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ORIGINAL RESEARCH

Acute Pulmonary Thromboembolism: A Retrospective Study in a Nigerian Private Tertiary Hospital

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Abstract

Background: Pulmonary embolism (PE) is a disease associated with high morbidity and mortality in the more technically advanced western world. However, in Africa and Nigeria in particular, the burden of PE is largely poorly defined as few data are available.
Objectives: To characterize the clinical profile, management and outcomes in PE patients confirmed with Computerized Tomography Pulmonary Angiography (CTPA).
Methods: A retrospective study was conducted at Babcock University Teaching Hospital, Ilishan-Remo, Nigeria. The medical records of PE patients confirmed by CTPA and admitted to the intensive care unit of the hospital spanning July 2016 to June 2020 were retrieved for analysis.
Results: Thirty-one patients with the age range of 26 to 93 years were included and the mean age was 55.5±18.5 years. Breathlessness was the most prevalent presenting symptom. In the majority of patients (48.4%), the risk factors were not known. However, the most common risk factor and co-morbidity was pregnancy (16.1%). The in-hospital mortality rate was 9.7%.
Conclusion: The clinical characteristics of PE in this cohort were similar to those described in the literature. The high mortality rate in this study also underscores the need for large population studies in black Africans.

Keywords: Anticoagulants, Computerized Tomography Pulmonary Angiography, Intensive Care Unit, Pulmonary Embolism, Venous Thromboembolism.

Introduction

Venous thromboembolism (VTE) is the third most frequent cause of acute cardiovascular syndrome behind myocardial infarction and

stroke worldwide. [1] It usually presents as deep vein thrombosis (DVT) or pulmonary embolism (PE). Pulmonary embolism (PE) is defined as obstruction of the pulmonary arteries by thrombi usually originating from veins (venous thrombosis) outside the lung. It is potentially fatal if not diagnosed on time and treatment commenced immediately. [2] Epidemiological studies showed that the annual incidence rates for PE range from 39 to 115 per 100,000 population and 53-162 per 100,000 population for DVT. [2, 3] PE causes about 300,000 deaths per year in the US and about 370,000 deaths in six European countries with a total population of 454.4 million. [3, 4] The Surgeon General of the United States of America estimated that PE causes 100,000–180,000 deaths annually in the US. [5] The Virchow triad describes the three main aetiological factors associated with intravascular thrombus formation: blood stasis, hyper-coagulable states and endothelial injury. [6]

Risk factors for PE include [5]: long-distance travel (> 4 hours) in the past month, surgical procedure within the last three months, malignancy (such as lung cancer), present or previous history of thrombophlebitis, lower extremities injuries occurring within the previous three months, central venous catheterization within the past three months, prior pulmonary embolism, smoking, chronic heart diseases, cerebrovascular accidents, paresis/paralysis and chronic obstructive airway diseases (COAD). [7] Other predisposing factors include drug-induced lupus anticoagulant, haemolytic anaemia, heparin-associated thrombocytopaenia, hyperhomocysteinaemia/homocystinuria, hyperlipidaemias, phenothiazine, thrombocytosis and drugs such as warfarin [8] (within the first few days of commencement of therapy).

PE does not always present with the same clinical picture in all patients. [6] The symptoms and signs of PE vary and are often dependent on the size and number of branches of the pulmonary vessel that have been occluded. It can occur suddenly with a severe clinical presentation which may even lead to death. Dyspnoea that is progressively worsening may be the presenting symptom, though it may not always be due to PE. [9] Other clinical features of PE include tachypnea, coarse crepitations, loud second heart sound, tachycardia, and fever (temperature >37.8ºC). However, a temperature higher than 39.5°C is often not from PE. Others are excessive sweating, clinical features in keeping with thrombophlebitis, pedal oedema, presence of heart murmurs and cyanosis. [8]

