Prognostic Factors Associated With Development of Venous Thromboembolism in Critically Ill Patients—A Systematic Review and Meta-Analysis

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OBJECTIVE: To identify prognostic factors for the development of venous thromboembolism in the ICU.

DATA SOURCES: We searched MEDLINE, EMBASE, and Cochrane CENTRAL from inception to March 1, 2021.

STUDY SELECTION: We included English-language studies describing prognostic factors associated with the development of venous thromboembolism among critically ill patients.

DATA EXTRACTION: Two authors performed data extraction and risk-of-bias assessment. We pooled adjusted odds ratios and adjusted hazard ratios for prognostic factors using random-effects model. We assessed risk of bias using the Quality in Prognosis Studies tool and certainty of evidence using the Grading of Recommendations, Assessment, Development and Evaluations approach.

DATA SYNTHESIS: We included 39 observational cohort studies involving 729,477 patients. Patient factors with high or moderate certainty of association with increased odds of venous thromboembolism include older age (adjusted odds ratio, 1.15; 95% CI, 1.02–1.29 per 10 yr), obesity (adjusted odds ratio, 1.25; 95% CI, 1.18–1.32), active malignancy (adjusted odds ratio, 1.70; 95% CI, 1.18–2.44), history of venous thromboembolism (adjusted odds ratio, 4.77; 95% CI, 3.42–6.65), and history of recent surgery (adjusted odds ratio, 1.77; 95% CI, 1.26–2.47). ICU-specific factors with high or moderate certainty of association with increased risk of venous thromboembolism include sepsis (adjusted odds ratio, 1.41; 95% CI, 1.12–1.78), lack of pharmacologic venous thromboembolism prophylaxis (adjusted odds ratio, 1.80; 95% CI, 1.14–2.84), central venous catheter (adjusted odds ratio, 2.93; 95% CI, 1.98–4.34), invasive mechanical ventilation (adjusted odds ratio, 1.74; 95% CI, 1.36–2.24), and use of vasoactive medication (adjusted odds ratio, 1.86; 95% CI, 1.23–2.81).

CONCLUSIONS: This meta-analysis provides quantitative summaries of the association between patient-specific and ICU-related prognostic factors and the risk of venous thromboembolism in the ICU. These findings provide the foundation for the development of a venous thromboembolism risk stratification tool for critically ill patients.

KEY WORDS: critical care; prognostic; venous thromboembolism

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) or pulmonary embolism (PE), is a potentially preventable but frequently underrecognized cause of morbidity and mortality among critically ill patients (1, 2). It is often suspected to be responsible for unexplained hemodynamic and respiratory instability encountered during the course of ICU admissions (1) and is one of the most common missed diagnoses

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found at autopsy for patients dying in the ICU (3). Various risk factors in this population have been identified, including comorbidity, hypercoagulability from acute illness, invasive procedures, and immobilization from sedation for mechanical ventilation (2, 4–6). For this reason, the use of empiric thromboprophylaxis has been shown to provide better value and efficacy in terms of monetary costs and health gains compared with routine screening for DVT (7).

Although pharmacologic thromboprophylaxis is recommended in this population and endorsed by several societal guidelines (8–10), provision is often challenging due to competing bleeding risks or the need for frequent invasive procedures (11). Despite these recommendations, there continues to be practice variation with regard to indications for interruption, choice of pharmacologic agent, and institution-specific facilitating factors (12, 13). Much of this uncertainty and variability in practice probably relate to insufficient evidence examining VTE in this population, which is particularly challenging due to unique subpopulation characteristics and influences of practice setting (14). Randomized trials are often limited by the enrollment of large, heterogeneous populations of critically ill patients (trauma, surgical, and medical) with variable risk profiles (15–18). Enrollment of heterogeneous populations makes it difficult to identify the patients most likely to benefit from specific intervention (19). Prognostic enrichment that is the identification of patients most likely to have the event of interest for risk-reduction studies offers the potential for the delineation of a more homogenous, high-risk patient group suitable for focused study and optimization of care. A comprehensive and evidence-based understanding of VTE risk factors among critically ill patients could improve patient-specific risk stratification and provide the potential for individualized care. Thus, we conducted a systematic review and meta-analysis summarizing the association between clinical risk factors and the development of VTE among critically ill adult patients.

