Acute Pulmonary Embolism: Situational Analysis at a Single Tertiary Hospital

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Abstract

Objectives: Pulmonary embolism-PE is a type of venous thromboembolism-VTE, which is globally considered the third most common acute cardiovascular disease that causes hospital admission and death after acute myocardial infarction and stroke. In Oman, PE is increasingly becoming a major issue among our patients especially in those who have various medical conditions in addition to the sedentary lifestyle which renders them susceptible to various risks for PE.

Methods: This is a cross-sectional Situational analysis study of all patients with computed tomography pulmonary angiogram-CTPA proven with PE that was approved by the local ethics committee. All data related to acute PE cases from 2010 to 2021, were collected from an electronic medical system called "Al Shifaa".

Results: Patients who presented with PE were young and overweight, but males were noted to be older compared to females who had a higher Body mass index-BMI. Surgery was the commonest risk factor reported in our study. However, two-thirds of the patients who were presented with PE had hypertension and one-third had diabetes mellites. Most PE patients presented with dyspnea and chest pain. However, syncope was more common in females compared to males who mostly presented with hemoptysis. In addition to CTPA, an echocardiogram was included as one of the investigations to diagnose PE. Almost half of the patients had abnormal ECHO with significant gender differences in ejection fraction where males had a lower ejection fraction compared to females. Different modalities of management are used to treat PE such as Heparin which is the most used anticoagulant followed by warfarin and then Direct oral anticoagulants-DOACs. The total number of deaths in our study is 122, of which 68 of these patients had PE as the cause of their death and high mortality in males than in females.

Conclusions: The incidence of acute PE is similar among females and males. However, there were gender differences in risk factors, symptoms, investigations, and management of PE. Females presented with more severe PE as higher numbers were found to receive thrombolysis compared to males. In addition, mortality was higher in males than in females.

Keywords: Acute Pulmonary Embolism; Computed Tomography Pulmonary Angiogram-CTPA; Gender; Hypertension; Diabetes; Obesity.

Introduction

Pulmonary embolism (PE) is the third most common acute cardiovascular disease that can lead to death after myocardial infarctions and Stroke.[1] Epidemiological studies reported that the incidence rate per year of PE is from 39 to 115 per 100 000 population.[2] PE is one of the most important causes of death in the United States (US) as it can lead to almost 300000 deaths per year.[2] However, studies showed a decrease in acute PE fatality rates in Asia, North American, and European populations.[2]

Both genetic and environmental factors can participate in the development of PE.[3] The risk factors for PE include a hypercoagulable state where there is a stasis of blood such as in pregnancy, surgery, immobilization, traveling, and malignancy.[3] PE might be asymptomatic and is discovered incidentally during investigations for another disease.[4] On the other hand, patients can present with symptoms and signs that are vague and non-specific.[5]

Toll-like receptors, mainly Toll-like receptors 2 and 4 (TLR2 and TLR4), play an important role in the host defense mechanism against different microorganisms.[6] The expression of TLR2, TLR4, and Interleukin 1 beta (IL 1β) was increased in patients with PE.[7] Other interleukins such as Interleukin 10 (IL-10) are considered an immune-regulatory cytokines having an anti-tumor effect.[8] The level of IL-10 is significantly raised in massive PE in comparison to patients with low-risk and sub-massive disease, reflecting the inflammatory response with larger embolism.[9] Circulating Vascular Cell Adhesion Molecule-1 (sVCAM-1) is a cytokine-inducible endothelial cell adhesion molecule (CAM).[10] Also, sVCAM-1 is a platelet activation marker that is significantly increased in patients with pulmonary embolism.[11] Immune thrombocytopenia (ITP) is one of the autoimmune diseases where patients present with an increased risk of bleeding and thrombocytopenia.[12] Heavy use of glucocorticoids in patients with ITP can result in a hypercoagulable state complicated with PE which is not always clinically easy to prevent or detect, and it can even be missed.[13]

Upon clinical suspicion of PE, diagnosis starts with the clinical evaluation and laboratory markers such as D-dimer which has a highly sensitive assay. In a high-risk PE with a hemodynamically unstable patient, an echocardiogram (ECHO) at the bedside or an emergency Computed tomography pulmonary angiogram (CTPA) is recommended.[14] Other investigations that can be used are V/Q scintigraphy, and Lower-limb ultrasound, which is used to rule out deep vein thrombus (DVT) in patients who are suspected to have PE. Other imaging modalities such as chest X-ray findings are not specific to PE; but can be used to exclude other causes for dyspnea and chest pain.[15] Electrocardiographic (ECG) findings such as S1Q3T3 can indicate right ventricle (RV) strain that may be found in severe PE.[16] However, in less severe cases, ECG might only show sinus tachycardia.

