ORIGINAL ARTICLE

SaO$_2$ / FiO$_2$ Ratio as Mortality Predictor in COVID-19 : A Meta-Analysis

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ABSTRACT

Background: SARS CoV-2 known as COVID-19 spreads rapidly achieve effective and sustainable human-to-human transmission by contact, droplets, and possible airborne routes. Respiratory failure is one of the deadliest manifestations with poor prognosis related comorbidity. Predictor of the deterioration is useful for making decisions on the management of oxygen administration from non-invasive to invasive ventilation. Studies report the SaO$_2$/FiO$_2$ ratio is a reliable method to predict the mortality rate in COVID-19 infection.
Aim: In this meta-analysis, we will measure the Sao2/FiO2 ratio as a predictor of mortality in COVID-19 infection.
Methods: We included all research articles in adult patients diagnosed with COVID-19 with information on SaO$_2$/FiO$_2$ ratio available. The SaO$_2$/FiO$_2$ ratio (mmHg) is divided into non-severe (101-300) and severe (≤100). The mortality rate is defined in each SaO$_2$/FiO$_2$ ratio noticed in the first examination.
Result: There were 850 patients included in this study. We separate the mild and moderate against severe SaO$_2$/FiO$_2$ ratio. The meta-analysis showed that there are no significant difference in both results (OR 1.06 [0.78 - 1.44], p = 0.69; I^2: 95%, p<0.00001).Severity of respiratory failure in COVID-19 patient is important to determine the prognostic factor. COVID-19 is related to lung injury contribute to acute respiratory distress syndrome. From meta-analysis, we found no significant finding in SaO$_2$/FiO$_2$ ratio as a prognostic factor for mortality comparing mild and moderate to severe classification. No RCT study included and only 3 studies were analyzed. Further study and strong design are needed to prove this finding.
Conclusion: SaO$_2$/FiO$_2$ ratio in COVID-19 infection cannot be used for the predictor of mortality when distinguished from mild to severe forms.
Keywords: SaO$_2$/FiO$_2$ ratio, Mortality rate, COVID-19

INTRODUCTION

Coronavirus disease (COVID-19) is a disease announced as pandemic by World Health Organization on March 11, 2020. It spread qucikly throughout the world (Li et al., 2020). As the disease spread worldwide in fast manner, predictor of deterioration of the disease is not clear enough because no definite causation can be taken. Recent autopsies studies suggest that coagulopathy and damage to pneumocyte is one of complication which increase the mortality in COVID-19 patients related respiratory failure (Attalah et al., 2020).

Respiratory failure is one of the deadliest manifestations with poor prognosis related comorbidity in SARS-CoV-2 infection.The pathophysiology of COVID-19 will lead to acute respiratory distress syndrome (ARDS) and presenting as respiratory failure manifestation (House et al., 2020; Rodrigues-Morales, et al., 2020). To our knowledge, there are no prognostic factors with large scale research to determine if the patient will likely undergo this condition. Predictor of the deterioration is useful for making decisions on the management of oxygen administration from non-invasive to invasive ventilation. Studies report the SaO$_2$/FiO$_2$ ratio is a reliable method to predict the mortality rate in COVID-19 infection(Vopelius-Feldt et al., 2020; Lu et al., 2020). In this meta-analysis, we will measure the Sao2/FiO2 ratio as a predictor of mortality in COVID-19 infection.

METHODS

Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) were used to accomplished this meta-analysis (Moher et al., 2009). We systematically searched PubMed, SCOPUS, EuropePMC, ProQuest, and Cochrane Central Databases with the search terms "COVID-19" or "SARS-CoV-2" and " SaO$_2$" or "FiO$_2$" and "Mortality" that were published within the year of 2020. Duplicate results were excluded. The remaining articles were independently screened for relevance by its abstracts with all authors. The full-text of the selected abstract then were thoroughly read, and those that fulfilled our criteria were included in the study. The final inclusion of studies was based on the agreements of all investigators. Any disagreement was resolved by consensus of all authors. The outcome was mortality related SaO$_2$/FiO$_2$ ratio.
Study Selection: We included cohort prospective, retrospective study, and preprinted study. We included all research articles in adult patients diagnosed with COVID-19 with information on SaO$_2$/FiO$_2$ ratio available. The SaO$_2$/FiO$_2$ ratio (mmHg) is divided into non-severe (101-300) and severe (≤100). The mortality rate is defined in each SaO$_2$/FiO$_2$ ratio noticed in the first examination. Study without divided SaO$_2$/FiO$_2$ ratio were excluded from the selection. We found 3 studies fulfilled our criteria and Von Vopelius-Feldt et al study was preprinted.
Quality Assessment ; The quality of the studies was appraised independently by two authors using the Modified Newcastle-Ottawa Scale (NOS). A score of 0–9 was allocated toeach study, with studies having a total score of ≥ 7 defined as high quality. Any disagreement in the quality assessment was resolved by discussion with both author.
Statistical Analysis: To perform a meta-analysis, Review Manager (RevMan) 5.4 (Computer program, The Cochrane Collaboration, London, UK) and Comprehensive Meta-Analysis (CMA) 3.3 (Computer program, New Jersey, USA) were used to perform all statistical analysis.The heterogeneity was considered significant for a P-value less

than 0.05, and its magnitude wassubstantial when I2 was greater than 50%. A random-effects model was used to report the results of heterogeneous data,otherwise a fixed-effects model was used. Dichotomous variables were analyzed with the Mantel-Haenszel statistical method using risk ratio (RR) as the summary statistic and reported with95% confidence intervals (CI).

