Post-traumatic pulmonary embolism in the intensive care unit

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Abstract:

OBJECTIVE: To determine the predictive factors, clinical manifestations, and the outcome of patients with post-traumatic pulmonary embolism (PE) admitted in the intensive care unit (ICU).

METHODS: During a four-year prospective study, a medical committee of six ICU physicians prospectively examined all available data for each trauma patient in order to classify patients according to the level of clinical suspicion of pulmonary thromboembolism. During the study period, all trauma patients admitted to our ICU were classified into two groups. The first group included all patients with confirmed PE; the second group included patients without clinical manifestations of PE. The diagnosis of PE was confirmed either by a high-probability ventilation/perfusion (V/Q) scan or by a spiral computed tomography (CT) scan showing one or more filling defects in the pulmonary artery or its branches.

RESULTS: During the study period, 1067 trauma patients were admitted in our ICU. The diagnosis of PE was confirmed in 34 patients (3.2%). The mean delay of development of PE was 11.3 ± 9.3 days. Eight patients (24%) developed this complication within five days of ICU admission. On the day of PE diagnosis, the clinical examination showed that 13 patients (38.2%) were hypotensive, 23 (67.7%) had systemic inflammatory response syndrome (SIRS), three (8.8%) had clinical manifestations of deep venous thrombosis (DVT), and 32 (94%) had respiratory distress requiring mechanical ventilation. In our study, intravenous unfractionated heparin was used in 32 cases (94%) and low molecular weight heparin was used in two cases (4%). The mean ICU stay was 31.6 ± 35.7 days for patients with and without PE. The predictive factors of PE were: Age > 40 years, a SAPS II score > 25, hypoxemia with PaO₂/FiO₂ < 200, the presence of a spine fracture, and the presence of meningeal hemorrhage.

CONCLUSION: Despite the high frequency of DVT in post-traumatic critically ill patients, symptomatic PE remains, although not frequently observed, because systematic screening is not performed. Factors associated with poor prognosis in the ICU are the presence of circulatory failure (shock) and thrombocytopenia (OR = 32.5). Moreover, comparison between patients with and without PE showed that the predictive factors of PE were: Age > 40 years, a SAPS II score > 25, hypoxemia with PaO₂/FiO₂ < 200 mmHg, the presence of spine fracture, and the presence of meningeal hemorrhage.

Key words:

Anticoagulation, ICU, predictive factors, pulmonary embolism, trauma patients

Venous thromboembolism (VTE) remains a major challenge in critically ill patients. Subjects admitted to the Intensive Care Unit (ICU), in particular, trauma patients, are at a high risk for both deep vein thrombosis (DVT) and pulmonary embolism (PE). Pulmonary embolism is a cardiovascular emergency. Occluding the pulmonary arterial bed may lead to an acute life-threatening condition, due to a potentially reversible right ventricular failure. The diagnosis of PE is usually suspected by the presence of common symptoms (including breathing difficulties, chest pain on inspiration, and palpitations) and clinical signs, including low blood oxygen saturation, tachypnea, and tachycardia.[1,2] However, in the ICU, most of patients require sedation and mechanical ventilation. The clinical manifestations usually observed in this condition (PE) cannot be exhibited by these patients and clinical presentation is usually atypical.[3] In trauma patients, venous thromboembolic events comprise deep vein thrombosis and pulmonary embolism. The latter represents a significant cause of death, disability, and discomfort after trauma-associated hospitalization. In fact, while DVT may be clinically silent, PE is the third most common cause of death in patients who survive after the first 24 hours of trauma.[3-5] Moreover, post-traumatic pulmonary embolism traditionally occurs after a period of at least five days from trauma. Patients with pelvic or...
lower limb fractures are at a higher embolic risk, as well as patients with severe head traumas or spine traumas.\[^{10}\] Despite the complexity of establishing the diagnosis of PE and its management in critical trauma patients, this pathology is, to our knowledge, rarely studied.\[^{10,11}\] The aim of our study is to determine the predictive factors and the clinical and demographic characteristics of patients with post-traumatic PE admitted to our ICU. Moreover, we aim to define the simple predictive factors, which can be routinely used in general ICUs as indicators of poor prognosis in patients with post-traumatic PE.