Acute PE, especially high-risk PE, is usually managed with anticoagulation and thrombolytic therapy. An example of anticoagulation medications is heparins (low molecular weight heparin or unfractionated), Direct oral anticoagulants (DOACs), or vitamin K antagonists such as Warfarin. Another way to manage patients who have absolute contraindications to systemic anticoagulation; is the insertion of an inferior vena cava filter (IVC) filter.

There is one study that was done in 2016 in Oman and published by Oman Medical Journal (OMJ) that looked into the Usefulness of Clinical Prediction Rules (CPR), D-dimer, and Arterial Blood Gas Analysis to Predict Pulmonary Embolism in Cancer Patients.[17] The study found that all three CPRs can be used to help exclude PE in patients with malignancy. However, the study did not look into other diagnostic parameters that are used in diagnosing PE. Another study was done in Oman in 2021 that investigated Predicting risk factors for thromboembolic complications in patients with sickle cell anemia (SCA).[18] This study reported that PE in patients with SCA has a high impact on morbidity and mortality. However, no study has evaluated the clinical situation and adherence to guidelines for PE management. Other predictors such as higher mean-platelet volume are associated with an immediate diagnosis of acute PE[19] and it can as well predict serious infections such as spontaneous bacterial peritonitis, which is a major cause of mortality in patients with liver cirrhosis.[20]

This situational analysis will help us to provide a proper view of the predisposing factors, diagnostic issues, and adherence to the UpToDate management strategies.

Methods

This is a cross-sectional Situational analysis study that was approved by the Ministry of Health ethical committee with the serial number SRC#94/2021. All data related to acute pulmonary embolism cases were collected from a medical record system where data was computerized and received a well-recognized international certificate of excellence for the electronic medical system called "Al Shifaa".

We reviewed all patients, who were diagnosed with acute pulmonary embolism during the study period from 2010 and 2021 based on the following criteria:

- Confirmed on CTPA, as shown in Figure 1 A-D
- Omani
- Adult > 13 years
- From Jan 2010 to December 2021

All cases without available CTPA were excluded.

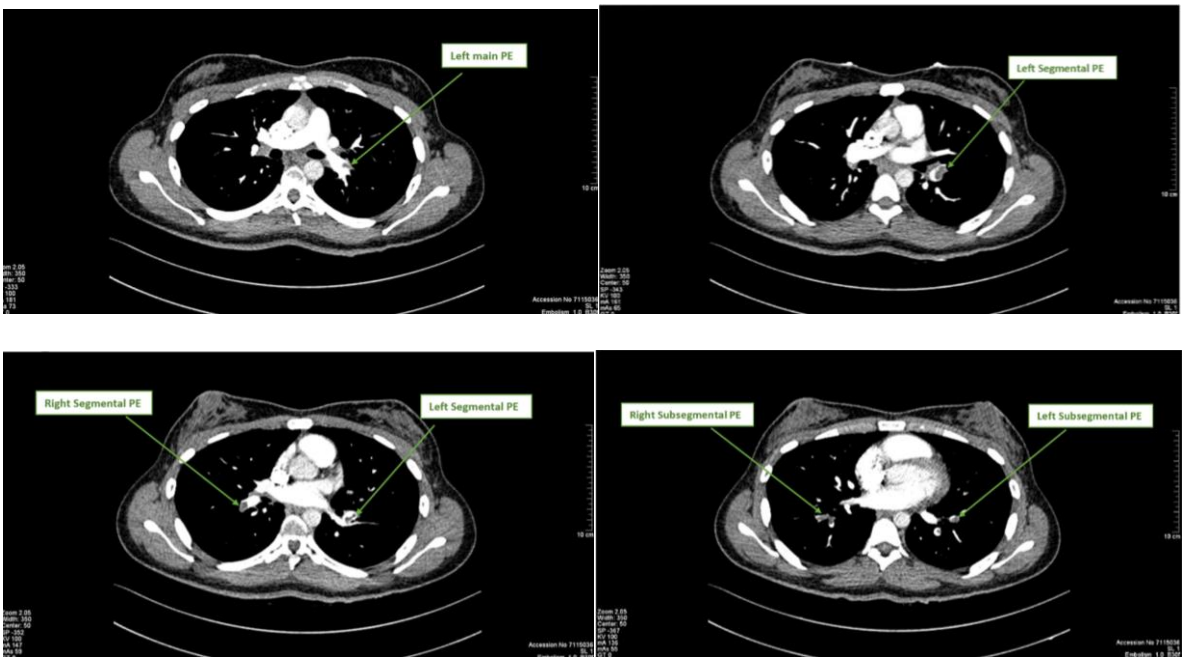

Figure 1: A-D shows the computed tomography pulmonary angiogram.

The following clinical and laboratory data were retrieved including the patient's demographic data, risk factors for PE, history of chronic conditions, symptoms of PE on presentation, laboratory parameters, radiographic data including ultrasound (US) and chest X-ray (CXR,) different management of PE and finally mortality associated with PE.