MATERIALS AND METHODS

We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (20), the Prognosis Research Strategy Group (PROGRESS) recommendations (21–24), the Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modeling Studies (CHARMS) checklist (25), as well as guidelines for meta-analyses of prognostic factor studies (26). We registered our protocol with the Open Science Framework (https://osf.io/ak89g).

Search Strategy

We searched MEDLINE, EMBASE, and Cochrane CENTRAL from inception to March 1, 2021. An experienced health sciences librarian assisted in development of the strategy. The strategy used clinical content terms, in combination with terms related to prognostic research, consistent with similar prognostic meta-analyses (27–30), and is included in **Supplementary Figure 1** (http://links.lww.com/CCM/G888).

Study Selection

We included all English-language studies describing retrospective and prospective observational studies. We included studies meeting the following criteria: 1) enrolled adult patients (≥ 16 yr old) admitted to any mixed medical-surgical or subspecialty ICU and 2) evaluated clinical risk factors associated with the development of any VTE as defined by study authors but including limb DVT (distal and/or proximal) and/or PE objectively confirmed with diagnostic imaging. Lower limb DVT could be symptomatic or identified on routine ultrasound surveillance. We excluded studies that did not provide odds ratios (ORs) or hazard ratios (HRs) with corresponding CIs and which were adjusted for confounding by accounting for at least one patient demographic factor (age, sex, obesity, or any medical comorbidity composite index), one prothrombotic patient factor (prior VTE history, active malignancy, or recent surgery), and one ICU admission factor (admission diagnosis, any illness severity score, or use of mechanical ventilation). We contacted the corresponding author where these values could not be obtained from the reported data.

We screened studies using the Covidence software (Melbourne, Australia). We imported titles into Covidence directly from the search databases and removed duplicates. Two reviewers (A.T., S.M.F.) independently screened the titles and abstracts of all identified citations.

We resolved disagreements by discussion; no third-party adjudication proved necessary. The same reviewers (A.T., S.M.F.) subsequently independently

assessed full texts of the selected articles following screening, and again disagreements were resolved by discussion.

Data Extraction and Quality Assessment

Two investigators (A.T., S.M.F.) abstracted the following variables: author information, year of publication, study design, study dates, eligibility criteria, clinical risk factors, and development of VTE. Clinical risk factors included patient demographic factors such as age, sex, and obesity (as defined by the study authors); prothrombotic factors such as prior VTE history, active malignancy, and recent surgery (as defined by study authors); and ICU admission factors such as admission diagnosis, any illness severity score and invasive procedures, central venous catheters (CVCs), vasoactive medications, and provision of pharmacologic and/or mechanical thromboprophylaxis. For each prognostic factor, two investigators (A.T., S.M.F.) independently collected or calculated adjusted ORs (aORs) for development of VTE for each study, where available. In the event of overlapping patient cohorts, we preferentially included data from the larger patient cohort. We performed extraction using a tool modified from the CHARMS checklist for prognostic factors (25).

Using the Quality in Prognosis Studies (QUIPS) tool, two reviewers (A.T., S.M.F.) independently assessed the risk-of-bias of included studies (31). Disagreements were resolved by consensus following discussion. The QUIPS tool includes six domains for bias and applicability: study participation, study attrition, prognostic factor measurement, outcome measurement, adjustment for other prognostic factors, and statistical analysis and reporting.

Data Synthesis

We extracted aORs or HRs based on the available data. We performed meta-analysis of aORs and HRs using the random-effects method for estimation of between-study variances (32) and the Review Manager software (Version 5.3, Copenhagen, Denmark). In accordance with Cochrane guidance, we combined studies with dichotomous outcome data (OR) and time-to-event data (HR) when the event rate was low (less than 10%) (33). We present results as pooled aORs with 95% CIs. We assessed heterogeneity using the I^2 statistic, the chi-square test for homogeneity, and visual inspection of the forest plots. We conducted two post hoc sensitivity analyses. The first sensitivity analysis included data only from studies with prespecification of variables based on clinical importance as determined by study authors, as advocated for by the PROGRESS guidelines for model development (24). The second sensitivity analysis included data only from studies not using screening ultrasound regimens. These sensitivity analyses were not preplanned and, therefore, not included in our registered protocol.

