	*p* value
Spring	Summer	10	1.03	0.93–1.14	random effects model	0.550
Spring	Autumn	10	0.95	0.86–1.05	random effects model	0.310
Spring	Winter	10	0.93	0.85–1.02	random effects model	0.110
Summer	Autumn	10	0.93	0.89–0.97	random effects model	0.002
Summer	Winter	10	0.90	0.84–0.98	random effects model	0.010
Autumn	Winter	10	0.98	0.91–1.06	random effects model	0.590
DVT	References	Number of included literatures	RR	95% CI	Model	*p* value
Spring	Summer	8	0.98	0.87–1.10	random effects model	0.750
Spring	Autumn	8	0.94	0.78–1.14	random effects model	0.510
Spring	Winter	8	0.85	0.72–1.00	random effects model	0.050
Summer	Autumn	8	0.93	0.80–1.08	random effects model	0.330
Summer	Winter	9	0.80	0.66–0.96	random effects model	0.020
Autumn	Winter	8	0.89	0.73–1.08	random effects model	0.250

RR, relative risk.

rate and weather. Meta-analysis results revealed a significantly lower incidence rate of VTE in spring compared to winter (RR = 0.83, 95% CI: 0.72–0.96; p = 0.010) (refer to Fig. 5). However, no statistically significant differences were observed in the incidence rates of VTE between winter and summer or autumn in our country.

Discussion

VTE risk factors include a history of malignant tumors, recent surgery, fractures, and estrogen therapy [43]. However, the role of short-term exposure to climatic conditions in VTE incidence remains unclear. Through a meta-analysis and systematic review of the literature, we have preliminarily identified the relationship between VTE incidence and seasonal variations, as well as the association between seasonal changes and PE or DVT incidence. We observed a significantly higher incidence of VTE (both pulmonary embolism and deep vein thrombosis) during winter compared to summer.

Several aspects may explain the heightened risk of VTE during winter. For instance, the cold temperature effect is often associated with winter, and an Italian study suggests that the high coagulation state during winter leads to decreased fibrinolytic activity and increased fibrinogen [44]. Additionally, reduced physical activity during winter, coupled with the vasoconstrictive effects of cold temperatures, may impact the formation of VTE or DVT [45]. Moreover, certain risk factors affecting vascular walls, such as abnormal lipid levels and hypertension, exhibit distinct seasonal patterns and may influence the occurrence and development of VTE [46]. A recent *in vivo* study in mice indicated that exposure to cold air significantly reduces adiponectin concentration in serum, suggesting a potential role of adiponectin in protecting against atherosclerosis [47].

Before conducting our meta-analysis, we identified conflicting conclusions in international literature regarding the relationship between meteorological factors and VTE incidence. Three studies we included [34,37] reported a peak in VTE incidence during seasons with lower temperatures. Conversely, four studies [25,30,36,41] indicated an increase in VTE incidence during winter. Anar *et al*. [33] proposed an increase in VTE incidence during autumn. Simultaneously, one literature piece argued no association between VTE incidence and seasonal changes [23], while another study suggested a peak in VTE incidence during summer [22]. Meta-analysis, also known as a systematic review, addresses the issue of disparate results in a multitude of scientific papers on the same study. Therefore, considering the divergent conclusions, we gathered small sample and single clinical center results globally regarding the impact of seasonal changes on VTE. We conducted a systematic evaluation and statistical analysis to promptly provide as accurate scientific conclusions as possible to meteorological service departments and clinical practitioners, serving as a basis for health meteorological forecasts and public defense against venous thromboembolism.

The comprehensive analysis of global VTE incidence across the 24 studies provides valuable insights into the seasonal variations of this condition. The meta-analysis revealed distinct patterns, with a significantly lower incidence of VTE during summer compared to winter. The observed rates were 24.3% in spring, 24.3% in summer, 24.8% in autumn, and 26.5% in winter. The statistically significant reduction in VTE incidence during summer (RR = 0.90, 95% CI: 0.84–0.98, p = 0.010) supports the notion of a seasonal influence on the occurrence of VTE. The lower incidence during summer aligns with findings from subgroup analysis, which focused on the two main subtypes of VTE, PE, and DVT. The analysis demonstrated a significantly lower incidence of PE during summer compared to autumn/winter (RR = 0.93, 95% CI: 0.89–0.97 summer/autumn; RR =

