

Incidence And Risk Factors Of Venous Thromboembolism (Vte) In Hospitalized Patients: A Systematic Review

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Abstract

Background: Venous thromboembolism (VTE) is a major healthcare problem that has resulted in a significant increase in mortality, morbidity, and healthcare cost. Our knowledge of the incidence and risk factors of VTE differs among various ethnic backgrounds and nationalities, therefore, there is a need to explore the incidence of VTE and to understand the role of risk factors that require a pooled analysis. The aim of this review is to assess the incidence and risk factors of venous thromboembolism (VTE) in hospitalized patients. Methods: We searched PubMed, Embase, Scopus and Web of Sciences databases from 2015 to 2022, to identify studies reporting the incidence and risk factor of VTE among hospitalized patients. Descriptive statistics were described to present the results. Results: We identified 17 studies comprising 17703 participants, and only 1132 (6.4%) of them developed VTE. 12 studies were retrospective, while 5 studies were prospective. The majority of participants 9573 (54%) were female, while 8130 (4645.9%) were male. 13 (76%) studies reported a low incidence of VTE, while 2 (12%) studies concluded high incidence and 2 (12%) studies reported moderate incidence of VTE. 12 (70%) studies revealed low risk factors associated with VTE, while 3 (18%) studies found high risk factors associated with VTE and 2 (12%) studies described moderate risk factors related to VTE. Conclusions: Despite universal thromboprophylaxis, medical and surgical ill patients continue to be at risk for VTE. Incidence of VTE among hospitalized patients was low and associated with several risk factors. All patients need to undertake dynamic and constant risk¹ assessment for VTE with laboratory monitoring, associated medications, invasive procedures, and previous medical history considered, particularly for severe and critically ill patients. We strongly urge clinicians to be conscious of VTE risk factors and highlight on optimizing patients' comorbidities before admission to the hospital.

Keywords Venous, thromboembolism, hospitalized, patients, incidence, risk, factors.

Introduction

Plain language summary

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Venous thromboembolism (VTE) is a common and serious health problem, especially among hospitalized patients. Therefore, it is necessary to explore how large this problem and what risk factors are associated with its occurrence. We conducted a systematic review searching multiple medical databases to summarize the incidence and risk factors of this issue. This review revealed that VTE is still prevalent and associated with multiple risk factors, such as hypertension, diabetes mellitus, obesity, longer hospital stays, immobility, age, surgery or trauma, oncology patients and positive personal or family history of VTE. We strongly urge healthcare practitioners at all settings to look for those who are at risk of developing VTE before their admission to hospital.

Introduction

Venous thromboembolism (VTE) is a major healthcare issue, that has resulted in a significant increase in mortality, morbidity, and healthcare cost (Guyatt et al., 2012; Nkoke et al., 2020). VTE occurring in hospitalized patients and after discharge is becoming more common worldwide, and, hence, hospitalization is the most important risk factor for the development of VTE (Ambra et al., 2022).

The prevalence and incidence of VTE is high worldwide (Zhang et al., 2019), with an approximate annual incidence rate of 1–2 per 1000 persons a year and with an approximate death of 60,000–100,000 in the United States of America (Al-Hameed et al., 2015; Scheres et al., 2018). Moreover, a study revealed that the incidence of VTE was highest in patients who were in a critical care setting (Puri et al., 2022). Furthermore, a study conducted in Saudi Arabia reported that 21.4% and 78.6% of confirmed VTE occurred in surgical and medical patients, respectively (Al-Hameed et al., 2017).

Internationally, the incidence of VTE rises during hospitalization as a result of an increase in risk factors (Nkoke et al., 2020). VTE risk factors are revealed to be previous diagnosis of VTE, the occurrence of surgery within the past 30 days and an admission diagnosis of pulmonary disease (Anderson et al., 2007; Khalafallah et al., 2016).