Certainty of Evidence

An investigator with expertise in Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology (B.R.) assessed overall certainty in pooled estimates using the GRADE approach (34). The overall certainty in estimates was categorized into one of four levels: high, moderate, low, or very low. In keeping with GRADE guidance for prognostic studies, cohort data start as high certainty evidence but could be lowered for concern in any one of the following domains: precision, consistency, risk of bias, directness, or publication bias. A GRADE evidence profile was created using the guideline development tool (gradepro.org). In accordance with GRADE guidance, high certainty associations are characterized as "is associated," moderate certainty as "probably associated," low certainty as "may be associated," and very low certainty as "uncertain" (35).

RESULTS

Search Results

Of 2,092 citations (**Fig. 1**), 181 underwent full-text review, and we included 39 observational cohort studies involving 729,477 patients in the meta-analysis (**Table 1**). Studies were predominantly observational cohorts from North America involving mixed medical-surgical ICU patient populations. There was one study (198 patients) involving a specialized cardiac ICU (36), three studies (3,317 patients) involving neurologic ICUs (37–39), and four studies (1,101 patients) involving trauma ICUs (40–43). Most studies evaluated any symptomatic VTE (DVT or PE) as the primary outcome, though some studies evaluated only DVT (2, 44–47), only PE (6, 36, 37, 40, 48–50), or only CVC-associated DVT (39, 51). Of the 20 studies evaluating lower

