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ORIGINAL ARTICLE

Acute Pulmonary Embolism in an Intensive Care Unit Setting in Sierra Leone

Embolie Pulmonaire Aiguë dans une Unité de Soins Intensifs au Sierra Leone

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ABSTRACT

INTRODUCTION: In Sierra Leone, the lack of information on pulmonary embolism (PE) limits the access to evidence-based standard of diagnostic work-up and management of the disease. The objective of this study was to describe the clinical characteristics and management of acute pulmonary embolism in our setting and to determine whether the pre-test probability scoring algorithms were used prior to Computed Tomography Pulmonary Angiogram (CTPA) request.

METHODS: This retrospective observational study was conducted on CTPA-confirmed PE patients admitted to the Intensive Care Unit, Choithrams Memorial Hospital, in Freetown, Sierra Leone between July 2014 to June 2019. Clinical data, and pertinent investigations related to PE were determined. CTPA findings were correlated with the patient's hemodynamic status. The calculated pretest clinical probability scores (PCPS) for each patient were compared to the CTPA results.

RESULTS: CTPA-confirmed PE in the study cohort was 79, with a rate of 16 new PE per year. The frequency of PE was 1.9% of the total hospital admission per year. The mean age was 64.1 ± 17.9 years, median age was 63.3years (range: 23–89 years), with 55.7% of the cohort being females. Dyspnea (78.5%) and tachycardia (69.6%) were the commonest signs and symptoms documented, with immobilization (34.2%) being the prevalent risk factor, while hypertension (48.1%) was the most common co-morbidity. The PCPS algorithm was underutilized, as "Wells Score" was documented in only 9.5% while "modified Geneva score" was never used by hospital physicians. PE with hemodynamic stability was significantly more common than PE with unstable hemodynamic status [55 (69.6%) vs 24 (30.4%), p=0.015]. All patients were managed only with anticoagulants. The overall in-hospital mortality was 17.7%.

CONCLUSION: Since PCPS was hardly calculated by doctors in the diagnosis of PE, the study showed that the diagnostic algorithm for suspected PE was infrequently used in clinical practice. The use of empirical judgement by doctors in requesting for CTPA may have accounted for low rate in the diagnosis of PE per year. The establishment of P.E registry in Sierra Leone is imperative. **WAJM 2022; 39(10): 997–1006.**

Keywords: Pulmonary embolism, Clinical characteristics, Management, Sierra Leone.

RÉSUMÉ

INTRODUCTION: En Sierra Leone, le manque d'informations sur l'embolie pulmonaire (EP) limite l'accès à des normes de diagnostic et de prise en charge de la maladie fondées sur des preuves. L'objectif de cette étude était de décrire les caractéristiques cliniques et la prise en charge de l'embolie pulmonaire aiguë dans notre établissement et de déterminer si les algorithmes de notation de la probabilité pré-test étaient utilisés avant la demande d'angiographie pulmonaire par tomodensitométrie (CTPA).

MÉTHODES: Cette étude observationnelle rétrospective a été menée sur des patients atteints d'EP confirmée par CTPA admis à l'unité de soins intensifs, Choithrams Memorial Hospital, à Freetown, Sierra Leone, entre juillet 2014 et juin 2019. Les données cliniques, et les investigations pertinentes liées à l'EP ont été déterminées. Les résultats du CTPA ont été corrélés avec l'état hémodynamique du patient. Les scores de probabilité clinique prétest (PCPS) calculés pour chaque patient ont été comparés aux résultats du CTPA.

RÉSULTATS: Le nombre d'EP confirmées par CTPA dans la cohorte étudiée était de 79, avec un taux de 16 nouvelles EP par an. La fréquence de l'EP était de 1,9 % du nombre total d'hospitalisations par an. L'âge moyen était de 64,1 ± 17,9 ans, l'âge médian de 63,3 ans (fourchette : 23-89 ans), 55,7 % de la cohorte étant des femmes. La dyspnée (78,5 %) et la tachycardie (69,6 %) étaient les signes et symptômes les plus fréquemment documentés, l'immobilisation (34,2 %) étant le facteur de risque prévalent, tandis que l'hypertension (48,1 %) était la comorbidité la plus courante. L'algorithme PCPS était sous-utilisé, le " score de Wells " n'étant documenté que dans 9,5 % des cas, tandis que le " score de Genève modifié " n'était jamais utilisé par les médecins hospitaliers. L'EP avec stabilité hémodynamique était significativement plus fréquente que l'EP avec état hémodynamique instable [55 (69,6 %) vs 24 (30,4 %), p=0,015]. Tous les patients ont été traités uniquement par anticoagulants. La mortalité globale à l'hôpital était de 17,7 %.

