Impact of clinical pharmacist services on physicians' guideline compliance and prognosis of patients for venous thromboembolism prophylaxis in ICU

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Abstract

Purpose Whether the clinical pharmacist services (CPS) improve ICU physicians' compliance with venous thromboembolism (VTE) prophylaxis guidelines remains unclear, and its impact on VTE incidence and mortality in ICU patients should also be investigated.

Methods ICU patients were assigned to CPS group or control group according to the medical arrangements of the day of patient admission without any intervention. The impact of CPS on guideline compliance, VTE incidence, and mortality was assessed.

Results A total of 338 patients were included. With pharmacist intervention, ICU physicians' compliance with VTE prophylaxis guideline was improved by 7%–25% ($p < 0.001$). The incidences of VTE (9% vs 17%, $p = 0.037$) and bleeding events (5% vs 11%, $p = 0.042$) were both lower in the CPS group than in the control group. Multivariate Cox regression model showed that CPS was an independent risk factor for VTE events (HR = 0.438, 95% CI = 0.224–0.857, $p = 0.016$) and 14-day mortality (HR = 0.416, 95%CI = 0.25–0.692, $p = 0.001$).

Conclusion CPS could significantly improve ICU physician compliance with VTE prophylaxis guidelines and reduce the incidence of VTE events and mortality in ICU patients. Clinical pharmacists should be involved in the daily management of ICU patients as an important member.

Introduction

Venous thromboembolism (VTE), including pulmonary embolism (PE) and deep venous thromboembolism (DVT), is one of the diseases that seriously threaten public health [1]. Patients in intensive care unit (ICU) have not only general VTE risk factors (e.g., age, VTE history, obesity, trauma, or surgery, etc.), but also ICU-acquired risk factors (e.g., ventilator-assisted ventilation, use of vasoactive drugs, sepsis, or central venous catheterization, etc.), with a higher risk of VTE [2]. The incidence of VTE in ICU patients was 10–80% without any prophylaxis [3]. Autopsy results showed that the incidence of PE in ICU was 7–27% [4].

However, a study revealed that only 8% of ICU patients received VTE prophylaxis, and only 9.9–11.9% of patients received appropriate preventive measures during the study period [5]. Significantly higher mortality was found in ICU patients not receiving VTE prophylaxis within 24 hours [6]. Even with uncomplicated DVT, these populations still have longer ICU and hospital lengths of stay [2, 7]. Therefore, timely assessment of the risk of VTE in ICU patients and taking appropriate preventive measures are of great significance for improving their prognosis.

Due to the high incidence of VTE events and its significant impact on ICU patient prognosis, the 2018 National Institute of Health Excellence guidelines [8], 2018 American Hematological Association VTE practice guidelines [9], and the American Association of Trauma Surgeons in 2021 [10] all give positive

recommendations on VTE prophylaxis in these population. Nevertheless, the compliance of different centers to the guidelines is 33–100% [11, 12], presenting great heterogeneity.

Previous literatures have demonstrated that clinical pharmacists' participation in in-hospital VTE management programs can significantly improve physicians' compliance with guidelines for VTE prophylaxis in general ward [13–15], but little has been evaluated for the compliance of ICU physicians treating more complex patients. Hence, this study would like to focus on the impact of clinical pharmacist services (CPS) on ICU physicians' compliance with VTE guidelines. Furthermore, the second purpose was to determine whether the CPS could improve ICU patients' prognosis.

Methods

This retrospective cohort study was approved by the Ethics Committee of the Second Affiliated Hospital of Xi'an Jiaotong University (XJTUSAH-2020071). Since patient information was anonymous and no human samples were involved in this study, the informed consents were waived. The qualifications of clinical pharmacists to participate in the management of patients' anticoagulation therapy have been recognized and filed by the medical department of the hospital.

Study population and design

This retrospective, sequential cohort study was performed to assess the impact of CPS on physicians' VTE prophylaxis guidelines compliance and the prognosis of patients in ICU. The patients who have been admitted to ICU of the Second Affiliated Hospital of Xi’an Jiaotong University from January 2019 to September 2021 were included. The ICU of our hospital is divided into two medical groups, each with 6 beds. Patients were assigned to the intervention group (CPS group) or control group according to the medical arrangements of the day of patient admission without any intervention. All patients admitted to the ICU who met the criteria during study period were included.