At national level, a retrospective cohort study conducted in Madinah, Saudi Arabia, found 70.5% patients were at high risk to develop VTE and 17.6% at moderate risk (Kharaba et al., 2017). Another study conducted in the intensive care unit (ICU) revealed that central venous catheter use and length of stay were independent risk factors related to the incidence of VTE for patients admitted to the ICU (Zhang et al., 2019). Moreover, in a study carried out after major abdominal-pelvic surgeries, authors revealed that risk factors for VTE were history of VTE, anticoagulant use, postoperative chemotherapy, preoperative chemotherapy, and endometrium cancer (Taengsakul et al., 2021).

Saudi Ministry of Health (MOH), and the Saudi Association for Venous Thromboembolism (SAVTE) agreed to implement VTE prevention protocols in 2017 to cover all related clinical specialties for all adult patients admitted to MOH hospitals (Al-Hameed et al., 2017). As part of this initiative, it is imperative to highlight the incidence and risk factors of VTE. Our knowledge of the incidence and risk factors of VTE differs among various ethnic background and nationalities. Moreover, there is a need to understand the role of risk factors that required a pooled analysis. Hence, the aim of this review is to assess the incidence and risk factors of venous thromboembolism (VTE) in hospitalized patients.

Methods

This systematic review was conducted according to the Cochrane collaboration guidelines and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Page et al., 2021).

Search strategy

We performed a comprehensive search of PubMed, Embase, Scopus and Web of Sciences databases using the following search terms: incidence, risk factors, Venous thromboembolism, hospitalized patients from 2015 to 2022. Searches include MeSH and text words terms with combination using 'AND, OR' Boolean operator. The search words differed between databases, but were comparable. Obtained studies were screened by title and abstract. Manuscripts describing incidence and risk factors of VTE in hospitalized patients retrieved in their entirety and reviewed for potential inclusion. The last day of search was on August 2022

Inclusion and exclusion criteria

Articles were included if they described that they assessed the incidence and/or prevalence and risks factors of VTE as their purpose of the research in adult hospitalized patients, and were published between 2015 and 2022. Articles were also included if published in English and full texts can be accessed. Studies were excluded if they were narratives about VTE in general, studies conducted in children, articles with VTE cases diagnosed before hospital admission, articles with no reported clinical outcomes (PE, recurrence and mortality) of VTE and VTE cases under definite situations such as intensive care unit admission. Three authors were involved in determining whether a study would be included. Any disagreements were resolved by a fourth author.

Screening and data extraction

Data were extracted based on the method used in each study. The following pre-defined baseline and outcome variables were extracted: incidence of VTE, risk factors and use of pharmacological thromboprophylaxis. All data was independently extracted from eligible studies by two authors to ensure data reliability, and any inconsistencies were resolved by discussion with a third author. Other data extracted included: the surname of the author/s, the country where the study was conducted, the study design, sample size, total VTE, patient population, type of VTE and method of VTE diagnosis.

Synthesis methods

Extracted data were descriptively summarized in terms of the incidence of VTE and risk factors provided by each study. In Microsoft Word, we tabulated the surname of the author/s, the country where the study was conducted, the study design, sample size, total VTE, patient population, type of VTE and method of VTE diagnosis. VTE incidence was categorized into low, moderate and high (low incidence of VTE: < 2, moderate: 2–6, high: > 6).

Results

Searches revealed 8598 potentially eligible studies. After carrying out the initial search, 5309 studies were removed since they were duplicates. The remaining 3289 studies were screened and appeared to meet our inclusion criteria. However, 3107 studies were excluded because they were found to not be in accordance with the inclusion criteria. When screening the abstract, 165 studies were excluded due to the following reasons: 63 were found to use duplicate data, 100 had insufficient data and 2 studies had no literature review. After reviewing the full text, 17 studies were included for the final analysis (Figure 1).

Table 1 summarizes the characteristics of the included 17 studies. For each study, the following information was extracted: the surname of the author/s, the country where the study was conducted, the study design, sample size, total VTE, patient population, type of VTE and method of VTE diagnosis. The analyses included 12 retrospective and 5 prospective studies. The total number of patients involved in the 17 studies was 17703, and only 1132 (6.4%) of them developed VTE. Most of the studies used Doppler ultrasound, D-dimer screening, or computerized tomography (CT) scan to diagnose VTE. Deep vein thrombosis (DVT) and pulmonary embolism (PE) are the most common types of VTE seen in the 17 studies.

