Trajectories of Hypoxemia & Pulmonary Mechanics of COVID-19 ARDS in the NorthCARDS Dataset

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Abstract

Background: Understanding heterogeneity seen in patients with COVIDARDS and comparing to non-COVIDARDS may inform tailored treatments.

Methods: A multidisciplinary team of frontline clinicians and data scientists worked to create the Northwell COVIDARDS dataset (NorthCARDS) leveraging over 11,542 COVID-19 hospital admissions. The data was then summarized to examine descriptive differences based on clinically meaningful categories of lung compliance, and to examine trends in oxygenation.

Findings: Of the 1595 COVIDARDS patients in the NorthCARDS dataset, there were 538 (34.6%) who had very low lung compliance ($<20\text{ml/cmH}_2\text{O}$), 982 (63.2%) with low-normal compliance ($20\text{-}50\text{ml/cmH}_2\text{O}$), and 34 (2.2%) with high lung compliance ($>50\text{ml/cmH}_2\text{O}$). The very low compliance group had double the median time to intubation compared to the low-normal group (107 hours (IQR 26.3, 238.3) vs. 37.9 hours (IQR 4.8, 90.7)). Overall, 67.5% ($n=1049$) of the patients died during the hospitalization. In comparison to non-COVIDARDS reports, there were less patients in the high compliance category (2.2% vs. 12%, compliance $\geq 50\text{mL/cmH}_2\text{O}$), and more patients with $\text{P/F} \leq 150$ (57.8% vs. 45.6%). No correlation was apparent between lung compliance and P/F ratio. The Oxygenation Index was similar, (11.12 (SD 5.67) vs. 12.8 (SD 10.8)).¹

Introduction

A subset of patients with COVID-19 deteriorate despite supportive measures, requiring invasive mechanical ventilation for acute respiratory failure and the acute respiratory distress syndrome (ARDS).² Controversy has existed regarding the differences between COVID-related ARDS (COVIDARDS) versus other causes of ARDS.³⁻⁵ For example, there appear to be a subset of patients with higher lung compliance despite profound hypoxemia.⁶ The cohorts of COVIDARDS patients reported in the literature have been limited by sample size and have not included data on pulmonary mechanics. Herein, we describe the development of the NorthCARDS dataset which includes data on trajectories of illness, response to treatments and lung compliance for COVID-19 patients who were mechanically ventilated at one of the 12 acute care hospitals within the Northwell Health System. We then describe differences in demographics and treatments as well as trajectories of lung compliance and hypoxemia over the hospital course for patients with very low versus low-normal lung compliance. This work sets the stage for further data analytics among patients with COVIDARDS to better characterize phenogroups using readily available data elements from electronic health records.

Methods

Patients, Study Design and Data Collection

This is a retrospective study of intubated and mechanically ventilated patients with ARDS and COVID-19 who were admitted to one of 12 acute care hospitals within the Northwell Health System during the height of the pandemic in NYC (March 1 - April 30, 2020). Northwell Health is the largest academic health system in New York, serving approximately 11 million people. Discharge disposition was available until Sept 30th, 2020 for all patients in the cohort. Within the Northwell Health COVID-19 Research Consortium, the Northwell ARDS Research Collaborative was formed by a multi-disciplinary group of clinical providers and research scientists (data scientists, biostatisticians and clinical trialists) to work on the creation of the NorthCARDS dataset.

All patients admitted to one of the 12 hospitals within the Northwell Health system during the time period of March 1 through April 30, 2020 were screened. Inclusion criteria were: Age > 18 , COVID-19 polymerase chain reaction (PCR) test positive during the hospitalization, treatment with invasive mechanical ventilation, and PaO_2 : Fraction of inspired Oxygen (FiO_2) ratio, (referred to as P/F), of less than 300 for 2 consecutive measurements during the hospital admission. The requirement for bilaterality of infiltrates as per the Berlin ARDS definition was confirmed based on a random sample of one hundred patients who were reviewed for radiographic findings of bilateral pulmonary involvement based on attending radiologist read of chest x-rays or CT scan. Surgical patients, identified by the presence of a brief operative note within 24 hours of intubation time (Ti) were excluded unless the mechanical ventilation was for a post-operative state rather than for the procedure alone.

Features relevant for understanding patients' lung mechanics were extracted from the electronic health records of COVIDARDS patients. All available laboratory values, medications and oxygen supplementation concentration and mode as well as pulse oximetry results (SpO_2) were recorded.

This study was considered by Northwell Health Institutional Review Board (IRB) as minimal-risk using data collected for routine clinical practice, meeting the ethical standards framed in 1964 Declaration of Helsinki. The Northwell Health IRB waived the requirement for informed consent.

Data Definitions and Assumptions

Several data assumptions needed to be made to structure the data. These included which fields contained the most valid and reliable data, and how best to handle missing data. For transparency, we outline assumptions for data structuring below and how we tested these assumptions. The Northwell ARDS Research Collaborative discussed each assumption to ensure that they reflected the clinical practice of providers caring for patients and their data entry in to the electronic health record. Further details are provided in the Supplement.

Oxygen Delivery Method, Concentration, and Degree of Hypoxemia:

The FiO_2 delivered was calculated based on the following formula: for nasal cannula or non-rebreather face mask, each liter of oxygen flow added 0.04 to 0.21 (room air), with a maximum of 6 liters per minute for nasal cannula and 15 liters per minute for non-rebreather mask. In the instances where the delivery method was not recorded in the electronic medical record, the previous recorded method was presumed to have been continued, until change in flow rate or delivery method was noted. To be able to accurately map hypoxemia prior to intubation, we used both arterial blood gas data on partial pressure of oxygen (PaO_2) and peripherally measured oxygen saturation (SpO_2). We calculated $\text{SpO}_2:\text{FiO}_2$ ratios as well as $\text{PaO}_2:\text{FiO}_2$ ratios over time for each patient across their entire hospital stay. For separate analyses we converted $\text{SpO}_2:\text{FiO}_2$ to $\text{PaO}_2:\text{FiO}_2$ ratios ("derived P/F") to obtain an estimated trajectory of PaO_2 over time⁷ (derived P/F = $([\text{SpO}_2:\text{FiO}_2]-64)/0.84$). The assumption that derived P/F would have parallel trends compared to ABG based P/F was visually tested (Fig. 4).