Study or Subgroup	spring Events	spring Total	summer Events	summer Total	Weight	Odds Ratio M-H, Random, 95% CI
Lee CH, et al.2011	670	2774	713	2774	33.5%	0.92 [0.82, 1.04]
Li Y, et al.2017	371	1593	392	1593	27.9%	0.93 [0.79, 1.09]
Tan XY, et al.2006	198	763	162	763	19.5%	1.30 [1.03, 1.65]
Ma QB, et al.2011	168	727	179	727	19.1%	0.92 [0.72, 1.17]
Total (95% CI)		**5857**		**5857**	**100.0%**	**0.99 [0.86, 1.13]**
Total events	1407		1446			

Heterogeneity: Tau² = 0.01; Chi² = 6.99, df = 3 (P = 0.07); I² = 57%
Test for overall effect: Z = 0.18 (P = 0.86)

Study or Subgroup	spring Events	spring Total	autumn Events	autumn Total	Weight	Risk Ratio M-H, Random, 95% CI
Lee CH, et al.2011	670	2774	687	2774	30.6%	0.98 [0.89, 1.07]
Li Y, et al.2017	371	1593	309	1593	26.4%	1.20 [1.05, 1.37]
Tan XY, et al.2006	198	763	162	763	21.6%	1.22 [1.02, 1.47]
Ma QB, et al.2011	168	727	181	727	21.5%	0.93 [0.77, 1.11]
Total (95% CI)		**5857**		**5857**	**100.0%**	**1.07 [0.94, 1.22]**
Total events	1407		1339			

Heterogeneity: Tau² = 0.01; Chi² = 10.72, df = 3 (P = 0.01); I² = 72%
Test for overall effect: Z = 0.99 (P = 0.32)

Study or Subgroup	spring Events	spring Total	winter Events	winter Total	Weight	Risk Ratio M-H, Random, 95% CI
Lee CH, et al.2011	670	2774	704	2774	28.3%	0.95 [0.87, 1.04]
Li Y, et al.2017	371	1593	521	1593	26.8%	0.71 [0.64, 0.80]
Tan XY, et al.2006	198	763	241	763	23.2%	0.82 [0.70, 0.96]
Ma QB, et al.2011	168	727	199	727	21.7%	0.84 [0.71, 1.01]
Total (95% CI)		**5857**		**5857**	**100.0%**	**0.83 [0.72, 0.96]**
Total events	1407		1665			

Heterogeneity: Tau² = 0.02; Chi² = 15.29, df = 3 (P = 0.002); I² = 80%
Test for overall effect: Z = 2.51 (P = 0.01)

Study or Subgroup	summer Events	summer Total	autumn Events	autumn Total	Weight	Risk Ratio M-H, Random, 95% CI
Lee CH, et al.2011	713	2774	687	2774	33.0%	1.04 [0.95, 1.14]
Li Y, et al.2017	392	1593	309	1593	26.9%	1.27 [1.11, 1.45]
Tan XY, et al.2006	162	763	162	763	19.2%	1.00 [0.82, 1.21]
Ma QB, et al.2011	179	727	181	727	20.8%	0.99 [0.83, 1.18]
Total (95% CI)		**5857**		**5857**	**100.0%**	**1.08 [0.96, 1.21]**

Study or Subgroup	summer Events	summer Total	winter Events	winter Total	Weight	Risk Ratio M-H, Random, 95% CI
Lee CH, et al.2011	713	2774	704	2774	27.1%	1.01 [0.93, 1.11]
Li Y, et al.2017	392	1593	521	1593	26.3%	0.75 [0.67, 0.84]
Tan XY, et al.2006	162	763	241	763	23.4%	0.67 [0.57, 0.80]
Ma QB, et al.2011	179	727	199	727	23.3%	0.90 [0.76, 1.07]
Total (95% CI)		**5857**		**5857**	**100.0%**	**0.83 [0.68, 1.00]**
Total events	1446		1665			

