Evaluation of Oxygen Saturation as an Indicator for Tracheal Intubation in Patients With COVID-19: A Prospective Cohort Study

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Abstract

**Background:** Since the beginning of COVID-19 pandemic, lack of clinical criteria for intubation in critically ill patients with respiratory failure and simultaneous resource limitations became more noteworthy than before. This study is designed in order to investigate oxygen saturation as an indicator for tracheal intubation in COVID-19 patients.

**Methods:** This is a multi-center, prospective, observational cohort study. We included patients with COVID-19 who needed respiratory support between March to June 2021. Patients were intubated by each institute's protocol and the anesthesiologist's clinical judgement. Respiratory symptoms, methods of respiratory support and patients' outcome were recorded.

**Results:** In this study 117 patients were enrolled. Among 117 studied cases, 100 patients had O₂ saturation of 60-90% in whom 58 were intubated. During hospitalization, 56 intubated patients and 14 non-intubated patients died (96.6% Vs. 33.3%).

**Conclusion:** We found that oxygen saturation per se cannot be appropriate criteria for intubating decision.

**Background:**

In December 2019, in Wuhan (China) a previously unknown coronavirus, SARS-Cov-2 was identified that today is known as COVID-19. A virus with high level of contagion and high mortality rate of 2% due to respiratory distress in infected patients (1)(2). Despite massive effort to control viral transmission it became an enormous worldwide pandemic.

The most common and severe manifestation of COVID is hypoxic respiratory failure that is also the main reason of mortality (3). Thus, these patients need respiratory support to maintain adequate oxygenation, ventilation, prevention of lung injury and decrease respiratory work. Respiratory support could be in various levels and it depends on the degree of alveolar damage and the severity of Acute Respiratory Distress Syndrome (ARDS). Oxygen can be delivered via different devices. Nasal cannula, simple facial mask and reservoir bag increase FiO₂ by low flow oxygen. On the other hand, facial mask with venturi valve and high flow nasal cannula (HFNC) provide high flow oxygen support. Non-invasive ventilation (NIV) including continuous positive airway pressure (CPAP) and Bilevel positive airway pressure (BiPAP) deliver oxygen to airway by applying positive pressure (4). In severe forms of respiratory failure invasive mechanical ventilation by endotracheal tubes is inevitable.

The undetermined question is the time and criteria for using these supports especially invasive mechanical ventilation that seems to be the last step of respiratory support in patient suffering from COVID-19. In general, there are heterogeneities between studies to determine intubation criteria in respiratory failure even before COVID-19 pandemic. Although various elements such as respiratory rate, heart rate, non-specific blood gas factors, dyspnea, hemodynamic instability and neurologic deterioration
are suggested for decision making but at last there is lack of standard criteria for endotracheal intubation (5).

Certainly this question would become more serious in COVID-19 pandemic when scares of resources are accompanied by patients' abundant need for respiratory support. The decision of intubation may interfere with survival rate.

**Methods:**

This multi-center, prospective, observational cohort study was conducted in three tertiary public hospitals. Ethical Committee approved this study in February 2021 (Approval ID: IR.SBMU.MSP.REC.1399.677). Data were collected from March to June 2021. This time period was selected as peak of pandemic was risen and there was no consensus on criteria for intubation. The questionnaire was designed to collect data. Patients with positive polymerase chain reaction (PCR) for COVID-19 or characteristic findings in Chest-CT scan who were consulted by anesthetist for airway management were included. In all centers anesthesia consult was requested for patients who would need respiratory support during their hospital stay. Every institutes based on their skills and resources had their own criteria for intubation. Patients who were transferred to other hospitals or those who were lost to follow-up or intubation after cardiopulmonary arrest were excluded from this study.

In this time period detailed information of 117 patients were assessed by trained resident of anesthesiology under supervision of faculty members. Patients’ detailed medical history, O\textsubscript{2} Saturation, respiratory rate (RR), presence of cough (sporadic or heated), subjective dyspnea (mild or severe) and also signs of dyspnea (nasal flaring, rib retraction and abdominal breathing) were recorded in a questionnaire. We evaluated patient’ level of consciousness by using AVPU scale (Alert, Voice, Pain, Unresponsive) and the patients’ outcome as discharged or deceased was also pursuit. Patients were intubated based on institute’s criteria and also the faculty members’ clinical judgement.

We intent to compare mortality rate among patients with severe symptoms who were intubated with those who are not intubated. Severe symptoms were defined by O\textsubscript{2} Saturation of 60-90% with non-invasive oxygen support, respiratory rate of more than 30/minute, level of consciousness described by AVPU scale as P & U, heated cough, severe subjective dyspnea, presence of nasal flaring, rib retraction and abdominal breathing.

Qualitative data were shown by frequency and percentage, and analyzed by chi square, and fisher exact tests. Quantitative data were shown by mean, and SD (standard deviation). The P-value less than 0.05 considered statistically significant difference. All statistically were analyzed. Analyses were conducted using the statistical software environment R, version 4.1.1.