PE can be classified as: (a) acute/chronic (b) massive/ sub-massive/ low risk (c) central /peripheral. [8] Massive pulmonary embolism is characterized by symptoms that are a result of a disorder of cardiac function and severe haemodynamic instabilities. Sub-massive PE is characterized by right ventricular dysfunction despite normal systemic arterial pressure. Sudden onset of chest pain, which is the dominant symptom, is characteristic and often resembles the pain of acute myocardial infarction. This pain is associated with a significant drop in blood pressure leading to shock, tachycardia, tachypnea, restlessness, pallor, sweating and classical electrocardiographic features of deep S in lead I, deep Q in lead III, inverted T in V1, V2, V3, V4 leads, transient right blockade and high pulmonary P signifying a right-sided strain in the heart. [10]

Evidence-based literature supports the practice of determining the clinical probability of PE before proceeding with testing. [10] The modified Wells score and the revised Geneva score are the most common clinical rules used for excluding PE. Relevant investigations in PE include chest X-ray, electrocardiography, echocardiography, D-Dimer, compressive ultrasonography, pulmonary angiography, ventilation-perfusion

scanning, N-terminal Pro B-type Natriuretic Peptide (NT Pro-BNP assay) assay, and Computerized tomography with pulmonary angiography, which is regarded as the gold standard investigation for PE. [11]

The case-fatality rate for venous thromboembolism was reportedly twice as high for African Americans (4.1%) than for Caucasians and 1.8% for Hispanics. [12] The prevalence of DVT in Africa varies between 2.4% and 9.6% in patients after surgery, and between 380 and 448 per 100 000 births per year in pregnant and postpartum women. [13] In Nigeria, little data are available on the prevalence and treatment of PE. [14 – 16] In Africa, the prevalence of PE in medical patients varies between 0.14% - 61.5% with a mortality rate of between 40% – 61.5%. [17, 18] This study was born out of the need to improve knowledge about cardiovascular diseases in Nigerians and black Africans. Therefore, the study aimed to describe the epidemiology, clinical profile, management and outcomes of patients in patients diagnosed of PE and confirmed with Computerized Tomography Pulmonary Angiography (CTPA).

Methods

This retrospective study was conducted at the Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, south-west Nigeria. The study was carried out in accordance with the Helsinki Declaration and with adherence to the ethical guidelines of the institution. The medical records of all patients admitted to the ICU and Medical wards of the hospital from July 2016 to June 2020 were retrieved for analysis. Suspicion of a PE case was based on symptoms at presentation, physical signs and probable risk factor(s). All patients with clinical evidence of PE were included in the study if PE was confirmed by computed tomographic pulmonary angiography (CTPA). Demographic variables such as age, sex, weight, height, BMI and marital status of the patients, the suggestive symptoms and signs and risk factors were recorded. The cases were grouped and evaluated according to PE risk scores (modified Wells score). The following diagnostic tests were analysed in terms of frequency and positivity rates.

a) Laboratory tests: D-Dimer assay (Normal value is <400ng/ml).
b) Chest X-Ray: Presence of segmental atelectasis, parenchymal opacities, pleural effusion, cardiomegaly, regional oligaemia, enlarged pulmonary artery, unilateral diaphragmatic elevation.
c) ECG: Presence of sinus tachycardia, the pattern of deep S wave in lead 1, Q wave in lead 3, T wave inversion in lead 3 (S1Q3T3), tall P wave (P pulmonale), right bundle branch block, right ventricular hypertrophy and right axis deviation.
d) Echocardiogram: Presence of enlargement of the right chambers, thrombus in the right atrium or ventricle, right ventricle (RV) hypokinesia, McConnell sign, and evidence of pulmonary hypertension.
e) Compressive ultrasound scan of the extremities: To demonstrate the presence of blood clot or tram line. It has a sensitivity of 96% and a specificity of 99% for deep-vein thrombosis (DVT).
f) Computerized Tomographic Pulmonary Angiography (CTPA): The lesions were classified as massive PE if the thrombosis was located centrally in the main and lobar branches of the pulmonary artery or sub-massive PE if thromboses are located in the segmental and sub-segmental branches of the pulmonary artery.