Figure 2 shows the countries where the studies were conducted. It reveals that 3 studies were conducted in China, 3 studies in Saudi Arabia, 2 studies in Cameroon and 2 studies in Thailand, with one study in each of the following countries: Korea, Japan, Qatar, Holland, Portugal, Spain and Australia.

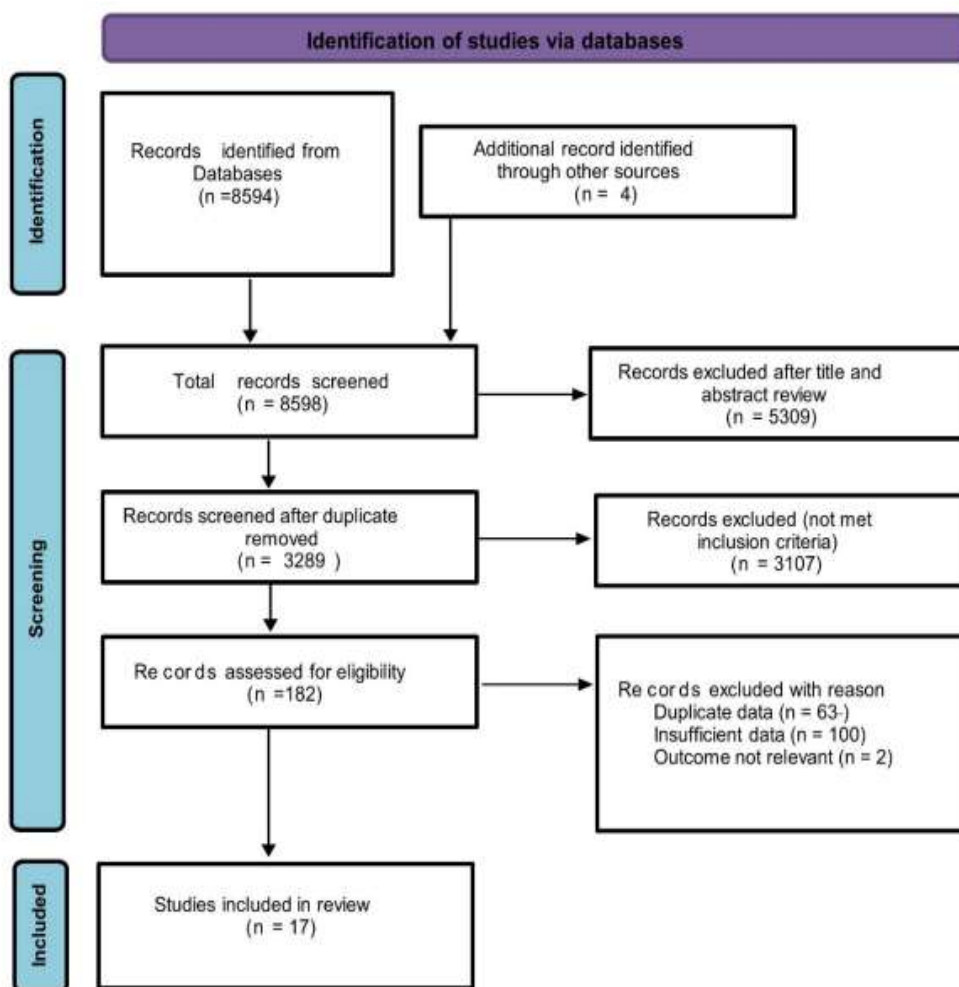


Figure 1. PRISMA flow flowchart for 'Incidence and risk factors of venous thromboembolism (VTE) in hospitalized patients: a systematic review'.

Table 1. Characteristics of included studies.

