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Pulmonary Thromboembolic Disease in COVID-19 Hospitalized Patients on CT Pulmonary Angiography-Prevalence, Pattern of Disease and Relationship to CT Scan Severity Score (CTSS)

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Abstract

Aims: Covid 19 is a multisystem disease that varies from mild to very severe and is fatal in different individuals. The exact cause of the deterioration of the disease in some people is not completely known, but various studies have shown that the risk of venous arterial embolism is higher in these patients for various reasons, and one of the reasons that worsen the clinical course and increases mortality in these patients, Pulmonary Emboli (PE). Due to the non-specific and non-diagnostic nature of clinical signs and laboratory tests (d-dimer) for the diagnosis of PE in patients with covid-19 and also the non-specificity of the findings in contrast-free CT, there is a possibility of delay in the diagnosis of PE. Since early detection of PE treatment and prevention of PE in high-risk individuals is very effective in the prognosis of covid-19 underlying disease, so careful study of the prevalence of PE in patients with covid-19 and also a careful study of underlying factors Which may increase the risk of PE in patients with covid-19, play an important role in designing appropriate diagnostic and therapeutic clinical trials for the prevention and treatment of PE in patients with covid-19 as well as preventing the inappropriate administration of anticoagulants. This study aimed to investigate the relationship between the frequency of pulmonary embolism and the severity of lung parenchyma involvement (CTSS) in hospitalized patients with covid-19.

Methods: This retrospective study was performed by examining the files of 211 patients with Covid-19 who were hospitalized in Baqiyatallah Hospital from 2020 to 2021. Variables such as age, sex, the severity of PE, D-Dimer, ward, Underlying diseases were extracted and finally analyzed with SPSS version 26.

Result: The results of this study showed that the mean age of 211 patients was 56.26±56.54 years, of which 55.5% were male. The prevalence of pulmonary thromboembolism in patients was 23.7%. There was no significant relationship between patients with pulmonary thromboembolism and severity of lung parenchyma involvement.

Conclusion: Based on the high number of patients diagnosed with PE among those scanned we recommend a low threshold for performing computed tomography angiography in patients with COVID-19 and respiratory deterioration.

Keywords: COVID-19; Pulmonary embolism; CT Scan Severity Score (CTSS)

Abbreviations: PE: Pulmonary Emboli; CTSS: Computed Tomography Severity Score; ARDS: Acute Respiratory Distress Syndrome; CTPA: Computed Tomography Pulmonary Angiogram; RUL: Right Upper Lobe; RML: Right Middle Lobe; RLL: Right Lower Lobe, LUL: Left Upper Lobe; LLL: Left Lower Lobe; ICU: Intensive Care Unit

Introduction

Covid_19 is an RNA virus from the Coronaviridae family the cause of the worldwide pandemic since 2019, starting in Wuhan, China. The clinical course, laboratory signs, and even radiological signs of patients on CT scans are highly variable. The exact cause of the worsening of the clinical course in some people is not clear, but in some articles development of Acute Respiratory Distress Syndrome (ARDS), progression of viral pneumonia, pulmonary embolism is three main causes of worsening the clinical course and even increasing mortality

rate in covid-19 patients. Non contrast-enhanced CT is commonly used routinely to assess disease severity in covid-19. However, this modality is not suitable for evaluating pulmonary embolism as a cause of respiratory deterioration and clinical signs or laboratory tests such as D-dimer are not specific evaluations [1,2]. The early diagnosis and treatment of pulmonary embolism have an effective role in the prognosis of covid-19 patients, it is important to identify high-risk patients as well as the clinical condition that raises suspicion of pulmonary embolism. In some studies, pulmonary embolism is suspected if complementary oxygen is needed if the severity of the involvement is limited or when CT does not justify respiratory failure contrast, and CTA (Computed Tomography Pulmonary angiogram) is performed for further evaluation [2,3].

Some other studies have focused on screening high-risk patients for the prevention of pulmonary emboli and various factors such as hemodynamic disorders, immobility, systemic inflammatory conditions, mechanical ventilation, central catheter, changes in liver function and nutritional and consequently the production of coagulation factors have been considered as risk factors for venous thromboembolism [4]. Also, the occurrence of a sudden decrease in oxygen saturation, respiratory distress, hypotension, and right ventricular dysfunction has been considered as predisposing factors for pulmonary emboli [4] because early detection of PE treatment and prevention of PE in high individuals risk is highly effective in the prognosis of covid-19 underlying disease, so carefully evaluate the frequency of PE in patients with covid-19 and also carefully examine the underlying factors that may increase the risk of PE in patients with covid-19, Such as patient age, the severity of lung parenchyma involvement in CT, inpatient ward, underlying patient, previous history of arterial and pulmonary embolism, an important role in designing ¬an appropriate diagnostic and therapeutic clinical trial for prevention and treatment of PE in patients with covid-19 and prevention Improper administration of procedures and inappropriate anticoagulants. Due to the lack of a similar study in our country, it is hoped that by carefully examining the underlying factors that may increase the risk of PE in patients with covid-19, such as patient age, severity in the lung parenchyma on CT, hospitalized disease, Underlying disease, history of pulmonary artery embolism, clinical design play an important role in the diagnosis and appropriate treatment for meteorology and PE treatment in patients with covid-19, as well as the prevention of inappropriate and inappropriate use of coagulant.

