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ORIGINAL ARTICLE

COVID-19

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Pulmonary Embolism Diagnosed by CT Pulmonary Angiography in Patients with COVID-19 and Features of the Associated Factors

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Abstract

Background: Since December 2019, when a new coronavirus disease 2019 (COVID-19) was detected in Wuhan, China, over 774 million confirmed COVID-19 cases and over seven million deaths have been reported globally, as of 7 January 2024 (WHO, 2024). Venous thromboembolism is a recognized complication of COVID-19. This study aimed to investigate the prevalence of pulmonary embolism (PE) diagnosed by CT pulmonary angiography (CTPA) in COVID-19 patients and the features of the associated factors.

Methods and Results: The study included 162 patients from the Imam Abdulrahman Al-Faisal Hospital who had COVID-19-confirmed infections while hospitalized in the ICU. Patients were diagnosed as COVID-19 positive by RT-PCR and underwent CTPA examination on the Discovery 16-slice CT scanner (Siemens, Germany) following standard protocol. For contrast enhancement, non-ionic, iodinated, intravenous contrast material (Omnipaque 350 mg) was used.

PE was detected by CTPA in 87(53.7%) COVID-19 patients. The D-dimer level was significantly higher in the PE group than in the non-PE group. The frequency of renal impairment in the PE group was 2.3 times higher than in the non-PE group. The ICU duration was longer in the PE group than in non-PE group (12.9±11.3 and 8.6±7.2 days, P=0.005). The death rate was 17.2% in the PE group and 1.3% in the non-PE group (P=0.001). The heart and respiratory rates, blood pressure, BMI, BUN, and creatinine levels did not differ in the study groups. The frequency of diabetes, hypertension, asthma, COPD, and smoking were comparable in the groups.

Conclusion: CTPA is very important in diagnosing PE in COVID-19 patients. CTPA-diagnosed PE is significantly associated with D-dimer, ICU duration, and death.**(International Journal of Biomedicine. 2024;14(2):305-311.)**

Keywords: COVID-19 • CT pulmonary angiography • pulmonary embolism • D-dimer

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Abbreviations

ARDS, acute respiratory distress syndrome; **AKI**, acute kidney injury; **BMI**, body mass index; **BP**, blood pressure; **DBP**, diastolic BP; **CT**, computed tomography; **CTPA**, CT pulmonary angiography; **COPD**, chronic obstructive pulmonary disease; **HR**, heart rate; **ICU**, intensive care unit; **PE,** pulmonary embolism; **RR**, respiratory rate; **RT-PCR**, reverse transcription–polymerase chain reaction; **SBP**, systolic BP.

Introduction

Since December 2019, when a new coronavirus disease 2019 (COVID-19) was detected in Wuhan, China, over 774 million confirmed COVID-19 cases and over seven million deaths have been reported globally, as of 7 January 2024.[1]

Patients with SARS-CoV-2 infection can experience a range of clinical manifestations, from no symptoms to critical illness. Venous thromboembolism is a recognized complication of COVID-19. Many studies have reported a higher incidence of deep vein thrombosis and PE in COVID-19.[2-4] PE in COVID-19 has been found to be different from traditional PE in terms of demographic and clinical characteristics and laboratory data.[5]

SARS-CoV-2 infection could increase predisposition to venous and arterial thromboembolism due to excessive inflammation, hypoxia, immobilization, and diffuse intravascular coagulation.[6] SARS-CoV-2 infection with a wide thrombotic response has become a factor in a sudden surge in the incidence of PE the world over. Data from numerous meta-analyses also strongly indicate a higher incidence of PE in COVID-19 patients, especially in ICU settings.[7] In a Chinese study, Miesbach et al.[8] reported that up to 40% of patients developed PE chiefly localized in small pulmonary artery branches. In a French study, Poissy et al.[9] reported PE in 20.6% of the patients during their stay in the ICU, with a median time of 6 days. Another French study by Bompard et al.[10] reported a PE incidence of 50% in ICU, COVID-19 patients.