The treatment type for each case was recorded and the clinical outcomes were classified as death or discharged alive.

The data were analysed and presented as absolute frequencies, means with standard deviations.

Results

A total of 31 cases were included in this study. The age ranged from 23 years to 91 years with a mean of 55.5±18.5 years. The 51-60 years age groups (19.4%) and 61 to 70 years (19.4%) were the most frequent. Nineteen (61.3%) of the cases were aged over 50 years. Close to three-quarters (71%) were female, 48.3% were married while 22.6% and 25.8% were overweight and obese respectively (Table I).

Table I: Demographic profile of the patients

Parameters		*Frequency*	*Percentage*
Age (Years)	20-30	3	9.6
	31-40	5	16.1
	41-50	4	12.9
	51-60	6	19.4
	61-70	6	19.4
	71-80	4	12.9
	81-90	2	6.5
	91-100	1	3.2
Gender	Female	22	71.0
	Male	9	29.0
BMI group	Underweight	2	6.4
	Normal weight	14	45.2
	Overweight	7	22.6
	Obese	8	25.8

BMI – Body Mass Index

The symptoms included breathlessness (87.1%), leg pain (54.8%), chest pain (45.2%), leg swelling (35.5%) and cough (25.8%) as depicted in Figure 1. In the majority of the cases (48.4%), the risk factors were not known. However, pregnancy (16.1%), immobilization for more than 72 hours, heart failure, malignancies (9.7%) and protein S and C deficiency (6.5%) were the identifiable risk factors and co-morbidities (Figure 2).

Using the modified Wells score for pre-test assessment of probability for PE, PE was likely in 19 (61.3%) cases while PE was unlikely in 12 (38.7%) of the cases. D-Dimer at presentation was within a normal range (<400ng/ml) in 21 (67.7%) but elevated in 10 (32.3%) of the cases (Table II). Fourteen (45.2%) had normal chest X-Ray. The most common chest X-Ray abnormalities included regional oligaemia (9.7%), atelectasis (9.7%), enlarged descending pulmonary trunk (9.7%) pleural effusion (9.7%), parenchymal opacities (6.5%) and unilateral diaphragmatic elevation (3.2%) (Table II). The electrocardiogram was normal in 54.8% of cases

while the classic S1Q3T3 pattern was found in only 6.5%. The presence of blood clot (deep-vein thrombosis) discoverable by Doppler ultrasound was documented in 54.8% of cases. About two-thirds (67.7%) of the cases had no abnormalities on echocardiogram. Only 16.1% had evidence of right ventricular enlargement, 9.7% had pulmonary hypertension and 3.2% had evidence of severe tricuspid regurgitations.