Material and Methods

In this retrospective study, all patients with covid-19 (positive PCR test) were admitted to Baqiyatallah Hospital in Tehran from March 2020 to the end of December 2021 with suspected pulmonary embolism under CTPA (Computed Tomography Pulmonary Angiogram) Are; They were included in the study by the census. Cases in which patients had a recent arterial and venous thrombosis before covid-19 infection (past three to six months) or incomplete information or CTPA images were excluded. On the one hand, CTPA findings of patients were re-evaluated and lung parenchyma was evaluated according to CTSS (Computed Tomography Severity Score) to assess the severity of lung parenchyma involvement and was rated from 1 to 5 based on the degree of lung parenchyma involvement. (Grade 1, severity of parenchymal involvement between 1 to 5%, grade 2, severity of involvement between 6 to 25%, grade 3 severity of involvement between 26 to 50%, grade 4 conflict between 51 to 75% and grade 5 severity of involvement greater than 75%). Pulmonary vascularity was also assessed to evaluate pulmonary embolism as a filling defect in the main pulmonary arteries and its branches, and in the case of pulmonary embolism, embolism is based on the involved artery or its branches into the saddle, central, lobar, segmental, and sub were segmented. Also, in the presence of pulmonary embolism, the involved pulmonary segment (Right Upper Lobe (RUL), Right Middle Lobe (RML), Right Lower Lobe (RLL), Left Upper Lobe (LUL), and Left Lower Lobe (LLL) separately Becomes. On the other hand, the information included in the records of patients with pulmonary emboli, including sex, age, ward of patients (emergency, normal ward, and ICU), history of venous thrombosis, the recent history of anticoagulant use in recent hospitalization, d-dimer level and the percentage of oxygen saturation as well as the possible underlying disease will be examined. And the information obtained from CTPA readings of patients and the data obtained from reading records will be statistically evaluated. After collection, the data were entered into SPSS software version 26, and based on the results of the Smirnov-Kolmograph test, the quantitative data of the study did not follow the normal distribution except for age; As a result, non-parametric tests were used to investigate the statistical relationship between the data. The types of statistical tests used to describe and analyze the results are as follows: Chi-square, Fisher's exact test, Frequency & Percent, mean ±SD, Student T-test, Mann-Whitney U test in all stages of the research, the principle of confidentiality and non-disclosure of patients 'information was observed and all patients' information was confidentially available only to the researcher. Also, all stages of the research are under the supervision of the professors of Baqiyatallah Hospital and approved by the ethics committee of Baqiyatallah University and in line with the Helsinki Declaration.

Result

In this study, 211 patients with Covid were studied. The mean age of patients was 56.26 14 14.54 with a minimum age of 21 years and a maximum age of 91 years. The frequency of men was 117 (55.5%) and the frequency of women in this study was 94 (44.5%). 127 patients (60.2%) were admitted to normal wards of the hospital, 42 patients (19.9%) were admitted to the intensive care unit and 42 patients (19.9%) were admitted to the emergency department. The incidence of venous thromboembolism in patients was 12 (5.7%) and 207 (98.1%) had a history of anticoagulant use. The presence of active malignancy was observed in 18 patients equal to 8.5% of patients. 9.5% of patients had right ventricular dysfunction and 6.78% had significant underlying disease. The prevalence of pulmonary thromboembolism was 23.7% (50 patients). The most affected areas of the lung were observed as unilateral involvement

of the right side and the lower right lobe with a frequency of 6.2%. Segmental and sub-segmental conflicts had the highest frequency of 7.1% and 6.6%, respectively. The severity of lung parenchyma involvement was reported to be 14.7% of grade 1 and 25.6% of grade 2, 19% of grade 3, 22.7% of grade 4, and 18% of grade 5. Of the 211 patients studied, 22.3% died and 77.7% survived.

The mean level of D-dimer in patients was 33.75±18.45 with a minimum of 0.1 and a maximum of 99. 23.7% had a D-dimmer level of less than one and 76.3% had a D-dimer level of more than one. 68% of patients with pulmonary thromboembolism were male and 32% were female. The incidence was significantly higher among men (P=0.041). 54% of patients with pulmonary thromboembolism were hospitalized in general wards, 26% in intensive care units, and 20% in emergency wards, and there was no association between hospitalization and thromboembolism (P=0.440). 18% of patients with pulmonary thromboembolism also had venous thromboembolism and 82% did not have venous thromboembolism (p<0.001). 98% of patients with pulmonary thromboembolism had a history of anticoagulant use which was not statistically significant (p=1). 14% of patients with pulmonary thromboembolism had active malignancy which was not statistically significant (P=0.145). 14% of patients with pulmonary thromboembolism had right ventricular dysfunction, which was not statistically significant (P=0.267). 84% of patients with pulmonary thromboembolism had a significant underlying disease that was statistically significant (P=0.005). 74% of patients with pulmonary thromboembolism survived and 26% died, with no statistically significant difference between them (P=0.469). The severity of pulmonary parenchyma involvement in patients with pulmonary thromboembolism was 10% first degree and 25% fifth degree. This difference was not statistically significant (P=0.070). The mean age of patients with pulmonary thromboembolism was 58.15 years. There was no statistically significant difference between patients with pulmonary thromboembolism and healthy individuals (P=0.347).