CTPA, a gold standard,[11] should be performed on admission if PE is suspected, or if there is acute degradation of hemodynamic or respiratory status, or if the patient presents with minimal pulmonary infiltrates or signs of acute right ventricular overload.[12,13]

This study aimed to investigate the prevalence of PE diagnosed by CTPA in COVID-19 patients and the features of the associated factors.

Materials and Methods

The study included 162 patients from the Imam Abdulrahman Al-Faisal Hospital who had COVID-19-confirmed infections while hospitalized in the ICU. The baseline characteristics of COVID-19 patients are shown in Table 1.

Table 1.
Baseline characteristics of COVID-19 patients.

Patient group	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)	HR (bpm)	RR (bpm)
Male	52.2±13 (18-92)	169.4±6 (150-188)	80.8±11 (52-119)	28.1±4 (18.1-37.5)	79.5±8 (22-100)	21.3±6 (17-78)
Female	50.8±15 (22-84)	161±7 (134-188)	78.4±15 (52-120)	30±5 (21.4-45.7)	81.4±12 (52-146)	21.1±2 (18-25)
Total	51.8±14 (18-92)	167±7 (134-188)	80.1±12 (52-120)	28.7±4 (18.4-45.7	80.1±9 (22-146)	21.2±5 (17 -78)

Patients admitted for treatment or isolation had to meet the following criteria: (a) positive SARS-CoV-2 RT-PCR testing on pharyngeal swabs; (b) a thin-section chest CT scan indicating any signs of pneumonia; and (c) patients hospitalized for treatment or isolation. All patients were examined based on the World Health Organization's interim recommendations for the clinical care of COVID-19 patients (WHO, 2022).

All patients were identified via the electronic record system, and their demographic, clinical, and radiological data were extracted and reviewed. Patients were diagnosed as COVID-19 positive by RT-PCR and underwent CTPA examination on the Discovery 16-slice CT scanner (Siemens, Germany) following standard protocol. We used non-ionic, iodinated, intravenous contrast material (Omnipaque 350 mg) for contrast enhancement. CTPA images were double-reviewed by radiologists with more than 10 years of experience. If PE was detected in the CTPA, the location, distribution, size, and type were documented.[14]

Statistical analysis was performed using the statistical software package SPSS version 21.0 (SPSS Inc, Armonk, NY: IBM Corp). Baseline characteristics were summarized as frequencies and percentages for categorical variables and mean ± SD for continuous variables. For data with normal distribution, inter-group comparisons were performed using Student's t-test. The frequencies of categorical variables were compared using a chi-squared test. A probability value of $P<0.05$ was considered statistically significant.

Results

The patients ranged in age from 18 to 92 years. The largest age group was 56-60 years (Table 2). The distribution of symptoms in COVID-19 patients is shown in Table 3.

Table 2.
Patient distribution by age group.

Age group (year)	N	%	Cumulative Percentage
<20	2	1.2	1.2
20-25	2	1.2	2.5
26-30	6	3.7	6.2
31-35	8	4.9	11.1
36-40	18	11.1	22.2
41-45	20	12.3	34.6
46-50	19	11.7	46.3
51-55	23	14.2	60.5
56-60	25	15.4	75.9
61-65	18	11.1	87.0
66-70	7	4.3	91.4
>70	14	8.6	100.0
Total	162	100.0	

Table 3.

The distribution of symptoms in COVID-19 patients.

Signs and symptoms	N	Percent
Fever	19	11.7%
Cough	11	6.8%
General symptoms	49	30.2%
General symptoms & pneumonia	30	18.5%
Breath shortness	39	24.1%
Sore throat	2	1.2%
Diarrhea	4	2.5%
Body pain	4	2.5%
Vomiting	2	1.2%
Others	1	0.6%
General symptoms & pneumonia & other symptoms	1	0.6%
Total	162	100%

PE was detected by CTPA in 87(53.7%) COVID-19 patients. In general, the death rate was 9.87%, and the causes of death are presented in Table 4. Three images demonstrate features of COVID-19 on CT (Figures 1-3).