CONCLUSION: Étant donné que le PCPS était rarement calculé par les médecins pour le diagnostic de l'EP, l'étude a montré que l'algorithme diagnostique pour l'EP suspectée était rarement utilisé dans la pratique clinique. L'utilisation d'un jugement empirique par les médecins pour demander un CTPA peut expliquer le faible taux de diagnostic de l'EP par an. L'établissement d'un registre de l'E.P. en Sierra Leone est impératif. **WAJM 2022; 39(10): 997–1006.**

Mots-clés: Embolie pulmonaire, caractéristiques cliniques, gestion, Sierra Leone.

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Abbreviations: CTPA, Computed Tomography Pulmonary Angiogram; PCPS, Pretest Clinical Probability Scores; PE, Pulmonary Embolism.

INTRODUCTION

Pulmonary Embolism (PE) is not uncommon in sub-Saharan African (SSA) countries,[1–3] as it represents one of the greatest cardiovascular burdens in developing countries, with a potentially lethal outcome if not timely diagnosed and managed. It is a preventable cause of hospital deaths in developed nations but in Africa, it carries a high mortality rate in the range of 9.2% to 64%.[4–6] The clinical presentation of PE can be subtle and as a great mimicker of other diseases, it may result in a low threshold of clinical suspicion and diagnostic work-up among clinicians.[7–9] PE should be included in the list of differential diagnosis for clinical presentations with chest pain, shortness of breath or unexplained collapse. Clinicians should be familiar with the validated risk stratification tools in establishing the diagnosis of PE.[10,11]

Several diagnostic tools are now available for the investigation of PE, with few providing definitive answers. Investigations such as Computed Tomography Pulmonary Angiogram (CTPA) may be helpful in establishing the diagnosis of PE, but this is not readily available in most tertiary hospitals in SSA.[12,13] The pre-test probability score as a workup tool for PE has been validated to improve the diagnosis of PE but these tools are still under-utilized by clinicians in these countries.[11,14,15]

In Sierra Leone, little is known about the frequency of pulmonary embolism, as there are no available published data, prior to this study. A 64 slide Multi-detector CT scan was introduced at the Choithrams Memorial Hospital (CMH) in 2013 and since then, it has been a useful diagnostic tool in the investigation of suspected cases of pulmonary embolism.

The overall aim of this study is to assess the clinical characteristics, diagnostic work-up and management of acute pulmonary embolism in patients hospitalized in an Intensive Care Unit (ICU) at CMH, Freetown, Sierra Leone. The study also evaluated whether the pre-test probability scoring tools were used by clinicians prior to the request of CTPA. The Well's score and modified Geneva Score were calculated retrospectively for every patient and were then compared to the CTPA results.

METHODS

Ethics Approval and Registration

The study was written in accordance with the STROCSS statement guidelines[16] and was approved by the Sierra Leone Ethics and Scientific Review Committee. It was also registered under Research Registry with the unique identification number research registry6514, that is available at https://www.researchregistry.com/browse-the-registry#home/. Anonymity was maintained by using independent serially coded numbers which were then assigned to the case records. The extracted data was then handled with strict confidentiality.

Study Design, Setting and Cohort Group

We conducted this descriptive, retrospective single center cohort study on all patients with a confirmed CTPA diagnosis of acute pulmonary embolism. These patients were admitted to the ICU at the CMH from July 2014 to June 2019. CMH is a premier private hospital serving an approximate population of one million people in the capital city, Freetown. It accepts referrals from other hospitals within the city of Freetown and district hospitals country wide. It is a 52-bed hospital with well-equipped laboratories, electrocardiogram (ECG), Echo-cardiogram, doppler ultrasound, a 64 Multi-Detector CT (MDCT) scanner and intensive care unit. Patients using this facility are those who could afford "out of pocket payment" for health services, as there is no extensive functional Health Insurance Scheme in the country. Hence, patients admitted to this private facility are assumed to be in a higher socioeconomic and professional class.

Sample Size, Sampling Method and Data Collection Instrument

As a retrospective study, an *a priori* sample size was not calculated. We searched the ICU registry database for patients above 18 years of age, for the identification of CTPA confirmed diagnosis of PE. Patient's electronic clinical notes and laboratory information were then obtained from a database computer-generated archiving system, in the Information and Records Department of the hospital. The medical case records of the patient with acute pulmonary embolism were then manually retrieved from the patient's folder. All information were entered into a data extraction form, which has an advantage of reducing the likelihood of missed data and improving the standardization of medical information.

