Acute Pulmonary Embolism at Tanta University Hospital: Single Centre Registry

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Authors’ contributions

This work was carried out in collaboration among all authors. Author AREE designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors SFB, TMA and AFA managed the analyses of the study, managed the literature searches and revised the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background: Pulmonary embolism (PE) is a major cause of morbidity and mortality worldwide, and has significant negative impacts on quality of life, healthcare costs, and longevity. Registries have been created to record ‘real-life’ clinical features and management of patients with PE. 

Aim: We aimed to describe a comprehensive view of the clinical presentation, demographic data, treatment modalities and short-term outcome at hospital discharge and 3 months after discharge for patients presented with acute pulmonary embolism at Tanta university hospital to improve the level of care of those patients.

Methods: This study was conducted on 150 patients with confirmed acute PE presented to Tanta university hospitals. The study duration was 1 year from April 2019 to May 2020.

Results: We focused on a group of common risk factors for PE and determined prevalence of each in our enrolled patients, we found increase some risk factors obesity and bed rest > 3 days were the most prevalent risk factors followed by active cancer, estrogen use and lower limb fracture. Symptoms in this study are near to other registries and ESC guidelines 2019 with the commonest symptom was dyspnea and chest pain and the least symptom was hemoptysis. Certain ECG signs

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more prevalent in our patients and these signs related to RV strain with sinus tachycardia the commonest sign followed by S1Q3T3 sign and the least was right axis deviation.  

**Conclusion:** Presence of active cancer and patients with high risk stratification were independent predictors of mortality. Other factors associated with increased mortality were impaired RV systolic function, high PESI score, presence of RBBB in ECG and presence of congestive heart failure. Increased risk of bleeding in male patients with intermediate high or high risk category especially those received UFH and fibrinolytic therapy. Previous history of VTE was independent predictors of VTE recurrence.

**Keywords:** Acute Pulmonary Embolism.

**ABBREVIATIONS**

RV= Right Ventricle,  
RBBB= Right Bundle Branch Block,  
VTE= Venous Thromboembolism,  
CT= Computed Tomography,  
UFH= Unfractionated Heparin,  
LMWH= Low Molecular Weight Heparin,  
NOACs = New Oral Anticoagulants,  
OAT = Oral Anticoagulant Therapy  
PE = Pulmonary Embolism,  
ROC= Receiver Operating Characteristic,  
VKA= Vitamin K Antagonist.

**1. INTRODUCTION**

Acute pulmonary embolism is the most serious clinical presentation of venous thromboembolism, pulmonary embolus (PE) refers to obstruction of the pulmonary artery or one of its branches by material (e.g., thrombus, tumor, air, or fat) that originated elsewhere in the body [1].

It is one of the most common causes of sudden death overall, it is important to make studies about characteristics of patients presented with pulmonary embolism for early diagnosis and better treatment modalities. Diagnosis of pulmonary embolism is difficult that may be missed because of non-specific clinical presentation that may range from simple dyspnea up to sudden death. However, early diagnosis is fundamental, since immediate treatment is highly effective. Depending on the clinical presentation, initial therapy is primarily aimed either at life-saving restoration of flow through occluded pulmonary arteries (PA) or at the prevention of potentially fatal early recurrences. Both initial treatment and the long-term anticoagulation that is required for secondary prevention must be justified in each patient by the results of an appropriately validated diagnostic strategy [2].

PE represents a major and growing public health problem worldwide, since there are no enough data documenting the national impact of this disease in Egypt, the following figures are related to the United States and have been used as an example to reflect the serious impact of this problem on the health care of cardiac patient, the estimated incidence of diagnosed PE is 71 to 117 per 100,000 person-year, but the true incidence likely to be much more than this rate because studies showed that for every case of diagnosed, non-fatal PE, there are 2.5 cases of fatal PE diagnosed only after death, other studies have estimated that more than one million people in the United States are affected per year [3,4].

**1.1 Objectives**

We aimed to describe a comprehensive view of the clinical presentation, demographic data, treatment modalities and short-term outcome at hospital discharge and 3 months after discharge for patients presented with acute pulmonary embolism at Tanta university hospital to improve the level of care of those patients.

**2. PATIENTS AND METHODS**

**2.1 Study Design and Population**

This study was a prospective observational cohort registry including all consecutive patients with proven acute pulmonary embolism that were admitted at cardiology department of Tanta university hospital.

**2.2 Duration of the Study**

The study had been run for 12 months from April 2019 to May 2020, during which data collection and follow up have been done.
2.3 Inclusion Criteria

All patients with proven acute pulmonary embolism with symptoms suggestive of acute pulmonary embolism, positive D-dimer test and visualization of the pulmonary embolus by CT pulmonary angiography were included.