Comparative observational statistics are used to present the percentage of people with clinical data, laboratory parameters, and various comorbidities and outcomes. Data were described as frequencies and percentages of categorical variables. Continuous variables were reported as median and ranges or as mean and standard deviation. Univariate comparisons between various lab findings were calculated using independent samples median tests. The data entry was rechecked by 2 researchers. All statistical calculations were performed using the STATA 16 software (version 16.0, STATA Inc, Chicago, Illinois, USA).

Results

During the study, 438 patients were proven to have PE on CTPA and were included in the analysis. Males represented 223 (50.9%) of the study population. Of all patients, 278 (63.5%) were from the Muscat governate and-the rest were from outside the capital area. The mean (SD) age of the patients was 53.35 (18.5); Males have a mean (SD) of 55.05 (18.5) compared to females who have a mean (SD) of 51.6 (18.4) years, P= 0.048, as shown in table1. Body mass index (BMI) mean (SD) was 29.7 (7.36); Females with a mean (SD) of 30.93 (8.02) compared to males' means (SD) of 28.45 (6.37), P= 0.0056, as shown in **Table 2.**

Table 1: Shows the various demography (with gender differences) of 438 patients with pulmonary embolism.

	All patients	Female	Male	P
Patients Number (%)	438 (100%)	215 (49.1%)	223 (50.9%)	
Age in years, Mean (SD)	53.35 (18.5)	51.57 (18.38)	55.05 (18.53)	0.0488
Muscat Region, Number (%)	278 (63.5%)	140 (31.96%)	138 (31.5%)	0.482

Table 2: Shows the clinical risk factors (with gender differences) of 438 patients with pulmonary embolism.

	All patients	Female	Male	P
Number (%)	438 (100%)	215 (49.1%)	223 (50.9%)	
BMI, Mean (SD)	29.73 (7.36)	30.93 (8.02)	28.45 (6.37)	0.0056
Pregnancy, Number (%)	21 (4.79%)	21 (4.79%)		
Malignancy, Number (%)	73 (16.67%)	42 (9.6%)	31 (7%)	0.114
Trauma, Number (%)	24 (5.48%)	11 (2.5%)	13 (3%)	0.743
Surgery, Number (%)	109 (24.89%)	58 (13.2%)	51 (11.6%)	0.320
Bed bound, Number (%)	49 (11.19%)	23 (5.25%)	26 (5.9%)	0.750
Travel, Number (%)	33 (7.5%)	12 (2.7%)	21 (4.79%)	0.128
Smoking, Number (%)	29 (6.6%)	1 (0.22%)	28 (6.39%)	0.0001
Family history, Number (%)	5 (1.1%)	1 (0.22%)	4 (0.9%)	0.191
SCD, Number (%)	16 (3.6%)	10 (2.28%)	6 (1.36%)	0.457
DVT, Number (%)	72 (16.4%)	33 (7.5%)	39 (8.9%)	0.546
COVID, Number (%)	48 (10.9%)	19 (4.3%)	29 (6.6%)	0.163
DM, Number (%)	97 (22.1%)	45 (10.27%)	52 (11.87%)	0.547
HTN, Number (%)	152 (34.7%)	72 (16.4%)	80 (18.26%)	0.600
CLD, Number (%)	39 (8.9%)	24 (5.47%)	15 (3.4%)	0.103
CLiD, Number (%)	9 (2.05%)	1 (0.22%)	8 (1.8%)	0.021
No CKD, Number (%)	391 (89.26%)	196 (44.75%)	195 (44.52%)	
CKD 1, Number (%)	2 (0.46%)	2 (0.46%)	0 (0%)	0.035
CKD 2, Number (%)	1 (0.23%)	1 (0.22%)	0 (0%)	0.035
CKD 3, Number (%)	6 (1.37%)	0 (0%)	6 (1.37%)	0.035
CKD 4, Number (%)	3 (0.69%)	0 (0%)	3 (0.69%)	0.035
CKD 5 , Number (%)	34 (7.7%)	15 (3.4%)	19 (4.3%)	0.035

BMI: body mass index, SCD: Sickle cell disease, DVT: Deep vein thrombus, DM: Diabetes mellites, HTN: hypertension, CLD: Chronic lung disease, CLiD: Chronic liver disease, and CKD: chronic kidney disease.

Of 215 females that were included in the study, 21 (4.79%) females reported pregnancy at the time of the presentation. Malignancy was found in 73 (16.67%) of all patients; 42 of these patients were females and 31 were males. The number (%) of patients who presented with trauma was 24 (5.48%); the number of females was 11 compared to males who were 13. Surgery was reported in 109 (24.89%) of all patients; 58 were females and 51 were males. Only 49 (11.19%) who had PE were bedbound, with not much gender difference. The number (%) of patients who had a travel history was 33 (7.5%); males presented 21 of the total number compared to females which were 12 with no statistical significance. Smoking was reported in 29 (6.6%); 28 of them were males and only 1 female, P= 0.0001. Family history of PE was only found in 5 (1.1%) patients, as shown in **Table 2.**

The total number (%) of patients who had hypertension (HTN) and diabetes mellites (DM) was 152 (34.7%) and 97 (22.1%) respectively. The number of males who had HTN and DM was 80 and 52 respectively. The number of females who had HTN and DM was 72 and 45 respectively. DVT was reported in 72 (16.4%) of patients; 39 were males and 33 were females. The total number of patients who had coronavirus disease of 2019 (COVID-19) was 48 (10.9%); 29 of them were males and 19 were females. Chronic lung disease was found in 39 (8.9%); of these 24 were females and 15 were males. Only 16 (3.6%) sickle cell disease patients were presented with PE with no statically significant gender difference, as shown in Table 2.