The following variables were recorded at presentation: demographics, signs and symptoms, previous medical history, vitals on admission, duration of symptoms, and presence or absence and location of DVT, and findings on physical examination. The risk factors related to PE and comorbidities were also recorded. Electrocardiogram (ECG), echocardiography and oxygen saturation on room air were done for all patient and results were retrieved. Laboratory parameters such as D-dimer, troponins, white blood cell count, HIV results and blood sugar were also recorded. Findings of the chest x-ray, doppler ultrasound of the lower limbs, echocardiogram and CTPA were also documented.

The hemodynamic status on presentation was documented for every PE patient. A patient was classified as being hemodynamically unstable or "high-risk" if pulmonary embolism resulted in hypotension with a systolic blood pressure <90 mmHg or a drop in systolic blood pressure of $\geq$40 mmHg from baseline for a period >15 minutes. Hypotension is further defined as the circulatory collapse requiring vaso-pressors or inotropic support that is not explained by arrhythmias, hypovolemia, left ventricular dysfunction and sepsis. The hemodynamically stable PE patient are those without hypotension. If the hemodynamically stable patient has right ventricular strain, it is referred to as "intermediate risk" PE patient while without right ventricular strain it is referred to as "low risk".[17]

The pretest clinical probability scores (Wells and modified Geneva scoring systems) were retrospectively calculated from the medical records of each patient and these were then compared to the reference standard (evidence of PE on CTPA).

The route (Emergency Room, Surgical Ward, Medical Ward, or Obstetric ward) or mode of referral

(another hospital, self-presentation, or ward transfer) for admission into the ICU were documented. If a patient was referred from another hospital, the duration before transfer and outcomes were documented. The treatment type and duration were analyzed. Complications whilst on admission in the ICU were recorded, while treatment given to the patients were also documented.

Statistical Analysis

All data was analyzed using STATA version 15.0. Descriptive statistics were determined. All categorical variables were expressed as frequency and percentage, while continuous variables were expressed as median with interquartile ranges (IQRs) or means with standard deviations (SDs). *P* value < 0.05 was considered statistically significant. The non-parametric chi-squared test was used to test heterogeneity of proportions.

RESULTS

Demographics and Baseline Characteristics of all Patients

During the 5-year study period, 79 patients with confirmed clinical diagnosis of acute pulmonary embolism by CTPA were hospitalized in the Intensive Care Unit (ICU), irrespective of their hemodynamic status. The frequency of PE was 1.9% (79 of the 4181) total hospital admission per year. The baseline clinical characteristics of these patients are shown in Table 1. The mean age at diagnosis was 64.1 ± 17.9 years, median age was 63.3years (range: 23–89 years), with 55.7% of the cohort being females, while 84% of the patients were over the age of 50 years (Figure 1). The time interval from onset of clinical symptoms to diagnosis of PE was 6.0 ± 3.0 days. The mean blood pressure was 122.8 ±16.5 mmHg and 71.2 ±11.6 mmHg, for systolic and diastolic, respectively.

Clinical Presentation, Risk Factors and Co-morbidity

The clinical signs and symptoms, including risk factors and co-morbidity are represented in Table 1. Respiratory symptoms were the most frequent presentation on admission, with the most common being dyspnoea in 62 (78.5%)

Table: 1 Clinical and Socio-demographic of Patients with Pulmonary Embolism

Variable	Frequency (n)	Percentage (%)
Genders		
Male	35	44.3
Female	44	55.7
Signs and Symptoms		
Dyspnoea	62	78.5
Chest pain	47	59.5
Tachycardia	55	69.6
Palpitation	56	70.9
Cough	34	43.0
Hypotension	19	24.0
Sputum	29	36.7
Haemoptysis	11	13.9
Oxygen Sat < 90%	22	27.8
Syncope	2	2.5
Tachypnoea	55	69.6
Fever (Temp > 37.5 °C)	6	7.6
Other non-specific symptoms	20	25.3
DVT	6	7.6
Risk Factors and Morbidity		
Trauma	7	8.9
Hypertension	38	48.1
Stroke	5	6.3
Contraceptive	2	2.5
Immobilization	27	34.2
Smoking	6	7.6
Pulmonary Tuberculosis	4	5.1
Chronic Liver Disease	3	3.7
Heart Failure	4	5.1
Recent surgery (< 3months)	12	15.2
Recent air travel	2	2.5
Malignancy	9	11.4
COPD	5	6.3