Inclusion criteria: (1) length of hospital stay ≥ 72 hours; (2) age ≥ 16 years. Exclusion criteria: (1) Patients who had been diagnosed with PE or DVT on admission; (2) patients were receiving anticoagulation therapy.

CPS

CPS is an intervention by clinical pharmacists in the management of drug therapy in ICU patients. VTE prophylaxis and anticoagulation management are important components of CPS. Clinical pharmacists provide 3–4 hours a day of pharmacy services for physicians, nurses, and patients on their medical team. The contents of VTE prophylaxis management in CPS include: (1) collecting patients' past medication history, assessing the VTE risk (Caprini or Padua) and bleeding risk on admission, and giving VTE prophylaxis recommendations; (2) evaluating the patients' VTE-related risks daily, giving VTE prophylaxis plan and adjustment suggestions through laboratory examination, imaging examination, and related

physical signs; (3) providing medication consultation to physicians, nurses and patients at any time during service. The workflow of CPS is shown in Fig. 1.

Prior to CPS implementation, two clinical pharmacists and an ICU senior physician reviewed guidelines related to VTE prophylaxis in ICU patients and identified six recommendations from the 2018 NICE guidelines [8] as the evaluation criteria for evaluating physicians' compliance with this guideline. Clinical pharmacists trained all ICU physicians and confirmed that the evaluation criteria were approved by all ICU physicians before the project started. The criteria and methods for evaluating compliance with the guidelines are presented in Table 1.

Data collection

Patient demographics, days of ICU hospitalization, Acute Physiology and Chronic Health Assessment II (APACHE II) scores, VTE risk score (Caprini score or Padua score), laboratory tests (hemoglobin concentration, platelet count, blood coagulation, liver function, and renal function, etc.), VTE preventive measures (including anticoagulants, dosing, frequency, and course of treatment; whether intermittent pneumatic compression[IPC] is used), thrombotic events, bleeding events, central venous catheterization, hospitalization cost, and 14-day all-cause mortality were collected. The adoption rates among physicians who received pharmacist recommendations in the CPS group were also calculated.

Statistical analysis

Continuous variables were presented as the mean ± standard derivation (SD) for normal distribution, and median (interquartile range [IQR]) for non-normal distribution. Categorical variables were expressed as percentages (%). Continuous variables were analyzed by the Mann-Whitney U test. Percentages were compared by using the χ^2 test or Fisher exact test as appropriate. The univariate and multivariate Cox regression was employed to estimate the risk factors of the incidence of VTE and 14-day all-cause mortality. Covariates with $p < 0.15$ in the univariate analysis were considered candidates for building multivariable models. A multivariate stepwise COX regression model with forward selection was used and variables with $p < 0.05$ in the final model were considered as statistical differences. All statistical analyses were performed using the SPSS 22.0 software (IBM SPSS Inc., Chicago, USA).

Results

Patient characteristics

A total of 773 patients were admitted to ICU from January 2019 to September 2021. Four hundred and thirty-five patients were excluded, mainly due to length of ICU stay < 72h (323 patients) or a diagnosis of PE or DVT on admission (66 patients). There were 176 patients in the CPS group and 162 patients in the control group (Fig. 2). The mean age of the patients was 67 years, and 140 (41.4%) were female. The medicine expenses in the CPS group were significantly lower than in the control group (16783 RMB vs 20152 RMB, p = 0.017) (Table 2). CPS provided 176 recommendations, which were adopted 140 times, with an adoption rate of 79.5%.

Guideline compliance

Guideline compliance rates for VTE prophylaxis among ICU physicians were higher in the CPS group. Clinical pharmacists assessed VTE and bleeding risk in all patients in the CPS group (Criterion 1, 100% vs 93% [CPS vs control], $p < 0.001$). Chemoprophylaxis rates (Criterion 2, 91% vs 67%, $p < 0.001$) and IPC usage (Criterion 2 4,84% vs 59%, $p < 0.001$) were significantly higher in the CPS group compared with the control group. Clinical pharmacists could promptly assess and adjust prophylaxis for patients with VTE and bleeding risk or when clinical circumstances change (Criterion 5, 98% vs 65%, $p < 0.001$; Criterion 6, 89% vs 68%, $p < 0.001$) (Table 3).