As shown in Table 2, the number (%) of patients who had chronic kidney disease is 46 (10.53%); 28 were males and 18 were females, P = 0.035. Chronic Liver disease was only reported in 9 (2.05%) patients, 8 were males compared to 3 were females, P = 0.021.

Table 3 shows the various clinical presentation, where Dyspnea was reported in 293 (66.89%); of these patients 150 were females and 143 were males. We found that 162 (36.98%) of the patients presented with chest pain; 86 in males compared to 76 in females. Cough is another presentation that was reported in 123 (28.1%) patients; 68 of them were males comparing to 55 were females. Syncope was reported in 23 (5.2%) compared to hemoptysis which was reported in 18 (4.1%); 15 males and 3 females, P= 0.005.

Table 3: Shows the analysis by presentation (with gender differences) of 438 patients with pulmonary embolism.

	All patients Number (%)	**Female Number (%)**	**Male Number (%)**	**P**
Number	438 (100%)	215 (49.1%)	223 (50.9%)	
Dyspnea	293 **(66.89%)**	150 (34.24%)	143 (32.64%)	0.185
Chest pain	162 (36.98%)	76 (17.35%)	86 (19.6%)	0.509
Cough	123 (28.1%)	55 (12.55%)	68 (15.5%)	0.265
Hemoptysis	18 (4.1%)	3 (0.68%)	15 (3.4%)	0.005
Syncope	23 (5.2%)	13 (2.96%)	10 (2.28%)	0.457

Table 4 shows the various laboratory parameters. The study showed that most patients had a mean (SD) hemoglobin (Hb) of 11.68 (2.34); females had Hb mean (SD) of 11.24 (2.06) compared to males' Hb mean (SD) of 12.10 (2.52), P= 0.0001. Platelets level was on the lower side of normal for most patients with a mean (SD) of 282.4(144.19), males mean (SD) of 261.21 (139.06) compared to females mean (SD) 304.28 (146.43), P= 0.0017.

Table 4: Shows analysis by laboratory parameters (With gender differences) of 438 patients with pulmonary embolism.

	All patients	**Female**	**Male**	**P**
Number (%)	438 (100%)	215 (49.1%)	223 (50.9%)	
Hb, Mean (SD)	11.68 (2.34)	11.24 (2.06)	12.10 (2.52)	0.0001
Platelet count, Mean (SD)	282.40 (144.19)	304.28 (146.43)	261.21 (139.06)	0.0017
Platelet Volume, Mean (SD)	8.19 (1.64)	8.15 (1.79)	8.23 (1.48)	0.5807
HbA1c %, Mean (SD)	6.82 (2.31)	6.68 (2.18)	6.94 (2.43)	0.4238
HbA1c count, Mean (SD)	50.53 (24.48)	48.46 (21.94)	52.47 (26.59)	0.2520
RBS, Mean (SD)		7.17 (3.46)	7.36 (3.56)	0.6744
LDL, Mean (SD)	2.9385 (1.3)	3.05 (1.29)	2.82 (1.305)	0.2263
PT, Mean (SD)	14.50 (10.87)	14.95 (14.04)	14.06 (6.34)	0.3980
APTT, Mean (SD)	40.23 (24.62)	38.93 (25.59)	41.53 (23.60)	0.2753
INR, Mean (SD)	1.38 (.99)	1.42 (1.19)	1.35 (.773)	0.4623

Albumin, Mean (SD)	28.85 (7.26)	28.57 (7.20)	29.14 (7.32)	0.4154
Protein C low, Number (%)	2 **(0.46%)**	0 (0%)	2 (0.46%)	0.073
Protein S low, Number (%)	2 (0.46%)	0 (0%)	2 (0.46%)	0.046
Antiphospholipid, Number (%)	59 (13.5%)	11 (2.5%)	48 (10.95%)	0.365

Hb: hemoglobin, HbA1c: glycated hemoglobin, RBS: random blood sugar, LDL: Low density lipoprotein, PT: Prothrombin time, APTT: Activated partial thromboplastin time, INR: international normalized ratio.