**Methods**

Between January 2005 and December 2008, we prospectively included 34 consecutive patients with a positive diagnosis of post-traumatic pulmonary thromboembolism developed on ICU admission and/or during ICU stay (Sfax - Tunisia).

**Management of trauma patients on ICU admission**

In Sfax city, severe trauma patients were usually admitted directly from the scene of the accident within six hours of injury. They were all examined and scored according to the Glasgow coma scale (GCS) score on arrival. A cranial CT-Scan was done in all patients with a head trauma. When extra cranial pathology was suspected, appropriate investigations were performed. All clinical, biological, and radiological parameters and the relevant therapeutic measures were registered on admission and during the ICU stay. In the present study, for all included patients, the following data were collected: Age, gender, vital signs, body temperature in degrees centigrade (°C Temp), Glasgow coma scale score (GCS score),\[^{14}\] injury severity score (ISS),\[^{7}\] the simplified acute physiology score (SAPS II), calculated within 24 hours of admission,\[^{8}\] cause of injury, use of mechanical ventilation, presence of shock or arterial hypotension, cardiac arrest, fluid intake volume, brain CT-scan result, and the use of catecholamine.

**Diagnosis and management of pulmonary embolism**

In our institution, the diagnosis of PE is usually suspected by the presence of tachypnea, dyspnea, pleuritic chest pain, and hemoptysis. However, in our ICU, most of the severe trauma patients have required sedation and mechanical ventilation and the diagnosis of PE is usually suspected in patients with unexplained hypoxemia and/or shock and arterial hypotension. A medical committee of six ICU physicians examine prospectively all available data in order to classify patients according to the importance of the clinical suspicion of pulmonary thromboembolism. The diagnosis of PE is confirmed by a high-probability ventilation/perfusion (V/Q) scan\[^{9}\] or by a spiral computed tomography (CT) scan showing one or more filling defects or obstructions in the pulmonary artery or its branches.\[^{10}\] The diagnosis is also confirmed when echocardiography shows a thrombus in the pulmonary artery.\[^{12}\]

The V/Q scan and/or spiral CT scan were performed after correction of hemodynamic instability (using fluid resuscitation and/or catecholamine) and improvement of hypoxemia (using mechanical ventilation, high fraction of O\(_2\)). Massive PE was defined by the presence of hemodynamic instability, arterial hypotension, and cardiogenic shock. Arterial hypotension was defined as a systolic arterial pressure < 90 mm Hg or a drop in systolic arterial pressure of at least 40 mm Hg for at least 15 minutes. A data entry form was designed to collect the demographic, clinical, and radiological data on admission and during the ICU stay. The systemic inflammatory response syndrome (SIRS)\[^{11}\] was also researched on admission and during the ICU stay. The biochemical parameters measured on admission and during the ICU stay were arterial blood gases, acid–base status (pH and HCO\(_3\)), hemoglobin concentration, and so on.

Moreover, the risk factors of PE were also collected. The use of preventive anticoagulant agents, the delay of development of PE, and the clinical manifestations associated with the PE were also recorded for each patient. On the other hand, chest X-ray findings and arterial blood gas values were recorded. Chest X-rays were analyzed by a radiologist who was blinded to the patient’s diagnosis. The ECG abnormalities were also recorded. As echocardiography was not available, only few patients had this investigation. For each patient, clinically symptomatic DVTs were researched. Leg ultrasonography also known as Leg Doppler was performed when DVT was suspected, and at the same time it was possible to perform Leg ultrasonography, in association with a spiral CT scan. Estimation of the clinical probability of PE was performed in all patients according to the two scoring systems: The Wells’ score\[^{12}\] and the Geneva revised score.\[^{13}\] Massive PE was defined as the presence of hypotension or shock, whereas, submassive PE was defined as stable hemodynamics in the presence of echocardiographic right ventricular (RV) dysfunction, based on RV dilatation (end diastolic diameter > 30 mm) or hypokinesia or abnormal movement of the interventricular septum, with or without tricuspid regurgitation.\[^{14}\] The therapeutic agents given, either unfractionated heparin alone or a thrombolytic agent, were noted. During the ICU stay, all complications were recorded: Nosocomial infections,\[^{15}\] pneumonia, thrombocytopenia, gastrointestinal bleeding, cerebral hemorrhage, and hematomas. For each patient, the number of organ failures\[^{16}\] was calculated on admission and when the diagnosis of PE was established. Moreover, for each patient the severity of illness was estimated with the simplified acute physiology score (SAPS II), calculated within 24 hours of admission,\[^{9}\] and according to the APACHE categorization, at admission.\[^{16}\] The number of patients who died in the ICU and in the hospital was recorded as the primary clinical outcome and the patients were classified as survivors or nonsurvivors.