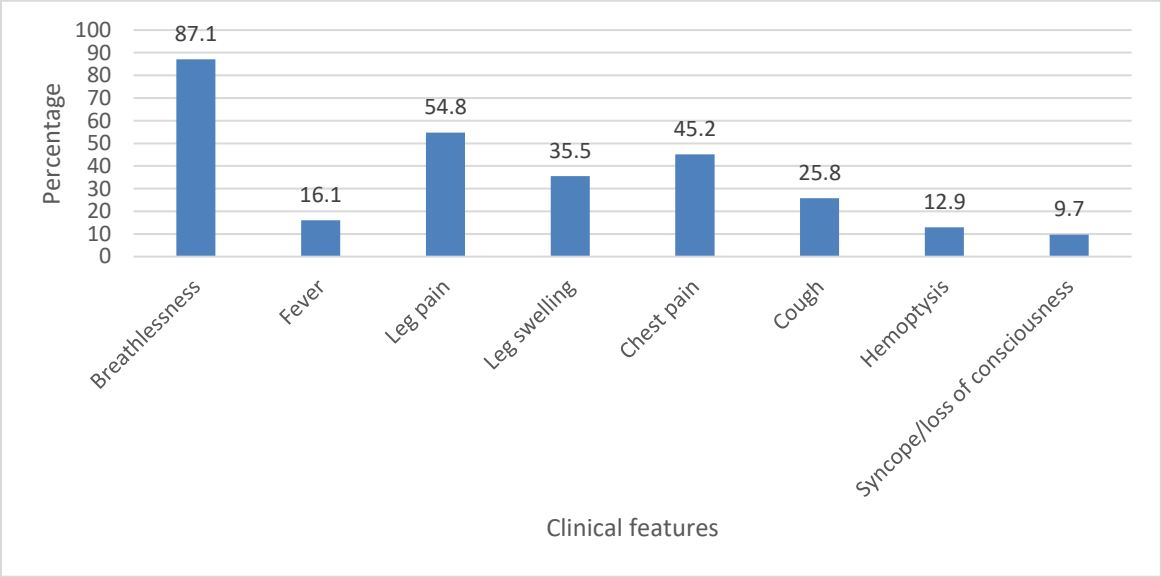

Figure 1: Distribution of the clinical features in the patients at presentation

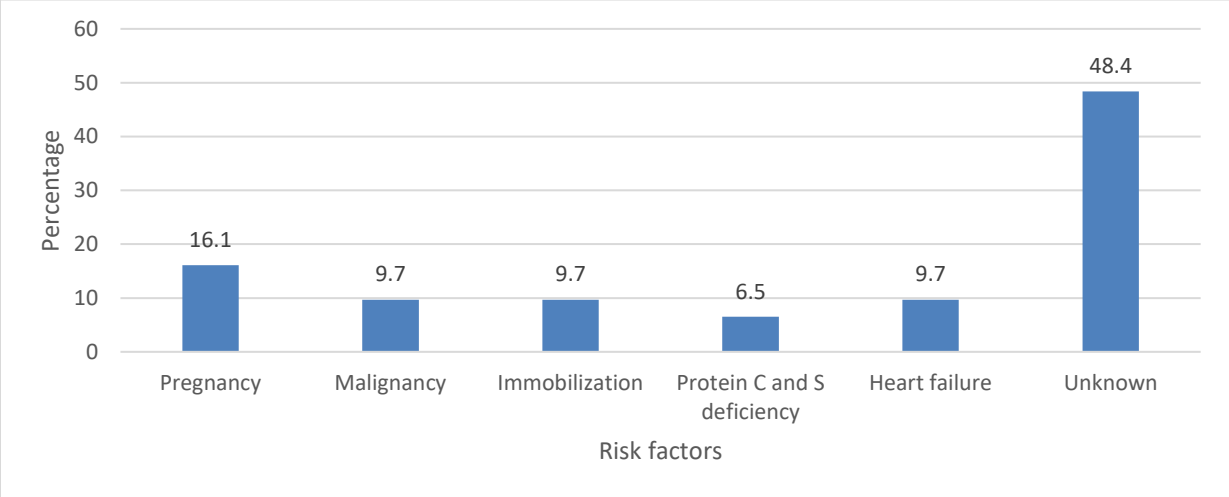

Figure 2: Distribution of the risk factors among the patients

Table II: Pattern of the results of laboratory investigations among patients

Parameters		*Frequency*	*Percentage*
Wells Score	PE unlikely	12	38.7
	PE likely	19	61.3
Chest X-Ray	Normal chest X-Ray	14	45.2
	Regional oligaemia	3	9.7
	Enlarged descending pulmonary trunk	3	9.7
	Atelectasis	3	9.7
	Pleural effusion	3	9.7
	Parenchymal opacities	2	6.5
	Unilateral diaphragmatic elevation	1	3.2
	Cardiomegaly	2	6.5
Electrocardiography	Normal ECG	17	54.8
	Tachycardia	6	19.4
	ST abnormalities	2	6.5
	P wave abnormalities	1	3.2
	Right Axis Deviation	3	9.7
	S1q3t3	2	6.5
Compressive Doppler Ultrasound	Clot seen	17	54.8
	Loss of compressibility	8	25.8
	No abnormality detected	6	19.4
D- Dimer assay	Positive	10	32.3
	Negative	21	67.7
Echocardiography	Normal ECHO	21	67.7
	Pulmonary hypertension	3	9.7
	Right ventricular Enlargement	5	16.1
	Tricuspid regurgitation	1	3.2
	McConnel's sign	1	3.2
CTPA	Low risk	0	0.0
	Sub massive	27	87.1
	Massive	4	12.9

CTPA - Computerized Tomographic Pulmonary Angiography

At presentation, CTPA changes were correlated with haemodynamic stability in all the patients. Four cases (12.9%) had massive PE, of whom 50% were haemodynamically unstable, while 27 (87.1%) had sub-massive PE. Anticoagulation was the treatment mostly used among 27 patients (87.1%) while 2 (6.5%) each received anticoagulation with vena cava filter and thrombolytic therapy respectively. Heparins were the most common form of in-hospital anticoagulation. Low-molecular-weight heparins were used in 93.6% of the cases and the mean duration of anticoagulation therapy was 7.6±2.3 days. Among these patients on anticoagulation therapy, 77% were on a combination of parenteral anticoagulation with warfarin while 10.1% used new oral anticoagulants (NOAC).

Table III: Treatment modalities and outcome among patients with PE

Parameters		*Frequency (n = 31)*	*Percentage*
Treatment	Anticoagulant	27	87.0
	Thrombolytic	2	6.5
	Anticoagulant and Vena cava filter	2	6.5
Outcome	Died	3	9.7
	Discharged alive	28	90.3

Table III shows that the in-hospital mortality rate was 9.7% (3/31), 2 of whom received thrombolytic therapy. Twenty-eight cases (90.3%) were discharged alive. All the mortalities were recorded among patients with massive embolism.