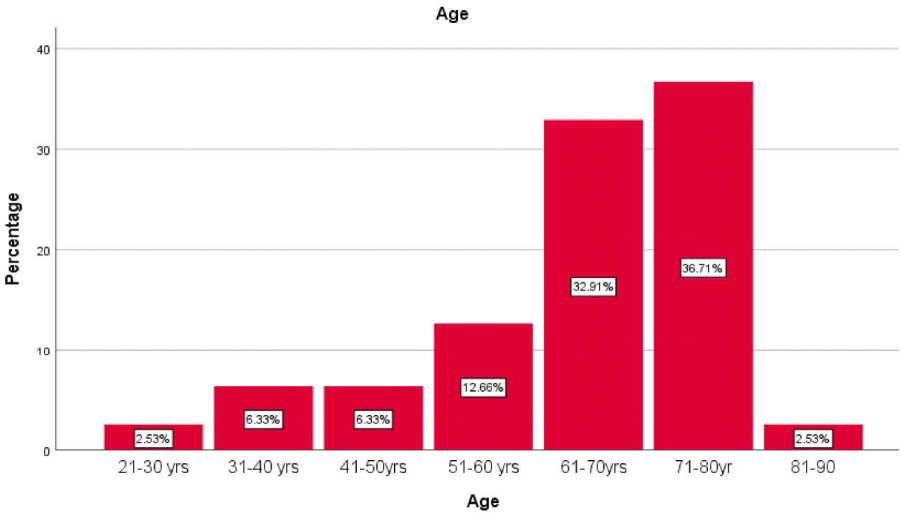

Fig. 1: Age Distribution of Participants with Pulmonary Embolism

patients, followed by palpitation in 56 (70.9%) and chest pain in 47 (59.5%) patients. The other symptoms were cough in 34 (43.0%), haemoptysis in 11 (13.9%), and fever in 6 (7.6%) patients. The commonest signs were tachycardia in 55 (69.6%) and tachypnoea in 53 (67.1%) patients. Only 2 (2.5%) patients presented with syncope, whilst the remaining 20 (25.3%) presented with non-specific symptoms. During evaluation for underlying comorbidities and risk factors, hypertension 38 (48.1%) was the most common co-morbidity whilst the most prevalent risk factor was immobilization 27 (34.2%) for more than 72 hours.

Investigations

About three-quarter of the patients with pulmonary embolism 57 (72.2%) had normal chest x-ray, while pulmonary parenchyma infiltrations 9 (11.4%) was the most frequent abnormal chest x-ray findings. The most common ECG abnormality was sinus tachycardia 52 (65.8%), followed by normal ECG findings (16.5%). Other abnormal ECG findings were Q3T3S1 (10.1%), non-specific T-wave inversion (8.9%), atrial fibrillation (3.8%), right bundle branch block (RBBB) (2.5%) and right ventricular hypertrophy (3.8%).

According to echocardiographic assessment, the main findings were RV/RA enlargement in 25 (31.6%), pulmonary arterial hypertension in 7 (8.9%), right ventricular hypokinesia 6 (7.6%) and McConnell sign in 6 (7.6%). The median Left Ventricular Ejection Fraction was 55.0 % (55.0–60.0).

D-Dimer levels were elevated in 61 (77.2%) patients, while the mean D-Dimer level was 1710.3± 130.7(µg/mL). With a troponin cut-off level >0.1ng/ml, 9 (11.4%) patients had an elevated troponin level while the mean level of troponin for all participant was 0.06 ±1.2ng/ml. WBC was raised in 12 (15.2%) while the mean level of the study population was 9.2 ± 3.6 >10 × 109 cells/l. Likewise CRP was elevated in 12 (15.2%) of the cohort with a mean CRP level documented as 3.2 ± 1.3. At the time of diagnosis of PE, CTPA findings as presented in Table 3, were classified into massive, sub-massive and low risk.

Table 2: Baseline Characteristic of PE Positive Patients

Variable	Mean ± SD
Age (years)	64.1 ± 17.9
Respiratory frequency (breaths/min)	24.3± 11.6
Heart rate, (rates/min)	104.3 ± 23.3
Systolic blood pressure, (mmHg)	122.8 ±16.5
Diastolic blood pressure, (mmHg)	71.2 ±11.6
Temperature, °C	36.9 ± 9.3
PaO_2, pulse oximeter (%)	89.2 ± 43.4
D-dimers (>500 ng/l)	1710.3 ± 130.7
Troponin-I, (>0.1ng/mL)	0.06 ±1.2
C-Reactive Protein (>5mg/L)	3.2 ± 1.3
White Blood Cell (>10 × 10^9 cells/l)	9.2 ± 3.6
Interval between onset of symptoms and diagnosis (days)	6.0 ± 3.0
Hospital duration (days)	7.9 ± 5.9