**Determination of associated factors with pulmonary embolism**

Finally, during the study period, all the patients admitted to our ICU were classified into two groups. The first group included all patients with confirmed PE. The second group included patients without clinical manifestations of PE (in this group, pulmonary thromboembolism was not suspected by our medical staff). From this group, 42 patients were included in a random way and were analyzed in this study. The files of the patients without PE were drawn randomly according to the Injury Severity Score (±3) and mechanism of injury. In order to identify the predictive factors of pulmonary thromboembolism we compared these two groups with and without PE.

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Results

Clinical characteristics of population with confirmed pulmonary embolism on ICU admission

During the study period, 1067 trauma patients were admitted in our ICU. The diagnosis of PE was confirmed in 34 patients (3.2%), who were all included in this study. In this study, the causes of ICU admission were: Traumatic head injury in 15 patients (44%), multiple trauma in 16 (47%), and respiratory distress in three (9%). There were 26 males (76%) and eight females (24%). The mean age (±SD) was 42.1 ± 16.3 years, with a range of 15 to 69 years. Most patients (56%) were older than 40 years. The trauma was usually caused by traffic accidents (85%). The clinical presentations of the study group on admission are shown in Table 1.

In our study, 32 patients (94%) had head trauma, it was isolated in 15 (46.8%). Extra-cranial pathology was present in 19 patients (56%) including fracture of long-bones in 10 (52.6%), chest trauma in 13 (38.2%), abdomen trauma in six (17.6%), pelvic trauma in four (11.7%), and spine trauma in 11 patients (32.3%). The brain CT-scan was performed in 32 patients with head trauma. It showed a meningeal hemorrhage in 20 patients (58.8%), cerebral contusion in 14 (41%), Subdural hematoma in eight patients (23.5%), extradural hematoma in four (11.8%), cerebral edema in four (11.8%), and brainstem injury in three (8.8%). A total of 32 (94%) needed intubation, mechanical ventilation, and sedation on admission.

Twenty-one patients (61.8%) had an SAPS II score of > 30, confirming the severity of the patients in the current study. Moreover, 25 patients (73.5%) had an ISS score > 25, and 31 patients (91%) had one or more organ failures on ICU admission [Table 2]. Neurological failure was the most common organ failure observed (79.5%), followed by respiratory and circulatory failures, observed in 53 and 38.5%, respectively. Eighteen patients (52.9%) underwent a surgical intervention before the development of thromboembolic complication. Ten patients (29.3%) required craniotomy, while nine patients (26.4%) needed extra-cranial surgery. An orthopedic surgery was applied in seven patients (20.5%).