2.4 Exclusion Criteria

1. Patients with end stage kidney disease.
2. Patients with end stage liver disease.
3. Patients with chronic obstructive lung disease.
4. Patients with symptoms suggestive of pulmonary embolism and not confirmed with CT pulmonary angiography.

2.5 Statistical Analysis

Normally distributed scale variables were expressed as mean ± standard deviation. Non-normally distributed variables were expressed as median and range. Categorical variables were expressed in numbers and percentages. Analyses of categorical variables were performed by chi-square test. Parametric scale variables were analyzed by independent sample t test, and nonparametric scale variables were analyzed by Mann-Whitney U test. Multivariate logistic regression analyses were performed to determine the independent predictors of remodeling. No normality test was used as all patients were presented to our center during study period who met the inclusion criteria included in the study.

3. RESULTS AND DISCUSSION

3.1 Predisposing Factors of Acute Pulmonary Embolism (Table 1)

Thirty-nine patients (26.0%) have history of smoking, 23 patients (15.3%) had lower limb fracture, 28 patients (18.7%) were on oral contraceptive pills containing estrogen from reviewing of the drug history, 9 patients (6%) had thrombophilia based upon previous documented data or investigations that included anti thrombin III, protein C and S, lupus anticoagulant and factor V leiden, 14 patients (9%) had autoimmune diseases based upon previous documented data or investigations, 21 patients (14%) had previous VTE at any time during their life, 15 patients (10%) had history of abdominal or pelvic surgery within one month, 33 patients (22%) had active cancer on admission, 17 patients (11.3%) had congestive heart failure on patient words, other previous documented data and investigations as echocardiography showed impaired LV systolic function, 34 patients (22.7%) were obese after calculating their BMI which was >30 and 40 patients (26.7%) had a history of bed ridden within 3 days.

3.2 ECG findings on Admission (Table 2)

Ninety-eight patients (65.3%) had sinus tachycardia with heart rate >100 b.p.m, 37 patients (24.7%) had RBBB either complete or incomplete in their ECG, 15 patients (10.0%) had right axis deviation, 47 patients (31.3%) had evidence of S1Q3T3 in their ECG, 41 patients (27.3%) had T wave inversion from V1 to V4 in ECG and 10 patients (6.66%) had no from these signs in their ECG.

Univariate and multivariate analysis were performed to investigate the possible predictive factors affecting mortality.

In univariate analysis: (presence of active cancer, congestive heart failure, presence of RBBB in ECG, impaired RV systolic function, sPESI score 1 and patients with intermediate high and high risk stratifications) were correlated with increased mortality.

In multivariate analysis, using model adjusted for previously mentioned parameters, (presence of active cancer and patients with intermediate high and high risk category) independently predicting mortality.

As regard to sPESI score it was associated with increased mortality if the score was 1 in univariate analysis but couldn’t included in the multivariate analysis as there were no patients died had score.

Univariate and multivariate analysis were performed to investigate the possible predictive factors affecting occurrence of bleeding.

In univariate analysis: (male sex, impaired RV systolic function, intermediate-high, high risk patients, UFH and fibrinolytic therapy) were correlated with increased risk of bleeding.

In multivariate analysis, using model adjusted for previously mentioned parameters, (Male sex and fibrinolytic therapy) independently predicting occurrence of bleeding complications.
Table 1. Distribution of the studied cases according to predisposing factors of pulmonary embolism (n = 150)

<table>
<thead>
<tr>
<th>Predisposing factors of pulmonary embolism</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>39</td>
<td>26.0</td>
</tr>
<tr>
<td>Lower limb fracture</td>
<td>23</td>
<td>15.3</td>
</tr>
<tr>
<td>Estrogen use</td>
<td>28</td>
<td>18.7</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Autoimmune disease</td>
<td>28</td>
<td>18.7</td>
</tr>
<tr>
<td>Previous VTE</td>
<td>21</td>
<td>14</td>
</tr>
<tr>
<td>Abdominal and pelvic surgery within one month</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Active cancer</td>
<td>33</td>
<td>22</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>17</td>
<td>11.3</td>
</tr>
<tr>
<td>Obesity</td>
<td>34</td>
<td>22.7</td>
</tr>
<tr>
<td>Bed rest &gt; 3 days</td>
<td>40</td>
<td>26.7</td>
</tr>
</tbody>
</table>

Table 2. Distribution of the studied cases according to ECG findings (n = 150)