Discussion and Conclusion

Numerous different complications have been reported following the Covid-19 disease. However, pulmonary involvement is still the leading cause of death. Although the disease often improves after undergoing various clinical phases, short-term or long-term complications are found in some patients. Sustained fibrosis changes following clinical improvement, bacterial or fungal infections, ARDS, pneumomediastinum and pneumothorax, myocardial infarction and pericardial involvement, and pulmonary artery embolism are all reported major complications following coronavirus infection. Many of the variables studied in this study were not studied in other similar studies abroad and it was not possible to compare the results for those variables. However, our main findings were that at the time of respiratory failure in COVID-19, the prevalence of PE varied and was not associated with disease severity on CT (CTSS). This study is clinically more significant than the screening or PE diagnosed by autopsy in previous studies [5-7]. The prevalence of PE varied from study to study, with one study finding that the prevalence of PE was much higher than in other studies. However, all studies, like the results of the present study, have reported conflicts in the segmental and sub-segmental sections above the size of the sections. However, different percentages have been reported, and it seems that the difference in the prevalence of PE between studies can be explained by the algorithms used to perform a CTPA, thus increasing the probability of PE a priori, in which case it is also the optimal use of available resources. In patients with proven Covid-19, there is usually no clinical suspicion of PE in the presence of a reliable differential diagnosis (e.g., progression of pneumonia). This may indicate that when using standard diagnostic algorithms caution is required in COVID-19 because it is not approved in this population and relevant studies are not currently available. A previous study, conducted in the ICU, reported a cumulative incidence of 31% for thrombotic complications [8] and 49% after an updated analysis, the majority of which was PE [9].

In the present study, the incidence of thromboembolism was reported to be 23.7%. Another screening study found a very high cumulative incidence of VTE (47%) in ICU patients. Recently, studies support the use of Doppler ultrasound as a method for systematic screening for thromboembolic events in COVID-19 pneumonia [9]. However, we believe that a cautious approach to the deterioration of respiration in patients for several reasons. It is preferred over VTE screening in hospitalized patients with COVID-19. A previous prospective study showed that the incidence of asymptomatic DVT was similar to that of other series [10,11]. Other studies have previously reported the occurrence of PE in environments other than the ICU. A French study examined the prevalence of PE in 100 COVID-19 patients with severe clinical features of COVID-19 (e.g., need for mechanical ventilation or underlying disease) in both ICU and normal wards, and they measured PE in 23 patients and found (23%) percentage of patients with 17 patients in ICU and 6 patients in the normal ward [12]. A retrospective cohort study in Italy showed 10 (2.8%) PE in 362 patients, of whom 2 (4.2% of the population (ICU in the ICU) and 8 (2.5% of the general ward population) resided in the public ward. They are probably greatly underestimated because they performed imaging tests on only 44 (11% of the total) patients [13].

In this study, we also compared the inpatient ward to cover the shortcomings of previous studies, but no significant relationship was found between the inpatient ward (emergency, intensive care, and normal wards) and venous thromboembolism. The results of the present study showed that the history of anticoagulant use was not related to the prevention of side effects. Another study stated that the current standard thromboprophylaxis is not sufficient to prevent thrombotic complications in patients with Covid-19(2), however, recommendations for thromboprophylaxis await further research specifically to evaluate the effectiveness of thromboprophylaxis. The current Covid-19 should be designed. These data also emphasize the need to include unselected patients in RCTs, which addresses the benefits of increasing the dose of thromboprophylaxis, and not just patients in high-risk

environments. As a result, we found PE in a significant proportion of patients admitted for COVID-19 with respiratory failure. An important outcome of this study is the low clinical threshold for CTPA in patients with rapid respiratory failure.

Our study has strengths and limitations. Strengths include the use of simple, clearly defined, and predetermined criteria for respiratory deterioration that make it directly applicable in the daycare of COVID-19 patients. In addition, we enrolled patients from the ED and normal wards, both of which are underrepresented in existing studies, and add valuable information to the expanding COVID-19 literature. But on the other hand, the volume of our sample for a subject of this importance is small and needs extensive research. It was also a retrospective study that errors in the writing of files may have occurred, so we cannot rule out the possibility that clinical judgment may also influence the decision to order a scan. Selection bias may have been identified as patients who were diagnosed as unsuitable for CT scanner transport, and patients who began palliative care due to their respiratory failure did not undergo CTPA and possibly some patients We have lost and not considering these patients has probably led to the underestimation of the prevalence of PE because these patients are among the patients with a high a priori probability for PE and show a very high prevalence of PE in this population. Finally, more research should be done on exploring the mechanisms of preventive treatment and preventive strategies for all COVID-19 patients to optimize the treatment of these patients.

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