RESULTS

Characteristic of study included an initial search generated 315 potentially relevant papers, of which 96 were immediately excluded due to duplication. After the first screening of titles and abstracts, 201 papers were excluded. An additional 15 papers were excluded after the full-text review, which resulted in 3 studies included in this meta-analysis (Figure 1).

The baseline characteristics of the included studies are presented in Table 1. The mean age of the patients in the included studies was 64,2 years old.A total of 3 publications were included, all of which areretrospective studies (evidence level II). There are unfortunately no randomized-controlled trials (RCT) found on our search. All of the studies was perform in Europe (England, France, Italy). For quality evaluation through NOS, studies were considered high quality if they received ascore of 7 stars or more. In this analysis, all studies considered high quality, with no study receiving fewer than 7 stars (Table 2).
SaO2/FiO2 Ratio related Mortality: There were 850 patients included in this study. We separate the mild and moderate against severe SaO_2/FiO_2 ratio. The meta-analysis showed that there are no significant difference in both results (OR 1.06 [0.78 - 1.44], p = 0.69; I^2: 95%, p < 0.00001) (Figure 2).

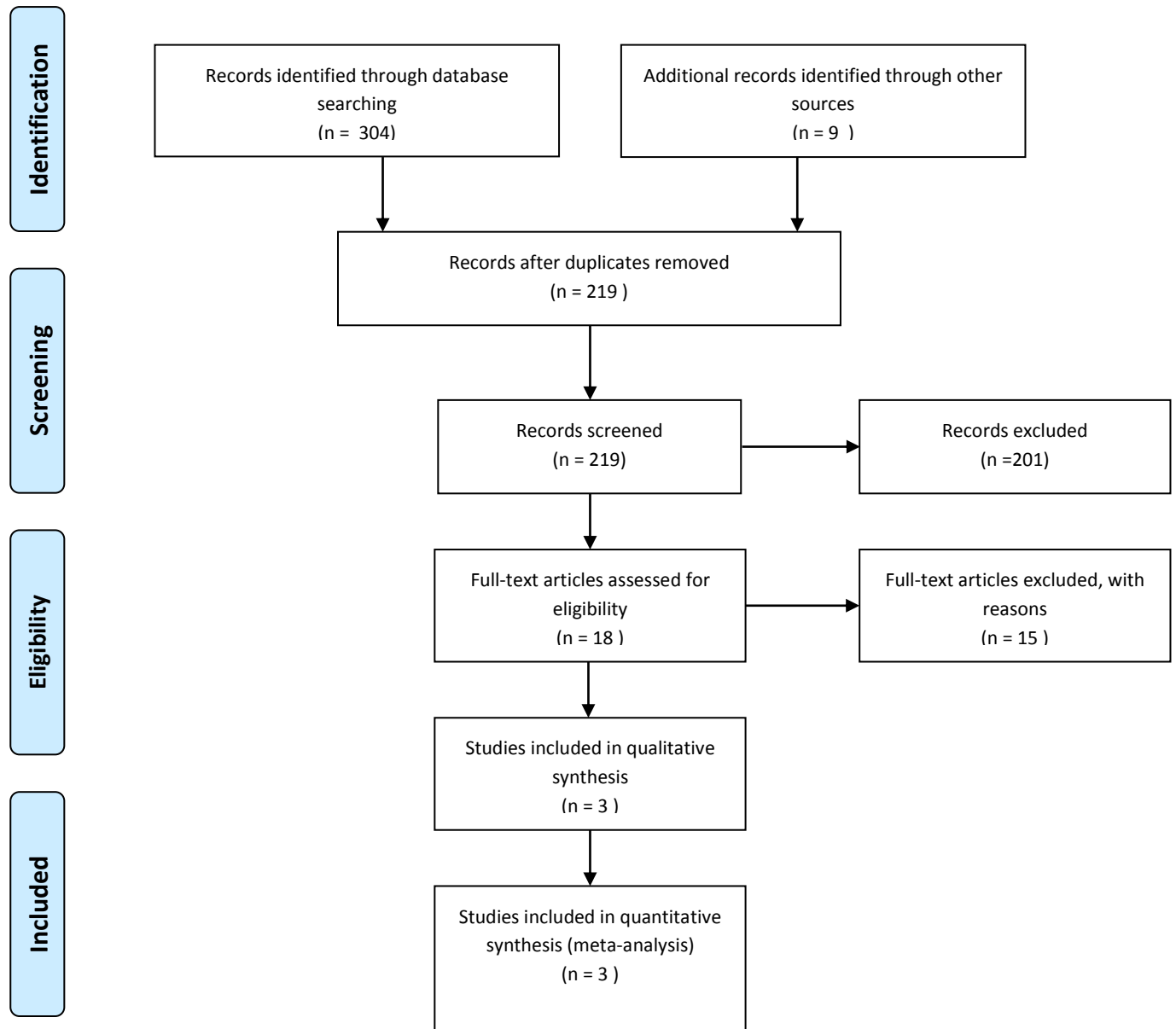Figure 1. PRISMA flow diagram for the included studies.