Table 4.

Causes of death.

Causes of death among 162 COVID-19 patients	N	Percent
Irreversible cardiogenic shock	1	0.617
Metabolic acidosis	1	0.617
Irreversible shock/cardiac arrest	1	0.617
ARDS/septic shock	2	1.234
ARDS/septic shock/cardiac arrest	1	0.617
Septic shock/ARDS /AKI	1	0.617
ARDS/PE/septic shock	1	0.617
ARDS/respiratory failure	1	0.617
Metabolic acidosis/shock	1	0.617
Cardiovascular collapse/refractory hypoxia	1	0.617
ARDS /cardiogenic shock	1	0.617
Shock/metabolic acidosis/AKI/cardiac arrest	1	0.617
ARDS/septic shock/cardiac arrest/PE	1	0.617
Severe ARDS/shock/AKI/pneumothorax/PE	1	0.617
Chronic renal failure/septic shock	1	0.617
Total	16	9.872%

A comparison of the demographic and clinical characteristics of COVID-19 patients with PE and without PE is presented in Table 5. Mean levels of SBP and DBP were within the recommended values in both groups. The D-dimer level was significantly higher in the PE group than in the non-PE group (4.7±11.2 vs.1.8±2.8 µg/mL, *P*=0.031). The frequency of renal impairment in the PE group was 2.3 times higher than in the non-PE group (27.6% vs.12.0%, *P*=0.014). The ICU duration was longer in the PE group than in non-PE group (12.9±11.3 and 8.6±7.2 days, *P*=0.005). The death rate was 17.2% in the PE group and 1.3% in the non-PE group (*P*=0.001). The heart and respiratory rates, blood pressure, BMI, BUN, and creatinine levels did not differ in the study groups. The frequency of diabetes, hypertension, asthma, COPD, and smoking were comparable in the groups.

Table 5.

Demographic and clinical characteristics of the studied groups.

Variable		PE (n= 87)	Non-PE (n=75)	*P*-value
Demographic data				
Age, years		50.8±12.9	52.2±15.2	0.527
Sex	Female	30 (34.5%)	22 (29.3%)	0.485
	Male	57 (65.5%)	53 (70.7%)	
Nationality	Non-Saudi	56 (64.4%)	37 (49.3%)	0.054
	Saudi	31 (35.6%)	38 (50.7%)	
Height, cm		166.6±8.1	167±6.6	0.734
Weight, kg		78.6±12.7	81.2±13.5	0.209
BMI, kg/m^2		28.3±4.3	29.0±3.8	0.277
Vital signs				
SBP, mmHg		128±12	129±11	0.583
DBP, mmHg		77.8±5.8	78.7±6.0	0.334
HR, bpm		80±10.8	80±6.8	1.000
RR, bpm		21.5±6.4	20.9±2.2	0.441
History of risk factors				
Diabetes Mellites		50 (57.5%)	33 (44.0%)	0.088
Hypertension		31 (35.6%)	30 (40.0%)	0.569
Asthma		11 (12.6%)	10 (13.3%)	0.897
COPD		1 (1.1%)	0.0(0.0%)	0.353
Smoking		2 (2.3%)	1 (1.3%)	0.813
Laboratory investigations				
D-dimer, µg/mL		4.7±11.2	1.8±2.8	0.031
BUN, mg/dL		8.2±8.4	7.1±4.0	0.301
Creatinine, µmol/L		73.6±28.9	79.2±43.2	0.328
AKI, n %		24 (27.6%)	9 (12.0%)	0.014
Outcomes				
ICU duration, days		12.9±11.3	8.6±7.2	0.005
Death		15 (17.2%)	1 (1.3%)	0.001

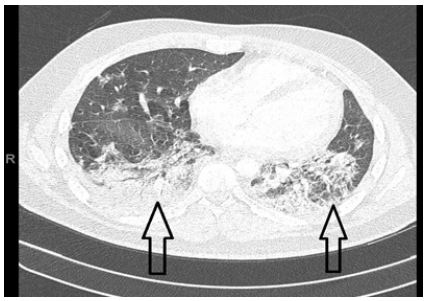

Fig.1. *A 22-year-old Saudi female patient. Bilateral patchy consolidated opacities at the lower lobes.*