Discussion

The findings in this study showed that PE may not be as uncommon among Nigerians as was widely believed and the availability of appropriate diagnostic tools will improve prompt diagnosis and treatment. In concordance with the findings reported by Manuel Ana *et al.* in Angola [14] and Tambe *et al.* in Cameroun, [17] PE may not be as rare in Africa as was previously believed. The non-unavailability of CTPA in hospitals in sub- Saharan Africa impairs the confirmation of most cases of PE. [18] The availability of CTPA and other diagnostic tests at the facility where the present study was conducted allowed the confirmation of PE cases and excluded other differential diagnoses. This afforded better accuracy and consistency of the findings.

The mean age of PE cases in the present study (55.5±18.5 years) is similar to 56.5 ± 18.1 years reported in the Emergency Medicine Pulmonary Embolism in the Real World Registry (EMPEROR) study, [19] but higher than 50.5 ± 17.8 years reported in the Angolan study () [14] but lower than the median ages described in some other studies. [20, 21] The differences noted with these other studies may be as a result of the small sample size used in the present study.

The most common symptom in this cohort was breathlessness. The spectrum of features in this present study is similar to the report in the Japanese Society of Pulmonary Embolism Research (JASPER) study [22] and the Angolan study. [14] However, compared to the findings in the present study, higher frequencies of tachycardia and tachypnoea have been reported in other studies. [22] The symptoms of PE are in most cases not specific; therefore, a high index of suspicion is needed to ensure the diagnosis is not missed. Breathlessness often constitutes the main symptom of PE in most cases with an array of probable differential diagnoses. However, the sudden onset of breathlessness should raise suspicion about PE. [23]

The most prevalent co-existing risk factor in our study included pregnancy and immobilization for more than 72 hours. The low frequencies of these factors in the present study may be due to the small sample size used in the study. However, these values are similar to the findings in the International Cooperative Pulmonary Embolism Registry (ICOPER) [24] and Estudo