Table 3: Frequency and Positivity of the Diagnostic Tests in Patients with Pulmonary Embolism

	Frequency (n) = 79	Percentage (%) = 100
Chest X-ray		
Lung parenchymal infiltrate	9	11.4
Pleural Effusion	5	6.3
Cardiomegaly	5	6.3
Wedge Shaped opacity	3	3.8
Normal	57	72.2
ECG		
Tachycardia	52	65.8
Non-specific T wave inversion	5	10.1
Q3T3S1	4	6.3
Atrial Fibrillation	3	3.8
Right Bundle Branch Block	2	2.5
Right Ventricular Hypertrophy	3	3.8
Normal	10	12.7
ECHO		
RV/RA enlargement	25	31.6
Pulmonary Arterial Hypertension	7	8.9
McConnell sign	6	7.6
RV Hypokinesia	6	7.6
Other findings	10	12.7
Normal	25	31.6
Labs		
Troponins (>0.1ng/ml)	9	11.4
CRP (>5mg/L)	12	15.2
WBC (>10 × 109 cells/l)	12	15.2
D-dimers (>500 ?g/l)	61	77.2
CT Classification		
Massive	19	24.1
Sub massive	25	31.6
Low risk	35	44.3

Correlation of Pre-test Probability, Hemodynamic Stability and Pulmonary Embolism Severity Index

The hemodynamic status for every ICU patient was correlated with the risk of PE and of these patients, 35 (44.3%) were documented as "Low-risk PE". "Intermediate risk PE" was documented in 20 (25.3%) of admitted patients in the ICU, while "High risk PE" was noted in 24 (30.4%) of the study population. PE with hemodynamic stability was significantly more common than PE with unstable hemodynamic status [55 (69.6%) vs 24 (30.4%), p = 0.015)]. (Table 4a).

The Pulmonary Embolism Severity Index (PESI) score was analyzed for every patient admitted and 16.5% of these patients had a very high (Class V) mortality risk (Table 4b).

Wells Score was documented in only 9.5% patients with PE, while modified Geneva score was not documented in any of the reviewed clinical notes. Analyzed pre-test probability score for Wells and modified Geneva score for every patient, is represented in Table 4c.

Route of Admission into the Intensive Care Unit and Duration of Admission

There were three different routes of admission into the ICU, with 9 (11.4%) patients directly shifted from the General Medical/Surgical wards in Choithrams Hospital, while 43 (54.4%) patients were admitted directly from home. About one-third of the admitted cohort 27 (34.2%) were referred from another hospital on account of diagnostic dilemma by the primary clinician or need for ICU management. Duration of ICU admission was classified into 1st week, 2nd week and 3rd week. More than half of the study cohort 42 (53.2%) were admitted in the ICU for a duration of 2 weeks. The duration of hospitalization in the Intensive Care Unit (ICU) for all patients diagnosed with PE was 7.9 ± 5.9 days.

Management and Outcomes of Patients with Pulmonary Embolism

The commonest anticoagulants used in the ICU management of PE were heparin and warfarin. Unfractionated heparin was used in 55 (69.6%) patients for 5.2 ± 1.8 days, while Low-molecular-

Table 4: PE Classification, PESI, Pre-test Probability Score, Admission and Mortality

Table 4a: Pulmonary Embolism Classification according to Computer Tomography Pulmonary Angiography and Correlation with Hemodynamic Stability at Admission

CTPA Classification	Hemodynamically Stable		Hemodynamically Unstable		Sub-Total		p-value
	n	%	n	%	n	%	
Massive PE	2	2.5	17	21.5	19	24.1	0.015
Sub-massive PE	18	22.8	7	8.9	25	31.6	0.241
Low risk PE	35	44.3	–	–	35	44.3	–
Total	**55**	**69.6**	**24**	**30.4**	**79**	**100**	

Table 4b: The Pulmonary Embolism Severity Index (PESI)

30-day Mortality Risk Classes (%)	Frequency	Percentage (%)
I (0–1.6)	20	25.3
II (1.7–3.2)	19	24.1
III (3.2–7.1)	16	20.3
IV (4.0–11.4)	11	13.9
V (10.0–24.5)	13	16.5
Total	**79**	**100.0**

Table 4c: Estimated Pre-test Probability of PE Stratification according to the Modified Wells and Geneva Revised Scoring Systems

PE Probability	Wells Scoring		Geneva Scoring	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Low	11	13.9	12	15.2
Moderate/Intermediate	43	54.4	45	57.0
High	25	31.6	22	27.8
Total	**79**	**100.0**	**79**	**100.0**

