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The Relationship between Pulmonary Embolism and Prone Position among Covid-19 Patients in King Abdulaziz Medical City

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Abstract

Background: Corona virus disease 19 (COVID-19) is a disease caused by SARS-CoV-2 virus, where the majority of infected individuals will have mild respiratory symptoms. Prone position is used to correct ventilation-perfusion mismatch by increasing the flow of air and blood to the dorsal region of the lung lifting the weight of the heart and abdominal compartments. Patients with COVID-19 are at high risk of developing pulmonary embolism (PE), which can result in one-third of severely ill COVID-19 patients who need intensive care units (ICUs) admission.

Objectives: To study the relationship between pulmonary embolism and prone position among COVID-19 patients in King Abdulaziz Medical City.

Method: 383 patients in adult critical care units enrolled to the study and were divided to control group and prone position group. CT angiography, D dimer tests, total hours of prone

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positioning and mortality data was collected for both groups. Nonprobability convenience sampling was used to select the samples. Pearson Chi square test and Fisher Exact test was used for analysis of data with significance level at 5%.

Results: A total of 383 patients enrolled to this study, 290 (75.7%) were male and 93 (24.3%) were female. 150 (43.4%) did prone position comparing to 195 (56.5%) did not do prone position. The median (IQR) in years, total hours of prone position and length of stay in ICU (in days) were 56(45,63), 20.5(8.5, 48) and 9(4, 17), respectively. Out of 150 samples with prone position only 12 (8%) had Pulmonary Embolism of which 11 (91.7%) were alive and was statistically significant with p value 0.020. Whereas in the non-prone position (control) group the mortality rate was 16.7% which was higher as compared to those in prone position P= 0.236) (Table 1). Moreover, 95 (97.9) patients tested positive on the final D-dimer test acquired were expired (Statistically significant, p= 0.001) comparing to the first D-dimer result which found to be not conclusive (p= 0.142). Relation of total hours of prone position with either incidence of PE or mortality were not statistically significant (p= 0.732, p= 0.200, respectively).

Conclusion: in summary, there is a significant relationship between prone position and pulmonary embolism. Mortality rate between patients in prone position group who were diagnosed with PE was 8.3% comparing to 16.7% in non prone group. The extra precaution during COVID pandemic prevented the possibility of testing patients for CT angiography which we believe that it is considered as a limitation of this study.

Introduction

REVIEW OF LITERATURE

Corona virus disease 19 (COVID-19) is a disease caused by SARS-CoV-2 virus, where is the majority of infected individuals will have mild respiratory symptoms. [(1)] However, people with specific medical conditions and older people are more likely to have severe symptoms such as acute respiratory distress syndrome (ARDS). The Berlin definition defines ARDS as an acute onset of lung inflammation with bilateral opacities on chest radiograph not fully explained by cardiac failure or fluid overload with ratio of the partial pressure of arterial oxygen (PaO_2) to the fraction of inspired oxygen (FiO2) of less than 300 mm Hg [(2)]. COVID-19 might damage the alveolar sacs and increase the vascular permeability leading to ventilation-perfusion mismatch [(3)]. Therefore, prone position is used to correct ventilation-perfusion mismatch by increasing the flow of air and blood to the dorsal region of the lung lifting the weight of the heart and abdominal compartments [(4)]. Study done by Claude Guérin et.al. has showed that prone position improves oxygenation and decrease mortality [(5)]. In patients with normal lung mechanics, the perfusion is mostly distributed at dependent lung tissue in supine position [(6)]. In contrast, ARDS patients may have factors worsening the perfusion such as hypoxic