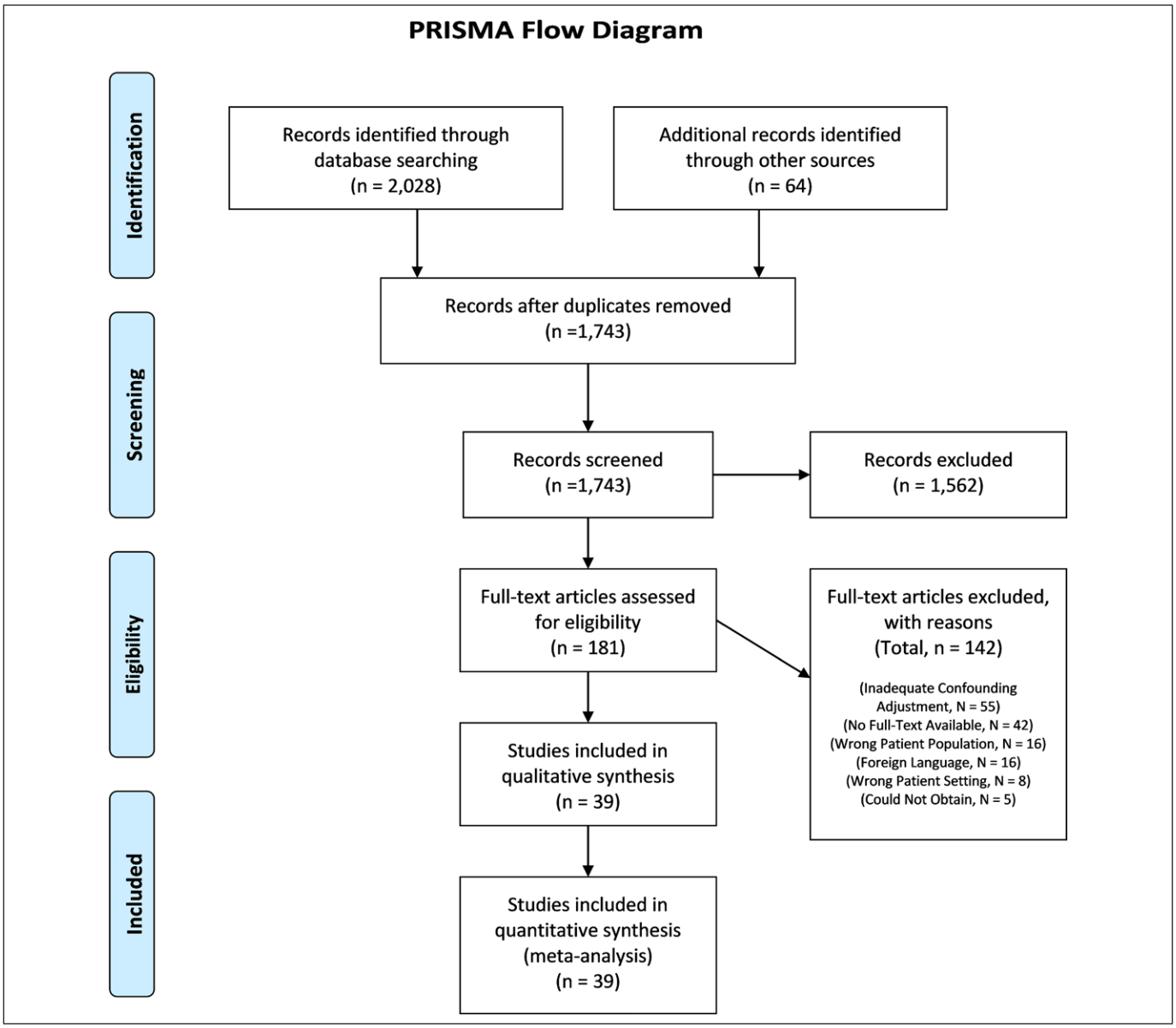

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

extremity DVTs, nine studies included both proximal and distal DVTs (38, 43, 47, 52–56). The study-specific definitions for VTE are included in **Supplemental Figure 2** (http://links.lww.com/CCM/G888). Although the majority of studies did not perform routine ultrasound surveillance, there were 11 studies with reported surveillance protocols (2, 41, 42, 46, 51, 52, 56–60) (**Supplemental Fig. 4**, http://links.lww.com/CCM/G888). Studies with reported ultrasound surveillance regimens typically demonstrated higher VTE risk, with a median rate (Q1–Q3) of 9% (6–26%) compared with studies without ultrasound surveillance that reported a median VTE rate of 6% (3–10%) (Supplemental Fig. 4, http://links.lww.com/CCM/G888).

Risk of Bias

Using the QUIPS tool for evaluation of prognostic studies (31), most studies were judged to be at low risk in the domains of study attrition, prognostic factor measurement, and confounding adjustment. Some studies were judged to be at moderate risk of bias for study participation due to targeted subpopulation diagnoses at admission (36, 37, 52, 57, 61–63), inclusion of only patients with contraindications to pharmacologic prophylaxis (42, 46, 60), or inclusion of only patients undergoing diagnostic imaging for potential VTE (44,50,51,55), which may limit external generalizability. A few studies were judged to be at moderate risk of bias