No.	The study	The risk factors
1	<i>Ambra et al. (2022)</i>	Hypertension, diabetes mellitus.
2	<i>García Adrián et al. (2022).</i>	pancreatic cancer
3	<i>Hayashida et al. (2022)</i>	age ≥ 60 years, tumor location in the lower limbs, and D-dimer
4	<i>Eissa et al. (2022)</i>	longer hospital stay and ICU length of stay, low GCS, and severe injury severity score,
5	<i>Ma et al. (2021)</i>	Current smoking, gender, time from injury to DUS, ASA class, ASIA grade, D-dimer.
6	<i>Chen et al. (2021)</i>	hypoalbuminemia, Sequential Organ Failure Assessment (SOFA) score, and D-dimer.
7	<i>Taengsakul et al. (2021)</i>	History of pulmonary embolism, obesity, anticoagulant use, postoperative & preoperative chemotherapy, endometrium cancer, tumor-node-metastasis stage 4.
8	<i>Nkoke et al. (2020)</i>	age >40 years (57.6%), long-term immobility, and swollen legs, immobility, bed confinement, and complete immobilization.
9	<i>Abduljabbar et al. (2020).</i>	elderly patients, diabetes mellitus, hypertension, bed-ridden patients, ischemic heart disease, breast cancer, and obese patients.
10	<i>Kaewborisutsakul et al. (2020).</i>	diabetes mellitus (DM), operative duration of >420 min, blood transfusion, and new-onset postoperative motor deficits. Female and the presence of a central catheter.
11	<i>Middeldorp (2020).</i>	Patients with COVID-19 were at high risk
12	<i>Zhang et al. (2019)</i>	length of stay and CVC in the location of the femoral vein were the independent risk factors of VTE. femoral catheter had developed VTE.
13	<i>Jang et al. (2018).</i>	Surgery or trauma, immobilization, and cancer
14	<i>Aedh (2018)</i>	Advanced age, stroke, Renal diseases and on dialysis, Positive personal or family history of VTE, Immobility, as well as malignancy
15	<i>Kamdem et al. (2018)</i>	Obesity, hypertension, immobility, and long-haul travel.
16	<i>Ferreira et al. (2017)</i>	oncology patients, followed by orthopedic patients, surgical patients and internal medicine patients.
17	<i>Khalafallah et al. (2016)</i>	prolonged length of stay, Patients who had a surgery within the past 30 days, Previous VTE.

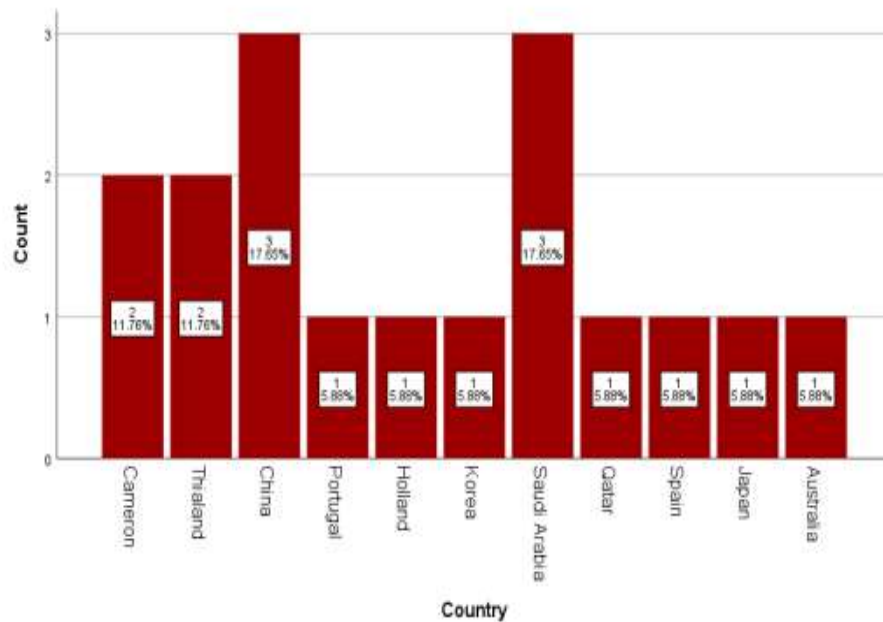


Figure 2. Distribution of the studies by country.