Multicentrico de Embolia Pulmunar (EMEP) [25] studies. In a large proportion of cases in the present study (48.4%), the risk factors for PE were not known. This suggests that there some risk factors predisposing to PE are unknown in the setting of the study. [26]

Although the Wells score is a subjective clinical tool of predicting VTE and PE, [26] the modified tool predicted PE in 61.3% of the cases in the present study which is similar to findings in other studies. [15, 31] D-Dimer assay were suggestive of PE in only 32.3% of cases confirmed by CTPA. This low yield of D-Dimer assay is similar to the findings in another study. [15]

More than half of the cases had Chest X-Ray abnormalities. These findings are similar to those reported in the Angolan [14] and EMEP [26] studies. However, inter-observer variability and subjectivity in the interpretation of chest radiographs may have influenced the results in these studies. ECG is frequently used to evaluate patients for PE. It is non-invasive and inexpensive. [27] Electrocardiographic (ECG) changes were identified in close to half of the cases in the present study. This is similar to the finding (48%) in the Angolan [14] study. The ECG changes observed in the present cohort included sinus tachycardia and right axis deviation. An echocardiogram is often used in the investigation of PE patients and it is not invasive or expensive. In about a third of the cases who had echocardiographic abnormalities, right ventricular enlargement and pulmonary hypertension were frequently encountered, similar to the finding in the EMEP study. Evidence of deep vein thrombosis using compressive ultrasonography (CUS) of the veins of the limbs was evident in 80.6% of PE patients confirmed by CTPA. This investigation has a sensitivity of 96% and a specificity of 99% for deep-vein thrombosis (DVT). This is not surprising as a study had shown that about 70% of patients with PE had DVT of the lower limbs. [28]

The treatment of pulmonary embolism (PE) in the acute phase was based on the use of heparin and other anticoagulants. They prevent the propagation of old thrombi and the formation of new ones. Most of our patients received low-molecular-weight heparins and warfarin. In our study, thrombolytic therapy was used in only 6.5% of PE patient. This is different from findings in the EMEP study [25] which showed that thrombolytic was used in only 15% of patients. The use of thrombolysis allows for early reperfusion of the pulmonary vessel. Even at increased risk of major bleeding, it is indicated in unstable patients. [26]

In our study, the mortality rate was 9.7%. This is small compared to that described in the EMEP study (22%) [25] but similar to the rates described in other PE studies. [27 - 29] The fact that the study involved only 31 patients and mostly intermediate-risk patients with hemodynamic stability may have contributed to the low mortality rate.

The retrospective design of the study is a limitation, in addition to the small size of the study subjects. The challenge of missing data is also acknowledged as another limitation.

Conclusion

This study confirmed that pulmonary embolism (PE) is not as rare in the African and Nigerian population as widely believed. The clinical presentations and investigation findings in PE cases were similar to the descriptions available in the literature. There is a need for other studies with larger sample sizes in different centres all over black Africa, to generate robust data using the findings in the present study as a template.

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Authors' Contributions: OJO conceived and designed the study, literature search, data acquisition and manuscript drafting. OAO, ABO, AYAO and EO participated in the literature review, manuscript drafting and revision of the manuscript for sound intellectual content. EO also participated in data acquisition. All the authors approved the final version of the manuscript.

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References

1. Raskob GE, Angchaisuksiri P, Blanco AN, Buller H, Gallus A, Hunt BJ, *et al.* Thrombosis: a major contributor to global disease burden. Arterioscler Thromb Vasc Biol 2014; 34: 2363–2371. https://doi.org/10.1161/ATVBAHA.114.304488

2. Wendelboe AM, Raskob GE. Global burden of thrombosis: epidemiologic aspects. Circ Res 2016; 118: 1340–1347. https://doi.org/10.1161/CIRCRESAHA.115.306841