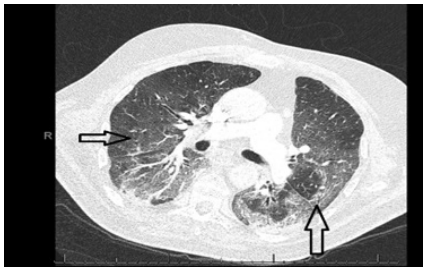

Fig.2. *A 65-year-old non-Saudi male patient. Bilateral ground glass opacity, the middle and lower consolidation.*

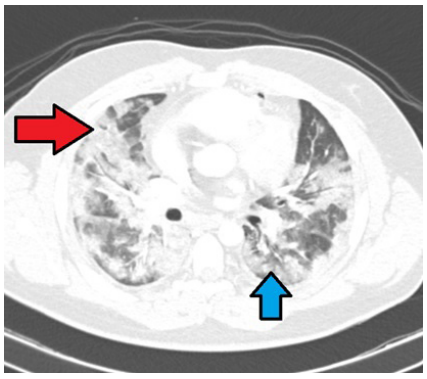

Fig.3. *A 31-year-old non-Saudi male patient. Crazy paving (red arrow) and areas of consolidation (blue arrow)*

Discussion

Pulmonary embolism is highly associated with COVID-19 disease and should be further explored and characterized for each patient.[15] Our study detected PE, diagnosed by CTPA, in 87(53.7%) COVID-19 patients. This result is much higher than that of Kyriakopoulos et al.[16] in Greece (6%). In a study by Abohamr et al.,[17] the incidence of acute PE was 22% [95% confidence interval (95% CI): 19%-39%], detected by chest CT. Overall, a higher prevalence of PE can be assumed among COVID-19 patients in Saudi Arabia. This study examined a wide range of variables associated with PE in patients with COVID-19. Regarding the gender of patients in this study population, males were more affected by COVID-19 than females, which agrees with a study by Abohamr et al.[17] from Saudi Arabia and Espallargas et al.[18] from Spain. This might be attributed to a higher probability of contact and exposure to sources of SARS-CoV-2 virus due to the nature of work among male rather than female patients.

Among factors predisposing to increased mortality with COVID-19 infection, male sex, hypertension, obesity, and increasing age are most important, but multiple studies have shown that excess weight is also significantly associated with severe COVID-19 disease.[19] The body mass index (BMI) of 28.7±4.0 kg/m^2 of participants in our research, which corresponds to the overweight range according to NHLBI (2022),[20] was found to be close to the mean BMI of 30.8 kg/m^2, which is within the obese range found in a US study of 20,736 COVID-19 patients.[21]

By analyzing the relationship between known risk factors for poor prognosis in COVID-19 and the development of PE, we found that COVID-19 patients with PE were characterized by significantly higher D-dimer level and ICU duration than non-PE patients [4.7±11.2 vs.1.8±12.8 µg/mL (P=0.031), 12.9±11.3 vs. 8.6±7.2 days (P=0.005), respectively]. Abohamr et al.[17] found that COVID-19 patients with PE had significantly higher levels of D-dimer, C-reactive protein, cardiac troponin, and lactate dehydrogenase than those in patients without PE. In a study by Mouhat,[22] elevated D-dimers (>2590 ng/mL) and the absence of anticoagulant therapy predicted PE in hospitalized COVID-19 patients with clinical signs of severity. D-dimers ≥2000 ng/mL (26.3 [4.1–537.8]) and neutrophils ≥7.0 g/L (5.8 [1.4–29.5]) were two biomarkers associated with a higher risk of PE (P=0.0002) and death or intensive care unit (ICU) transfer (HR [95%CI], 12.9 [2.5–67.8], P<0.01) in a study by Thoreau et al.[23] According to Kaminetzky et al.,[24] the D-dimer level can be used to stratify patients according to PE risk and severity.