VTE events and 14-day all-cause mortality

The incidence of VTE events (9% vs 17%, $p = 0.037$), bleeding events (5% vs 11%, $p = 0.042$), and 14-day all-cause mortality (14% vs 28%, $p = 0.001$) were significantly lower in the CPS group than in the control group (Table 2).

In the univariate analysis, the variables with $p < 0.15$ (age, APACHE II score, IPC to prevent VTE and CPS) were used as candidates for further analysis. Multivariate Cox regression analysis found CPS still significantly reduced VTE events (HR = 0.438, 95% CI = 0.224–0.857, $p = 0.016$) after adjustment for age (HR = 1.037, 95% CI = 1.015–1.06, $p = 0.001$) and APACHE Ⅱ score (OR = 0.912, 95% CI = 0.864–0.962, $p = 0.001$) (Table 4).

Univariate Cox analysis showed that only age and CPS were risk factors for 14-day mortality ($p < 0.15$). After adjusting for age (HR = 1.021, 95% CI = 1.006–1.037, $p = 0.007$), multivariate analysis found that CPS (HR = 0.416, 95% CI = 0.25–0.692, $p = 0.001$) was still significantly correlated with the reduction of 14-day all-cause mortality (Table 5).

Discussion

This study investigated the value of pharmacists in ICU patients and demonstrated that CPS could improve ICU physician compliance to VTE prophylaxis guidelines and improve patient prognosis.

Guideline compliance

ICU patients are at high risk of VTE. High compliance of ICU physicians with VTE prophylaxis guidelines could significantly reduce the risk of VTE and death in patients [16]. Pharmacists are already actively involved in patient medication management. Quantifying the role of CPS in VTE prophylaxis management could help to formulate more reasonable VTE prophylaxis management measures for ICU patients with pharmacist participation, and optimize the allocation of clinical pharmacist resources.

ICU physicians' compliance with VTE prophylaxis management guidelines increased by 7–25% under CPS intervention. “Assessment of VTE and bleeding risk in each ICU admission” (Criterion 1) is a prerequisite for developing preventive measures. However, few studies have assessed the compliance

with this recommendation. It is surprised to find that even in the control group, compliance with Criterion 1 was as high as 93%. This means that ICU physicians already have a good awareness of VTE prophylaxis. The main purpose of VTE prophylaxis with anticoagulants is to prevent fatal PE associated with reduced patient mortality [17].

Improving the use of anticoagulants in VTE prophylaxis is the main indicator for evaluating pharmacist participation in VTE management. In this study, 91% of the patients in the CPS group received chemoprophylaxis, which was significantly higher than that in the control group (76% vs 41%, $p < 0.001$) (Criterion 2), and the incidence of bleeding events in the control group was lower than that in the control group (5% vs11%, $p = 0.042$). This also confirmed the role of pharmacists in the management of anticoagulant therapy. The overall low compliance of Criterion 3 and Criterion 4 possibly because the efficacy of IPC for DVT prophylaxis in ICU patients has been controversial [18], which has shaken the confidence of physicians and pharmacists in he use of IPC in patients.

VTE incidence and 14-day all-cause mortality under CPS

After adjusting for other risk factors (age, APACHE II score for VTE occurrence, age for 14-day all-cause mortality), CPS still significantly reduce the occurrence of VTE events in patients.

Although the incidence of VTE in the intervention group was significantly lower than that in the control group, ICU patients had a high incidence of VTE even after VTE prophylaxis according to guidelines, which was similar to the results of previous studies [19]. The overall incidence of VTE in this study was 12%. Several studies have found that VTE prophylaxis strategies recommended in the guidelines may not be effective in patients with sepsis and septic shock [20]. The newly published AAST/ACSC expert consensus on the VTE prophylaxis in trauma patients also recommends that dose adjustment may be required according to anti-FXa levels after the first use of enoxaparin [21]. Individualized use of anticoagulants to prevent VTE in critically ill patients may be the focus of future pharmacists.