Figure 3 shows the gender of the participants in the 17 studies. The majority of the participants (54%; 9573) were female, while 8130 (46%) were male.

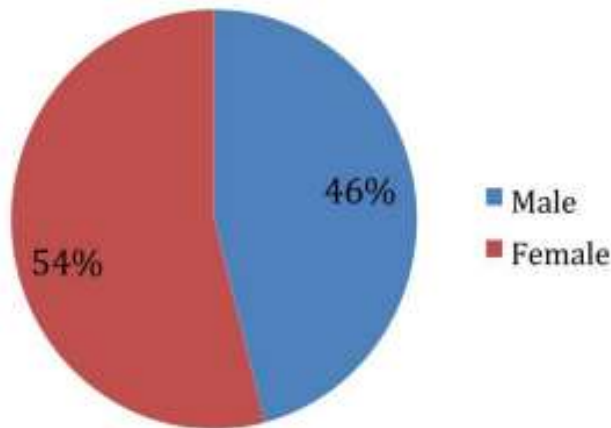


Figure 3. Distribution of participants in the included studies by gender.

Regarding the data collection tool, Figure 4 shows that 7 studies used an institutional database, 4 studies used medical records and D-dimer cut-off value, 3 studies used medical records and ultrasound result, 2 studies used structure questionnaire and medical records, and only 1 study used assessment of venous thromboembolism risk.

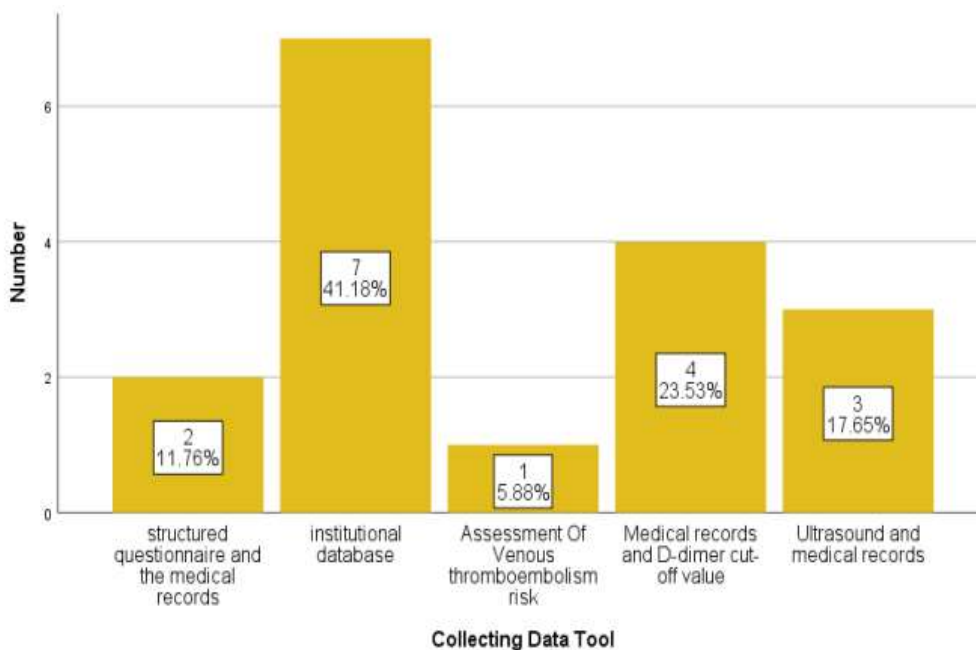


Figure 4. Distribution of studies according to data tools used.

Figure 5 shows the distribution of the 17 studies according to the incidence of VTE. It reveals that 13 (76%) studies reported a low incidence of VTE, while 2 (12%) studies concluded high incidence and 2 (12%) studies reported moderate incidence of VTE. Table 2 shows the most common risk factors reported in the 17 studies. The most common risk factors reported were hypertension, diabetes mellitus, obesity, ↑D-dimer, longer hospital stay, immobility, age, surgery or trauma, oncology patients and positive personal or family history of VTE.