Clinical characteristics and investigations at pulmonary embolism diagnosis

In our study, 21 patients (61.8%) received pharmacological prevention of venous thromboembolism before development of pulmonary embolism. However, in 13 patients (38.2%) these therapies were not given because of the presence of contraindications, although, all these patients had received mechanical device for prevention of DVT. The mean delay of development of PE was 11.3 ± 9.3 days (range 3-46 days). Eight patients (24%) developed this complication within five days of ICU admission [Figure 1]. On the day of PE diagnosis, pulmonary auscultation was performed in all patients. It was normal in 27 patients (79.4%) and showed lung crackles on auscultation of one or both lungs in four (11.7%). Table 3 shows the clinical characteristics of all population groups on the day of PE diagnosis. The quantitative plasma D-Dimer dosage was performed in six patients: It was > 500 ng/l in all cases. Ultrasonography of the legs was performed in 11 patients (32.3%). It showed DVT only in five patients (45%). Chest X-ray was performed in all patients and it was normal in 17 (50%) patients. An electrocardiogram was performed in all patients. The most frequent abnormalities recorded were sinus tachycardia in 89.3% of the cases, complete or incomplete right bundle block in four patients (11.7%), and T-wave inversion over the right or the left precordial leads (T-wave inversion in leads V2-V3) in seven (20.5%). Echocardiography was performed in one (2.9%) case. It showed a left ventricular dysfunction, with neither right ventricular dilatation nor pulmonary artery

### Table 1: Patients’ characteristics at the time of admission to the medical intensive care unit

| Parameters               | Results (Range) | % |
|--------------------------|-----------------|---|
| Age (years)              | 42 ± 16.3 (15-69)| - |
| Sex M/F                  | 26/8            | - |
| SAPS II                  | 31.6 ± 13.5     | - |
| ISS                      | 25 ± 11.4 (4-51)| - |
| HR (beats/minute)        | 97 ± 25         | - |
| SBP (mmHg)               | 112 ± 15        | - |
| Class ’A’ in the APACHE system | 31    | 91 |
| Shock/Use of catecholamine | 13    | 38 |
| Use of mechanical ventilation | 32   | 94 |
| Hypoxemia (PaO2/FiO2 < 300) | 23   | 67 |
| Glasgow Coma Scale score | 9 ± 3.9        | - |
| Anisocoria               | 4               | 11.7 |
| Motor deficit            | 5               | 14.7 |
| Convulsions              | 2               | 6 |
| Other injury             | 19              | 56 |
| SIRS (Yes)               | 19              | 56 |
| Multi organ failure      | 19              | 56 |
| Fracture of long bones   | 10              | 52.6 |
| Pathological antecedent  | 5               | 14.7 |

### Table 2: Frequency of each organ failure on ICU admission

| Type of organ failure                  | Number (Total number 34) | Percentage  |
|----------------------------------------|--------------------------|-------------|
| Neurological failure                    | 27                       | 79.5        |
| Circulatory failure                     | 13                       | 38.5        |
| Respiratory failure                     | 18                       | 53          |
| Kidney failure                          | 3                        | 8.8         |
| Liver failure                           | 4                        | 11.6        |
| Hematological failure                   | 1                        | 2.9         |
hypertension. The diagnosis of PE was made by spiral CT in 33 patients (97%) [Table 4] or by a V/Q scan in one (3%). Estimates of the clinical probability of PE were performed in all patients according to the two scoring systems; the Wells’ score and Geneva revised score. Only two (5.9%) patients had a high probability according to the first score and two (5.9%) patients had a high probability according to the second score [Figure 2].

Management and outcome of pulmonary embolism
Specific treatment (anticoagulant therapy) is the mainstay of treatment. In our study, 34 patients (100%) received parenteral anticoagulants. Intravenous unfractionated heparin was used in 32 cases (94%) and low molecular weight heparin was used in two cases (6%). Inferior vena cava filter and thrombolysis were not used in any of the cases. Under anticoagulant therapy, three patients (9%) developed a bleeding complication, including two patients (6%) who had gastrointestinal bleeding and one patient with epistaxis. Moreover, eight patients (23.5%) developed thrombocytopenia. The mean ICU stay was 31.6 ± 35.71 days (range: 1-203 days) and the mean hospital stay was 32.77 ± 35.31 days (range: 3-205 days). During their ICU stay, 32 (94%) patients developed one or more organ failures. Respiratory failure was the most commonly observed (29.4%) followed by cardiovascular failure (23.6%). Furthermore, 27 (79.4%) developed nosocomial infections. The mortality rate in the ICU was 38.2% (13 patients) and the in-hospital mortality rate was at 41% (14 patients). Univariate analysis showed that factors associated with poor outcome were: Shock (P = 0.003), age > 55 years (P = 0.014), and a number of organ failures > 3 (P = 0.02). Table 5 shows factors associated with poor outcome in the ICU. The multivariate analysis showed that factors associated with poor prognosis were the presence of circulatory failure (Shock) (P = 0.02; Odds ratio (OR) = 9.96; 95% CI = 1.4-70) and thrombocytopenia (P = 0.028; OR = 32.5; 95% CI = 1.45-72.5). The in-hospital mortality rate was at 41% (14 patients). Factors associated with poor hospital outcome were the presence of circulatory failure (Shock) (P = 0.004; Odds ratio (OR) = 8.4; 95% CI = 1.1-65), and a number of organ failures associated with PE ≥ 3 (P = 0.002, OR = 3.7; CI: 1.4-31).