Mortality, as one of the important outcomes of ICU patients, could better reflect the significance of intervention in improving patient prognosis. In this study, VTE events did not affect 14-day all-cause mortality ($p = 0.109$). This might be due to the fact that the main thrombotic events in this study was DVT (16 patients in the CPS group, all of which were lower extremity venous thrombosis; 27 patients in the control group, including 6 PE patients [medium-low risk]), rather than fatal PE. Improvement in thrombotic events did not directly affect the patient survival. Survival benefits of CPS for patients might come from other drug treatment management, such as reducing medication errors and reducing the overall workload of ICU staff [22].

Finally, this study also investigated the impact of CPS on patient hospitalization costs. Pharmacists were not statistically different in saving overall patient costs, but could reduce drug costs ($p = 0.017$).

Strengths and limitations

This study is a “pseudo-random” controlled study. Patients were randomly assigned to the CPS group or control group for treatment. Unlike previous studies that used the “before-after” control design to compare the effects of intervention measures before and after intervention [14, 15, 23–26], we used a parallel control method (simultaneous intervention and control group) to eliminate the effects of other treatment measures over time. Moreover, the similarity of baseline levels (age, gender, degree of critical illness, biochemical test results, etc.) between the two groups in this study also further confirmed the high comparability and homogeneity of the patient population in this study.

Our research also has some limitations. First, due to the retrospective nature of the study, there may have been omissions in the selection of variables that may have influenced the findings. In addition, although the “pseudo-random” design used in this study would reduce patient selection bias, due to the large heterogeneity of patients in a single-center ICU, it will inevitably introduce some inter-group bias. However, baseline levels and severity of critical illness were similar between the two groups in this study, which makes our results more robust. Additionally, due to the limited sample size, the low incidence of endpoint events (thrombotic events) in this study also prevented further group discussion of the outcomes. And it also limited the number of independent variables in multivariate analysis, but we used a forward regression model and did not include more than 4 independent variables at the end.

Conclusion

This study demonstrated that CPS could significantly improve ICU physicians' compliance with VTE prophylaxis guidelines and that patients could benefit from CPS. Clinical pharmacists should be involved in the daily management of ICU patient as an important member. In future work, pharmacists should pay more attention to the individual administration of anticoagulants in VTE prophylaxis in ICU patients, so that patients could obtain appropriate drug prophylaxis strategies.

Declarations

Author contributions All author contributed to the study conception and design. Data collection and analysis were performed by Li Zhang, Yuan Qiao and Haitao Wang. The first draft of the manuscript was written and edited by Yan Wang. Clinical data collected by Ping Li who is an ICU physician.: CPS performed by Yan Cai, Na Wang, and Chenwei Liu. Critically reviewed the manuscript by Kanghuai Zhang. Conceptualization, methodology, validation, oversight the study by Yu Fang. All authors declare that they have read and approved the final manuscript.

Ethics approval Not applicable.

Consent to participate Not applicable.

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Data availability statement Data are available on request to the authors.

Conflict of interest disclosures The authors declare no conflict of interest during the time involving the work, from initial conception and planning to present.

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Tables

Table 1 The criterion and methods for evaluating compliance with the guidelines.

