

Thromboembolic complications in patients with septic shock requiring invasive mechanical ventilation: Incidence, risk factors, and outcomes

Dear Editor,

Patients are at high risk for both deep vein thrombosis (DVT) and pulmonary embolism (PE) during a stay in an intensive care unit (ICU).^[1-5] The majority of ICU patients are severely ill requiring sedation and mechanical ventilation.^[4,5] However, little is known about the incidence and particularities of venous thromboembolic complications (VTE) in patients with septic shock requiring ICU admission. In the best of our knowledge, only one prospective study was done on this subject showing a high incidence of VTE in patients with severe sepsis and/or septic shock, regardless of the use of universal, guideline-recommended thromboprophylaxis.^[1] During the period from January 01, 2017 to December 31, 2017, we prospectively studied 60 successional enrolled patients with established septic shock in the ICU of Habib Bourguiba University Hospital, Tunisia. Patients that were recruited in the study included those that developed septic shock as a result of bacterial infection during the study period. Thromboprophylaxis was recorded for all patients. Spiral computed tomography scan and venous compression ultrasound were used to confirm the diagnosis of thromboembolic complications (TEC). PE is suspected by the presence of un-explicated hypoxemia and/or shock as well as arterial hypotension during diagnosis in our institution, and spiral computed tomography is used for PE confirmation.

However, venous compression ultrasound is performed when the patient developed clinical features of thrombophlebitis and/or when there are contraindications of spiral computed tomography.

During the study period, 24 patients (40%) developed VTE complications, despite all patients receiving guideline-recommended thromboprophylaxis. Mean Simplified Acute Physiology Score II (SAPSII score),^[6] which is intended to evaluate the severity of disease for patients admitted to Intensive care units aged 15 or more, was significantly higher in the thromboembolic complications free group [Table 1].

VTE was found to be associated with prolonged ICU stay and longer mechanical ventilation. However, the mortality rate was not significantly higher in patients with acute thromboembolic complications [Table 1].

Critically ill patients are usually at high risk for PE and DVT. Also, TEC is a crucial challenge these patients face. Moreover, septic shock is considered a risk factor for VTE, including upper and lower extremity DVT and pulmonary embolism (PE).^[1,2] The underlying pathogenesis of VTE in sepsis remains incompletely understood but is believed to be the result of multiple factors. In addition to risk factors for hypercoagulability, as originally described by Virchow, incorporating the 3 original triad (stasis; endothelial injury; and hypercoagulability), severe inflammation observed in patient with sepsis and/or septic shock represents the fourth factor for thromboembolic complications.^[1] Inflammation increases pro-coagulant factors, and also inhibits natural anticoagulant pathways and fibrinolytic activity, leading to DVT and PE.^[2] In fact, the inflammatory process initiated by septic shock may be strained by coexisting tissue hypoxia and systemic inflammation leading to endothelial damages and DVT complications.

Table 1: Comparison between the two groups (with and without VTE)

Characteristic	VTE Group (n=24)	VTE-FREE Group (n=36)	P
Age (years)	51.8±16.4	45.1±20.3	0.183
Sex ratio (M/F)	21/3	25/11	0.105
SAPS II on ICU admission	35.3±14.5	44.3±16.2	0.032
SOFA	5.5±1.3	8±4.1	0.017
GCS on ICU admission	10.6±4	9.5±4.3	0.329
Type of admission:			
Medical	10	22	
Traumatism	11	11	0.335
Surgical	3	3	
Duration of mechanical ventilation (days)	32.7±11.4	12.9±9.3	<0.001
Tracheotomy	23	23	0.004
DIC	6	17	0.083
Acute kidney failure	18	23	0.365
Dialysis	2	13	0.015
Length of stay (days)	37.3±11.6	16.3±11.7	<0.001
Mortality rate	58.3%	63.9%	0.665
pH on ICU admission	7.39±0.09	7.37±0.10	0.740
PACO ₂ (mmHg) on ICU admission	38.13±8.38	37.45±9.66	0.779
PAO ₂ /FiO ₂ ratio on ICU admission	270±112.8	267.4±109.8	0.931
HCO ₃ ⁻ (mmol/l) on ICU admission	22.47±4.41	21.88±6.10	0.751
Troponin (ng/l)	0.079±0.086	0.57±1.03	0.869
SGOT (UI/l)	71.4±59.3	91.5±142.6	0.952
SGPT (UI/l)	57.6±65.8	54.3±55.5	0.922
Bilirubin (μmol/l)	45.9±51.1	56.4±118.6	0.717
Blood urea (mmol/l)	12.4±7.5	17±16	0.763
Blood creatinine (μmol/l)	109±72	157±126	0.381
CRP (mg/L)	231.9±103	230±138	0.594
Procalcitonin (ng/mL)	14.6±20.9	11.3±15.5	0.682
SChEA (UI/L)	3391±1430	3423±1151	0.922

VTE=Venousthromboembolism, GCS=Glasgow coma scale score, SAPSII=Simplified acute physiology score, DIC=Disseminatedintra-vascularcoagulation, SOFA score=Sepsis-related Organ Failure Assessment score, SGOT=Sérum Glutamooxaloacétate Transférase, SGPT=Sérum Glutamopyruvate Transférase, SChEA=Serum CholinesteraseActivity

Our study confirms the high incidence of TEC (37.2%) in patients with sepsis despite the use of universal, guideline-recommended thromboprophylaxis reported by Kaplan *et al.*^[1] As a consequence, it underlines that current recommendations of VTE prophylaxis strategies may not be as efficient and should be revised in severe sepsis and septic shock compared with non-septic-critically ill patients. As a matter of fact, it is clear that the preventive dose used of unfractionated heparin (equivalent of 40mg of enoxaparine) in our ICU, is not sufficient and must be revised in this specific condition. Therefore, to improve the prevention of VTE in patients with severe sepsis and septic shock, other clinical trials specifically studying thromboprophylaxis in patients with severe sepsis and septic shock are advised.

In our study, the comparison between the TEC (+) group and TEC free group, showed that the development of this complication was not associated with a high mortality rate. However, the development of TEC was associated with increased length of stay and longer mechanical ventilation. Our

study confirms the results of previously reported studies^[1,3-5] and underlines the importance to prevent this type of complications.

We concluded that patients with sepsis and/or septic shock are considered at high risk for developing VTE. It is the result of multiple factors including immobility, activation of thrombo-inflammatory pathways and disseminated intravascular coagulation. The development of TEC was associated with increased length of stay and longer mechanical ventilation. Thus, more effective VTE prevention strategies are necessary for patients with sepsis and/or septic shock.

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Conflicts of interest

There are no conflicts of interest.

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