Respiratory System Compliance

We used both static compliance (change in lung volume per unit change in pressure in the *absence of flow*) using the plateau pressure recorded in the electronic medical record, (Tidal Volume/ [Plateau Pressure – Peak End Expiratory Pressure (PEEP)]); and dynamic compliance using the Peak Inspiratory Pressure (PIP) (change in lung volume per unit change in pressure in the *presence of flow*), (Tidal Volume/ [PIP – PEEP]) when patients were deeply sedated/paralyzed as described below. We only included values obtained at the time of full patient sedation, which was defined as the administration of intermittent bolus or continuous infusions of paralytics and difference in patient respiratory rate and set respiratory rate < 2 breaths/minute (Figure S-7). We made the assumption that patients would not have a significant component of airway resistance for most COVID-19 respiratory failure patients in the early stage of disease (no more than a difference of 5–7 cmH₂O between PIP and Plateau pressures), and that therefore this added pressure due to flow would have a minimal contribution to overall measured compliance. This assumption was tested by visualizing the difference between static and dynamic compliance seen over time (Figure S-3).

Outcomes measured

In addition to establishing the NorthCARDS dataset, we sought to explore whether there were different phenogroups of COVIDARDS. The primary outcome was the number of patients in categories of lung compliance on the first day of ARDS, and the characteristics seen descriptively in each category. The secondary outcome was hospital mortality and discharge location. Ventilator parameters and respiratory mechanics were reported for each group of pre-defined compliance. While oxygenation, pulmonary mechanics and therapeutics were censored on June 23rd, the hospital disposition data was available through the end of September.

Statistical analyses

Descriptive statistics included proportions for categorical variables, and mean (standard deviation) and median (interquartile range) for continuous variables. We used the independent-samples t-test, proportions z-test, and/or Mood's median test to compare very low and low-normal compliance categories, and two-sided p-value < 0.05 as the threshold of statistical significance. The data was analyzed using Python 3.7 and several libraries including pandas, numpy, matplotlib, scipy, nltk, and re. Because the size of our dataset could lead to finding statistically significant associations without clinical significance, each outcome was reviewed for clinical significance by the clinicians in the Northwell ARDS Collaborative and results are discussed in the context of pathophysiological validity and other investigators' results.

Role of the Funding Source

This work was supported by philanthropic funds to the Feinstein Center for Health Outcomes and Innovation Research. The funding source did not control any aspect of the study and did not review the results. All authors had full access to the full data in the study and accept responsibility to submit for publication.

Results

We identified 3176 patients who were admitted between March 1 and April 30, 2020 to one of the Northwell Health System hospitals, and who were mechanically ventilated. Of these, 2020 patients were COVID-19 PCR positive and 1554 met inclusion criteria with reliable lung compliance data (Fig. 1). Data for patients who were excluded are presented in the supplement (Table S1). Discharge disposition for index hospitalization was available for all patients except two patients.

Lung Compliance categories

The average lung compliance for the whole cohort was 24.44 mL/cm H₂O (SD 11.69). Frequencies per decile of compliance are presented in Fig. 2. Based on clinical observations, the Northwell ARDS Collaborative chose to categorize the cohort into three categories: very low compliance (< 20 mL/cm H₂O); low-normal (20–50 mL/cm H₂O) and high (> 50 mL/cm H₂O) measured by the dynamic compliance over the first 24 hours of intubation in the setting of paralytics or deep sedation. There were 538 (34.6%) patients with very low compliance; 982 (63.2%) with low-normal compliance, and 34 (2.2%) with high compliance. Given the very small sample size in the higher compliance category, comparators of prevalence and exploratory statistical testing is limited to the very low versus low-normal compliance groups. The average median difference between static

and dynamic compliance overall was 6.41 mL/cm H₂O (IQR 3.16, 11.42, n = 1053). For the very low compliance group median difference was 4.60 mL/cm H₂O (IQR 2.05, 8.10, n = 429); and for the low-normal group 7.89 mL/cm H₂O (IQR 4.19, 12.64, n = 610).

COVIDARDS Demographics

Patient demographics are detailed in Table 1. Overall, average age was 65 years, 32% were female, 35% were white, and the average Charlson comorbidity index was 4.9 (SD 3.3) (corresponding to a roughly 52% estimated 1-year survival).⁸ The MEWS score was also high (4.1, SD 1.9) (corresponding to a roughly 12.7% chance of ICU admission or death within 60 days).⁹ There was a greater percentage of females in the very low compliance category (43.7%, vs. 24.9%, low-normal; and 29.4%, high), and more were non-white/multi-racial. The most common comorbidity was hypertension (65.1%, n = 1012) and diabetes (43.4%, n = 675). The overall cohort included 16% (n = 251) with BMI indicating extreme obesity (BMI > 40).