Criteria	Assessment standard	Assessment methods	Assessment result
Criterion 1	Assessment of VTE and bleeding risk in each ICU admission.	If there was a documented VTE or bleeding evaluation, then YES	Yes/No
Criterion 2	Initiation LMWH at admitted the ICU if pharmacological VTE prophylaxis is not contraindicated [a].	If prescribing LMWH/UFH for VTE prophylaxis when the patient has no contraindications to anticoagulation, then YES	Yes/No
Criterion 3	If pharmacological prophylaxis is contraindicated, given mechanical VTE prophylaxis for patient admitted to the ICU.	If IPC therapy was used to prevent VTE when the patient has contraindications to anticoagulation, then YES. IF the patient was using LMWH/UFH to prevent VTE then defaults to YES.	Yes/No
Criterion 4	If using mechanical VTE prophylaxis for people admitted to the critical care unit, start it on admission and continue until the person on longer has reduced mobility relative to their normal or anticipated mobility.	If the patient started IPC therapy within 72 hours of admission and the course of treatment continue until the patient could get off the ground on their own or start anticoagulant drugs to prevent VTE, then YES.	Yes/No
Criterion 5	Reassess VTE and bleeding risk daily for people in ICU.	If the patient was assessed daily for VTE and bleeding risk, then YES.	Yes/No
Criterion 6	Assess VTE and bleeding risk more than once a day in people admitted to the ICU if the person's condition is changing rapidly.	Assessed VTE and bleeding risk at any time if the patient's clinical symptoms changed, then YES.	Yes/No

[a] Contraindications to anticoagulation: sever active bleeding, subarachnoid hemorrhage, cerebral hemorrhage.

ICU: intensive care unit, VTE: venous thromboembolism, LMWH: low molecular weight heparin, UFH: unfractionated heparin; IPC: intermittent pneumatic compression

Table 2 Baseline characteristics of patients

	Control group (n = 162) Frequency (%) or median (25^{th}–75^{th})	Intervention group CPS(n = 176) Frequency (%) or median (25^{th}–75^{th})	p value	All patients (n = 338) Frequency (%) or median (25^{th}–75^{th})	Normal range
Characteristics					
Age-yr	68 (56, 77)	66 (60, 77)	0.399	67 (54, 77)	NA
Female sex-no. (%)	63 (38.9)	77 (43.8)	0.365	140 (41.4)	NA
Hospitalization time in ICU, days	7 (4, 10)	11 (6, 17)	**<0.001**	10 (5, 14)	NA
Severity of illness score					
APACHE score on day 1	17 (13, 23)	18 (13, 25)	0.247	18 (13, 23)	NA
VTE risk calculator					
Padua score	5 (5, 6)	6 (4, 7)	0.256	5 (5, 6)	NA
Caprini score	7(5, 9)	6 (7, 9)	0.819	7 (5, 9)	NA
Catheter					
Central venous catheter no. (%)	93 (57)	129 (73)	**0.001**	222 (66)	NA
Hematologic					
HB (g/L)	108 (89, 127)	105 (91, 123)	0.711	107 (90, 126)	130-175
PLT, $\times 10^9$/L	157 (91, 234)	152 (112, 216)	0.462	153 (103, 225)	125-350
HCT, %	34 (27, 39)	34 (28, 38)	0.9	34 (28, 39)	40-50
Coagulation function					
PT, s	12.9 (11.4, 15)	12.5 (11.4, 13.7)	0.068	12.55 (11.4, 14.3)	9.8-12.1
APTT, s	30.3 (24.6, 39.9)	31.4 (25.2, 38.4)	0.94	30.6 (24.9, 38.8)	22.7-31.8
FIB, (g/L)	300 (166, 467)	365 (213, 530)	**0.016**	361 (195, 494)	1.8-3.5
D-dimer,	3765 (1778, 9785)	6880 (2773, 13820)	**<0.001**	5925 (2240,	0-1000

(ng/mL)				12495)	
Biochemical					
AST (U/L)	31 (21, 72)	38.5 (22, 71)	0.41	35.5 (21.5, 72)	15-40
ALT (U/L)	22 (12, 64)	26 (13, 62)	0.571	24.6 (12, 64)	9-50
Cr (μmol/L)	71 (47, 143)	62 (43, 115)	0.052	62 (46, 131)	57-111
VTE prophylaxis	66 (41)	133 (76)	**<0.001**	199 (59)	NA
LMWH no. (%)	48 (30)	126 (72)		174 (52)	NA
UFH no. (%)	18 (11)	7 (4)		25 (7)	NA
IPC no. (%)	42 (26)	52 (30)	0.458	94 (28)	NA
Vein thrombosis no. (%)	27 (17)	16 (9)	**0.037**	43 (12)	NA
All bleeding no. (%)	18 (11)	9 (5)	**0.042**	27 (8)	NA
Expenses					
Total hospitalization expenses	52738 (27537, 90416)	56973 (31222, 94598)	0.281	55008 (29788, 93473)	NA
Medicine expenses	16783 (8117, 30613)	20152 (10649, 38861)	**0.017**	18385 (9548, 33945)	NA
Overall death at 14 days no. (%)	46 (28)	25 (14)	**0.001**	71 (21)	NA