Table 4d: Admission and Outcomes of Patients with Pulmonary Embolism

	Frequency (n)	Percentage (%)
Transfer Route to ICU		
Ward transfer in CHM	9	11.4
Direct Home or self-reported transfer	43	54.3
From another hospital transfer (Referral)	27	34.2
ICU Duration (Days)		
1–7	32	40.51
8–14	42	53.16
15–21	5	6.33
Mortality (Hours)		
Mortality > 48	8	10.1
Mortality <48	6	7.6
Overall Mortality	**14**	**17.7**

Table 4e: Mortality Rates

Admission Route	Mortality					
	< 48hrs		> 48hrs		Overall	
Transfer from ward (CMH)	n	%	n	%	n	%
Transfer from home	1	7.1	2	14.3	3	21.4
Transfer from ward (CMH)	1	7.1	2	14.3	3	21.4
Transfer from another hospital	4	28.6	4	28.6	8	57.2
Total	**6**	**42.9**	**8**	**57.1**	**14**	**100**

weight heparins were used in 22 (30.4%) patients for 5.1 ± 2.9 days. Warfarin accounted for 86.1% of oral anti-coagulant use while 13.9% were on Direct Oral Anticoagulant (DOAC). Thrombolytic agents and other surgical procedures for the management of PE were not utilized.

The first 48hrs case fatality rate was 7.6% while the overall in-hospital mortality was 17.7%. Six (42.9%) out of the 14 deaths in the study cohort occurred within 48 hours of admission into the hospital. Two-thirds (66.7%) of those who died within the first 48 hours of ICU admission were referred from another hospital.

DISCUSSION

In this 5-year retrospective single-center-study, we reported the first PE study in the era of CT scan in Sierra Leone. All newly diagnosed PE patients hospitalized in the ICU were confirmed by CTPA. The high index of suspicion of PE (gestalt), the availability of CTPA and other ancillary diagnostic tools have enabled the confirmation of PE by clinicians at the CMH.

The frequency of PE in our study was 1.9% and this was similar to the 1.7% reported by Diall, *et al* in Mali[18] but lower than the 3.1% reported by Pessinaba, *et al* in Togo.[19] However, much higher rates were documented in Tunisia (17.5%) and Congo Brazzaville (20.5%).[20] The variation in the prevalence rate of admission of PE across African studies, reflect the differences in access to quality healthcare systems, the study population, and diagnostic facilities.

The mean age (64.9±17.9 years) in this study was similar to the JASPER study (60±15years),[21] while studies from Africa, reported age range of 60–65 years.[20,22–25] Higher mean age, ranging between 70 to 75 years, have been reported by the RIETE registry[26] while a relatively younger mean age, between 40–50 years, have been reported in SSA.[19,27,28] The disparity in age for PE across African countries could be attributed to the study setting and design, age distribution of the population, risk factor profiling, admission policy and diagnostic accuracy between different countries. Since our study was conducted in a private hospital, age selection bias is highly probable. This notwithstanding, there was an increased PE frequency with ageing, with peak age documented in the 7th decade of life.

Dyspnea, palpitations, and chest pain were the commonest clinical symptoms while tachypnea and tachycardia were the most common clinical signs. The symptoms and signs of PE in our study is similar to the JASPERS study[21] and other publications from Africa.[18,28,29] Since dyspnoea, palpitation and chest pain may suggest a plethora of disease differential, the presentation of sudden onset of these symptoms either in combination or in isolation, should alert a clinician to be highly suspicious of PE.

In developed countries, extensive investigations are often carried out in patients with confirmed PE, and this may result in the identification of risk factors in more than 90% of these patients.[30] In SSA, most PE related risk factors like cancer and thrombophilia are grossly under reported.[12,19,30] The main risk factor for PE in this study was immobilization (32.3%), which is almost similar to the 28% reported by the ICOPER studies[31] but lower than the 48% and 38.5% respectively reported by the Angola and EMEP studies.[29,32] Malignancy as a risk factor for PE was 11.4% in our study, which is similar to the 10% reported in Angola[29] but much lower than the 18.3 to 24.3% reported in other studies.[19,21,32] Many African studies have reported HIV as a major risk factor for PE[15,33] but in our study, there were no cases of HIV as a risk factor. The absence of HIV as a risk factor in our cohort could be attributed to the study setting (private hospital) and the low prevalence of HIV infection in Sierra Leone.[34,35]

D-dimer was routinely done in 95% of the patients and was positive in 77.2% of our cohort. Abolfotouh, *et al* reported a D-dimer positivity of 61.7% in their studied population,[36] while Manuel, *et al* reported a D-dimer elevation above normal in 50% of their cohort.[29] This clearly suggests that D-dimer should not be used in isolation in making the diagnosis of PE.