Interventions/treatments

Almost all patients (89%, n = 1383) received hydroxychloroquine, 62% (n = 963) received azithromycin, 82% (n = 1278) received steroids, 52% (n = 815) received paralytics, and 49% (n = 769) were prone. IL-1 and IL-6 inhibitors were given to 30% (n = 475) of the patients, while 7% received convalescent plasma (n = 109). During the first 48 hours, 83.5% (n = 449) received at least one vasopressor in the very low compliance category, compared to 77.2% (n = 758) in the low-normal group. (Table 2)

Time to Intubation

On average, COVIDARDS patients were intubated within 50.8 hours (IQR 7.5, 123.7) from the time of admission. Patients in the very low compliance group had the longest time between admission and intubation, 107 hours (IQR 26.3, 238.3), compared to 37.9 hours (IQR 4.8, 90.7) in the low-normal compliance group. Prior to intubation, 77% (n = 1196) of patients were receiving oxygen supplementation via non rebreather masks, with 2.1% (n = 33) on HFNC, and 3.3% (n = 51) on NIV, which reflects infection control practices at the time discouraging NIV use. (Table 2)

P/F ratios and blood gas results

The average blood gas pH in the 24 hour period before intubation was 7.29 (SD 0.14), and PaCO₂ was 51.4 mmHg (SD 19.31). (Table 3) Patients in the very low lung compliance category had higher levels of PaCO₂ and lower mean arterial pH. ABG was not performed in 70.8% cases during the 12 hours prior to intubation. The overall mean derived P/F ratio in the 12 hours prior to intubation was 95 (SD 85), which was lowest for those in the high compliance group (P/F 66, SD 33) (Fig. 5). When including PEEP in the calculation of P/F ratio, the P/FPEEP (PFP)¹⁰ also appeared lowest for those in the highest compliance category. There was no correlation between P/F and compliance. (Fig. 2)

In the 12 hours post intubation, the mean ABG P/F ratio was 155.33 (SD 88.47) for the overall group, and similar across groups. (Fig. 2) Those in the very low compliance categories received higher FiO₂ for longer periods of time prior to intubation (in the setting of also having longer average time to intubation). Prior to intubation, the group with normal to high compliance were exposed to FiO₂ > 60% for 57.53 hours (IQR 6.68, 181.66) compared to 12.82 hours (IQR 0.45, 44.59) in the low-normal category (Table 3).

Duration of intubation

The average duration of intubation was 14.25 days (SD 13.69). Among those who survived, median duration was 11.9 days (IQR 4.8, 29.3) and mean was 18.26 (STD 16.91) days. Among those who died, median duration was 8.8 days (IQR 4.0, 17.1) and mean was 12.32 (STD 11.35). It should be noted that the length of intubation for survivors is an underestimation due to the fact that 19.8% of survivors were discharged while still mechanically ventilated.

The general trend of derived P/F ratios paralleled the ABG P/F ratios prior to intubation, although with high degree of variability among the ABG P/F ratios prior to intubation (wide 95% CI, shaded gray), due to many ABGs not being performed. Post-intubation, where many more ABGs were drawn, the two curves diverge for the first 48 hours, and then trend together over time. (Fig. 4)

Oxygenation Index (OI)

The mean OI for the entire cohort in the 24 hours after intubation was 11.12 (5.67), and was slightly worse in the very low compliance group 12.29 (5.70).

Lung Mechanics and Ventilator Settings

Lung compliance for the whole cohort decreased over time, with a steeper trajectory among those who died (Fig. 3). This was seen more clearly in the low-normal compliance group and high compliance groups likely secondary to the 'floor effect' (very low compliance numbers starting at a very low value) (Figure S-4). On average, patients received 6.9 cc/kg (SD 1.2) of ideal body weight as the ventilator setting. (Table 4) As expected, the very low lung compliance group had the highest average peak airway pressure, plateau pressure, and resulting driving pressures. The mean driving

pressure for the whole cohort was 16·24 (SD 6·37), and 20·54 (SD·77) for the very low compliance group compared to 13·38 (SD 3·88) for the low-normal compliance group.

Proportion of Deaths and Discharge to Home

Table 5 presents the disposition status of patients based on the index hospitalization which was available for all patients (unknown for 2 patients). Overall, of the 1554 patients, 67·5% (n = 1049) died during the index hospital stay. Of the 505 patients who survived to hospital discharge, 100 (19·8%) were discharged while still on a mechanical ventilator. Of those who survived, 44·4% (n = 224) were discharged home and the rest to rehabilitation or longer term care facilities. The very low compliance group had the highest mortality (70·1% versus 66·2%) and fewer survivors were discharged home (41·0% versus 46·0%).

Discussion

Patients with COVIDARDS in the NorthCARDS dataset had heterogeneous lung compliance, as measured in the first 24 hours of intubation. Three observations were particularly notable and include the longer time to intubation for patients with very low lung compliance, the steeper trajectory of compliance decrease seen among those who died, and the severity of hypoxemia in those with high lung compliance. As others have noted, the course of COVID19 pneumonia and ARDS appears to start with a highly compliant lung but with profound hypoxemia.^{11,12} Therefore, it is possible that ARDS patients with low compliance detected at the time of intubation may well have started with a normal lung compliance with deterioration during the course of illness, in part due to the disease process itself, and possibly due to treatments administered. For example, it is possible that prolonged exposure to high concentrations of oxygen contributed to the low compliance seen once patients were intubated. High concentrations of oxygen have been demonstrated to cause lethal lung injury in animal models,^{13–15} and have been associated with increased mortality,^{16,17} severe lung injury, and pneumonia¹⁸ in humans. A recent study linked hyperoxia to microbial dysbiosis in both the lung and gut microbiome which could contribute to the lung injury.¹⁹ It is unclear whether earlier intubation, and/or lower oxygen saturation thresholds would have mitigated worsening of lung compliance. The recent ICU-ROX study did not find that conservative oxygen thresholds (SpO₂ 90–97%) decreased ventilator days in intubated ICU patients,²⁰ and the recent LOCO2 trial, conservative therapy (SpO₂ 88–92%) was associated with increased mortality among intubated patients.²¹ However, these results may not apply to non-intubated patients. Many COVID-19 patients who were maintained without intubation had uniquely preserved mentation despite very low SpO₂ levels (likely due to right-shifted oxygen dissociation curves) and did not meet conventional thresholds for intubation. Alternatively, clinicians have posited that PSILI (patient self-induced lung injury)²² due to extreme respiratory drives could exacerbate lung damage in COVID-19 disease. Prior to intubation patients were not receiving sedation and strong respiratory drives may have contributed to the lower lung compliance seen due to PSILI. Of course, these patients could have had very low compliance at the time of hospital presentation. In addition, the persistence of active disease itself could have led to progressively lower compliance due to persistent severe inflammation. A prospective study that includes a surrogate measure for compliance prior to intubation, ideally with serial measurements over time, and documentation of progression of ventilation and perfusion mismatch (including ultrasound or other radiography and dead space estimation) will help answer these questions. These investigations are relevant for ARDS in general and learnings will have implications for the management of ARDS beyond COVID19.