<table>
<thead>
<tr>
<th>ECG findings</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus tachycardia &gt;100</td>
<td>98</td>
<td>65.3</td>
</tr>
<tr>
<td>RBBB (right bundle branch block )</td>
<td>37</td>
<td>24.7</td>
</tr>
<tr>
<td>Right axis deviation</td>
<td>15</td>
<td>10.0</td>
</tr>
<tr>
<td>S1Q3T3</td>
<td>47</td>
<td>31.3</td>
</tr>
<tr>
<td>T wave inversion in V1-V3</td>
<td>41</td>
<td>27.3</td>
</tr>
<tr>
<td>No specific signs</td>
<td>10</td>
<td>6.66</td>
</tr>
</tbody>
</table>

4. DISCUSSION

The mean age of our patients was 51.92 ± 14.74, the relatively younger age of our patients confirmed when compared with the RIETE [5] registry which is a multicenter registry that was conducted on 23,858 patients in which the mean age was 67.3 ±17.0. Also the mean age of our patients was less than that in the study made by Garvey S et al [6], that was conducted on 1121 patients in which the mean age was 60.1 ± 16.7, also in the study made by Jiménez D et al, [7] that was conducted on 2096 patients the mean age was 68.7±16.6.

In this study female were more than males, 64% of patients are females and 36% are males. Similarly females were higher in RIETE registry [8], 46% males and 54% females.

In contrast the percentage of males was higher in the study made by Garvey S et al [6] 52% males and 48% females.

4.1 Risk factors of PE

4.1.1 As regard to active cancer

In our registry 22% of patients have history of active cancer, this was close to RIETE registry 8 that reported that 22.6 % patients have active cancer. In contrast to the Italian pulmonary Embolism Registry(IPER) [9] that was conducted on 1716 patients it had higher percentage of patients with cancer by about 26%.

The lower percentage of cancer may be because cancer underdiagnosed in Egypt or many cancer patients are accidentally diagnosed during work up.

As regard to estrogen use 18.7 % of patients were on medications containing estrogen on admission.

In contrast the percentage of patients using estrogen was less in IPER [9] (Italian pulmonary embolism registry) that was conducted on 1716 patients about 5% and also in EMPEROR study [10] that was conducted on 1880 patients the percentage was 5.7%

The higher percentage of estrogen use in this study may be due to high percentage of females.

In our study it represents 9% of patients. This was higher than that in the EMPEROR study [10] it was 4.2% of patients.

The increased percentage of autoimmune diseases in the study may be due to increase percentage of females and younger age group of patients and autoimmune diseases is more prevalent in middle aged females [11].
Table 3. Univariate and multivariate analysis for the death for total sample (n=150)

<table>
<thead>
<tr>
<th>Death</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
<td>OR (95%C.I)</td>
</tr>
<tr>
<td>Age (years) (&gt;50)</td>
<td>0.973</td>
<td>1.017 (0.379 – 2.728)</td>
</tr>
<tr>
<td>Male</td>
<td>0.370</td>
<td>1.545 (0.596 – 4.005)</td>
</tr>
<tr>
<td>Active cancer</td>
<td>&lt;0.001</td>
<td>24.889 (7.471 – 82.915)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>0.001</td>
<td>6.462 (2.103 – 19.857)</td>
</tr>
<tr>
<td>Obesity</td>
<td>0.163</td>
<td>0.340 (0.075 – 1.547)</td>
</tr>
<tr>
<td>Bed rest &gt; 3 days</td>
<td>0.472</td>
<td>0.653 (0.204 – 2.084)</td>
</tr>
<tr>
<td>Sinus tachycardia &gt;100</td>
<td>0.148</td>
<td>2.341 (0.740 – 7.410)</td>
</tr>
<tr>
<td>RBBB</td>
<td>0.002</td>
<td>4.889 (1.835 – 13.028)</td>
</tr>
<tr>
<td>Right axis deviation</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>S1Q3T3</td>
<td>0.103</td>
<td>0.345 (0.096 – 1.241)</td>
</tr>
<tr>
<td>T wave inversion in V1-V3</td>
<td>0.432</td>
<td>0.628 (0.197 – 2.004)</td>
</tr>
<tr>
<td>s PESI score (One or more)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Risk stratification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low/ Intermediate low</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Intermediate high/ High</td>
<td>&lt;0.001</td>
<td>9.681 (2.697 – 34.749)</td>
</tr>
<tr>
<td>Impaired RV systolic function</td>
<td>0.041</td>
<td>2.786 (1.042 – 7.449)</td>
</tr>
</tbody>
</table>