TABLE 1.
Characteristics of Included Studies

Study	Continent	Design	Population	*n*	VTE Outcomes	VTE Risk
Bahloul et al (40)	Asia	Prospective cohort	Mixed medical surgical	4,408	PE	2%
Bahloul et al (37)	Asia	Retrospective cohort	Neurologic	694	PE	11%
Bahloul et al (48)	Asia	Prospective cohort	Trauma	365	PE	18%
Blaivas et al (73)	Europe	Retrospective cohort	Mixed medical surgical	320	UE DVT	11%
Chaari et al (49)	Asia	Retrospective cohort	Mixed medical surgical	175	PE	9%
Cloney et al (61)	North America	Retrospective cohort	Surgical	1,269	DVT + PE	10%
Cook et al (2)	North America	Prospective cohort	Mixed medical surgical	261	DVT	3%
Cook et al (57)	North America	Prospective cohort	Mixed medical surgical	138	DVT + PE	5%
Darze et al (36)	South America	Prospective cohort	Cardiac	198	PE	9%
Eck et al (5)	Europe	Prospective cohort	Mixed medical surgical	2,166	DVT + PE	2%
Fontaine et al (74)	North America	Retrospective cohort	Mixed medical surgical	3,563	DVT + PE	6%
Gaspard et al (75)	North America	Retrospective cohort	Medical	748	DVT + PE	2%
Gibson et al (44)	North America	Retrospective cohort	Medical	243	DVT	16%
Gupta et al (45)	North America	Retrospective cohort	Mixed medical surgical	193	DVT	25%
Hamada et al (58)	Europe	Prospective cohort	Surgical	153	DVT + PE	31%
Ho and Chavan (6)	Australia	Retrospective cohort	Mixed medical surgical	609,367	PE	1%
Hrdy et al (51)	Europe	Prospective cohort	Mixed medical surgical	198	CVC DVT	24%
Kaplan et al (52)	North America	Prospective cohort	Medical	113	DVT + PE	37%
Lamontage et al (76)	Multicontinental	Retrospective cohort	Mixed medical surgical	3,746	UE DVT	2%
Lee and Blanco (77)	North America	Retrospective cohort	Mixed medical surgical	3,056	DVT + PE	2%
Lim et al (59)	Multicontinental	Retrospective cohort	Mixed medical surgical	3,746	DVT + PE	8%
Malinoski et al (42)	North America	Prospective cohort	Trauma	411	DVT + PE	7%
Minet et al (50)	Europe	Prospective cohort	Medical	176	PE	20%
Obi et al (53)	North America	Retrospective cohort	Surgical	4,844	DVT + PE	6%
Obi et al (62)	North America	Retrospective cohort	Medical	71	DVT + PE	51%
Pannucci et al (72)	North America	Retrospective cohort	Surgical	2,285	DVT + PE	6%
Patel et al (60)	North America	Prospective cohort	Surgical	204	DVT + PE	10%
Peters et al (78)	North America	Retrospective cohort	Medical	561	DVT + PE	5%
Prichayudh et al (46)	Asia	Retrospective cohort	Surgical	305	DVT	4%
Reynolds et al (79)	North America	Retrospective cohort	Mixed medical surgical	36,925	DVT + PE	6%
Shorr and Williams (63)	North America	Retrospective cohort	Mixed medical surgical	1,592	DVT + PE	5%
Van Haren et al (41)	North America	Prospective cohort	Trauma	121	DVT + PE	28%
Viarasilpa et al (80)	North America	Retrospective cohort	Mixed medical surgical	37,050	DVT + PE	1%
Viarasilpa et al (81)	North America	Retrospective cohort	Neurologic	2,188	DVT + PE	3%
Voils and Carlson (47)	North America	Retrospective cohort	Mixed medical surgical	920	DVT	6%
White et al (55)	North America	Retrospective cohort	Mixed medical surgical	5,788	DVT + PE	10%
Wilson et al (39)	North America	Retrospective cohort	Neurologic	431	CVC DVT	8%
Yumoto et al (43)	Asia	Retrospective cohort	Trauma	204	DVT + PE	32%
Zhang et al (56)	Asia	Prospective cohort	Mixed medical surgical	281	DVT + PE	9%

CVC = central venous catheter, DVT = deep vein thrombosis, PE = pulmonary embolism, UE = upper extremity, VTE = venous thromboembolism.

for outcome measurement if they included only PE (6, 36, 37, 40, 48–50) or only CVC-related DVT (39, 51) as the primary outcome. Most studies were judged to be at moderate risk of bias for statistical analysis and reporting, most commonly due to a failure to best practice guidelines for prognostic model development and validation (24). This included a failure to conduct a priori selection of variables based on clinical relevance (23, 24) or failure to adhere to the recommended minimum event-per-variable ratio of greater than 10, which can lead to potential overfitting and inappropriately optimistic model performance (64).

Predictors of VTE

We present the Forest Plots in **Supplemental Figure 5** (http://links.lww.com/CCM/G888) and the summary of findings in **Table 2**. The GRADE certainty assessments and rationale are included in **Supplemental Figure 6** (http://links.lww.com/CCM/G888). Of the patient demographic factors, older age (aOR, 1.02; 95% CI, 1.00–1.03 per 10-yr increase, high certainty) and obesity (aOR, 1.25; 95% CI, 1.18–1.32, high certainty) were associated with increased odds of VTE. Male sex may increase odds of VTE (aOR, 1.20; 95% CI, 0.90–1.60, low certainty). However, this finding is limited by serious inconsistency, as demonstrated by the high I^2 and important heterogeneity on visual inspection of the Forest Plots. This finding is additionally limited by serious imprecision, as demonstrated by the wide CIs.

With regard to patient prothrombotic factors, prior history of VTE (aOR, 4.77; 95% CI, 3.42–6.65, high certainty) and history of recent surgery (aOR, 1.77; 95% CI, 1.26–2.47, high certainty) were associated with increased odds of VTE. Active malignancy (aOR, 1.70; 95% CI, 1.18–2.44, moderate certainty) is probably associated with increased odds of VTE.

