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Shahid Javed Husain  
*Aga Khan University*

Ali Bin Sarwar Zubairi  
*Aga Khan University*

Kulsoom Fatima  
*Aga Khan University*

Muhammad Irfan  
*Aga Khan University*

Muhammad Atif  
*Aga Khan University*

*See next page for additional authors*

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**Authors**

Shahid Javed Husain, Ali Bin Sarwar Zubairi, Kulsoom Fatima, Muhammad Irfan, Muhammad Atif, and Muhammad Ammad Saeed

## **Clinical characteristics, Management and Outcome of Major Pulmonary Embolism: an experience from a tertiary care center in Pakistan**

Shahid Javed Husain,<sup>1</sup> Ali Bin Sarwar Zubairi,<sup>2</sup> Kulsoom Fatima,<sup>3</sup> Muhammad Irfan,<sup>4</sup>  
Muhammad Atif,<sup>5</sup> Muhammad Ammad Saeed<sup>6</sup>

Pulmonary & Critical Care, Department of Medicine,<sup>1,2,4</sup> Department of Radiology,<sup>3</sup> Department of Medicine,<sup>5,6</sup>  
The Aga Khan University Hospital, Karachi, Pakistan.

### **Abstract**

**Objective:** To evaluate the clinical characteristics, risk factors, management and outcome of major pulmonary embolism (PE) in a tertiary care center of Karachi.

**Methods:** Medical records of all patients who underwent a spiral CT scan of the chest for suspected pulmonary embolism were reviewed between January 2000 and June 2007 at the Aga Khan University Hospital, Karachi. Patients having evidence of major pulmonary embolism on spiral CT scan were selected.

**Results:** A total of 30 patients (10 males, 20 females) with mean age  $52 \pm 14.59$  years were identified who fulfilled our predefined criteria for major pulmonary embolism. Risk factors for thromboembolism were identified in 22 (73%) patients, prolonged immobilization in 8 (27%) and recent surgery in 8 (27%) patients being the commonest. All patients were symptomatic on presentation. Tachypnea and tachycardia were present in 27 (90%) patients. Refractory hypoxia was present in 18 (60%) patients and 3 (10%) were hypotensive on presentation. On spiral CT scan, 8 (27%) patients had embolus in the main pulmonary trunk, 26 (87%) patients in main right pulmonary artery and 20 (67%) patients had left main pulmonary artery embolus. Echocardiography was done in 22 (73%) patients with the findings of right ventricular dysfunction in all of them. All patients except one were treated with anticoagulation with either heparin infusion or low molecular weight heparin. In addition, thrombolytics were given in 7 (23%) patients and five (17%) underwent surgical embolectomy. Four (13%) patients died during hospitalization with a total of 26 (87%) surviving till hospital discharge.

**Conclusion:** Major pulmonary embolism is an uncommon but potentially life threatening entity. Early diagnosis and aggressive therapy improves the clinical outcome (JPMA 59:372; 2009).

### **Introduction**

Despite advances in prophylaxis, diagnostic modalities, and therapeutic options, pulmonary embolism (PE) remains a commonly underdiagnosed and potentially lethal entity. Studies have estimated an annual incidence of over 600,000 cases of PE in the US with a related mortality of almost 200,000 deaths.<sup>1</sup> According to various autopsy series, the ante mortem diagnosis of pulmonary embolism (made in only 30% of cases) and the PE related mortality either directly or indirectly has not improved over the last four decades.<sup>2,3</sup> PE related mortality ranges from 4.1% in haemodynamically stable patients to 31% for those patients presenting with massive pulmonary embolism.<sup>4</sup>

Major pulmonary embolism (MPE) is defined as an embolus on spiral CT scan involving either the main pulmonary trunk or the ascending or descending branches of right and left pulmonary arteries or both along with either hypotension due to the embolus (massive PE) or evidence of right ventricular dysfunction on echocardiography without hypotension (sub massive PE).<sup>5</sup>

Pulmonary embolism in Pakistan remains largely

unrecognized, underdiagnosed and undertreated clinical problem amongst hospitalized patients due to non-availability of objective tests and lack of awareness among physicians. There are very few reports available from Pakistan on pulmonary embolism and in fact there is no data on major pulmonary embolism.

We conducted this study to evaluate the clinical features, management strategies and outcome of major pulmonary embolism (MPE) in a tertiary care center of Karachi.

### **Material and Methods**

A retrospective chart review of all hospitalized patients who had a spiral CT of the chest done for suspected pulmonary embolism between January 2000 and June 2007 at Aga Khan University Hospital was done using a computerized database.

Patients who fulfilled the criteria of major pulmonary embolism anatomically ie pulmonary emboli in the main pulmonary trunk or the ascending or descending branches of main pulmonary arteries with or without hypotension were selected. All others were excluded from our study.

Data on demographics, clinical features, radiographs, echocardiography, management and outcome was collected.