APACHE: Acute Physiology and Chronic Health Evaluation, HB: hemoglobin, PLT: platelet, HCT: hematocrit value, PT: prothrombin time, APTT: activated prothrombin time, FIB: fibrinogen, AST: glutamic oxalacetic transaminase, ALT: glutamic-pyruvic transaminase, VTE: venous thromboembolism, LMWH: low molecular weight heparin, UFH: unfractionated heparin; IPC: intermittent pneumatic compression

Table 3 Guideline compliance rates between the CPS group and control group

	Control group (n = 162) no. (%)	Intervention group (n = 176)CPSno. (%)	p value
Criteria 1			
Yes	150 (93)	176 (100)	<0.001
Criteria 2			
Yes	109 (67)	160 (91)	<0.001
Criteria 3			
Yes	98 (61)	149 (85)	<0.001
Criteria 4			
Yes	96 (59)	148 (84)	<0.001
Criteria 5			
Yes	105 (65)	172 (98)	<0.001
Criteria 6			
Yes	110 (68)	157 (89)	<0.001

CPS: clinical pharmacist services

Table 4 Univariate and Multiple Cox regression models analysis of VTE events

	Vein thrombosis (n = 43) Frequency (%) or median (25^{th}–75^{th})	Non-vein thrombosis (n = 295) Frequency (%) or median (25^{th}–75^{th})	p value	HR	95% CI	p value
Age-yr	73 (66–80)	66 (53–77)	**0.028**	1.037	1.015–1.06	**0.001**
Female sex-no. (%)	15 (35)	125 (42)				
APACHE Ⅱ score on day 1	16 (12–20)	18 (13–24)	**0.005**	0.912	0.864–0.962	**0.001**
Padua score	6 (5–7)	5 (5–6)	**0.057**			
Caprini score		7 (5–9)	0.878			
Central venous catheter no. (%)	31 (72)	189 (64)	0.349			
HB (g/L)	106 (87–125)	107 (90–126)	0.419			
PLT, $\times 10^9$/L	122 (88–189)	156 (106–232)	0.068			
HCT, %	31.8 (23.1–36.9)	33.8 (28.3–38.7)	0.774			
Coagulation function						
PT, s	12.9 (11.8–14.2)	12.7 (11.4–14.4)	0.15			
APTT, s	31.6 (26.4–42.1)	30.7 (24.8–38.1)	0.436			
FIB, (g/L)	262 (55–421)	352 (201–500)	0.331			
D-dimer, (ng/mL)	6010 (2570–11730)	4600 (2230–12900)	0.968			
Biochemical						
AST (U/L)	28 (18–66)	36 (22–72)	0.962			
ALT (U/L)	22 (11–47)	25 (13–67)	0.432			
Cr (μmol/L)	74 (51–161)	65 (45–126)	0.146			
Anticoagulants VTE prophylaxis	27 (63)	172 (58)	0.472			
LMWH no. (%)	22 (81)	152 (88)				
UFH no. (%)	5 (19)	20 (12)				
IPC no. (%)	5 (12)	89 (30)	**0.028**			

All bleeding no. (%)	3 (7)	24 (8)	0.797			
Intervention group□CPS□no. (%)	16 (37)	160 (54)	**0.004**	0.438	0.224–0.857	**0.016**

HR: hazard ratio, CI: confidence interval

Table 5 Univariate and Multiple Cox regression models analysis of 14-day all-cause mortality