χ²: Chi square test  MC: Monte Carlo  FE: Fisher Exact  p: p value for association between different categories
*: Statistically significant at p ≤ 0.05
### Table 4. Univariate and multivariate analysis for the occurrence of bleeding (n=150)

<table>
<thead>
<tr>
<th>Occurrence of bleeding</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
<td>OR (95%C.I)</td>
</tr>
<tr>
<td>Age (years) (&gt;50)</td>
<td>0.554</td>
<td>0.757(0.300 – 1.908)</td>
</tr>
<tr>
<td>Male</td>
<td>0.027*</td>
<td>0.238(0.067 – 0.847)</td>
</tr>
<tr>
<td>Estrogen use</td>
<td>0.226</td>
<td>0.392(0.086 – 1.787)</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>0.513</td>
<td>1.729(0.335 – 8.921)</td>
</tr>
<tr>
<td>Autoimmune disease</td>
<td>0.651</td>
<td>0.700(0.149 – 3.282)</td>
</tr>
<tr>
<td>Previous VTE</td>
<td>0.534</td>
<td>1.417(0.473 – 4.248)</td>
</tr>
<tr>
<td>Abdominal and pelvic surgery within one month</td>
<td>0.103</td>
<td>2.602(0.824 – 8.219)</td>
</tr>
<tr>
<td>Active cancer</td>
<td>0.994</td>
<td>1.004(0.341 – 2.955)</td>
</tr>
<tr>
<td>Obesity</td>
<td>0.103</td>
<td>2.242(0.850 – 5.911)</td>
</tr>
<tr>
<td>Bed rest &gt; 3 days</td>
<td>0.335</td>
<td>0.568(0.180 – 1.793)</td>
</tr>
<tr>
<td>Impaired RV systolic function</td>
<td>&lt;0.001*</td>
<td>7.755(2.477 – 24.285)</td>
</tr>
<tr>
<td>s PESI score (One or more)</td>
<td>0.094</td>
<td>3.617 (0.803 – 16.300)</td>
</tr>
<tr>
<td>Risk stratification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low/ Intermediate low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate high/ High</td>
<td>&lt;0.001*</td>
<td>18.444 (4.123 – 82.509)</td>
</tr>
<tr>
<td>Starting anticoagulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UFH</td>
<td>0.010</td>
<td>7.092 (1.583 – 31.777)</td>
</tr>
<tr>
<td>LMWH</td>
<td>0.078</td>
<td>0.257 (0.057 – 1.162)</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>0.999</td>
<td>–</td>
</tr>
<tr>
<td>NOACs</td>
<td>0.999</td>
<td>–</td>
</tr>
<tr>
<td>Thrombolytic therapy</td>
<td>&lt;0.001*</td>
<td>51.571 (13.528 – 196.598)</td>
</tr>
<tr>
<td>Long term anticoagulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>0.078</td>
<td>2.625 (0.897 – 7.682)</td>
</tr>
<tr>
<td>NOAC</td>
<td>0.194</td>
<td>0.464 (0.146 – 1.478)</td>
</tr>
<tr>
<td>LMWH</td>
<td>0.387</td>
<td>0.398 (0.049 – 3.211)</td>
</tr>
</tbody>
</table>

* Chi square test MC: Monte Carlo FE: Fisher Exact p: p value for association between different categories
* *: Statistically significant at p ≤ 0.05
4.1.2 As regard to autoimmune diseases

4.1.3 Previous history of VTE

In our study 14% of patients had previous history of VTE at any time throughout life. Similarly it was 12.3% in EMPEROR study [10].

In contrast it was higher in the study made by Chuang LH, [12] et al that was conducted on 1399 patients about 20.2% of patients had previous history of VTE.

4.1.4 Abdominal and pelvic surgery

In this study 10% of patients had history of abdominal and pelvic surgery within one month, similarly in COMMAND VTE Registry [13] it was 9.4%.

In contrast it was higher in the IPER study [10] about 15% of patients had abdominal or pelvic surgery within one month.

4.1.4.1 Obesity BMI > 30

In this study 22.7% of patients who had BMI >30 kg-m2 while it was higher in the EMPEROR study [10] it was 26.9%.

In contrast it was less in the study made by Chuang LH [12], about 6% of patients had BMI >30kg-m2.

4.1.4.2 Immobility > 3 days

26.7% of patients in this study had history of decrease activity and bed rest > 3 days, similarly in the IPER study [9] it was near to our result by about 27% of patients.

In contrast in the study that made by Chuang LH, et al. [12] 11.2 % of patients had bed rest > 3 days.