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vasoconstriction and extrinsic factors compressing the pulmonary vessels [7]. Moreover, the trans-pulmonary pressure is less than that on airway opening leading to more collapsed alveolar units in dorsal regions [8]. In uncorrected perfusion, prone position showed that perfusion was steadier than those patients on supine position [12]. Moreover, lung perfusion was redistributed in nondependent regions which is normally has less perfusion than dependent region [12]. Furthermore, the contribution of gravity on perfusion heterogeneity of lung sections (dependent to nondependent) was 22-31% in supine position and 27-41% in prone position [12]. A study searched four animals and found that dorsal areas have more uniform perfusion during prone position [8]. These findings support the idea of lung perfusion differences between supine and prone positions. Patients with COVID-19 are at high risk of developing pulmonary embolism (PE), which can result in one-third of severely ill COVID-19 patients who need intensive care units (ICUs) admission [9]. In COVID-19 patients, thromboprophylaxis should be initiated, intervene in the anticoagulant doses may be suggested in patients in need of ICU admission, or those with several risk factors for venous thromboembolism [9]. Anticoagulant therapy is the basis of the management of PE patients [9]. To prevent comorbidities and organ failure, selecting an appropriate agent and dose should be taking in consideration [9]. The gold standard in the diagnosis of PE is Computed tomography pulmonary angiography (CTPA). CTPA is commonly used to diagnose PE due to its availability and high accuracy. A study searched the probability of D-dimer test to exclude PE in 808 suspected PE patients with threshold of 750 µg. D-dimer was negative in 52% and positive in 48% [10]. A predictive negative value of almost 99.8% in negative d-dimer group excluded PE but one patient showed PE after three months follow up [10, 11]. In relation to our research objective, a case study looked at seventeen years old young man with fat syndrome embolism who developed hypoxemia, which was successfully managed with prone position after failure of conventional ventilation [14]. Up to our knowledge, there is lack of data of prone position effect on perfusion in covid-19 patients and we assume that there is a relationship between pulmonary embolism and prone position among covid-19 patients. Our aim is to study the relationship between pulmonary embolism and prone position among COVID-19.

MATERIALS AND METHODS

Aim of the Study:

To study the relationship between pulmonary embolism and prone position among COVID-19 patients in King Abdulaziz Medical City.

The study conducted in all adult intensive care units in King Abdulaziz Medical City and the subjects will be all adult inpatients with COVID-19 between (MARCH 2020 - March 2021) in in King Abdulaziz Medical City. The study design was quantitative, Cohort retrospective study design.The sample size was 184 patients. Inclusion criteria included all patients diagnosed with positive PCR covid-19 in King Abdulaziz Medical City and the age group from 18 to 70. Those

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patients who had at least one organ failure or recived chemical therapy and the patients admitted from other hospitals were excluded from the study. The Data entered in Microsoft Excel sheets, and statistical analysis of the variables carried out by using SPSS software version 22. The categorical variable expressed as frequencies and percentages. Mean and SD were used for continuous variable.

Results

A total of 345 patients enrolled to this study, 260 (75.7%) were male and 85 (24.3%) were female. 150 (43.4%) did prone position comparing to 195 (56.5%) did not do prone position. The median (IQR) in years, total hours of prone position and length of stay in ICU (in days) were 56(45,63), 20.5(8.5, 48) and 9(4, 17), respectively.

Demographic details of subjects:

Variable	Frequency (Percentage)/(Descriptive Statistics*)
Gender	
Male	260(75.7)
Female	85(24.3)
Total	345(100)
Prone Position	
Yes	150(43.4)
No	195(56.5)
Total	345(100)
Age in years	Median (IQR) : 56(45,63)
Total hours of proning	Median (IQR) :20.5(8.5, 48)
Length of stay in ICU	Median (IQR) :9(4, 17)

The first D-dimer test upon admission to ICU was done to 364 (95%) against 19 (5%) which were not tested for both groups. The result of the first d-dimer was positive to 287 (78.8%) in which 187 (65.1) were alive comparing to 100 (34.9%) were expired and was negative to 77(21.2%) in which 57 (74%) were alive while 20 (26%) were expired with (p=0.142). Final D-dimer test was taken for 310 (80.9%) where 73 (19.1%) were not. Results of final D-dimer test was positive to 274 (88.4%), among them 179 (65.3) were alive in contrast to 95 (34.6%) were expired, versus 36 (11.6%) were negative in which 34 (94.4%) were alive while 2 (5.6%)

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were expired. Total of 97 expired patients who had final d-dimer test, 95 (97.9%) were positive (Statistically significant, p= 0.001). Out of 150 samples with prone position CT angiography done for 41 (27.3%) patients and 109 (72.7%) did not had CT angiography.

Various tests done for the subjects

Tests done	No. (%)
First D dimer	
Yes	328(95)
No	17(5)
Total	345(100)
Final D dimer	
Yes	279 (80.9)
No	66 (19.1)
Total	345(100)
Result of First d dimer	
Positive	272(78.8)
Negative	73(21.2)
Total	345(100)
Result of final d dimer	
Positive	274(88.4)
Negative	36(11.6)
Total	310(100)
CT done	
Yes	345(90.1)
No	38(9.9)
Total	383(100)
CT result	
Positive for Pulmonary embolism	31(9)
Negative	314(91)
Total	345(100)
Mortality outcome	
Alive	251(65.5)
Expired	132 (34.5)
Total	383(100)

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Out of 150 in prone position group, only 11 (7.3%) tested positive for PE with zero mortality outcome (p=0.083), while the other 30 patients who were negative for PE had 8 (26.7%) expired patients and 22 (73.3%) were alive.