3. Keller K, Hobohm L, Ebner M, Kresoja KP, Munzel T, Konstantinidis SV, *et al*. Trends in thrombolytic treatment and outcomes of acute pulmonary embolism in Germans. Eur Heart J 2020; 41: 522-529. https://doi.org/10.1093/eurheartj/ehz236

4. ISTH Steering Committee for World Thrombosis. Thrombosis: a major contributor to global disease burden. J Thromb Haemost 2014; 12: 1580–90. https://doi.org/10.1111/jth.12698

5. Galson SK. The surgeon general's call to action to prevent deep vein thrombosis and pulmonary embolism. Available at: http://www.surgeongeneral.gov/topics/deepvein/. Accessed 19 April 2010.

6. Deitelzweig SB, Lin J, Johnson BH, Schulman KL. Venous thromboembolism in the US: does race matter? J Thromb thrombolysis 2011; 31: 133-138. https://doi.org/10.1007/s11239-010-0503-3

7. Cohen AT, Agnelli G, Anderson FA, Arcelus JI, Bergqvist D, Brecht JG, *et al.* Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality. Thromb Haemost 2007; 98: 756–764.

8. Heit JA. Epidemiology of venous thromboembolism. Nat Rev Cardiol 2015; 12: 464–474. https://doi.org/10.1038/nrcardio.2015.83

9. Lambrini K, Konstantinos K, Christos I, Petros O, Areti T. Pulmonary Embolism: A Literature Review. Am J Nurs Sci 2018; 7: 57-61. https://doi.org/10.11648/j.ajns.s.20180703011.19

10. Kapetaniou A. Pulmonary embolism-Diagnosis and treatment. Medical Analects 2011; 9: 390-394.

11. Doğan H, de Roos A, Geleijins J, Huisman MV, Kroft LJ. The role of computed tomography in the diagnosis of acute and chronic pulmonary embolism. Diagn Interv Radiol 2015; 21: 307–316. https://doi.org/10.5152/dir.2015.14403

12. White RH, Zhou H, Murin S, Harvey D. Effect of ethnicity and gender on the incidence of venous thromboembolism in a diverse population in California in 1996. Thromb Haemost 2005; 93:298–305. https://doi.org/10.1160/TH04-08-0506

13. Mbatchou Ngahane BH, Kamdem F, Njonnou SRS, Chebou N, Dzudie A, Ebongue SA, *et al.* Epidemiology, clinical and paraclinical presentations of pulmonary embolism: A cross-sectional study in a sub-Saharan Africa setting. Open J Respir Dis 2019; 9: 89-99. https://doi.org/10.4236/ojrd.2019.93008.

14. Awotedu AA, Igbokwe EO, Ekang EE, Aghadiuno PO. Pulmonary embolism in Ibadan, Nigeria: five years autopsy report. Cent Afr J Med 1992; 38:432-435.

15. Manuel A, Aufico A, Africano R, Peralta T, Salas A, Silva A, *et al.* Clinical profile, management and outcomes of patients with pulmonary embolism: a retrospective tertiary centre study in Angola. Cardiovasc J Afr 2017; 28: 356-361. https://doi.org/10.5830/CVJA-2017-017

16. Igun GO. A 10-year review of venous thromboembolism in surgical patients seen in Jos, Nigeria. Niger Postgrad Med J 2001; 8: 69–73.

17. Tambe J, Moifo B, Fongang E, Guegang E, Juimo AG. Acute pulmonary embolism in the era of multidetector CT: a reality in sub-Saharan Africa. BMC Med Imaging 2012; 12: 31. https://doi.org/10.1186/1471-2342-12-31

18. Danwang C, Temgoua MN, Agbor VN, Tankeu AT, Noubiap JJ. Epidemiology of venous thromboembolism in Africa: a systematic review. J Thromb Haemost 2017; 15: 1770–1781. https://doi.org/10.1111/jth.13769