The increased percentage in our study may be due to decrease awareness of the care of the bed ridden patients.

4.2 Thrombophilia

In this study 9% of patients had thrombophilia.

In contrast it was 3.9% in RIETE registry [8] and in the study made by Chuang LH, et al [12] it was about 5.1%.

In our study ECG findings were:

a) Sinus tachycardia with heart rate > 100 b.p.m in 65.3% of patients
b) RBBB either complete or incomplete in 24.7%
c) S1Q3T3 in 31.3% of patients
d) T wave inversion from v1 to v4 in 27.3% of patients
e) Right axis deviation in 10.0% of patients

In meta-analysis of Shopp JD, et al [14] that made by reviewing 45 studies on 8209 patients that

a) Sinus tachycardia in (38%) of patients.
b) S1Q3T3 in 24 % of patients
c) T wave inversion in leads v1 to v4 in 29 % of patients
d) RBBB either complete or incomplete in 24 % of patients

e) Right axis deviation in 10.6 of patients

These ECG signs are the most prevalent as they are indication of RV strain in ECG. Still sinus tachycardia is the commonest sign in ECG of a patient with acute PE.

4.3 Mortality

In our study, in hospital death was 8.7% and death after 3 months was 6.2% of patients. In the study made by Holder et al [16] that was conducted on 829 patients in-hospital mortality rate was 3.7% of patients.

In RIETE registry [8], in hospital mortality rate was 1.8 % and 30-day mortality of 5.9%.

In COMMAND VTE [17] registry in-hospital death occurred in 4.4% of patients and 30-day mortality 5.4% of patients.

The increased rate of mortality in our may be due to increased percentage of patients with active cancer, intermediate-high and high risk category patients as these are associated risk factors for mortality.

Also the small number of patients in our study in compare to other large studies.
4.3.1 Predictors of mortality

In this study we found in univariate analysis that (presence of active cancer, congestive heart failure, presence of RBBB in ECG, impaired RV systolic function, sPESI score 1 and patients with intermediate high and high risk stratifications) were correlated with increased mortality.

while in multivariate analysis, (presence of active cancer and patients with intermediate high and high risk category) were independently predicting mortality.

In RIETE registry [5] (increasing age, active cancer, immobilization, obesity and high PESI score) are factors associated with increasing mortality.

In the study made by Chuang et al [13] it showed also increasing age, obesity, active cancer, and high sPESI associated with increased mortality.

In the meta-analysis made by Zhou et al [18], that showed that PESI has discriminative power to predict the short-term death and in patients with acute pulmonary embolism, the PESI and the sPESI have similar accuracy.

Patients with co-morbid disease as active cancer and congestive heart failure have increased risk of mortality from their co-morbid diseases and also this make them more liable to fatal complications from PE due to their bad general condition.

Also it is important to assess RV systolic function by echo and risk stratification of patients as these can predict patients at increased risk of mortality.

4.3.2 Bleeding complications

In our study bleeding complications occurred in 7.3% of patients in-hospital and 8.4% in follow up. In the in RIETE registry [5] the 30-day bleeding occurred in 3.2%, while it was 12.8% of patients in the COMMAND VTE [17].

In univariate analysis we found that male sex, impaired RV systolic function, intermediate-high, high risk patients, UFH and fibrinolytic therapy are associated with increased risk of bleeding. Patients received UFH may had increased risk of bleeding due to difficulty in adjusting aPTT and complications from UFH as HIT (heparin induced thrombocytopenia).

Fibrinolytic therapy increase risk of bleeding and this consistent with the meta-analysis that made by Bundhun et al. [19] that showed increased risk of bleeding in patients received fibrinolytic.

Patients with RV systolic function, intermediate high and high risk category usually received UFH and may receive fibrinolytic if become hemodynamically unstable so more liable to bleeding complications.

5. CONCLUSION

1. We found that presence of active cancer and patients with high risk stratification were independent predictors of mortality. Other factors associated with increased mortality were impaired RV systolic function, high PESI score, presence of RBBB in ECG, and presence of congestive heart failure.

2. We found increased risk of bleeding in male patients with intermediate high or high risk category especially those received UFH and fibrinolytic therapy.

3. We also found that previous history of VTE was independent predictors of VTE recurrence.

CONSENT AND ETHICS APPROVAL

This study was approved by the local ethics committee of faculty of medicine Tanta university, Egypt. Written informed consent was obtained from all patients in this study.

AVAILABILITY OF DATA AND MARTHAL

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

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COMPETING INTERESTS

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REFERENCES


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