Predictive factors of pulmonary embolism
As previously shown, during the study period, we included a second group of 42 trauma patients without clinical manifestations of PE (in this group, pulmonary thromboembolism was not suspected by our medical staff). Comparison between the two groups showed that factors associated with PE in univariate analysis were: Age > 40 years (P = 0.03), SAPS II > 25 (P = 0.013), the presence of meningeal hemorrhage (P = 0.004), the presence of spine fracture (P = 0.005), hypoxemia with PaO₂/FiO₂ < 200 (P = 0.0054),

Table 3: Patients’ characteristics on the day of diagnosis of PE

| Parameters                  | Results (Total number 34) | %    |
|-----------------------------|---------------------------|------|
| HR (beats/minute)           | 109 ± 23                  | -    |
| SBP (mmHg)                  | 122 ± 15.8                | -    |
| Tachycardia (>90 beats/minute) | 28                      | 82   |
| Shock                       | 13                        | 38.2 |
| Use of catecholamine         | 13                        | 38.2 |
| Use of mechanical ventilation| 32                       | 94.1 |
| Hypoxemia (PaO₂/FiO₂ < 300) | 28                        | 84.8 |
| Chest pain                  | 2                         | 5.9  |
| Hemoptysis                  | 0                         | 0    |
| Normal pulmonary auscultation| 27                       | 79.4 |
| SIRS (Yes/No)               | 23                        | 67.6 |
| Clinical manifestations of deep vein thrombosis | 3              | 8.8  |
| Fever (≥38°C)               | 12                        | 35.3 |
| Clinical symptoms of right ventricular dysfunction | 1              | 2.9  |

Table 4: Chest CT scan findings of all patients on the day of diagnosis of pulmonary embolism

| Findings                              | Number (Total number 33) | %    |
|---------------------------------------|---------------------------|------|
| Main branch (unilateral or bilateral) thrombi | 18                        | 54.5 |
| Lobar and segmental thrombi             | 20                        | 60.6 |
| Sub-segmental thrombi                  | 3                         | 9    |
| Normal lung parenchyma                  | 17                        | 51.5 |
| Volume loss/atelectasis                 | 6                         | 18   |
| Infiltrate                              | 7                         | 21   |
| Pneumothorax                            | 4                         | 12   |
| Pleural effusion                        | 4                         | 12   |

Figure 1: Temporal distribution of PE incidence in 34 patients. Eight patients (24%) developed this complication within five days of ICU admission, and 14 (41%) within seven days of ICU admission

Figure 2: Probability of all patients according to the Wells and Geneva revised score
and a platelet level > 150 cells/mm³ (P = 0.049) [Table 6]. Multivariate analysis showed that factors associated with PE were: Age > 40 years (P = 0.038, OR: 4.57, and 95% CI: 1.08-19.2), a SAPS II score > 25 (P = 0.046, OR: 4.48, and 95% CI: 1.02-19.6), hypoxemia with PaO₂/FiO₂ < 200 (P = 0.025, OR: 1.26, and 95% CI: 1.26-31), the presence of spine fracture (P = 0.007, OR: 13.6, and 95% CI: 2-93), and the presence of meningeal hemorrhage (P = 0.001, OR: 12.8, and 95% CI: 2.7-60).