19. Pollack CV, Schreiber D, Goldhaber SZ, Slattery D, Fanikos J, O'Neil BJ, *et al.* Clinical characteristics, management, and outcomes of patients diagnosed with acute pulmonary embolism in the emergency department: initial report of EMPEROR (Multicenter Emergency Medicine Pulmonary Embolism in the Real World Registry). J Am Coll Cardiol 2011; 57: 700–706. https://doi.org/10.1016/j.jacc.2010.05.071

20. Eng J, Krishnan JA, Segal JB, Bolger DT, Tamariz LJ, Streiff MB, *et al.* Accuracy of CT in the Diagnosis of Pulmonary Embolism: A Systematic Literature Review. Am J Roentgenol 2004; 183: 1819-1827. https://doi.org/10.2214/ajr.183.6.01831819

21. Vamsidhar A, Rajasekhar D, Vanajakshamma V, Lakshmi AY, Latheef K, Siva Sankara C, *et al.* Comparison of PESI, Echocardiogram, CTPA and NT-ProBNP as risk stratification tools in patients with acute pulmonary embolism. Indian Heart J 2017; 69: 68-74. https://doi.org/10.1016/j.ihj.2016.07.010

22. Nakamura M1, Fujioka H, Yamada N, Sakuma M, Okada O, Nakanishi N, *et al.* Clinical characteristics of acute pulmonary thromboembolism in Japan: results of a multicenter registry in the Japanese Society of Pulmonary Embolism Research. Clin Cardiol 2001; 24: 132–138. https://doi.org/10.1002/clc.4960240207

23. International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM). Available at: http://www.icd10cmtool.cdc.gov. Accessed March 2021.

24. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet 1999; 353: 1386–1389. https://doi.org/10.1016/s0140-6736(98)07534-5

25. Volschan A, Albuquerque DC, Tura BR, Knibel Mde F, Souza PC, Toscano ML. Pulmonary embolism: multicenter registry in tertiary hospitals. Rev Bras Ter Intensiva 2009; 21: 237–246. https://doi.org/10.1590/S0103-507X2009000300002

26. Goldhaber SZ. Deep venous thrombosis and pulmonary thromboembolism. In: Kasper D, Hauser S, Jameson JL, Fauci A, Longo DL,

Loscalzo JL (Eds). Harrison's Principles of Internal Medicine. 19th Edition. London: McGraw-Hill, 2015: p.1631–1637.

27. Danielsbacka JS, Hanssonc PO, Mannerkorpi K, Olsén MF. Physical activity and respiratory symptoms after pulmonary embolism. A longitudinal observational study. Thrombosis Res 2020; 189: 55–60. https://doi.org/10.1016/j.thromres.2020.02.014

28. Penaloza A, Kline J, Verschuren F, Courtney DM, Zech F, Derrien B, *et al*. European and American suspected and confirmed pulmonary embolism populations: comparison and analysis. J Thrombosis Haemostasis 2012; 10: 375–381. https://doi.org/10.1111/j.1538-7836.2012.04631

29. Ibrahim SA, Stone RA, Obrosky S, Sartorius J, Fine MJ, Aujesky D. Racial Differences in 30-Day Mortality for Pulmonary Embolism. Am J Public Health 2006; 96: 2161-2164. https://doi.org/10.2105/AJPH.2005.078618

30. Mousa AY, Broce M, De Wit D, Baskharoun M, Abu-Halimah S, Yacoub M, *et al*. Appropriate use of venous imaging and analysis of the D-Dimer/ Clinical Probability Testing Paradigm in the diagnosis and location of deep venous thrombosis. Ann Vasc Surg 2018; 50: 21-29. https://doi.org/10.1016/j.avsg.2017.12.006

31. Mousa AY, Broce M, Gill G, Kali M, Yacoub M, AbuRahma AF. Appropriate use of D-Dimer Testing can minimize overutilization of Venous Duplex Ultrasound in a contemporary High-Volume Hospital. Ann Vasc Surg 2015; 29: 311-317. https://doi.org/10.1016/j.avsg.2014.07.032