The mean (SD) of Glycated hemoglobin (HbA1c) and low-density lipoprotein (LDL) in most patients was 6.82 (2.31) and 2.9385 (1.3) respectively with no significant gender diffidence. The mean (SD) of albumin was 28.85 (7.26), the females' mean (SD) was 28.57 (7.20) and the males' mean (SD) was 29.14 (7.32), as shown in Table 4.

In regard to coagulation parameters, the mean (SD) of Prothrombin time (PT), Activated Partial Thromboplastin Clotting Time (APTT) and international normalized ratio (INR) was 14.50 (10.87), 40.23 (24.62) and 1.38 (0.99) respectively with no significant gender difference.

Unfortunately, protein S and protein C tests were rarely done. However, the positive antiphospholipid test was more in males compared to females with no significant P value, as shown in Table 4.

Table 5 shows the various imaging modalities that were included in the study apart from the CTPA. Ultrasound kidney ureter bladder (US KUB) was found to be abnormal in 68 (15.5%) of patients; 42 of them were males and 26 were females. Nonspecific abnormal chest X-ray (CXR) was reported in 265 (60.5%), 136 were males and 129 were females. More than half of the patients had abnormal ECHO with a total number of 216 (49%). Males were found to have a mean (SD) ejection fraction (EF) of 48.46 (14.53) compared to females' ejection fraction mean (SD) of 52.52(11.98), P= 0.008. The total number (%) of patients who had diastolic dysfunction was 125 (28.5%); 70 were males and 55 were females. The number (%) of patients who had systolic dysfunction was 54 (12%); of those 31 were males and 23 were females. Valve abnormalities were found in 121 (27.6%) of patients; 64 were females compared to 57 males.

Table 5: Analysis by radiological parameters (with gender differences) of 438 patients with pulmonary embolism.

	All patients Number (%)	**Female Number (%)**	**Male Number (%)**	**P**
Number (%)	438 (100%)	215 (49.1%)	223 (50.9%)	
Abnormal ECG	189 (43.1%)	94 (21.46%)	95 (21.68%)	0.477
Abnormal US KUB	68 (15.5%)	26 (5.9%)	42 (9.58%)	0.256
CTPA Main	238 (54%%)	120 (27.39%)	118 (26.9%)	
CTPA Segmental	343 (78%)	164 (37%)	179 (40.86%)	
CTPA Subsegmental	280 (63.9%)	135 (30.8%)	145 (33%)	
Abnormal ECHO	216 (49%)	99 (22.6%)	117 (26.7%)	0.040
EF	50.49 (13.45)	52.52 (11.98)	48.46 (14.53)	0.0080
Valve Abnormal	121 (27.6%)	64 (14.6%)	57 (13%)	0.330
Diastolic Dysfunction	125 (28.5%)	55 (12.55%)	70 (15.98%)	0.121
Systolic Dysfunction	54 (12%)	23 (5%)	31 (7%)	0.263
Abnormal CXR	265 (60.5%)	129 (29%)	136 (31%)	0.599

ECG: Electrocardiography, US KUB: ultrasound kidney ureter bladder, CTPA: Computed tomography Pulmonary angiogram, ECHO: echocardiography, EF: ejection fraction, CXR: chest x ray.

In the acute presentation of PE, 38 (8.7%) of patients received Reteplase; 23 were females and 15 were males. 399 (91.30%) of patients received heparin; 204 in which were females and 195 were males. The total number (%) of patients who received Warfarin was 281 (64.30%); 143 in males and 138 in females. 134 (30.66%) of patients received DOACs; 78 were females compared to 56 were males. IVC filter was only inserted in 11 (2.51%) of the patients 7 of them males and 4 were females, as shown in Figure 2.