TABLE 2.
Prognostic Factors Associated With Development of Venous Thromboembolism

Prognostic Factor	Studies (*n*)	Pooled OR (95% CI)	*p*	I^2 (%)	Grading of Recommendations, Assessment, Development and Evaluations Certainty
Patient demographics					
Age (per 10-yr increase)	9	1.15 (1.02–1.29)	0.08	82	High
Sex (male vs female)	10	1.20 (0.90–1.60)	0.21	86	Low
Obesity (obese vs nonobese)	6	1.25 (1.18–1.32)	< 0.00001	3	High
Patient prothrombotic factors					
Active malignancy (yes vs no)	10	1.70 (1.18–2.44)	0.005	68	Moderate
History of VTE (yes vs no)	16	4.77 (3.42–6.65)	< 0.00001	75	High
Recent surgery (yes vs no)	7	1.77 (1.26–2.47)	0.0008	84	High
ICU admission					
Sepsis (yes vs no)	7	1.41 (1.12–1.78)	0.004	51	High
Acute Physiology and Chronic Health Evaluation II score (per 10-point increase)	5	0.99 (0.83–1.18)	0.88	71	Moderate
Pharmacologic VTE prophylaxis (no vs yes)	7	1.80 (1.14–2.84)	0.01	52	High
Central venous catheter (yes vs no)	12	2.93 (1.98–4.34)	< 0.00001	92	High
Invasive mechanical ventilation (yes vs no)	8	1.74 (1.36–2.24)	< 0.0001	67%	High
Vasoactive medication (yes vs no)	7	1.86 (1.23–2.81)	0.003	87	High

OR = odds ratio, VTE = venous thromboembolism.

Of the factors related to ICU admission, a diagnosis of sepsis (aOR, 1.41; 95% CI, 1.12–1.78, high certainty) is associated with increased odds of VTE. Several ICU-related interventions including presence of CVC (aOR, 2.93; 95% CI, 1.98–4.34, high certainty), invasive mechanical ventilation (aOR, 1.74; 95% CI, 1.36–2.24, high certainty), and use of vasoactive medication (aOR, 1.86; 95% CI, 1.23–2.81, high certainty) were associated with increased odds of VTE. The lack of pharmacologic VTE prophylaxis (aOR, 1.80; 95% CI, 1.14–2.84, high certainty) was also associated with increased odds of VTE. The pharmacologic prophylaxis dosing regimens for each study are provided in **Supplementary Figure 3** (http://links.lww.com/CCM/G888). No studies reported on timing of initiation or dosing interruptions. Acute Physiology and Chronic Health Evaluation II score at admission (aOR, 0.99; 95% CI, 0.83–1.18 per 10-point increase, moderate certainty) probably had no impact on risk of VTE. We have rated down the certainty in this finding given the imprecision introduced by the width of CIs.

Sensitivity Analysis

We conducted two post hoc sensitivity analyses (**Supplementary Fig. 7**, http://links.lww.com/CCM/G888). In the first sensitivity analysis, we included data only from studies whereby variable selection for prognostic model development was prespecified based on clinical importance. In the second sensitivity analysis, we included data only from studies without ultrasound screening regimens. In both sensitivity analyses, there was some mild reduction in precision but minimal change in pooled effect size across most prognostic factors. The direction of association did not change for any prognostic factor.

DISCUSSION

In this systematic review and meta-analysis, we summarize the prognostic association between several clinical factors and the development of VTE in critically ill patients. Patient factors with moderate or higher certainty of association with increased odds of VTE include older age, obesity, active malignancy, history of VTE, and history of recent surgery. Factors specific to ICU admission with moderate or higher certainty of association with increased odds of VTE include a sepsis diagnosis, lack of pharmacologic VTE prophylaxis, presence of CVC, use of invasive mechanical ventilation, and use of vasoactive medication. These findings are supported by the sensitivity analyses.

The most important potentially modifiable variable we identified is the provision of pharmacologic VTE prophylaxis, a high certainty finding that is consistent with existing literature and supported by societal guideline recommendations (8–10). VTE prophylaxis is known to reduce preventable morbidity and mortality among critically ill patients and many other higher risk populations (65).