The Statistical package for social science SPSS version 11 was used for data analysis. The descriptive analysis was done for demographic, clinical, radiographic features and laboratory results. Results were expressed as mean  $\pm$  standard deviation, and number (percentage).

## Results

A total of 30 patients were identified over the study period that met our predefined criteria of major pulmonary embolism. The mean age was  $52 \pm 14.59$  years (range 23-75 years). Risk factors for thromboembolism were identified in 22 patients (73%), immobilization and recent surgery as the commonest recognized factors. Other important risk factors included previous history of Deep Vein Trocombosis (DVT), trauma and hypercoagulable state. Details of the demographics and risk factors are presented in Table.

**Table: Demographics and risk factors of massive PE patients.**

Demographics	Number (%)
Total no. of patients	30
<b>Sex:</b>	
Male	10 (33%)
Female	20 (67%)
<b>Age:</b>	
Mean (Range) years	52 (23-75)
<b>Risk factors:</b>	
Prolonged bed rest / immobilization	22 (73 %)
Recent surgery (past 3 months)	08 (27 %)
Trauma	08 (27 %)
Previous DVT	04 (13 %)
Hyper coagulable state	07 (23 %)
Malignancy	06 (20 %)

All patients were symptomatic, with dyspnoea and tachycardia present in 27 (90%), 9 (30%) presented with chest pain and 2 (7%) with haemoptysis. Twenty patients (67%) were hypoxic and 3 (10%) were hypotensive on presentation.

Arterial blood gases (ABG) were done in 27 patients (90%). Respiratory alkalosis (pH  $>7.45$ , PaCO<sub>2</sub>  $< 35$  mmHg) was the commonest finding, present in 26 patients (86%). Refractory hypoxia was present in 18 (60%) patients. D-dimer assay was tested in 17 (57%) patients, being positive (value  $> 0.5$ ) in 9 patients (30%) only.

The chest radiograph was abnormal in 20 (67%) patients with cardiomegaly as the commonest finding (33%, 10 patients). Other features included pleural effusion in 9 (30%), atelectasis in 8(27%), enlarged pulmonary artery in 7 (23%), focal oligoemia in 6 (20%) and elevated hemi diaphragm in 4 (13%).

All patients underwent spiral CT chest. The embolus was visualized in the main pulmonary trunk in 8 (27%) patients, in the proximal right pulmonary artery in 26 (87%) patients and in the left pulmonary artery in 20 (67%) patients. Four (13%) patients were noted to have pulmonary infarction and 10 (33%) patients showed concomitant thrombus in the deep veins of the extremities.

Echocardiography was done in 22 (73%) patients with evidence of right ventricular dysfunction in all of them. Right ventricular (RV) hypokinesis was present in 16 (72%) patients, right ventricular dilatation in 16 (72%) patients, tricuspid regurgitation in 18 (82%) patients, severe pulmonary hypertension in 10 (46%) patients and paradoxical interventricular septal shift in 6 (27%) patients.

All patients except one (95%) received anticoagulation with either intravenous heparin or subcutaneous low molecular weight heparin (LMWH, Enoxaparin). In addition intravenous thrombolytics (streptokinase) were given in 7 (23%) patients, five (17%) patients underwent surgical embolectomy and five (17%) patients had inferior vena cava filter placement. Three (10%) patients required mechanical ventilation for respiratory failure.

Four (13%) patients died due to refractory shock and hypoxia. One patient had arrived in the ER with severe shock and hypoxia and received intravenous streptokinase but did not survive; in the other three patients only subcutaneous low molecular weight heparin was used. Twenty six (87%) patients survived and were discharge from the hospital.

## Discussion

Traditionally major pulmonary embolism has been defined on anatomical grounds, as a greater than 50% obstruction of the pulmonary vasculature or the occlusion of two or more lobar pulmonary arteries. However, recently the term "massive PE" is being used based not only on the size of the embolus but also on the underlying cardio-respiratory status, such that the net effect results in haemodynamic instability.<sup>6,7</sup>

In our group we included all patients who had anatomically major PE even in the absence of hypotension on presentation. The group of patients with haemodynamically stable PE along with evidence of right ventricular dysfunction on 2D echocardiography has shown in numerous studies to have a much higher mortality compared to those without it.<sup>7</sup> A term of "submassive PE" has been coined to categorize this group. These patients require closer and more aggressive management due to high potential for deterioration and subsequent poorer outcome.<sup>7</sup> Our cohort included only three patients with hypotension on presentation (massive PE), the rest (90%) were haemodynamically stable (submassive PE). Also, in our cohort the commonest clinical presentation was of

dyspnea, tachycardia (90% each) and chest pain (28%) which is consistent with other studies.<sup>8</sup>

Despite the vast array of physiological abnormalities associated with PE, hypoxia is not a uniform finding.<sup>9,10</sup> In our study hypoxia was documented in 71% of patients only. Part of the reason could be that most patients who present with breathlessness and tachycardia are generally placed on supplemental oxygen before checking their pulse oximetry or arterial blood gases.