Heterogeneity: Tau² = 0.03; Chi² = 26.32, df = 3 (P < 0.00001); I² = 89%
Test for overall effect: Z = 1.93 (P = 0.05)

Study or Subgroup	autumn Events	autumn Total	winter Events	winter Total	Weight	Risk Ratio M-H, Random, 95% CI
Lee CH, et al.2011	687	2774	704	2774	26.1%	0.98 [0.89, 1.07]
Li Y, et al.2017	309	1593	521	1593	25.5%	0.59 [0.52, 0.67]
Tan XY, et al.2006	162	763	241	763	24.2%	0.67 [0.57, 0.80]
Ma QB, et al.2011	181	727	199	727	24.2%	0.91 [0.76, 1.08]
Total (95% CI)		**5857**		**5857**	**100.0%**	**0.77 [0.59, 1.01]**
Total events	1339		1665			

Heterogeneity: Tau² = 0.07; Chi² = 47.26, df = 3 (P < 0.00001); I² = 94%
Test for overall effect: Z = 1.92 (P = 0.05)

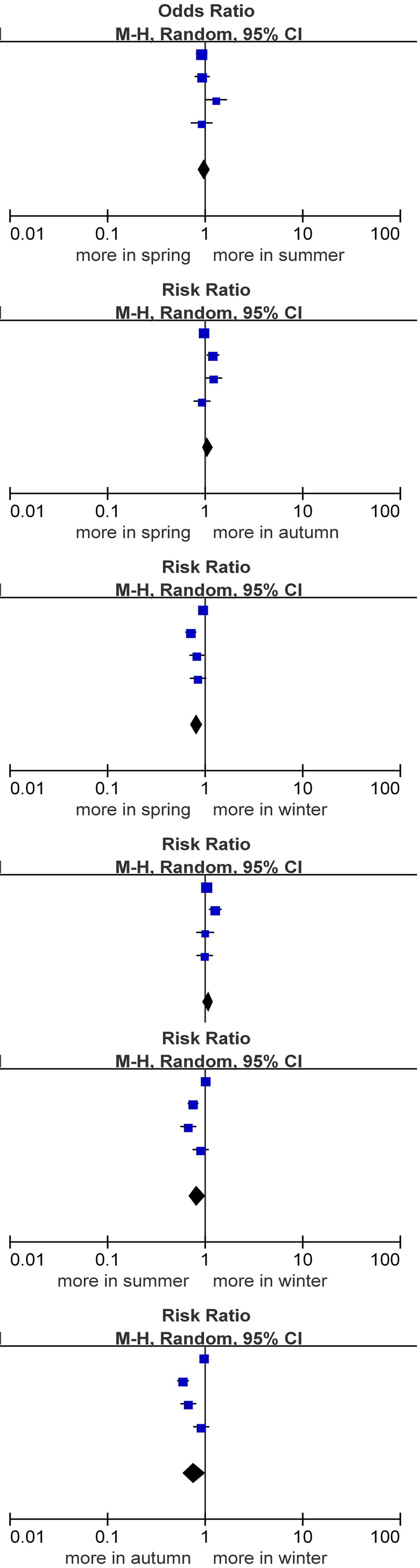

Fig. 5. Meta-analysis results of 4 studies based on data from China.

0.90, 95% CI: 0.84–0.98 summer/winter). Conversely, the incidence rate of DVT was found to be significantly higher in winter compared to summer (RR = 0.80, 95% CI: 0.66–0.86, $p = 0.02$). These findings suggest a distinct seasonal variation in the occurrence of PE and DVT globally. The observed seasonality in VTE incidence can be attributed to multiple factors identified in the literature. The cold temperature effect in winter, characterized by high coagulation states and reduced fibrinolytic activity, may contribute to the elevated risk of VTE. Additionally, decreased physical activity during winter, coupled with vasoconstriction due to cold temperatures, could further influence the formation of VTE or DVT. The seasonal variations in risk factors such as abnormal lipid levels and hypertension may also play a role in the observed patterns [48]. Furthermore, the winter season is associated with decreased physical activity, which, when combined with vasoconstriction due to cold temperatures, can further influence the formation of VTE or DVT. Reduced physical activity during winter has been identified as a risk factor contributing to venous thrombosis [49]. The vasoconstrictive effects of cold temperatures on peripheral blood vessels may exacerbate this risk, creating an environment conducive to the development of thrombotic events. Seasonal variations in risk factors such as abnormal lipid levels and hypertension also play a role in the observed patterns of VTE. These factors exhibit distinct seasonal patterns, and their influence on vascular walls may contribute to the occurrence and development of VTE. For example, abnormal lipid levels and hypertension have been linked to vascular dysfunction, potentially increasing the risk of venous thrombosis [50].