Table 1. Characteristics of the included studies

Author and Year	Study Design	Country	Quality Score	Characteristic of Participants	Age (mean)	SaO$_2$/FiO$_2$ in ARDS classification			Mortality Rate
						Mild	Moderate	Severe	
Von-Vopelius-Feldt et al, 2020[5]	Cohort prospective	England	7	117 patients with COVID-19 infection	63 years old	32 patients	27 patients	19 patients	9 normal 5 mild 8 moderate 13 severe
Santus et al, 2020[8]	Multicentre cohort prospective	Italy	8	412 patients with suspected COVID-19	65 years old	101 patients	90 patients	64 patients	10 normal 16 mild 43 moderate 35 severe
Ferrando et al, 2020[9]	Prospective multicentre	Spain	7	663 patients with COVID-19 infection	64 years old	109 patients	241 patients	167 patients	84 mild 182 moderate 104 severe

Table 2. Newcastle-Ottawa Scale

Study	Selection				Comparability	Outcome			Total stars
	Representativeness of the Exposed Cohort	Selection of the Non-Exposed Cohort	Ascertainment of Exposure	Demonstration That Outcome of Interest Was Not Present at Start of Study	Comparability of Cohorts on the Basis of the Design or Analysis	Assessment of Outcome	Was Follow-Up Long Enough for Outcomes to Occur	Adequacy of Follow Up of Cohorts	
Von-Vopelius-Feldt et al, 2020	1	1	1	1	0	1	1	1	7
Santus et al, 2020	1	1	1	1	1	1	1	1	8
Ferrando et al, 2020	1	1	1	1	0	1	1	1	7

Figure 2.The metaanalysis of SaO$_2$/FiO$_2$ on the mortality. Comparison mortality between SaO2/FiO2 mild against moderate-severe

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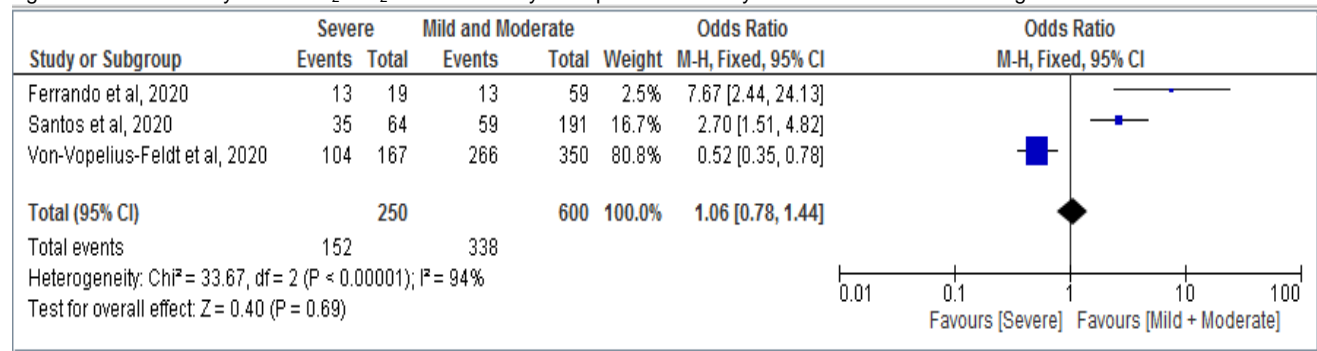
DISCUSSION

This study summarized the available study related severity of respiratory failure in COVID-19 patient. It is important to determine the prognostic factor of COVID-19 patient progression which COVID-19 is related to a progressive lung injury (Santus et al., 2020). From meta-analysis, we found no significant finding in SaO$_2$/FiO$_2$ ratio as a prognostic factor for mortality comparing mild and moderate to severe classification.

Hypoxemia degree in COVID-19 patient is one of risk factor in severity of COVID-19. Study from Xie et al shows patient with SpO$_2$< 90% has 84,6% sensitivity and 97,2% specificity for survival in COVID-19 patient regardless of age. Higher SpO2 levels after oxygen administration associated with lower mortality (Xie et al., 2020). When the ratio of SaO2/FiO2 is compared with ARDS Berlin's criteria (2020), the respiratory failure definition in this meta-analysis does not give significant difference to predict the mortality.

This study has some limitations. There are only few studies related to divide the severity of stratification degree on respiratory failure. There is no RCT study included and only 3 studies were analyzed. Further study and strong design are needed to prove this finding.

CONCLUSION

SaO$_2$/FiO$_2$ ratio in COVID-19 infection cannot be used for the predictor of mortality when distinguished from mild to severe forms.

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Conflict of interest: The authors report no conflict of interest.

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