**Results:**
In this study 117 critically ill patients that had anesthesia consult during their hospital stay from March to June 2021 were enrolled. COVID-19 infection were confirmed by PCR test (50.4%) or CT scan findings (49.6%). Among these patients, 48 were female and 69 were male (41% Vs 59% respectively). The mean age was 65.8 years old from minimum of 18 to maximum of 95. Among hospitalized patients who required anesthesia consult for respiratory support 80 died (68.4%) and 37 were discharged (31.6%). Also, 71% had at least one comorbidity; hypertension (46.2%), diabetes (25.6%), and ischemic heart disease (20.5%) were the most common comorbidities. History of smoking was presented in 24.8% of patients. The most common drug that had been using was Angiotensin Converting Enzyme Inhibitors (ACEI) (34.2%) (Table 1).

Table 1

| Demographic Characteristics | Mean (SD) | Count (%) |
|-----------------------------|-----------|-----------|
| Age (year)                  | 66 (16)   |           |
| Sex                         |           |           |
| Female                      | 48 (41)   |           |
| Male                        | 69 (69)   |           |
| Diagnosis                   |           |           |
| Missing                     | 0 (0)     |           |
| PCR                         | 59 (50.5) |           |
| Radiologic                  | 58 (49.5) |           |
| Clinical                    | 0 (0)     |           |
| Diabetes Mellitus           | 30 (25.6) |           |
| Hypertension                | 54 (46.1) |           |
| Ischemic Heart Disease      | 24 (20.5) |           |
| ACEIs                       | 40 (34.1) |           |
| Corticosteroids             | 1 (0.01)  |           |
| Intubated                   | 67 (57.2) |           |
| Outcome                     |           |           |
| Death                       | 80 (68.3) |           |
| Discharge                   | 37 (31.6) |           |

Patients who were visited had mean O2 saturation of 75.8% (30-96), respiratory rate of 26 (16-45). The most common respiratory symptoms were heated cough (70.1%), severe subjective dyspnea (56.4%), nasal flaring (48.6%), abdominal breathing (45.3%) and rib retraction (37.6%) (Table 2).
Table 2
Comparison of Clinical symptoms among intubated versus non-intubated patients

|                          | Non-Intubated (50) | Intubated (67) |
|--------------------------|--------------------|----------------|
|                          | Mean (SD)          | Count (%)      | Mean (SD)          | Count (%)      |
| **O₂ Saturation (%)**    | 81 (13)            | 72 (17)        |
| **Respiratory Rate (/min)** | 23 (5)            | 29 (8)         |
| **Temperature (°C)**     | 38.2 (0.8)         | 37.9 (0.7)     |
| **Cough**                |                    |                |
| Heated                   | 3 (6)              | 13 (20)        |
| Sporadic                 | 33 (66)            | 35 (52)        |
| Negative                 | 14 (28)            | 19 (28)        |
| **Subjective Dyspnea**   |                    |                |
| Severe                   | 1 (2)              | 31 (46)        |
| Mild                     | 37 (74)            | 31 (46)        |
| Negative                 | 11 (22)            | 5 (7)          |
| **Nasal Flaring**        | 2 (4)              | 23 (34)        |
| **Rib Retraction**       | 2 (4)              | 22 (32)        |
| **Abdominal Breathing**  | 4 (8)              | 28 (41)        |
| **Decreased level of consciousness** | 3 (7) | 43 (93) |
| **Outcome**              |                    |                |
| Death                    | 15 (30)            | 65 (97)        |
| Discharge                | 35 (70)            | 2 (3)          |

Among 117 studied cases, 100 patients had O₂ saturation of 60-90% in whom 58 were intubated. During hospitalization, 56 intubated patients and 14 non-intubated patients died (96.6% Vs. 33.3%). Of all cases, 56 patients had respiratory rate of greater than 30 per minute in whom 87% were intubated and all of them died. Among 16 patients with heated cough thirteen were intubated and mortality rate in these intubated patients were 92.3%. Ninety-six percent of patients with severe subjective dyspnea died and two were discharged. In evaluation of the other respiratory distress symptoms 3.9% of patients with nasal flaring, 4.9% of patients with rib retraction and 0% of patients with abdominal breathing were discharged after intubation. These statics in non-intubated patients were 16.7%, 33% and 75% respectively. Among 46 patients with decreased level of consciousness, all non-intubated patients had died whilst 3% of intubated ones had been discharged.

Results of Fisher's Exact Tests showed that intubation did not increase survival of patients with heated cough, Abdominal Breathing, Respiratory rate more than 30 and O₂ Saturation of 60-90% (p-value<0.001).
Subjective severe dyspnea and decreased level of consciousness did not correlate with survival after intubation although patients who were intubated discharged whilst there were not any survivals in patients with severe dyspnea and decreased level of consciousness who were not intubated (P-value=0.71).