Table 5: Factors associated with a poor outcome in ICU on univariate analysis

| Parameters                     | Survivors | Nonsurvivors | P   |
|--------------------------------|-----------|--------------|-----|
| On ICU admission               |           |              |     |
| Age (Years)                    | 38 ± 15   | 48.7 ± 16    | 0.049 |
| Age > 55 years (Yes/No)        | 3/18      | 7/6          | 0.014 |
| Sex M/F                        | 6/15      | 2/11         | 0.37  |
| SAPS II score                  | 32.8 ± 14.4| 29.6 ± 12.3  | 0.51  |
| ISS score                      | 25.3 ± 10.6| 25.5 ± 13   | 0.99  |
| Class ‘A’ in the APACHE system | 20        | 11           | 0.28  |
| Number of organ failures ≥ 3 (Yes/No) | 3/18 | 5/8          | 0.106 |
| Use of catecholamine (Yes/No)  | 6/15      | 7/6          | 0.14  |
| Blood urea > 8 mmol/l          | 19%       | 53.8%        | 0.035 |
| The day of diagnosis of pulmonary embolism |            |              |     |
| Blood glucose levels (mmol/l)  | 7.24 ± 1.5| 9.3 ± 3.9    | 0.038 |
| Shock (Yes)                    | 19%       | 69%          | 0.01  |
| Use of mechanical ventilation  | 90.4%     | 100%         | 0.25  |
| Abnormal chest X ray           | 63%       | 61.5%        | 0.16  |
| Platelets levels (cells/mm³)   | 278952    | 187750       | 0.03  |
| Potassium levels (mmol/l)      | 3.71 ± 0.48| 4.23 ± 0.88  | 0.036 |
| Right bundle branch block      | 5.8%      | 36.4%        | 0.04  |
| Thrombopenia under Heparine (%)| 9.52      | 46.15        | 0.014 |
| Number of organ failures > 3   | 0%        | 23%          | 0.021 |

Table 6: Factors associated with pulmonary embolism in univariate analysis

| Parameters                     | PE (+) | PE (-) | P   |
|--------------------------------|--------|--------|-----|
| Age > 40 years (%)             | 55.9   | 33.3   | 0.03 |
| ISS > 25 (%)                   | 76.2   | 73     | 0.79 |
| SAPSII ≥ 25 (%)                | 73.53  | 45.23  | 0.013|
| Meningeal hemorrhage (%)       | 58.82  | 26.2   | 0.004|
| Presence of spine fracture (%) | 32.35  | 7.14   | 0.005|
| PaO₂/FiO₂ < 200 mmHg (%)       | 54.83  | 15     | 0.005|
| Platelet levels > 150 cells/mm³ (%) | 76.47 | 54.76 | 0.049|

Discussion

Our study showed that pulmonary embolism is associated with poor outcome in trauma patients. Moreover we found that the factors associated with PE were older age, a SAPS II score of > 25, hypoxemia, the presence of spine fracture, and the presence of meningeal hemorrhage.

Incidence and risk factors of pulmonary embolism in trauma patients

Venous thromboembolic events (VTEs) involve deep vein thrombosis (DVT) and pulmonary embolism (PE), and represent a significant cause of death, disability, and discomfort, after trauma-associated hospitalization.[5] Data about thromboembolic event frequency among hospitalized trauma patients vary widely, ranging from less than 1% to 58%, depending upon the demographics of the study population and the nature of the injuries.[17-19] The incidence of post-traumatic PE in the ICU is poorly described, and systematic screening has not been performed.[4] The rate of symptomatic PE in injured patients has been reported previously to range from 2 to 6%.[4,18,19] In our study, the diagnosis of PE was confirmed in 34 (3.2%) out of 1067 patients. The low rate of PE in our study can be explained by the absence of systematic screening in patients who are clinically asymptomatic (false negative).