Degree of V/Q mismatch and hypoxemia does not appear to correlate with lung compliance, which corresponds to what colleagues have found in the non-ARDS analyses.²³ Indeed, 42% of the cohort with high lung compliance in non-COVID ARDS patients had P/F levels under 150, which is similar to our findings in COVIDARDS. The extremely low P/F ratio, P/FP and high Oxygenation Index seen among patients in the high compliance group suggests ventilation perfusion mismatch which could be explained by the extensive micro-thrombi that have been reported, and the involvement of the vascular endothelium with impaired hypoxic pulmonary vasoconstriction.²⁴ Questions have been raised about whether COVIDARDS should be treated differently than non-COVIDARDS. The more relevant question seems to be whether ARDS management should be different for patients with different severity of lung compliance impairment and different degrees of ventilation and perfusion mismatch. An index that takes into account oxygen impairment and compliance over time, pointing to predominance of dead space ventilation (thrombi) versus shunt physiology (alveolar and parenchymal pathology, and impaired vascular hypoxic vasoconstriction) may help clinicians tailor treatments for individual patients with ARDS.

Only 2·2% of patients were in the high compliance category (low elastance/ phenotype “L”).²⁵ This is lower than the 12% reported in the recent secondary analysis of the LungSAFE data of non-COVID ARDS patients.²³ However, it is important to note that our description of compliance variability is limited to ARDS patients who are mechanically ventilated. Many patients who met ARDS criteria based on hypoxemia and bilaterality of infiltrates did not receive mechanical ventilation until several days after admission. This period was likely prolonged compared to other viral pneumonia causes of ARDS due to the relatively preserved mental status in COVID-19 patients despite profound hypoxemia. Comparisons between studies need to consider the timing of intubation relative to symptom onset, and different practice patterns regarding thresholds for intubation. Disparate outcomes reported internationally are likely explained in large part by different comorbidity burden, severity of hypoxemia on hospital presentation, and different practice patterns regarding timing of intubation.

The strengths of this study include being the largest sample of COVIDARDS patients in a single health system which has granular patient-level data regarding respiratory mechanics and oxygenation. We have described methods for leveraging real-world data to determine lung compliance data in the absence of patient effort which could either over- or under-estimate true pressures. Our large sample size allowed us to maintain 1554 patients in the dataset who had reliable data on pulmonary mechanics.

Limitations of the present study are inherent to the retrospective nature of this data extraction from the electronic health record. We are unable to ensure that there was no significant airway resistance contributing to the measurement of dynamic compliance, and to account for the contribution of abdominal pressures and chest wall stiffness. The small and consistent margin of difference between static and dynamic compliance seen suggests that airway resistance contributed minimally to measured dynamic airway pressures. We assumed that the difference between dynamic and static compliance would be $< 10 \text{ mL/cm H}_2\text{O}$ due to airway resistance not being commonly observed in the early stages of COVIDARDS. In non-COVID-19 related ARDS the mean difference between peak and plateau pressures has been found to be $6\text{--}7 \text{ cmH}_2\text{O}$.²⁶ However, given that 50% ($n = 804$) of patients had a BMI of over 30, it is possible that chest wall compliance contributed to a decreased measured compliance in some patients. A further limitation is our inability to control for factors which influenced decisions about timing of intubation for COVID19 patients. For example, those who were intubated earlier may have had altered mental status which could confound differences seen in mortality associated with lung compliance. Limits to resuscitation due to patient and family preference have also not been presented in this descriptive analysis. These factors will need to be accounted for in future inferential studies

In summary, we present the methods for establishing the NorthCARDS dataset of COVIDARDS patients, and the range of lung compliance and oxygen trajectories seen in these patients. These data will inform phenogrouping research to further understand COVIDARDS towards tailored approaches to treatment which maybe also be applicable to non-COVID-19 related ARDS.

Conclusions

The respiratory system compliance distribution of COVIDARDS is largely similar to non-COVIDARDS, with most patients having low or very low lung compliance. Patients with high lung compliance had profound hypoxemia. In some patients, there may be a relation between time to intubation and duration of high levels of supplemental oxygen treatment on trajectory of lung compliance.

Declarations

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Ethics approval and consent to participate:

The Northwell Institutional Review Board has reviewed the application for creation of COVIDARDS database and approved the study with a waiver of consent.

Consent for publication:

Not Applicable

Availability of data and materials:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

Funding:

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Authors' contributions:

Daniel Jafari - literature search, figures, study design, data collection, data interpretation, writing

Amir Gandomi - figures, study design, data collection, data analysis, data interpretation, writing

Alex Makhnevich - literature search, figures, study design, data collection, data interpretation, writing

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Molly Stewart - literature search, data collection, writing

Meng Zhang - study design, data collection, data interpretation

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All authors have had access to and verified the underlying data. In Particular DJ, NH, AM, AT, EG independently chart reviewed random selections of patients to verify accuracy of data.