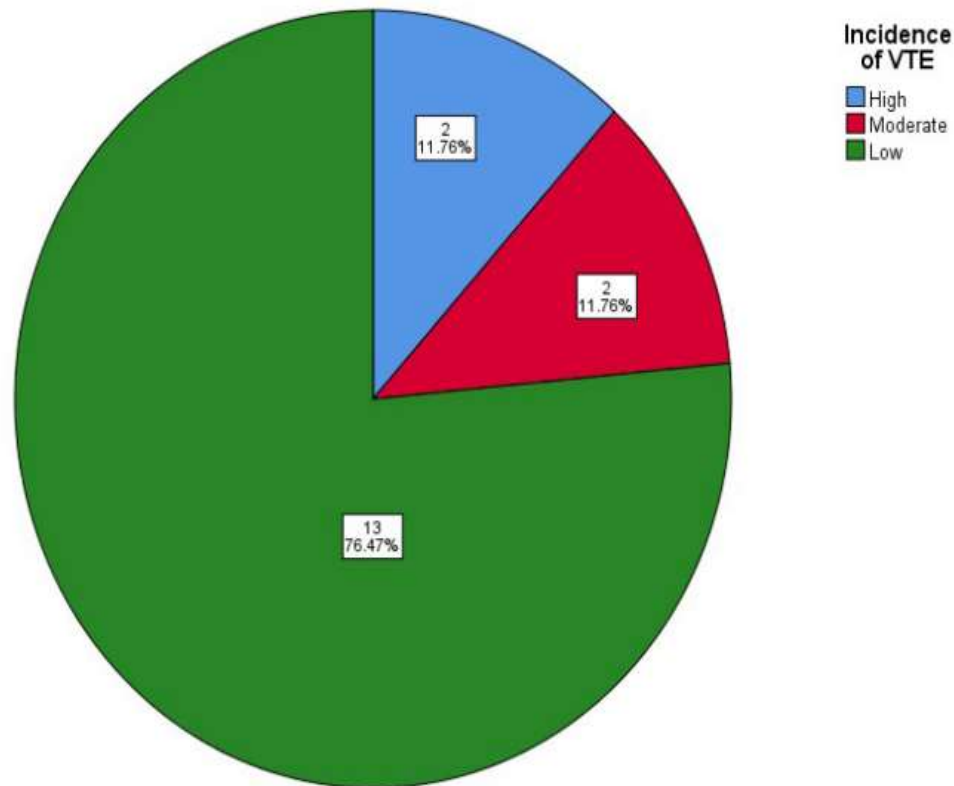


Figure 5. Distribution of the studies according to the incidence of VTE. Note: Low incidence of VTE: < 2, Moderate: 2-6, High: > 6.

Figure 6 shows the distribution of the studies according to the risk of VTE. It reveals that 12 (70%) studies mentioned low risk factors of VTE among the study sample, while 3 (18%) studies concluded high risk factors and 2 (12%) studies reported moderate risk factors of VTE.

Table 2. Common risk factors reported by the 17 studies.