The relationships we found between CTPA-diagnosed PE and studied parameters in our study were consistent with the results of a number of studies. Bompard et al.[10] showed that patients with PE were more frequently hospitalized in the ICU and more frequently under mechanical ventilation, with a longer median (IQR) hospitalization duration (15(9–17) vs. 8(4–12) days [P=0.04] in the PE-negative patients).

In our study, high levels of blood D-dimer, and ICU duration in PE patients were accompanied by more than 13 times higher mortality: 17.2% in the PE group and 1.3% in the non-PE group (P=0.001). Causes of death were irreversible cardiogenic shock, acute kidney injury, metabolic acidosis, large PE, respiratory failure, acute respiratory distress syndrome, septic shock, cardiovascular collapse, refractory hypoxia, and right-side pneumothorax. These causes of death were in accordance with data from Menter et al.[25] and Elezkurtaj et al.[26] Moreover, PE, in the study of Elezkurtaj et al.,[26] was the cause of death in 3.8% of cases.

As is known, comorbidities complicate the prognosis of COVID-19 patients. In our study, diabetes, identified in 57.5% of COVID-19 patients with PE and 44.0% of non-PE patients, was the most prevalent comorbidity, followed by hypertension. The high incidence of diabetes in our study is

explained by the high incidence of diabetes in the country. According to the International Diabetes Federation,[27] 17.7% of Saudi Arabia's adult population suffers from diabetes, which is the second highest diabetes prevalence in the region and seventh worldwide.

Hypertension is also the most common comorbidity in COVID-19 patients and increases in-hospital mortality. Blood pressure (BP) variability is associated with clinical outcomes in hypertensive patients. A study by He et al.[28] included 702 COVID-19 patients with hypertension from Huoshenshan Hospital (Wuhan, China). The authors demonstrated that day-by-day in-hospital systolic blood pressure variability can independently predict mortality and acute respiratory distress syndrome in COVID-19 patients with hypertension. In our study, the frequency of hypertension in the PE and non-PE groups was 35.6% and 40.0%, respectively, without statistical significance. However, mean levels of systolic blood pressure and diastolic blood pressure were within the recommended values in PE and non-PE patients. The heart and respiratory rates did not differ in the study groups.

Early reports indicate that acute kidney injury is common among patients with COVID-19 and is associated with worse outcomes and high mortality. In a study by Chan et al.,[29] of 3993 hospitalized patients with COVID-19, acute kidney injury occurred in 1835(46%) patients; 347(19%) of the patients with acute kidney injury required dialysis. In our study, renal impairment was found in 27.6% of COVID-19 patients with PE and only 12.0% of non-PE patients (P=0.014).

Compared to factors predisposing to increased mortality with COVID-19 infection, such as male sex, hypertension, obesity, and increasing age, airway diseases gave some contradictory results. Finnerty et al.,[30] in a systematic global review and meta-analysis, showed that for asthma and COPD, prevalence in patients hospitalized with COVID-19 varies markedly by region. The authors found no evidence that asthma predisposes one to increased mortality in COVID-19 disease. For COPD, there was clear evidence of an association with increased mortality. In our study, the prevalence of asthma and COPD was 12.6% and 1.1% in the PE group and 13.3% and 0% in the non-PE group, and no differences were found.

Conclusion

CT pulmonary angiography (CTPA) is very important in diagnosing PE in COVID-19 patients. CTPA-diagnosed PE is significantly associated with D-dimer, ICU duration, and death. The specified parameters, such as D-dimer levels in COVID-19 patients, as well as ICU duration, can be recommended as indicators or predictors of the development of PE in circumstances where immediate CT is unavailable.

Ethical Considerations

The study was conducted in accordance with ethical principles of the WMA Declaration of Helsinki (1964, ed. 2013) and was approved by the King Saud Medical City's institutional review board.

Competing Interests

The authors declare that they have no competing interests.

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