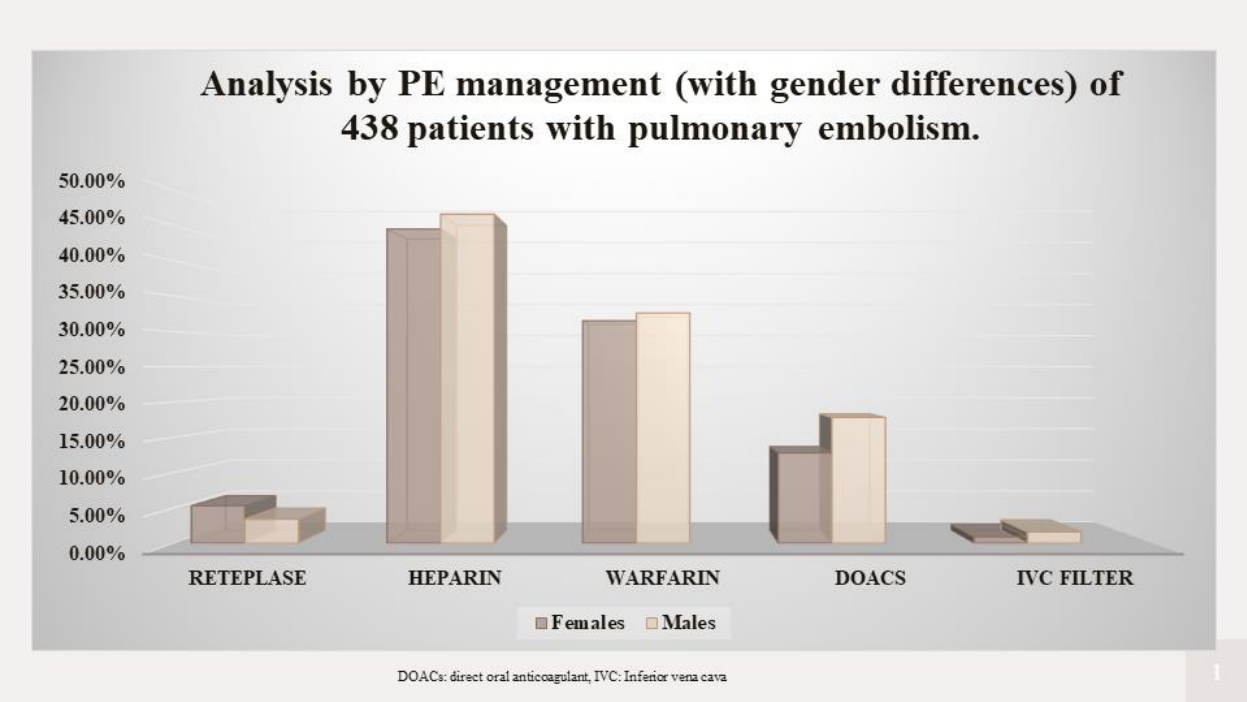

Figure 2: shows the analysis by clinical parameters (with gender differences) of 438 patients with pulmonary embolisms.

The total number of deaths was 122, which is 28% of the total 438 patients, as shown in Figure 3. The number (%) of death caused by PE is 68 (16%), malignancy is 18 (4.14%), septic shock is 21 (5%), cardiogenic shock is 5 (1.15%) and COVID-19 is 5 (1.15%). The study showed that 16 patients from the 68 patients who passed away due to PE, received reteplase. Deaths caused by PE have no significant differences between males and females (36 vs 32).

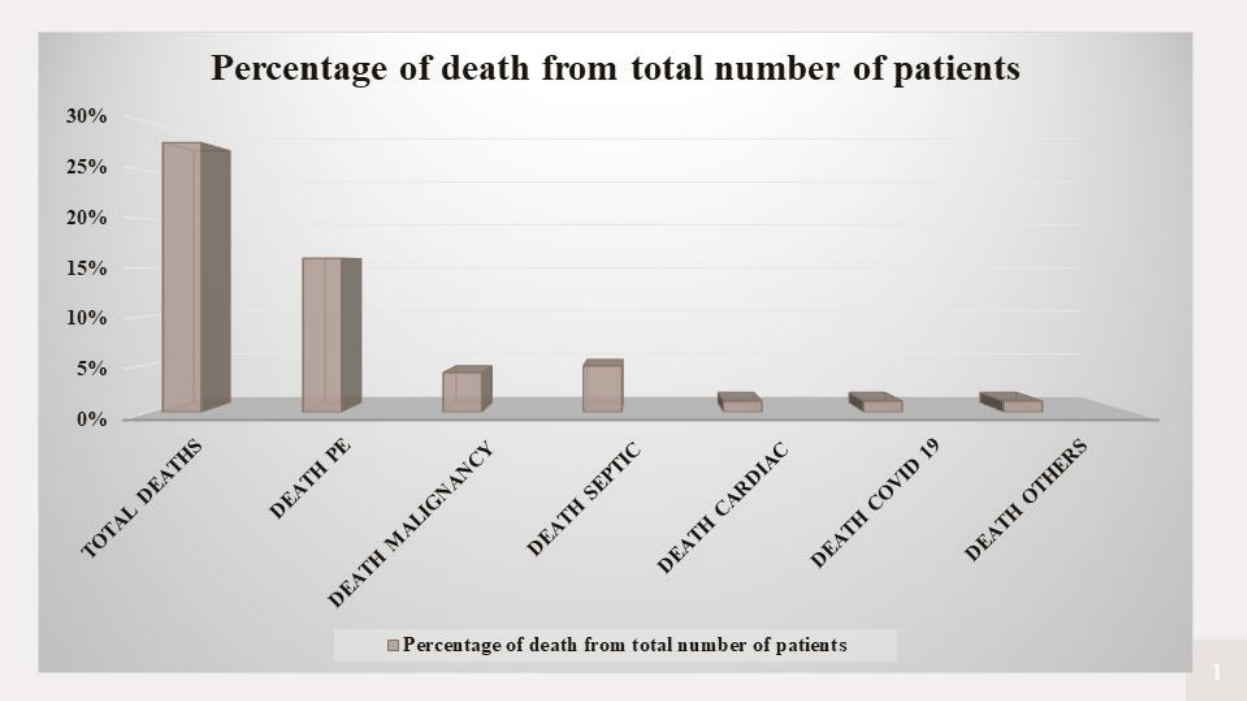

Figure 3: shows the causes of death by percentage among 122 deaths, which is 28% form 438 patients.