On ABG analysis 86% of patients had respiratory alkalosis (pH >7.45 & PaCO<sub>2</sub><35 mmHg) which is due to the tachypnea resulting from the sudden occlusion of the pulmonary arterioles by the thromboembolism.<sup>11</sup>

Spiral CT scan of chest has been considered a very good diagnostic tool due to its availability, noninvasiveness, rapidity and accurate results. Some studies have shown sensitivity and specificity in excess of 90% for proximal PE.<sup>12-14</sup> This has replaced ventilation perfusion scan due to its better sensitivity and specificity and also because it can give evidence of an alternate diagnosis if present. Studies have also suggested that this modality should replace pulmonary angiogram as a gold standard for the diagnosis of PE, particularly due to the invasiveness and the morbidity of the latter.<sup>15</sup> However, a word of caution; spiral CT can miss significant number of smaller peripheral emboli. In our institution the spiral CT has replaced the pulmonary angiogram as the diagnostic procedure of choice for PE.

Transthoracic echocardiography is of tremendous value in the setting of major pulmonary emboli, due to its ability to diagnose the severity and impact of the embolism and response to therapy.<sup>16</sup> In addition it is widely available, reproducible, and non-invasive. It also may detect emboli in transit or suggest alternative diagnosis. Echocardiographic findings in patients with MPE are signs of right ventricular pressure overload which include right ventricular dilatation, pulmonary artery dilatation paradoxical septal motion, right ventricular hypokinesis and tricuspid regurgitation.<sup>17</sup> Of our patients 73% had echocardiography done and all of them had signs of right ventricular dysfunction (100% sensitivity).

Anticoagulation with heparin should be initiated in the absence of contraindication, once the diagnosis of PE is considered. Early and adequate anticoagulation has shown to decrease mortality.<sup>18</sup> Subcutaneous low molecular weight heparin can be used as an alternative to intravenous heparin, however the experience is limited in the setting of massive PE.

Thrombolytic therapy for MPE has been studied extensively. When assessed by angiography, perfusion scans and echocardiography; thrombolytics have shown to produce more rapid clot lysis as compared to heparin therapy alone.<sup>19,20</sup> This however, has not shown to

significantly alter the outcome of such patients. Thrombolytic therapy is uniformly acknowledged as the treatment of choice for haemodynamically unstable patients. In case of submassive PE the data is less clear. Recently, two studies of submassive pulmonary embolism have shown a mortality advantage and reduced incidence of recurrent venous thromboembolism with intravenous thrombolytics.<sup>21,22</sup> Among the seven patients that received thrombolytics in our cohort, only one patient died and there were no bleeding complications.

Surgical embolectomy is generally reserved for patients with refractory shock despite aggressive medical therapy, ongoing cardiac arrest, or patients with contraindications to thrombolytics.<sup>23-25</sup> Recently a single center experience with massive PE without shock had a 86% survival at one year.<sup>25</sup> All five of our patients who underwent surgical embolectomy survived till discharge. Catheter thrombectomy is especially useful in the presence of an increased bleeding risk or if surgical embolectomy is not an option.

New catheter devices have broadened the role of this approach in the management of major pulmonary embolism.<sup>26-28</sup>

In our cohort all patients were started on treatment once the diagnosis was suspected. Anticoagulation was initiated on 95% of our patients with either heparin infusion or low molecular weight heparin. Five (17%) of our patients underwent surgical embolectomy and seven (23%) received intravenous thrombolytics. The indications for intravenous thrombolytics and surgical embolectomy included shock and refractory hypoxia.

Four patients (13%) died due to refractory shock and hypoxia. One patient had arrived in the ER with shock and received thrombolytics in the ER but did not improve; in the other two patients only subcutaneous low molecular heparin was used. In all 26 (87%) patients survived to discharge from the hospital. Our cohort had only confirmed cases of large pulmonary emboli, based on spiral CT findings. This is probably why mortality in our cohort is very low. We may have missed cases that were not diagnosed antemortem.

In our institution we follow an algorithm for major PE, which includes an urgent bedside echocardiogram and a spiral CT scan. A pulmonary angiogram is very rarely required. Anticoagulation is initiated as soon as PE is clinically suspected if there is no contraindication to it. Thrombolytics and surgical embolectomy are considered in patients presenting with shock and in those with refractory hypoxia.

The limitations of the study were the retrospective charts review so the complete data of all patients were not available. The rationale for giving thrombolytics was not uniform and was dependent on physician discretion.

## Conclusion

In conclusion, we need to maintain a high degree of clinical suspicion for major pulmonary embolism in patients presenting with shock and/or refractory hypoxia or unexplained tachypnea and tachycardia. 2D echocardiography is a good tool which assists in the diagnosis of major pulmonary embolism with an excellent sensitivity. Once diagnosed, early and aggressive management can result in good survival.

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