References

1. Go L, Budinger GRS, Kwasny MJ, et al. Failure to Improve the Oxygenation Index Is a Useful Predictor of Therapy Failure in Acute Respiratory Distress Syndrome Clinical Trials. *Crit Care Med* 2016; **44**: e40–e44.
2. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA* 2020; **323**: 2052–9.
3. Gibson PG, Qin L, Puah SH. COVID-19 acute respiratory distress syndrome (ARDS): clinical features and differences from typical pre-COVID-19 ARDS. *Med J Aust* 2020; **213**: 54–6.
4. Fan E, Beitler JR, Brochard L, et al. COVID-19-associated acute respiratory distress syndrome: is a different approach to management warranted? *Lancet Respir Med* 2020; **8**: P816–21.
5. Gattinoni L, Chiumello D, Caironi P, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? *Intensive Care Med* 2020; **46**: 1099–102.
6. Marini JJ, Gattinoni L. Management of COVID-19 Respiratory Distress. *JAMA* 2020; **323**: 2329–30.
7. Rice TW, Wheeler AP, Bernard GR, et al. Comparison of the SpO₂/FIO₂ ratio and the PaO₂/FIO₂ ratio in patients with acute lung injury or ARDS. *Chest* 2007; **132**: 410–7.
8. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373–83.
9. Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified Early Warning Score in medical admissions. *QJM* 2001; **94**: 521–6.
10. Sunitha P. The P/F Ratio (PaO₂/Fio₂ X PEEP) X 10: A Pilot Approach to Calculate the Severity of Oxygenation/ARDS with PEEP. *Am J Respir Crit Care Med* 2017; **195**.
11. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020; **323**: 1574–81.
12. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. *JAMA* 2020; **323**: 1612–4.
13. Frank L, Bucher JR, Roberts RJ. Oxygen toxicity in neonatal and adult animals of various species. *J Appl Physiol Respir Environ Exerc Physiol* 1978; **45**: 699–704.
14. Kallet RH, Matthay MA. Hyperoxic Acute Lung Injury. *Respir Care* 2013; **58**: 123–41.
15. Matute-Bello G, Frevert CW, Martin TR. Animal models of acute lung injury. *Am J Physiol Lung Cell Physiol* 2008; **295**: L379–99.
16. Chu DK, Kim LH-Y, Young PJ, et al. Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy. *Lancet* 2018; **391**: 1693–705.

17. Girardis M, Busani S, Damiani E, et al. Effect of conservative vs conventional oxygen therapy on mortality among patients in an intensive care unit: The oxygen-ICU randomized clinical trial. *JAMA* 2016; **316**: 1583–9.
18. Barber RE, Hamilton WK. Oxygen toxicity in man – A prospective study in patients with irreversible brain damage. *N Engl J Med* 1970; **283**: 1478–84.
19. Ashley SL, Sjoding MW, Popova AP, et al. Lung and gut microbiota are altered by hyperoxia and contribute to oxygen-induced lung injury in mice. *Sci Transl Med* 2020; **12**:
20. ICU-ROX Investigators, New Zealand Intensive Care Society Clinical Trials Group. Conservative Oxygen Therapy during Mechanical Ventilation in the ICU. *N Engl J Med* 2020; **382**: 989–98.
21. Barrot L, Asfar P, Mauny F, et al. Liberal or Conservative Oxygen Therapy for Acute Respiratory Distress Syndrome. *N Engl J Med* 2020; **382**: 999–1008.
22. Gattinoni L, Marini JJ, Busana M, Chiumello D, Camporota L. Spontaneous breathing, transpulmonary pressure and mathematical trickery. *Ann Intensive Care* 2020; **10**:
23. Panwar R, Madotto F, Laffey JG, van Haren FM, LUNG Safe Investigators, ESICM Trials Group. Compliance Phenotypes in Early Acute Respiratory Distress Syndrome before the COVID-19 Pandemic. *Am J Respir Crit Care Med* 2020; **202**: 1244–52.
24. Archer SL, Sharp WW, Weir K. Differentiating COVID-19 Pneumonia From Acute Respiratory Distress Syndrome and High Altitude Pulmonary Edema. *Circulation* 2020; **142**: 101–4.
25. Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. COVID-19 Does Not Lead to a "Typical" Acute Respiratory Distress Syndrome. *Am J Respir Crit Care Med* 2020; **201**: 1299–
26. Acute Respiratory Distress Syndrome Network, Brower R, Matthay M, et al. Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome. *N Engl J Med* 2000; **342**: 1301–8.

Tables

Table 1
Demographics stratified by high/normal/low compliance

	All patients with reliable compliance (n = 1554)	Patients with very low compliance < 20 ml/cm H2O (n = 538; 34.6%)	Patients with low-normal compliance 20–50 ml/cm H2O (n = 982; 63.2%)	Patients with high compliance > 50 ml/cm H2O (n = 34; 2.2%)	p-value (very low vs. low-normal compliance)
Age median, IQR	65.0 [56.0,73.0]	64.0 [56.0,73.0]	65.5 [56.0,74.0]	69.0 [60.2,73.0]	0.025
Female n (%)	490 (31.5)	235 (43.7)	245 (24.9)	10 (29.4)	< 0.001
Race n (%)					
Black/African American	290 (18.7)	113 (21.0)	172 (17.5)	5 (14.7)	0.096
Asian	154 (9.9)	70 (13.0)	82 (8.4)	2 (5.9)	0.004
Other/Multiracial	484 (31.1)	193 (35.9)	272 (27.7)	17 (50.0)	< 0.001
Unknown	81 (5.2)	25 (4.6)	54 (5.5)	2 (5.9)	0.47
White	545 (35.1)	137 (25.5)	400 (40.7)	8 (23.5)	< 0.001
Comorbidities (Charlson Index) mean (SD)	4.9 (3.3)	4.7 (3.2)	5.0 (3.3)	4.4 (2.2)	0.094
MEWS on admission mean (SD)	4.1 (1.9)	4.2 (1.8)	4.1 (1.9)	3.9 (1.6)	0.301
Chronic Lung Disease n (%)	102 (6.6)	33 (6.1)	67 (6.8)	2 (5.9)	0.60
Diabetes n (%)	675 (43.4)	211 (39.2)	378 (38.5)	14 (41.2)	0.28
HTN n (%)	1012 (65.1)	349 (64.9)	645 (65.7)	18 (52.9)	0.75
CHF n (%)	114 (7.3)	20 (3.7)	53 (5.4)	1 (2.9)	0.14
CAD n (%)	208 (13.4)	57 (10.6)	147 (15)	4 (11.8)	0.017
CKD n (%)	228 (14.7)	67 (12.5)	158 (16.1)	3 (8.8)	0.056
ESRD n (%)	85 (5.5)	24 (4.5)	60 (6.1)	1 (2.9)	0.178
Positive Smoking n (%)	195 (15.5)	63 (13.9)	131 (16.7)	1 (4.2)	0.18
Malignancy n (%)	147 (9.5)	51 (9.5)	94 (9.6)	2 (5.9)	0.037
BMI on admission mean (SD)	31.0 (7.8)	30.5 (7.4)	31.4 (8.1)	29.5 (4.3)	0.025
BMI Categories n (%)					
BMI < 18 underweight	10 (0.6)	7 (1.3)	3 (0.3)	0	0.0217
BMI 18 – <30 normal-overweight	740 (47.6)	267 (49.6)	457 (46.5)	16 (47.1)	0.25
BMI 30 – <40 obese	553 (35.6)	185 (34.4)	353 (35.9)	15 (44.1)	0.54
BMI >= 40 extremely obese	251 (16.2)	79 (14.7)	169 (17.2)	3 (8.8)	0.20