Discussion

The present study showed that the incidence of acute PE was common in the young and overweight populations with a similar number in both males and females. However, males were found to be older in age compared to females with higher BMI. Surgery was the most common risk factor reported in the study given the fact that Royal Hospital is the biggest tertial hospital that performs major surgeries. Almost two-thirds of the patients who were presented with PE had HTN and one-third had DM with fewer patients reporting other risk factors such as malignancy, smoking, and other organ failures. The most common presentation of PE was dyspnea and chest pain with fewer patients presenting with syncope and hemoptysis. Although most patients received anticoagulation, PE was the most common direct cause of mortality compared to other causes such as malignancy and shock.

A large Canadian study that included more than 55,000 patients over 5 years, reported that males had a 13% higher risk of VTE recurrence.[21] On the other hand, another study reported that the effect of gender on the incidence, severity, and treatment of PE was still not well understood and PE-specific data regarding gender differences were limited.[22] However, several studies showed that acute PE approximately affects males and females equally.[21,22]

Studies have shown that PE incidence generally was more common in the elderly.[23] However, there was a gender difference in the incidence of PE as they age.[23] A study from the US showed that women between the age of 20 - 40 had a higher risk of developing PE.[24] On the other hand, a study from the Netherlands reported that males had a higher risk of developing PE between the age of 60 -80.[25]

This study reported that most patients who presented with PE were having high BMI with a mean of 29.7 and it showed that females had higher BMI compared to males. A Saudi retrospective observational study that included 85 patients with PE reported that obesity is the commonest risk factor.[26] Another study had shown that both males and females who presented with PE had high BMI in general with no gender difference.[27]

This study found that surgery was the commonest risk factor for PE. This was as well showed by a Saudi study which reported that 20% of the patients who presented with PE, had a recent surgery.[26] A French study was done to assess the risk for PE postoperative among cancer-free middle-aged patients in all types of surgery, which showed that the risk for PE in early (1-6 weeks) and late (6-12 weeks) postoperative is high in all types of surgeries.[28]

Malignancy was one of the risk factors included in the study as it was an important predisposing factor for PE. Almost 17% of patients who presented with PE, had an underlying malignancy and it was more common in females compared to males. A study done in the United States reported that malignancy increases the risk for PE by fourfold compared to the general population.[29]

The present study found that 11.19% of patients who presented with PE were bedbound, but there was no gender difference. A retrospective Saudi study of 38 intensive care unit (ICU) patients showed that immobilization (23.7%) was the most common risk factor for PE.[30] A registry called Registro Informatizado de Enfermedad TromboEmbólica (RIETE) was done in Spain and included 18,023 patients with PE, showed that immobilization increases the risk for PE by two folds.[31]

Of the 215 females that were included in the study, 21 females reported pregnancy at the time of the presentation. A study in the US reported that 9% of all pregnancy-related deaths were caused by PE.[32] Those females who delivered by cesarean section had a higher risk for maternal morbidity and mortality.[32]

In general, smoking was one of the least risk factors reported in patients who presented with PE. However, it had the most significant gender difference as it was more common in males compared to females. A Saudi study done by Al Dandan et al; reported that smoking was a risk factor that was predominantly reported in males.[26] Several other studies reported that males with acute PE were more likely to be smokers.[33] This finding can reflect a behavior pattern in the population in that males are more likely to smoke compared to females.

HTN and DM were the most common diseases reported in PE patients. However, the study showed that a higher number of males compared to females had HTN and DM with no statistical significance. A meta-analysis of 63,552 patients with venous thromboembolism showed that HTN and DM were important risk factors for venous thromboembolism.[34]

Although only 46 patients of the total patients had chronic kidney disease (CKD), it was more common in males compared to females with a significant P value. The association between CKD and PE can be explained by the pathophysiology of the procoagulant state in CKD patients as a result of an increase in von Willebrand factor, fibrinogen, VIIa and XIIa, and the reduction in plasminogen activator inhibitor-1 (PAI-1).[35] In addition, the use of erythropoietin agents in CKD increases the risk of thrombosis. A meta-analysis that was done in 2020 and involved 225,000 patients reported that renal impairment is a predictor of short-term and long-term adverse outcomes and mortality in patients with acute PE.[36] One study showed that there was no gender difference in mortality in patients with CKD and PE.[37]

The present study showed that dyspnea was the most common presentation followed by chest pain and cough. Syncope and hemoptysis were the least clinical presentation reported in our study. All of these presentations had similar frequency in both males and females. However, hemoptysis is significantly more common in males compared to females. A Saudi study reported similar results regarding the PE presentation, and they found that the most common presentation is dyspnea followed by chest pain and hemoptysis which was a rare presentation.[26] Other studies showed that gender-based differences in acute PE presentation were relatively minor as both genders usually present with dyspnea (56%–89% of patients) and chest pain.[33,38,39] Although a small number of patients present with syncope (2%–7% of patients), it was still more common in females than males[40] which may reflect the fact that females usually have a more severe presentation. On the other hand, studies have shown that hemoptysis was somewhat more common in males.[33]