**Discussion:**

The most appropriate time for intubation per se is a dilemma in hypoxic patients due to lack of standard endotracheal intubation criteria (5) and it became more challenging in a pandemic with huge number of patients with severe COVID-19 and worldwide resource limitation. Also, invasive ventilation in COVID patients is being between Scylla and Charybdis (6) (7). It can be lifesaving by improvement in oxygenation and amelioration of virus spread, on the other hand it could be life threatening by increasing ventilator induced lung injury (VILI) and resource consuming (8).

In COVID patients it seems that the lower saturation could be better tolerated than the other hypoxic patients so maybe just the percent of O$_2$ saturation should not be considered as a trigger for intubation (8). Therefore, criteria for invasive ventilation in these patients is debatable. In this study discharge rate of intubated and non-intubated patients who had severe respiratory symptoms at the time of decision making for intubation, were compared. We found that 96.6% of patients that had O$_2$ saturation of 60-90% and were intubated died whilst in those who were not intubated with this range of O$_2$ saturation, mortality rate was 66.7%. This is obvious that mortality rate should be higher in intubated group, due to their worse general condition and their need for invasive respiratory support, but the interesting part in this result is discharge rate of 33.3% in patients with low O$_2$ saturation that were not intubated in compare to less than 4% in intubated group. It could show us maybe decreasing O$_2$ saturation below 90% even to 60% is not good criteria for starting mechanical ventilation of patients with COVID infection. The findings of Yong Hoon et al in 2020 can be in favor of ours that show early intubation is not associate with improvement in survival. In their study early intubation was defined as intubation in the first day of meeting ARDS criteria in patients with COVID-19 (9).

In evaluation of other signs and symptoms for intubation we found limited studies that mostly suggest their own clinical criteria and the lack of evidence based guidelines for the best time to start mechanical ventilation was noticeable. In an observational cohort study by Ahmad et al in 2020 on 150 intubated patients, association between early intubation and improvement in outcome was shown. As they mentioned their data is not a definitive evidence for early vs late intubation, but they suggest that if tracheal intubation is considered based on following criteria they could have better clinical outcome and staff safety. Their criteria is: O$_2$ Saturation<92%, FiO$_2$ requirement of more than 60%, respiratory rate of more than 25 per minute, increase work of breathing and failure adequate oxygenation in 4-hour prone position (10). In another study severity of respiratory failure, multi-organ failure, hemodynamic shock and multiple high risk condition are suggested as institutional intubation criteria. Of course all these conditions dependent on availability of ventilators and intensive care capacity (11). In our study we tried
to detect respiratory distress in detail. Among various respiratory symptoms, we found that mortality rate in patients with respiratory rate $\geq 30/\text{min}$ and abdominal breathing who were intubated are significantly higher than patients with these symptoms who were not intubated. We found that intubation did not decrease mortality in patients with respiratory rate $\geq 30/\text{min}$ and abdominal breathing and could not be suitable criteria for intubation.

In our cases with severe subjective dyspnea and decreased level of consciousness we had patients who were discharged after intubation but all of the non-intubated patients died. It was not statistically significant but clinically could be important. Therefore, evaluating patients’ subjective dyspnea and decreased level of consciousness could be considered as valuable variables for future studies (Table - 3).

| Clinical symptoms                  | Intubation criteria |
|------------------------------------|---------------------|
| $O_2$ Saturation 60-90%            | Not a good criteria |
| Respiratory Rate $> 30/\text{min}$ | Not a good criteria |
| Heated cough                       | Not a good criteria |
| Abdominal breathing                | Not a good criteria |
| Severe subjective dyspnea          | Could be a criteria |
| Decreased level of consciousness   | Could be a criteria |

Our limitation in this study was limited number of patients, because data gathering during pandemic situation was difficult. Also, in pandemic situation mortality rate can be affected by resource limitations. For defining a guideline for intubation in COVID patients maybe aggregation of more study with huge number of data could be helpful.

**Conclusion:**

In conclusion, our data showed that oxygen saturation of 60-90% could not be the correct key to unlock the problem of intubation decision in patients with COVID-19.

**Declarations:**

All methods were carried out in accordance with relevant guidelines and regulations and all experimental protocols were approved by ethical committee of Shahid Beheshti University of Medical sciences (Approval ID: IR.SBMU.MSP.REC.1399.677) also informed consent was obtained from all subjects or their legal guardian(s).
Consent for publication:

Not Applicable

Availability of data and materials:

The datasets generated and/or analysed during the current study are not publicly available due confidentiality reasons but are available from the corresponding author on reasonable request.

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The authors declare that they have no competing interests

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Authors’ contributions:

A. Tajbakhsh and S. Tabashi designed the study and wrote the paper

S. Behagh, P. Raji, M. Dahi, Sh. Dabir, B. Farzanegan and Sh. Sayadi gathered data

M. Moshari and M. Vosoughian analyzed data

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