No.	The Study	The risk factors
1	Ambra et al. (2022)	Hypertension, diabetes mellitus.
2	García Adrián et al. (2022)	pancreatic cancer
3	Hayashida et al. (2022)	age ≥ 60 years, tumor location in the lower limbs, and D-dimer
4	Eissa et al. (2022)	longer hospital stay and ICU length of stay, low GCS, and severe injury severity score,
5	Ma et al. (2021)	Current smoking, gender, time from injury to DUS, ASA class, ASIA grade, D-dimer.
6	Chen et al. (2021)	hypoalbuminemia, Sequential Organ Failure Assessment (SOFA) score, and D-dimer.
7	Taengsakul et al. (2021)	History of pulmonary embolism, obesity, anticoagulant use, postoperative & preoperative chemotherapy, endometrium cancer, tumor-node-metastasis stage 4.
8	Nkoke et al. (2020)	age >40 years (57.6%), long-term immobility, and swollen legs, immobility, bed confinement, and complete immobilization.
9	Abduljabbar et al. (2020)	elderly patients, diabetes mellitus, hypertension, bed-ridden patients, ischemic heart disease, breast cancer, and obese patients.
10	Kawborisutsakul et al. (2020)	diabetes mellitus (DM), operative duration of >420 min, blood transfusion, and new onset postoperative motor deficits. Female and the presence of a central catheter.
11	Middeldorp (2020)	Patients with COVID-19 were at high risk
12	Zhang et al. (2019)	length of stay and CVC in the location of the femoral vein were the independent risk factors of VTE. femoral catheter had developed VTE.
13	Jang et al. (2018)	Surgery or trauma, immobilization, and cancer
14	Aedh (2018)	Advanced age, stroke, renal diseases and on dialysis, Positive personal or family history of VTE, Immobility, as well as malignancy
15	Kamdem et al. (2018)	Obesity, hypertension, immobility, and long-haul travel.
16	Ferreira et al. (2017)	oncology patients, followed by orthopedic patients, surgical patients and internal medicine patients.
17	Khalafallah et al. (2016)	prolonged length of stay, Patients who had a surgery within the past 30 days, Previous VTE.

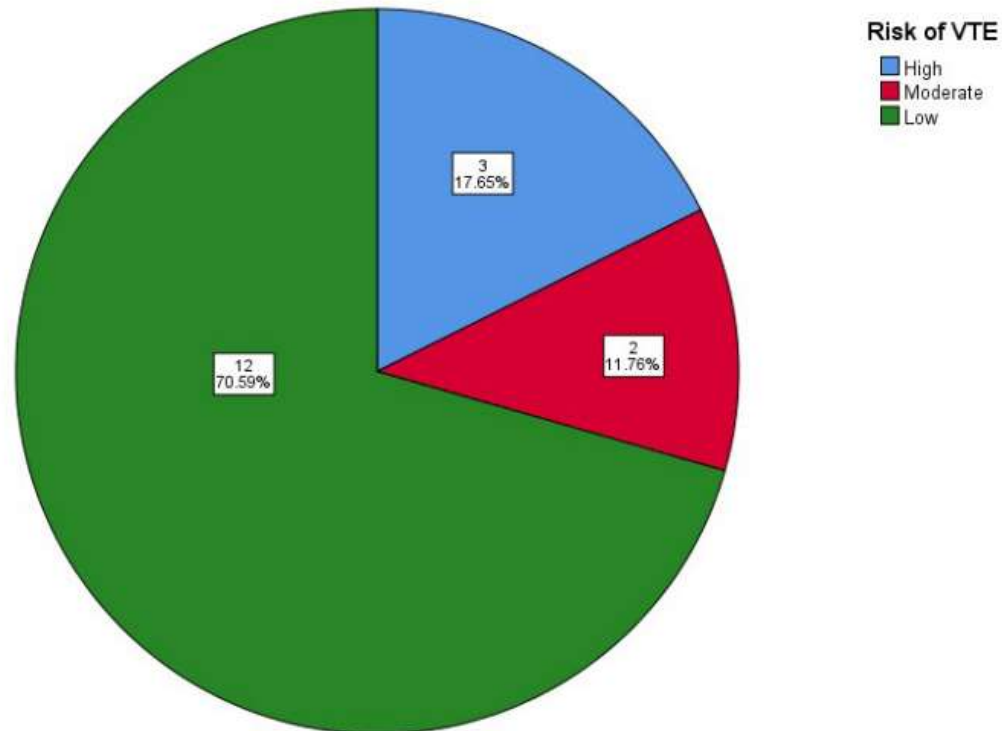


Figure 6. Distribution of types of studies according to the VTE risk.