Several blood tests were included in the data analysis. In general, patients who were presented with PE had a low Hb but a lower normal range of platelets. It was noticed that the most significant difference was that males had a lower platelet count compared to females who had a lower Hb level. Low Hb and low blood viscosity can lead to dysfunction in the vessel endothelium antithrombotic mechanism which makes the patient at high risk for developing thrombosis.[41]

This study showed no significant gender difference in CTPA and ECG findings. Although CTPA was a very important imaging modality in diagnosing PE, there were still few studies that investigated gender-related differences in CTPA to diagnose PE. A trial called Prospective Investigation of Pulmonary Embolism Diagnosis II (PIOPEDII)

done in New York showed that CTPA had a higher specificity but a similar sensitivity (93%vs97%, P=0.015) to diagnose PE in females compared to males.[42] However, a study from Germany reported that gender differences had no effect on the pulmonary blood flow in CTPA.[43]

More than half of the patients involved in the study had abnormal ECHO. In the present study, the average ejection fraction is 50, for males 48, and for females 52. In addition, males were noted to a have tendency for systolic and diastolic dysfunction compared to females who had more valvular dysfunction. A study from Germany that involved more than 47,000 patients identified a significantly higher number of females who had RV dysfunction on echocardiogram.[44] In addition, Keller et al identified in a 10-year prospective study reported that females are more likely to have right ventricle dysfunction evidence on echocardiography compared to males.[2]

Studies showed that patients with heart failure have a double risk of developing PE compared to patients with no heart failure.[45] In addition, large cohort studies reported that decompensated heart failure was an independent risk factor of mortality in patients with PE.[46] The increased incidence of PE in patients with heart failure can be related to the fact that reduced cardiac output can lead to reduced flow, abnormalities in platelet function, endothelial function, and hemostasis.[45,46]

Acute PE was managed with anticoagulation and thrombolytic therapy. An example of anticoagulation medications were heparins (low molecular weight heparin or unfractionated), DOAC, or warfarin. Another way to manage patients who had absolute contraindications to systemic anticoagulation was the insertion of an IVC filter.[45,46]

The study reported that only 38 patients received thrombolysis which was more used in females compared to males with no significant P value. Heparin was the most used anticoagulant in patients with PE, followed by warfarin and then DOACs. Those modalities of treatment showed no significant gender difference. IVC filter was the least utilized method of management, and it was used in males more than in females. Several studies have actually shown that females had a more severe presentation on admission as they have a higher rate of presentation with hypotension, shock, high B-type natriuretic peptide (BNP), and abnormal ECHO findings such as RV dysfunction.[22,38,39,44]

A German prospective observational trial suggested that compared to males, females were more likely to be managed with thrombolysis (9.2% vs 16.4%, P=0.013).[47] Nevertheless, a retrospective Japanese cohort study reported the opposite result that females were less likely to receive thrombolysis.[22] On the other hand, a number of studies from Spain, the United States, and Japan reported that there was no gender-related difference in the rate of thrombolysis.[38,39] Another study found that females were less likely to receive IVC filters in comparison to males.[39]

The total number of deaths in our study was 122, of which 68 patients had PE as the cause of their death. This study reported that mortality in males was higher than in females. A Saudi retrospective, observational study from 2021 to 2022 that included 92 patients reported mortality of 15.2% of total patients.[48] Data showed that females presented with more severe PE, but there was not enough evidence that females had higher mortality, although some studies had reported that females had higher mortality.[38,39] On the other hand, another study reported that males had higher mortality.[33] Another study suggested that there was no actual gender difference regarding mortality both in the short and long term.[49] This variation in mortality and morbidity can be due to genetic, environmental factors, and possibly health-system-related factors.

This study has a few limitations, including that it was a retrospective design, as well as the fact that it is a single-center study. Emphasizing the need for a large prospective multicenter trial that follows these patients for an extended duration of time.

Conclusion

The present study showed that the incidence of acute PE was common in the young and overweight populations. Surgery was the commonest risk factor reported in our study with fewer patients presenting with malignancy, smoking, and other organ failures. Almost two-thirds of the patients who were presented with PE had HTN and one-third had DM. The most common presentation of PE was dyspnea and chest pain with fewer patients presenting with syncope

and hemoptysis. Although most patients received anticoagulation, PE was the most common direct cause of mortality compared to other causes such as malignancy and shock.

We suggest that the clinician needs to focus on the various demography, comorbid, risk factors, and the in-hospital progress status of the patient. This study has shown the great need for an individualized patient assessment of the VTE assessment and regular follow-up of the patient, especially high-risk patients.

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