Table 2
Interventions stratified by compliance groups

During the entire hospital stay	All patients with reliable compliance N = 1554	Patients with very low compliance < 20 ml/cm H2O (n = 538; 34·6%)	Patients with low–normal compliance 20–50 ml/cm H2O (n = 982; 63·2%)	Patients with high compliance > 50 ml/cm H2O (n = 34; 2·2%)	p–value (very low vs. low–normal compliance)
Steroids* n (%)	1278 (82·1)	467 (86·8)	780 (79·4)	29 (85·3)	< 0·001
Hydroxychloroquine n (%)	1383 (89)	459 (85·3)	893 (90·9)	31 (91·2)	< 0·001
Azithromycin n (%)	963(62)	269 (50·0)	672 (68·4)	22 (64·7)	< 0·001
IL–1 or IL–6 inhibitor** n (%)	475 (30·6)	190 (35·3)	274 (27·9)	11 (32·4)	0·003
Remdesivir n (%)	12 (0·7)	5 (0·9)	7 (0·7)	0	0·650
Convalescent plasma n (%)	109 (7)	46 (8·6)	62 (6·3)	1 (2·9)	0·100
Proning	769 (49·4)	319 (59·3)	436 (44·4)	14 (41·2)	< 0·001
Paralytics***	815 (52·4)	313 (58·2)	487 (49·6)	14 (41·2)	0·001
Vasopressors (y/n) in first 48hrs n (%)	1,232 (79·2)	449 (83·5)	758 (77·2)	25 (73·5)	0·004
Inotropes (y/n) at any time count n (%)	64 (4·1)	28 (5·2)	0 (0·0)	36 (3·6%)	< 0·001
Pre–intubation O2 supplementation n (%) ****					
NRB	1196 (77)	426 (79·2)	743 (75·7)	27 (79·4)	0·119
NRB + NC	41(2·6)	18 (3·3)	23 (2·3)	0	0·248
NC	82 (5·3)	21 (3·9)	59 (6·0)	2 (5·9)	0·079
HFNC	33 (2·1)	13 (2·4)	20 (2)	0	0·628
NIV (BiPAP/CPAP)	51 (3·3)	23 (4·3)	27 (2·7)	1(2·9)	0·111
Venturi	15 (1)	2 (0·4)	13 (1·3)	0	0·072
Other*****	136 (8·8)	35 (6·5)	97 (9·9)	4 (11·8)	0·026
Median hours from hospital presentation to intubation (IQR)	50·8 [7·5,123·7]	107·0 [26·3,238·3]	37·9 [4·8,90·7]	29·4 [1·0,79·4]	< 0·001
<p>* dexamethasone, hydrocortisone, methylprednisolone, prednisone, prednisolone</p> <p>** Anikinra, Tocilizumab, Sarilumab</p> <p>***Rocuronium, Vecuronium, Cisatracurium</p> <p>**** NRB = Nonrebreather Mask; NC- Nasal Canula; HFNC = High Flow Nasal Canula; NIV = Non-Invasive Mechanical Ventilation; Venturi = Venturi Mask</p> <p>***** Other included room air; BVM; tracheostomy collar; simple face; bag mask; ambubag; T–piece; king airway;</p>					