In the context of China, the meta-analysis of five studies focusing on seasonal VTE incidence revealed intriguing findings. The incidence rate of VTE in spring was significantly lower than in winter (RR = 0.83, 95% CI: 0.72–0.96; $p = 0.010$). However, no statistically significant differences were observed in the incidence rates of VTE between winter and summer or autumn in the Chinese population. These results suggest that the seasonal patterns of VTE in China may differ from the global trends. The variations in VTE incidence patterns between different geographical regions could be influenced by a combination of genetic, environmental, and lifestyle factors unique to each population. Understanding these regional differences is crucial for tailoring preventive measures and healthcare strategies to specific populations. The variations in VTE incidence patterns between different geographical regions, such as China and the global context, could be influenced by a combination of genetic, environmental, and lifestyle factors unique to each population. Genetic predispositions, regional climate variations, and diverse lifestyle practices may contribute to the observed differences. For example, a study on genetic factors influencing VTE risk in different populations found variations in specific genetic markers associated with venous thrombosis risk across diverse ethnic groups [51]. Additionally, environmental factors such as air pollution levels and altitude, which vary between regions, have been linked to cardiovascular health and thrombotic events. Studies conducted in China have explored the impact of air pollution on cardiovascular diseases, indicating potential associations with thrombotic events [52]. Furthermore, lifestyle factors, including dietary habits and occupational activities, may contribute to the observed regional differences in VTE patterns. Understanding these regional differences is crucial for tailoring preventive measures and healthcare strategies to specific populations. Consideration of the unique factors influencing VTE risk in the Chinese population will aid in the development of targeted interventions and public health initiatives.

While our study provides valuable insights into the seasonal variations of VTE incidence, several limitations warrant consideration. Firstly, despite our efforts to include diverse datasets, the analysis heavily relies on available global and Chinese databases, which might not capture the entirety of regional variations. Additionally, the retrospective nature of our study introduces inherent limitations regarding data accuracy and potential biases in data collection methods across different regions. Secondly, although subgroup analyses were conducted to examine specific trends in DVT and PE, the heterogeneity among the included studies could influence the robustness of our findings. Variability in study methodologies, population demographics, and diagnostic criteria may contribute to inconsistencies in observed patterns. Furthermore, while we acknowledge the influence of seasonal factors on VTE incidence, our study primarily focuses on epidemiological associations, limiting our ability to elucidate the underlying mechanisms driving seasonal variations. Future research incorporating physiological and molecular investigations could provide deeper insights into the causative factors behind observed trends.

Conclusion

In conclusion, the meta-analysis provides robust evidence of seasonal variations in global VTE incidence, with a notable reduction during summer. Subgroup analysis indicates differing patterns for PE and DVT. The observed variations in China further emphasize the need for region-specific considerations in understanding and addressing VTE. The identified patterns underscore the importance of seasonal factors in the risk and occurrence of VTE, urging further research to unravel the underlying mechanisms and guide targeted interventions. the observed seasonality in VTE incidence can be explained by a combination of cold temperature effects, decreased physical activity, and seasonal variations in risk factors such as abnormal lipid levels and hypertension. These factors collectively contribute to the elevated risk of VTE during winter. Understanding these mechanisms is crucial for tailoring preventive measures and interventions to mitigate the seasonal variations in VTE risk.

Author Contributions

YNL and YML analyzed data; YML and YH conceived and supervised the study; YH, CS and YNL conceived and designed this study; JU, TY, and DJ searched the databases; YNL and YH conducted the meta-analysis, YML and DJ analyzed the data and drafted the manuscript; YNL, TY, YML checked all the data; DJ and YH contributed to reviewing. All authors reviewed the results and approved the final version of the manuscript. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.7251.

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