The current approach in the diagnosis of PE according to evidence-based protocol, is the use of non-invasive modalities like the pre-test probability score (PTPS) or clinical gestalt, either of which can be followed by D-dimer or CTPA.[37] These diagnostic algorithms have been validated in the work-up of PE but regardless of the overwhelming evidence to support its use, adherence in clinical practice is poor.[38] In this study, only 9% of our patients had documented clinical pre-test probability scoring by "Wells Score" while no documentation of the modified Geneva Score was noted. In the absence of written diagnostic algorithm or guidelines for PE in our hospital setting, it appears that patients were sent for CPTA by clinicians based on an unstructured analysis of the PTPS or by clinical gestalt. The poor adherence by clinicians to the clinical pre-test probability score is not unique to our study setting, as Sanjuán et al also reported a very low calculated clinical score of only 0.6% in their study.[39]

When the pre-test probability score for PE was retrospectively stratified according to Wells and Geneva revised scoring systems, more than half of the patients in this study were documented to have moderate (Wells score) and intermediate (Geneva revised score) probability for pulmonary embolism. Low

pretest probability scores for Wells and Geneva score were 11 (13.9%) and 12 (15.2%) respectively. Upon further evaluation of the pretest probability scoring tools, the Geneva score was comparable to the Well's score, with similar rates documented in the intermediate and high probability PE groups. Similar finding was reported in the Angola study by Manuel, *et al,* wherein 10 to 14% of the patients had a low probability score.[29]

Chest X-ray was normal in 72.2% of the patients with confirmed PE and this may suggest that the diagnosis of acute PE should be considered in any patient who presents with a dominant respiratory symptom but normal chest x-ray. Pulmonary parenchymal infiltration was the commonest abnormal radiological findings documented in this study and was similar to the PIOPED and Nepal studies that reported lung infiltration as the commonest radiological findings with a sensitivity of 68%[40,41] but differs from the 48% documented by the EMEP study.[32] The variation in chest x-ray reported across studies may be influenced by inter-observer variability and subjectivity. Even though chest x-ray has a low specificity for the diagnosis of PE, it is however recommended that chest x-ray should be carried out in every suspected PE patient because it provides a valuable alternative diagnosis.[42]

In PE with hemodynamic instability, there may be stretching of the right ventricle from pressure overload, and this may result in the release of troponins. Elevated serum troponin is associated with higher mortality in PE patients regardless of the troponin assay used. Troponin was done for all patients admitted with PE in the ICU. The mean troponin value was 0.06 ±1.2ng/ml, with a positivity rate of 11.4%. The finding of positive troponin in PE, in the absence of myocardial infarction has similarly been published by Manuel, *et al,* who reported an 8% troponin positivity in their PE cohort.[29] A higher troponin positivity rate of 68.5% in a PE cohort was also documented by the Indian study.[43] Therefore, a positive troponin in a patient with PE should be interpreted with caution, as troponin increase might be related to the stretching of the right ventricle rather than myocardial ischemia.

Echocardiography has always been a major diagnostic tool for high-risk patients with PE. In our study, RA/RV enlargement (31.6%) followed by pulmonary arterial hypertension (PAH) (8.9%) were the commonest Echo findings. Our study was contrary to the Nepal and Indian studies, that reported 88.5% and 100% RV dysfunction respectively.[41,43]

Arterial blood gases were not performed in this study but oxygen saturation by pulse oximetry and other baseline laboratory investigations were performed for all patients. About 30% of the population had an abnormal oxygen saturation with hypoxemia being the most frequently documented report. In a risk stratification study by Subramanian, *et al,* hypoxemia was an independent predictor of adverse outcome PE.[44]

The commonest ECG findings in our study was sinus tachycardia. This was followed by non-specific T wave inversion, Q3T3S1 and atrial fibrillation. While ECG is an integral diagnostic test in the investigation of patients suspected of having pulmonary embolism, the diagnosis of PE probably won't be confirmed, because ECG is neither a sensitive nor a specific clinical test. However, ECG is essential in assessing similar clinical presentations related to PE and the prognostication of the disease.[45]

Doppler ultrasonography is now the diagnostic method of choice for Deep Venous Thrombosis (DVT) due to its negative predictive value > 90%.[46] This non-invasive study was not routinely performed in our cohort, as less than a quarter of the study population had doppler screening, with 20.3% DVT cases confirmed on USG. The frequency of search for DVT in our study was less than the 69% reported by the JASPER study.[21]

Due to the high sensitivity and specificity of CTPA, it was used as the conventional diagnostic clinical tool in confirming the diagnosis of PE in our study. PE patients with hemodynamic stability were significantly more common than PE with unstable hemodynamic status [55 (69.6%) vs 24 (30.4%), p = 0.015). Similar findings have been reported by Manuel, *et al.*[29] Almost half of PE patients admitted to ICU were classified as low-risk PEs, and these patients generally and routinely could have been managed at the ward level or even in the outpatient settings. It therefore appears that one important factor leading to ICU admission was financial stability rather than true clinical indications. This significant percentage of low-risk PE admissions to ICU may add bias to the data.