Table 3
Oxygenation trends and duration of ventilation by compliance group

	All patients with reliable compliance N = 1554	Patients with very low compliance < 20 ml/cm H2O (n = 538; 34.6%)	Patients with low-normal compliance 20–50 ml/cm H2O (n = 982; 63.2%)	Patients with high compliance > 50 ml/cm H2O (n = 34; 2.2%)	p-value (very low vs. low-normal compliance)
P/F derived pre intubation (12hr mean)	94.64 (85.08)	81.50 (75.30)	102.73 (90.10)	66.20 (33.28)	< 0.001
Mean (SD)	60.13 (52.17,98.92)	58.04 (50.21,68.58)	61.90 (53.33,124.89)	58.29 (51.06,68.94)	
Median (IQR)	1419	489	900	30	
n					
P/F from ABG pre intubation (12hr mean)	109.32 (100.27)	110.72 (118.58)	109.49 (89.80)	81.32 (23.99)	0.90
Mean (SD)	75.31 (61.56,110.72)	71.30 (59.26,106.48)	77.57 (62.96,112.30)	74.07 (63.27,104.48)	
Median (IQR)	454	164	280	10	
n					
P/F derived post intubation, (12hr mean)	68.20 (38.77)	65.15 (36.46)	69.84 (39.95)	69.40 (38.22)	0.02
Mean (SD)	54.32 (40.97,83.07)	52.49 (40.25,77.12)	54.91 (41.14,86.03)	55.15 (41.07,88.11)	
Median (IQR)	1543	536	973	34	
n					
P/F from ABG post intubation (12 hr post, ABG)	155.33 (88.47)	140.56 (68.37)	163.36 (97.43)	160.98 (72.93)	< 0.001
Mean (SD)	136.31 (96.50,189.79)	120.00 (93.00,165.00)	144.71 (101.00,200.89)	162.89 (97.08,209.64)	
Median (IQR)	1484	519	933	32	
n					
First ABG P/F post intubation (within 4 hours after Ti),	149.39 (105.58)	130.24 (74.41)	160.49 (119.40)	161.01 (97.36)	< 0.001
Mean (SD)	120.00 (85.00,183.81)	107.50 (82.00,157.00)	127.50 (88.00,203.17)	133.75 (83.50,251.25)	
Median (IQR)	1116	410	682	24	
n					
P/F gradient derived 24 hrs pre intubation (derived P/F)	-321.66 (2054.35)	-266.31 (1508.05)	-360.98 (2340.15)	-92.62 (229.97)	0.42
Mean (SD)	-6.39 (-108.70,1.58)	-4.42 (-28.11,1.56)	-8.55 (-141.60,1.57)	-2.96 (-112.99,3.84)	
Median (IQR)	1345	482	836	27	
n					
Number of hours with FiO2 ≥ 60% pre intubation	63.34 (100.20)	112.25 (135.00)	36.27 (57.89)	57.12 (111.70)	< 0.001
Mean (SD)	20.72 (1.50,81.35)	57.53 (6.68,181.66)	12.82 (0.45,44.59)	13.85 (3.07,57.80)	
Median (IQR)	1489	522	936	31	
n					
Proportion of time on FiO2 ≥ 60% pre-intubation	61.86% (36.79%)	68.81% (34.47%)	57.45% (37.55%)	73.40% (32.24%)	< 0.001
Mean (SD)	73.31% (28.19%,97.91%)	84.50% (43.39%,98.55%)	64.14% (21.30%,96.37%)	89.45% (50.11%,100.00%)	
Median (IQR)	1380	497	856	27	
n					

	All patients with reliable compliance N = 1554	Patients with very low compliance < 20 ml/cm H2O (n = 538; 34·6%)	Patients with low-normal compliance 20–50 ml/cm H2O (n = 982; 63·2%)	Patients with high compliance > 50 ml/cm H2O (n = 34; 2·2%)	p-value (very low vs. low-normal compliance)
Proportion of time on FiO2 ≥ 60% post-intubation	2·62% (34·62%)	55·33% (35·84%)	51·12% (33·87%)	53·18% (35·04%)	< 0·001
Mean (SD)	48·78% (19·43%,89·65%)	55·24% (18·78%,95·70%)	46·44% (19·85%,84·55%)	50·31% (23·37%,88·06%)	
Median (IQR)	1554	538	982	34	
n					
Oxygenation Index*	11·12 (5·67)	12·29 (5·70)	10·47 (5·56)	8·28 (4·22)	0·002
Mean (SD)	10·17 (7·00,13·90)	11·48 (8·30,15·40)	9·47 (6·53,13·20)	7·25 (5·65,10·41)	
Median (IQR)	1341	508	810	23	
n					
PFP value**	96·41 (73·98)	100·68 (73·54)	94·76 (74·79)	76·74 (50·03)	0·138
Mean (SD)	76·57 (50·86,113·73)	80·47 (53·90,119·80)	74·67 (49·35,108·74)	57·57 (45·08,96·37)	
Median (IQR)	1554	538	982	34	
n					
pH within –24 to + 4 hours from T_i	7·29 (0·14)	7·26 (0·15)	7·31 (0·12)	7·33 (0·13)	< 0·001
Mean (SD)	7·31 (7·21,7·39)	7·26 (7·17,7·36)	7·33 (7·24,7·41)	7·35 (7·27,7·42)	
Median (IQR)	1123	414	687	22	
n					
PaCo2 within –24 to + 4 hours from T_i	51·43 (19·31)	58·51 (21·45)	47·80 (16·98)	42·29 (12·02)	< 0·001
Mean (SD)	47·00 (38·00,60·50)	54·50 (42·00,71·25)	44·00 (36·00,56·00)	40·00 (31·75,52·00)	
Median (IQR)	1207	424	755	28	
n					
Values are provided along with sample size (n) for patients with available data·					
*Oxygenation index = FiO2 x mean airway pressure]/PaO2 *100 [calculated using ABG PaO2 in the first 24 hours after T _i]					
**PFP Value = [P/{F x PEEP}] x 10					

Table 4
Mechanical ventilator obtained parameters (lung mechanics and ventilator settings)