	Bivariate analysis			Multivariate analysis		
	Survivors at days 14 (n= 267) Frequency (%) or median (25^{th}–75^{th})	Death at days 14 (n= 71) Frequency (%) or median (25^{th}–75^{th})	p value	HR	95%CI	p value
Age-yr	66 (54, 76)	71 (61, 81)	**0.004**	1.021	1.006–1.037	**0.007**
Female sex-no. (%)	113 (42)	27 (38)	0.386			
APACHE Ⅱ score on day 1	17 (13, 23)	18 (15, 24)	0.177			
Padua	5 (5, 6)	6 (5, 7)	0.053			
Caprini	7 (5, 9)	7 (6, 9)	0.764			
Central venous catheter no. (%)	110 (41)	52 (73)	0.345			
HB (g/L)	107 (106, 128)	106 (89, 123)	0.477			
PLT, $\times 10^9$/L	156 (106, 232)	147 (97, 201)	0.202			
HCT, %	34 (27, 39)	34 (30, 38)	0.667			
Coagulation function						
PT, s	12.7 (11.4, 14.1)	13 (11.9, 15)	0.739			
APTT, s	30.3 (24.6, 37.9)	34.4 (26.8, 41.6)	**0.141**			
FIB, (g/L)	353 (199, 495)	277 (140, 470)	0.473			
D-dimer, (ng/mL)	4550 (2230, 11740)	5810 (2270, 13880)	0.447			
Biochemical						
AST (U/L)	34 (20, 68)	22 (12, 65)	0.797			
ALT (U/L)	24 (12, 62)	39 (24, 74)	0.571			
Cr (μmol/L)	63 (44, 120)	79 (51, 147)	0.91			
VTE prophylaxis			0.882			
LMWH no. (%)	106 (39.7)	39 (55)				
UFH no. (%)	7 (3)	6 (8)				

IPC no. (%)	71 (27)	25 (35)	0.422			
Vein thrombosis no. (%)	33 (12)	10 (14)	**0.109**			
All bleeding no. (%)	23 (8.6)	4 (6)	0.457			
Intervention group□CPS□no. (%)	151(56.6)	25 (35)	**0.001**	0.416	0.25-0.692	**0.001**