Prone position and Pulmonary Embolism

Prone position * PE Crosstabulation

			Pulmonary Embolism		Total
			No	Yes	
Prone position	No	Count	176	19	195
		% within Prone position	90.3%	9.7%	100.0%
	Yes	Count	138	12	150
		% within Prone position	92.0%	8.0%	100.0%
Total		Count	314	31	345
		% within Prone position	91.0%	9.0%	100.0%

Chi square= 0.315, p= 0.575

Pulmonary Embolism and Mortality

mortality outcome * PE Crosstabulation

			PE		Total
			No	Yes	
mortality outcome	Alive	Count	202	27	229
		% within mortality outcome	88.2%	11.8%	100.0%
	Expired	Count	112	4	116
		% within mortality outcome	96.6%	3.4%	100.0%
Total		Count	314	31	345
		% within mortality outcome	91.0%	9.0%	100.0%

Chi square= 6.552, p= 0.010 (Statistically Significant)

In control group, 55 (28.2%) patients did CT angiography where 17 (30.9%) had PE of which 15 (88.2%) were alive and 2 (11.8%) expired. On the other hand, 38 (69.1%) tested negative

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for PE of which 29 (76.3%) were alive and 9 (23.7%) were expired (p= 0.471). Out of 150 patients in prone position group, only 12 (8%) had Pulmonary Embolism of which 11 (91.7%) were alive and was statistically significant with p value 0.020. Whereas in the non prone position group the mortality rate was 16.7% which was higher as compared to those in prone position P= 0.236) (Table 1). Moreover, 95 (97.9) patients tested positive on the final D-dimer test acquired were expired (Statistically significant, p= 0.001) comparing to the first D-dimer result which found to be not conclusive (p= 0.142). Relation of total hours of prone position with either incidence of PE or mortality were not statistically significant (p= 0.732, p= 0.200, respectively).

First d dimer and Mortality

result of first test (cutline of 0.5) * mortality outcome Crosstabulation

			mortality outcome		Total
			Alive	Expired	
result of first test (cutline of 0.5)	negative	Count	57	20	77
		% within mortality outcome	23.4%	16.7%	21.2%
	positive	Count	187	100	287
		% within mortality outcome	76.6%	83.3%	78.8%
Total		Count	244	120	364
		% within mortality outcome	100.0%	100.0%	100.0%

Chi square= 2.161, p= 0.142

Final d dimer and mortality

result of final test (cutline of 0.5) * mortality outcome Crosstabulation

			mortality outcome		Total
			Alive	Expired	
result of final test (cutline of 0.5)	negative	Count	34	2	36
		% within mortality outcome	16.0%	2.1%	11.6%
	positive	Count	179	95	274
		% within mortality outcome	84.0%	97.9%	88.4%
Total		Count	213	97	310
		% within mortality outcome	100.0%	100.0%	100.0%

Chi square= 12.547, p= 0.001 (Statistically significant)

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Discussion

While there is no clear evidence support the hypothesis of the effect of prone position on incidence Of pulmonary embolism among ARDS patients, this study shows no significant difference in the incidence of PE in patients who had prone position comparing to control group how did not have prone position. Moreover, there is no noticeable difference in numbers of PE incidence and mortality between patients who had more than 12 hours prone position cycles comparing to patients who had less than 12 hours cycles. In addition, this study found out that the mortality rate in patients with PE who did not have prone position was significantly higher comparing to those who had prone position. A case report study by Issac Cheong et al demonstrates the benefit of prone position for patient with right heart dysfunction due to pulmonary embolism. The beneficial impact of prone position was not only on improving the lung perfusion and oxygenation but also on the function of the right heart. A prospective study by Julie Helms et al compared the number of PE incidence between covied-19 patients and non covid-19 patients, 25(16.8%) patients had PE among 150 patients positively tested for covid-19, while 3(1.3%) patients had PE between 233 non covid-19 patients. On other hand, the results of d-dimer level duplicates our outcome where the level of d-dimer was elevated above normal range in the majority of the patients with covid-19 (95% vs 88.4). Furthermore, our study shows a high death rate in patients with high D-dimer level among patients with COVID-19 95 (97.9%) comparing to COVID-19 patients with normal D-dimer level 2 (2.1%).

Conclusion

With the large number of studies about the relation between COVID-19 and pulmonary embolism, up to our knowledge there was no mention to the effect of prone position which used to improve oxygenation in patients with covid-19 on incidence of pulmonary embolism among them. This study demonstrates no impact of prone position on number of PE incidence among COVID-19 patients. In contrast, it shows better in number in mortality rate among prone position group comparing to non-prone position group.

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