Traditional pulmonary emboli occur most commonly between the fifth and the seventh day post injury and are rare before the fourth day.[20,21] However, Owings et al.[20] showed that as many as 23.8% of the pulmonary emboli can occur within the first four days after injury. Sing et al.[22] showed that more than half of the pulmonary emboli diagnosed, occurred in the first seven days after trauma, and O’Malley et al.[23] reported that 70% of the pulmonary emboli were diagnosed within the first seven days after injury. Our results showed that eight patients (24%) developed this complication within five days of ICU admission and 14 (41%) occurred in the first week after injury. From this, the physicians must have a very high index of suspicion for PE from the time of admission after injury.[21,24]

Mechanisms of association between trauma and pulmonary embolism

Although DVT may be clinically silent, PE is the third most common cause of death in patients who survive after the first 24 hours of trauma.[4] In fact, fatal PE accounted for 11.9% of all post-traumatic deaths, although unfractionated heparin prophylaxis was used in 44% of these patients.[25] The high incidence of post-traumatic venous thromboembolic events is well known. In fact, major trauma is a hypercoagulable state often complicated by VTE and syndromes of ‘micro thrombosis,’ such as, disseminated intravascular coagulation (DIC), systemic inflammatory response syndrome (SIRS), and acute respiratory distress syndrome (ARDS), leading to poor clinical outcomes.[3,17] Several studies have established that the tissue factor (TF) and markers of thrombin generation increase after trauma[27,28] and that levels of natural anticoagulants, such as, antithrombin (AT), protein C (PC), and protein S.

References
(PS) are reduced. Several factors placing the individual patient at a higher risk for the development of DVT and PE have been suggested. For example, the magnitude of injury as reflected by the ISS score, has consistently been reported to be relevant in stratifying the risk for thromboembolic events. Moreover, spinal cord injuries have frequently been reported as a significant risk factor for VTEs after trauma. In other studies, it was shown that old age, head injury, chest injury with hypoxemia, lower extremity injury, and transfusion were associated with pulmonary embolism. Our study showed that the predictive factors of PE were: Age > 40 years, a SAPS II score > 25, hypoxemia with PaO2/FiO2 < 200, the presence of spine fracture, and the presence of meningeal hemorrhage. Moreover, in our study, 21 patients (61.8%) had a SAPS II score of > 30, confirming the severity of the included patients. Furthermore, 25 patients (73.5%) had an ISS score > 25, 19 (56%) had an SIRS on ICU admission, and 31 patients (91%) had one or more organ failures on ICU admission.

Clinical manifestations and diagnosis of pulmonary embolism in trauma patients
Symptoms of PE are a sudden-onset of dyspnea and pleuritic chest pain. In the ICU, these typical manifestations are rarely observed. In fact, in major trauma patients requiring ICU, intubation, mechanical ventilation, and sedation are usually needed. As a consequence, a classical presentation of acute PE may be lacking in these patients. For these reasons, the diagnosis of PE is usually suspected when unexplained hypoxemia and/or shock and arterial hypotension are observed. On account of the lack of sensitivity and specificity of clinical manifestations, some clinical pre-test probability scores, derived from large trials, which seek to determine the clinical signs and symptoms predicting the diagnosis of PE, are previously validated. In our study, estimates of the clinical probability of PE has been performed in all patients according to the two scoring systems, which have been tested prospectively and validated in large clinical trials: The Wells’ score and the Geneva revised score. These scores may be used to define the probability of PE as low, moderate, or high, with the prevalence of PE increasing across the three groups. However, in our study according to these scores, only two (5.9%) patients have a high probability according to the first score and two (5.9%) patients have a high probability according to the second score. When PE is suspected, diagnosis confirmation is needed. In fact, prompt and accurate diagnosis of PE greatly influences the patient outcome. In our study, the diagnosis of PE was made by spiral CT in 33 patients (97%) and a V/Q scan in 1 (3%).

Management and outcome of pulmonary embolism in trauma patients
Pulmonary embolism causing hemodynamic instability is termed massive; once it is suspected, a diagnostic plan and supportive measures are essential. In our study, all patients received saline infusion. Moreover 13 patients (38%) received catecholamine. The use of catecholamine was associated with poor outcome, and the multivariate analysis showed that the presence of circulatory failure (Shock) was an independent factor associated with death in the ICU and in hospital. Oxygen supplementation, intubation, and mechanical ventilation were instituted, when necessary, for respiratory failure. When mechanical ventilation was required, care had to be taken to limit its adverse hemodynamic effects. The use of mechanical ventilation was usually associated with a poor outcome. In our study, 32 (94%) patients required mechanical ventilation. Anticoagulant treatment played a pivotal role in the management of patients with PE. The objectives of the initial anticoagulant treatment of PE were to prevent death and recurrent events with a low rate of bleeding complications. Considering the high mortality rate in untreated patients, anticoagulant treatment should be considered in patients with suspected PE, while waiting for definitive diagnostic confirmation. In our study, 34 patients (100%) received parenteral anticoagulants.