Figures

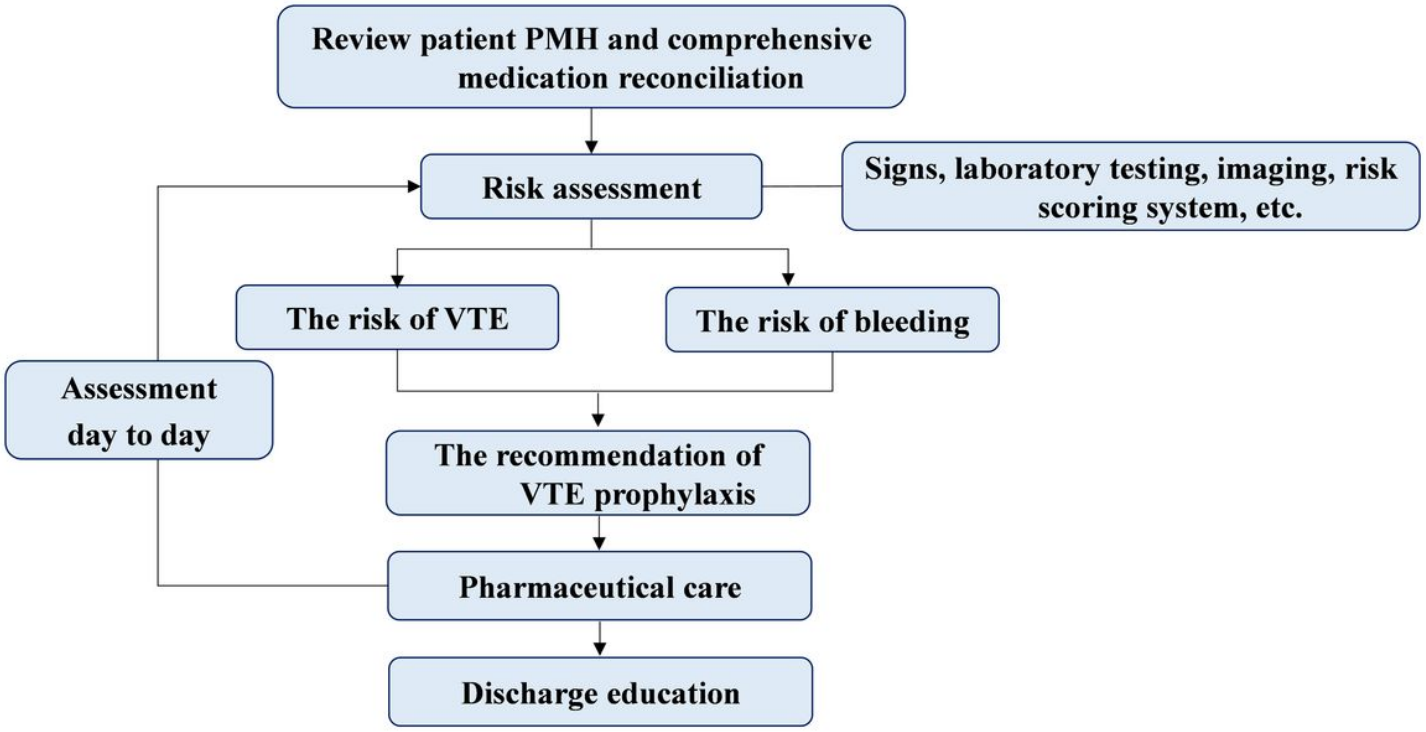

Figure 1

CPS workflow of VTE management of ICU patients

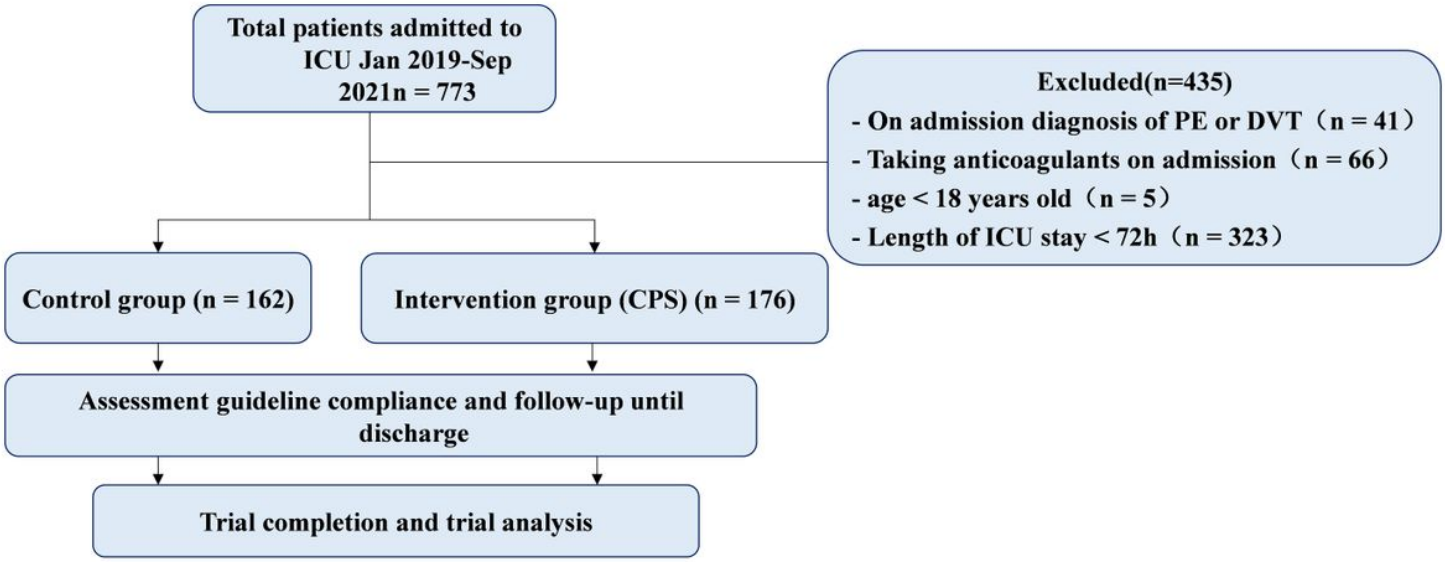

Figure 2

Patient flowchart