In this study, thrombolytic therapy was never used however 24 (30.4 %) patients presented with hemodynamic instability with hypotension documented in 24.0%. This report suggests the underutilization of thrombolytic therapy in our setting, despite the availability of streptokinase in our ICU. In the EMEP study, about 20% of the patients were hypotensive but thrombolytic agent (15%) was sparingly used[32] while in the retrospective Angolan study reported by Manuel, *et al,* thrombolytic therapy was used in 18% of patients.[29] Unlike our report, thrombolytic agent was widely used by the Ghanaians, but the reported in-hospital mortality was 35.5%.[24] Despite the superiority of thrombolytic therapy with respect to the resolution of radiographic and hemodynamic abnormalities within the first 24 hours, the use of this agent for the treatment of massive PE in SSA remains challenging, as these medications are not readily available in most African countries and if available, clinicians are wary of the bleeding complications associated with these agents.[47]

Anticoagulants either as unfractionated Heparin and or Vitamin K dependent, were the main stay of management for patients with PE. Low Molecular weight heparin or the DOACs were less frequently used as they were not readily available in early years (2014–2016) of the study. Despite the availability of DOACs in recent years, the high cost of these medications limited their use in this PE cohort.

When PESI clinical prediction rule for estimating the 30-day mortality risk was stratified, 16.5% of the cohort were categorized as Class V, thus highlighting a poor prognostic outcome in these patients. The in-hospital mortality rates from the Angola study (22%) and EMEP

study (20%), were slightly higher than the 17.7% mortality rates reported in our study.[29,32] A high mortality rate of 35.5% in a selected cohort of massive pulmonary embolism was reported by a Ghanaian study.[24] PE mortality lower than this study have been reported by Diall, *et al* in Mali 11.3 %, while Pessinaba, *et al* in Togo 13.7%, and Bakebe, *et al* in Kenya 7%.[18,19,48] There are diverse reasons for the differences in PE mortality across the reported studies, as this could be related to the availability of requisite medications, functional ICU, and supportive therapies.

Six (42.9%) patients died within the first 48 hours of admission, while 4 out of the 6 (66.7%) deaths were late referral. Co-morbidities such as cancer, chronic lung disease or congestive heart failure were documented among the deceased, with heart failure being the main cause of death. Delays in referral and associated co-morbidity remain a major gap in the care of patients. Such delays in PE diagnosis are associated with late initiation of therapy and worse disease outcomes.

Strengths and Limitations

As a hospital-based and single-center study, it has some limitations because it does not reflect the true picture of PE as patients with critical hemo-dynamically unstable PE may die before hospitalisation. As a private hospital there is referral bias, and this may not reflect the true burden and outcome of PE in our community. The small sample size, retrospective design of the study and large proportion of low-risk PE patients brought into the ICU, may create bias to the data. Despite these limitations, as the first documented report on PE in Sierra Leone, it will reduce the gap of data paucity in the epidemiology of PE in sub-Saharan Africa.

CONCLUSION

This study provides evidence that PE exists as a clinical diagnosis in Sierra Leone. The findings from this study are similar to other studies in SSA but different from published reports in Western countries. The validated pretest clinical prediction rules for PE were not strictly adhered by clinicians at the CMH, but rather tested for D-Dimer injudiciously. More than half of the patients admitted into the ICU were classified as low-risk PE. There was underutilization of thrombolytic agents, but heavy reliance on unfractionated heparin and warfarin. The hospital-mortality rate was comparable to other studies in Africa, with most patients dying from hemodynamically unstable PE. The high 48 hours case fatality rate among late referral cases from other hospitals, highlights the need for high index of suspicion and the need to investigate for PE as a possible cause for rapid cardiovascular deterioration in an African patient. Further prospective, and multicenter research is required to confirm our findings, as well as to address the limitations of our research.

Consent for Publication

Not applicable.

Source of Funding

None.

Registration of Research Studies

This study has been registered under the unique identifying number researchregistry6514, that is available at https://www.researchregistry.com/browse-the-registry#home/.

Declaration of Competing Interest

The authors declared no conflicts of interest.

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