Discussion

This systematic review confirmed that VTE incidence and its risk factors are variable in hospitalized patients. 17 included studies summarized the incidence and risk factors among the population of these patients. The results revealed that most of the studies (13; 76.4%) reported low incidence of VTE. Although the incidence is low, it should be considered as an important problem to the healthcare setting as it is affecting the patient safety and increasing the cost and length of stay in hospital. There are many studies that confirmed the increasing incidence of VTE among hospitalized patients in which they were considered as a problem related to patient safety and should be solved to prevent development of VTE, where the rate is supposed to be zero (Ambra et al., 2022; Lau et al., 2018).

We found that D-dimer, Doppler ultrasound and CT scan are the most commonly used procedures to confirm a diagnosis of VTE. Previous studies have reported that screening and diagnosis of VTE required specific diagnostic procedures such as D-dimer, Doppler ultrasound and CT scan (Kearon, 2016; Liederman et al., 2020; Vandenbrielle & Gorog, 2021). Furthermore, the findings of this study reported that DVT, PE or both usually occurred. Most of the patients develop one or both VTE types during hospitalization as reported in other studies (Agarwal et al., 2022; Puri et al., 2022; Subhani et al., 2022).

The variation in VTE incidence in the 17 studies could be attributed to some factors, including differences in implementation of the recommended guidelines and prophylaxis, under diagnosis and lack of reporting, or differences in patient safety monitoring systems (Wang et al., 2018). A systematic review of nine studies utilizing Asian hospital registries or databases showed that the incidence of VTE in hospitalized patients ranged from 0.11% to 0.88% (Lee

et al., 2017). While other data from the United States showed a higher incidence of VTE in hospitalized patients (Edelsberg et al., 2006) We believed that this heterogeneity was not only due to the differences in study population and outcome measures, but also due to the fact that screening in many studies was conducted in patients with venous thrombosis-related symptoms.

The risk factors for VTE were different according to the patients' populations. The main risk factors among the patients were: the presence of diabetes mellitus and hypertension, obesity, an increase in D-dimer, longer hospital stay, immobility, age, surgery or trauma, oncology patients and positive personal or family history of VTE. The risk of VTE increased in the ICU patients, and also patients with cancer. Our findings are consistent with nationwide studies confirming certain factors that increased the risk of VTE. The occurrence of VTE in most populations is associated with an increased in length of stay (Agarwal et al., 2022; Eissa et al., 2022; Khalafallah et al., 2016; Zhang et al., 2019). Diabetes mellitus and hypertension were significantly related to increasing the risk of VTE (Abduljabbar et al., 2020; Ambra et al., 2022; Kaewborisutsakul et al., 2020; Kamdem et al., 2018) as was immobility (Jang et al., 2018; Kamdem et al., 2018).

Conclusion

The incidence of VTE among hospitalized patients was low and associated with increased risk factors. The incidence increased in patients who were admitted to the ICU and those who are critically ill. Risk factors of VTE were hypertension, diabetes mellitus, obesity, an increase in D-dimer, longer hospital stay, immobility, age, surgery or trauma, oncology patients and a positive personal or family history of VTE. This review also found some factors that may increase the risk of venous thromboembolism in hospitalized patients despite giving prophylactic anticoagulation. Therefore, preventing these factors may decrease the morbidity and mortality rate among these patients.

VTE events were associated with increased length of stay, which can further increase the risk of additional VTE events.

The studies included in this review are limited. Risk factors and population in different studies were not similar. Additionally, studies were mostly observational, and some data were not reported. Therefore, given these limitations, the results of this review should be interpreted with caution.

Recommendations

All patients need to undertake dynamic and constant risk assessments for VTE with laboratory monitoring, associated medications, invasive procedures, and previous medical history considered, particularly for severe and critically ill patients.

Future large-scale prospective studies are essential to explain the prediction and prevention of VTE among hospitalized patients. Moreover, there is a need for wider awareness of VTE and its diagnosis and management in these patients. Prophylactic treatment against VTE is cost-effective for many hospitalized patients and should be applied across all clinical settings, where its effectiveness and safety has been recognized. All medical staff at every level should maintain a high suspicion and reinforce the prevention and screening of VTE to all hospitalized patients. We strongly urge clinicians to be conscious of VTE risk factors and highlight on optimizing patients' comorbidities before admission to the hospital.

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