Despite all advances made in diagnosis and therapeutic management of PE, mortality related to this complication remains as high as 15 to 18% after three-months of follow-up. In trauma patients, crude mortality depends on multiple factors such as injury severity, comorbidities, and thrombosis extent. However, when the diagnosis of pulmonary embolism is considered, mortality can be higher if prompt treatment is delayed. In fact, without appropriate treatment, mortality can reach 26 to 34%. In our study, the mortality rate in the ICU was 38.2% and the in-hospital mortality rate was at 41%. Factors identified by multivariate analysis as significantly correlated to the ICU poor outcome were shock and thrombocytopenia. Cardiogenic shock was found in almost all studies debating about pulmonary embolism as being correlated with poor outcome and mortality can be three-fold higher when compared to a patient in a stable hemodynamic state. In our study, the higher mortality compared to the literature can be explained by the contraindication of thrombolyis in almost all patients developing shock, which worsens patient prognosis. Thrombocytopenia was also significantly correlated with poor outcome in our patients; however, hemorrhagic complications were not identified as linked to mortality. In fact, in addition to acute hemorrhage, this hemostasis disorder could be the consequence of multi-organ failure or complicate the heparin use in these patients. Delayed Heparin-induced Thrombocytopenia (TTH) occurred in 1 to 5% of the patients treated with unfractioned heparin. The interpretation of the thrombocytopenia value as a prognosis factor in our patients should be taken with caution, as the exact cause of this disorder was not definitively established.

Role of the prevention
Prevention remains effective to reduce mortality attributable to pulmonary embolism, in critically ill patients. Several studies reported that pharmacological prevention is more effective than mechanical devices. Optimal delay for introducing this preventive measure remains a subject of debate. In fact, early administration of preventive anticoagulation may be complicated by hemorrhagic events that can be life-threatening, particularly in patients with head injuries. In a prospective study including 525 head trauma patients, enoxaparine was introduced 24 hours after ICU admission if the initial injuries did not worsen on a brain CT-scan. By applying this strategy, there was no pulmonary embolism reported and only six patients developed cranial hemorrhagic complications. Our study supports such a strategy, as 24% of our patients developed pulmonary embolism within the first five days following ICU admission. Further studies are needed to confirm the safety of this strategy.
Study limitations

The methodology used in our study, is usually used to study post-traumatic PE embolism. In fact it is not ethical to do a chest computed tomography (CT) scan without clinical suspicion of pulmonary embolism. However, there are some limitations to this study that need to be mentioned. In most of the remaining 1033 patients, PE was not suspected and we could not exclude that some patient had a PE. In fact, most of our patients were selected on the basis of a positive spiral CT result. Obviously this excluded those who did not have a CT performed in our ICU, because PE was not considered (biased against atypical cases). In fact, our study lacks systematic screening in clinically asymptomatic patients (false negative). Equally, false negative cases of PE and those who died from PE before a CT scan could be performed would have been excluded. Finally, to date, all studies of PE had some inherent bias in their selection of cases, often excluding atypical cases (not diagnosed as PE so not included in the studies) or massive PE where patients died quickly.

Conclusion

Pulmonary embolism is a thromboembolic event that can be life-threatening in trauma patients needing intensive care. Factors associated with poor prognosis in the ICU are the presence of circulatory failure (shock) and thrombocytopenia. Predictive factors of PE are: Age > 40 years, a SAPS II score > 25, hypoxemia with PaO\(_2\)/FiO\(_2\) < 200, the presence of a spine fracture and the presence of meningeal hemorrhage. Prevention is highly warranted.

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