Patient factors likely associated with VTE included older age, obesity, active malignancy, history of VTE, and history of recent surgery, a finding consistent with prior results (66, 67). ICU-specific factors likely associated with VTE included presence of CVC, use of invasive mechanical ventilation, and use of vasoactive medication. Sepsis in particular is associated with complex changes in hemostasis, predisposing some patients to a higher risk bleeding state and others to a prothrombotic state (68), and is known to have a high rate of VTE prophylaxis failure (69). CVCs are known to present an increased local risk of thrombosis (70), and the presence of a CVC is as a surrogate marker of patient illness severity. Similarly, use of invasive mechanical ventilation and use of vasoactive medication also likely function as direct or indirect indicators of acute illness severity, which may promote VTE risk by means of hypercoagulability, vascular injury, or immobilization (1). Although no ICU-specific risk stratification tool currently exists, prior practice audits have demonstrated that ICU clinicians are more likely to adhere to guideline-recommended thromboprophylaxis strategies for patients with higher body mass index, active malignancy, prior history of VTE, and use of mechanical ventilation (12), all of which are prognostic factors identified in this review.

Research efforts have focused on optimizing provision of timely and effective pharmacologic thromboprophylaxis (8–10). However, the ICU population is often heterogeneous and characterized by individual patient-specific risks for thromboprophylaxis nonuse (such as active bleeding and need for intervention), thromboprophylaxis failure (59, 69), and bleeding complications (71). Given that clinicians often underestimate VTE risk (72), a customized approach to thromboprophylaxis based on individual ICU patient risk stratification has been advocated (82). Individualized

VTE risk stratification for treatment determination has demonstrated feasibility, accuracy, and improved clinical outcomes in several studies (66, 83). Patient-specific risk algorithms have been employed in clinical trials with evidence of benefit with regard to improved prediction of patient outcomes, reduction in sample size requirements, and overall cost savings (84). As such, there is likely value in the development and validation of a VTE risk stratification tool specific to critically ill patients to identify the highest risk patients for targeted study and intervention. However, the fundamental basis for accurate prognostication begins with a comprehensive and evidence-based understanding of potentially important risk factors (23) that are summarized in this review.

This review used a comprehensive search, adhered to recommendations for meta-analysis of prognostic studies (26), and used GRADE to assess the certainty in the estimates (34). The face validity, consistency, precision, and generally robust effect sizes for the prognostic factors identified in this review justify their inclusion in any risk stratification framework. This review also has limitations. Although we prespecified the required coadjustment of several important clinical factors, the potential for residual confounding remains an unavoidable limitation of prognostic factor meta-analysis and is particularly relevant in this patient population given a high correlation between many of the identified risk factors (26). Importantly, the studies did not report on timing of initiation for pharmacologic prophylaxis, dosing interruptions, or competing risks such as bleeding or need for invasive procedures, which may also impacted the decision to use thromboprophylaxis. In addition, we note that all included studies were identified from the past 20 years. Although we searched from inception to present, we suspect that the prespecified minimum confounding adjustment requirement for this review may have acted as filter for modern methodological methods. Furthermore, significant clinical heterogeneity between studies was found with regard to differences in definitions for and surveillance of VTE. We are additionally limited by variability in practice and quality of the prognostic modeling strategies among included studies, which have low event rates and are prone to overfitting (24). The potential influence of methodological differences such as use of ultrasound surveillance would be addressable using meta-regression, although, unfortunately, we did not have sufficient studies to support this analysis. However, sensitivity analyses support our conclusions from the primary analysis. Finally, given the limitations of the available literature, we are unable to assess the potentially synergistic effect of combinations of the risk factors we identified. Such an analysis requires large cohort studies designed for the explicit purpose of methodologically rigorous development and validation of a prediction model specific to the critical care patient population. In order to better guide the decision to implement pharmacologic prophylaxis, such a model should additionally account for competing bleeding risks and the harm of late or interrupted dosing.

CONCLUSIONS

This meta-analysis confirms the association between several patient-specific and ICU admission-related prognostic factors and the risk of VTE development among critically ill patients. These findings provide the foundation for the development of a VTE risk stratification tool for critically ill patients.

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Drs. Tran, Fernando, Rochwerg, and Crowther conceived the idea and designed the study protocol. Drs. Tran and Fernando completed the search and extraction. Drs. Tran and Fernando completed the data analysis. All authors participated in the creation and revision of the article.

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