	All patients with reliable compliance (n = 1554)	Patients with very low compliance < 20 ml/cm H2O (n = 538; 34.6%)	Patients with low–normal compliance 20–50 ml/cm H2O (n = 982; 63.2%)	Patients with high compliance > 50 ml/cm H2O (n = 34; 2.2%)	p–value (very low vs. low–normal compliance)
Compliance in the first 24 hours of intubation	24.44 (11.69)	15.37 (3.26)	27.65 (6.48)	75.22 (26.54)	< 0.001
Mean (SD)	22.59 (17.96,28.21)	15.76 (13.20,18.18)	25.62 (22.71,31.03)	72.08 (53.72,79.50)	
Median (IQR)	1554	538	982	34	
n					
Mean PEEP (cm H2O) within 24 hrs of intubation	2.48 (3.72)	11.60 (3.53)	12.88 (3.69)	14.82 (4.42)	< 0.001
Mean (SD)	12.35 (10.00,15.00)	11.39 (9.33,14.00)	13.00 (10.00,15.24)	15.75 (10.38,18.40)	
Median (IQR)	1554	538	982	3	
n					
Mean Peak pressure (cm H2O) within 24 hrs of intubation	2.75 (6.43)	37.76 (5.96)	30.26 (4.83)	25.17 (4.87)	< 0.001
Mean (SD)	32.46 (28.50,36.25)	37.00 (34.00,41.71)	30.50 (27.00,33.40)	25.25 (23.00,28.15)	
Median (IQR)	1554	538	982	3	
n					
Ventilation duration (days)	14.25 (13.69)	14.45 (13.80)	14.03 (13.57)	17.22 (15.51)	0.56
Mean (SD)	9.65 (4.20,19.58)	9.94 (4.07,19.86)	9.57 (4.22,19.02)	10.56 (4.82,30.39)	
Median (IQR)	1554	538	982	34	
n					
Ventilation duration (days) among those who survived	18.26 (16.91)	19.58 (17.06)	17.63 (16.96)	17.77 (13.67)	0.42
Mean (SD)	11.91 (4.81,29.29)	13.40 (5.89,31.19)	11.19 (4.33,27.67)	12.23 (8.22,30.13)	
Median (IQR)	505	161	332	12	
n					
Ventilation duration (days) among those who died	12.32 (11.35)	12.27 (11.49)	12.19 (11.03)	16.92 (16.73)	0.38
Mean (SD)	8.84 (3.95,17.14)	8.36 (3.74,17.49)	9.16 (4.16,16.74)	8.29 (4.67,28.64)	
Median (IQR)	1049	377	650	22	
n					
Vt cc/Kg of IBW	6.91 (1.22)	6.74 (1.19)	7.01 (1.23)	7.00 (1.23)	< 0.001
Mean (SD)	6.76 (6.08,7.51)	6.62 (5.92,7.41)	6.80 (6.17,7.63)	6.90 (6.31,7.41)	
Median (IQR)	1423	502	891	30	
n					
Set respiratory rate (per minute)	24.75 (9.64)	26.84 (7.23)	23.69 (10.68)	22.30 (4.66)	< 0.001
Mean (SD)	24.00 (20.00,28.00)	27.00 (23.00,30.48)	23.33 (20.00,26.40)	22.00 (20.00,26.30)	
Median (IQR)	1554	538	982	34	
n					

	All patients with reliable compliance (n = 1554)	Patients with very low compliance < 20 ml/cm H2O (n = 538; 34.6%)	Patients with low-normal compliance 20–50 ml/cm H2O (n = 982; 63.2%)	Patients with high compliance > 50 ml/cm H2O (n = 34; 2.2%)	p-value (very low vs. low-normal compliance)
Total respiratory rate Mean (SD)	25.70 (4.79)	27.62 (4.92)	24.70 (4.40)	24.50 (4.20)	< 0.001
Median (IQR)	25.67 (22.25,29.24)	28.17 (24.38,31.24)	24.75 (21.60,27.84)	24.62 (21.55,27.92)	
n	1554	538	982	34	
Plateau pressure (cm H2O)	28.32 (6.58)	31.91 (6.61)	26.00 (5.18)	21.30 (7.89)	< 0.001
Mean (SD)	28.00 (24.25,32.00)	31.25 (27.50,35.73)	26.00 (22.27,29.8)	20.33 (17.00,28.00)	
Median (IQR)	1062	431	614	17	
n					
Driving pressure* (cm H2O)	16.24 (6.37)	20.54 (6.77)	13.38 (3.88)	9.27 (5.03)	< 0.001
Mean (SD)	15.00 (12.00,19.25)	19.50 (16.00,24.00)	13.00 (10.75,15.50)	11.00 (5.50,11.33)	
Median (IQR)	1055	429	611	15	
n					
*Driving pressures were reported only when plateau and PEEP was recorded at same time					

Table 5
Hospital Mortality and Discharge location stratified by compliance group

	All patients with reliable compliance N = 1554	Patients with very low compliance < 20 ml/cm H2O (n = 538; 34.6%)	Patients with low-normal compliance 20–50 ml/cm H2O (n = 982; 63.2%)	Patients with high compliance > 50 ml/cm H2O (n = 34; 2.2%)	p-value (very low vs. low-normal compliance)
Deceased % (n)	67.50% (1049)	70.07% (377)	66.19% (650)	64.71% (22)	0.122
Survived % (n)	32.50% (505)	29.93% (161)	33.81% (332)	35.29% (12)	0.051
Discharged while on mechanical ventilator, % of the survivors (n)	19.80% (100)	22.98% (37)	17.77% (59)	33.33% (4)	0.171
Discharged home, % of the survivors (n)	44.36% (224)	40.99% (66)	46.08% (153)	41.67% (5)	0.286
Discharged to another facility including acute care and longer-term rehabilitation, % of the survivors (n)	55.25% (279)	59.01% (95)	53.31% (177)	58.33% (7)	0.233

Figures

Figure 1

Flowchart of study population and exclusions

Figure 2

(a) Frequency of lung compliance seen in the first 24 hours of mechanical ventilation for the entire cohort with reliable compliance data (N=1554) by decile, and (b) Correlation between Compliance and P/F from ABGs in the first 24 hours of intubation.

Figure 3

Trends in compliance for the total cohort [N= 1554] for the first 5 days post intubation (top), and 30 day trends of dynamic compliance between survivors and non-survivors (bottom) indicating decreasing compliance over time with a steeper decline among non-survivors. Trends per compliance category are presented in supplement.

Figure 4

Trend over time in derived (from SpO₂ from peripheral pulse oximetry) versus measured (from PaO₂ in ABG) P/F ratio. The vertical black line denotes intubation time (T_i). Shaded areas indicate variability in measurements due to many missing measured PaO₂ values relative to continually available SpO₂ values. However, the direction of change over time is similar in derived and measured P/F values. The gap in derived and measured P/F during the first 24 hours of mechanical ventilation likely represents a combination of the maximum SpO₂ being 100% (as opposed to PaO₂ which can be over 600) which sets an upper limit to the derived P/F from SpO₂; and due to the shape of the oxygen dissociation curve wherein small changes in SpO₂ correspond to larger changes in PaO₂.

Figure 5

Frequency of ABG P/F by compliance category

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