

Natural History and Trajectory of non-COVID-19 Acute Respiratory Distress Syndrome patients. An observational study for comparison to COVID-19 populations.

Toal.C.M¹, Fowler.A.J¹, Patel.B.V², Puthuchery.Z¹, Prowle.J.R¹

1. William Harvey Research Institute, Queen Mary University of London.

2. Division of Anaesthetics, Pain Medicine & Intensive Care, Department of Surgery & Cancer, Faculty of Medicine, Imperial College London, London, UK



Introduction

Previous studies on acute respiratory distress syndrome (ARDS) relate trajectories to initial degree of hypoxia^{1,2}. Further work is required to deduce whether previous ARDS frameworks are applicable to COVID-19 ARDS patients. In our study, we assess how hypoxia progression affects outcomes in non-COVID ARDS patients and compare how this differs from COVID-19 ARDS patients. We hypothesized that that severity and progression of hypoxemia can predict outcomes in both populations but there remains significant differences in clinical and physiological characteristics between the two groups

Methods and Materials

This is a retrospective observational study analysing patients from the Medical Information Mart for Intensive Care³ (MIMIC-IV) database. Inclusion criteria required patients to be mechanically ventilated, have evidence of concurrent respiratory infection (microbiology or x-ray confirmed) and evidence of initial hypoxemia.

Patients were grouped into either resolvers or non-resolvers, based on their hypoxemia progression over the first 7 days of intubation.

Daily blood gas and ventilatory settings were analysed, from the point of intubation to death or discharge allowing longitudinal analysis with high granularity.

Our primary outcome was how the proportion and trajectory of patients varied between resolver status groups in non-COVID ARDS patients.

Secondary outcomes included how base characteristics and initial clinical parameters affect trajectory and outcomes. Comparative analysis was performed between the results of this study and a previous large multicentre COVID-19 ARDS⁴.

Results

Baseline characteristics

1,575 ICU admissions were included in the study. In the MIMIC cohort, 67.4% of the cohort were hypoxia resolvers and 32.6% were non-resolvers (Table 2). There were no significant differences in age, BMI or comorbidities between the resolver groups.

Comparison of progression of hypoxia between populations

The alluvial plot displays how the hypoxia status of patients varied from intubation to discharge or death for both our MIMIC study (top) and the COVID-19 study (bottom, Figure 1).

There was a much lower percentage of patients with initial moderate or severe hypoxia in this study compared to the COVID-19 study (54.5% vs 76.8% respectively). It also shows that a higher proportion of patients improved their hypoxia status.

Table one compares the hypoxia status on Day 0 and Day 7 of intubation between the two study populations. A much smaller proportion of non-COVID-19 patients had a worsening of hypoxia in the first 7 days compared to COVID-19 patients (shaded red, 18.9% compared to 31.8% respectively). A larger proportion of non-COVID patients improved their hypoxia status over the first 7 days (33.1%) compared to COVID patients (23.5%) shaded in blue.

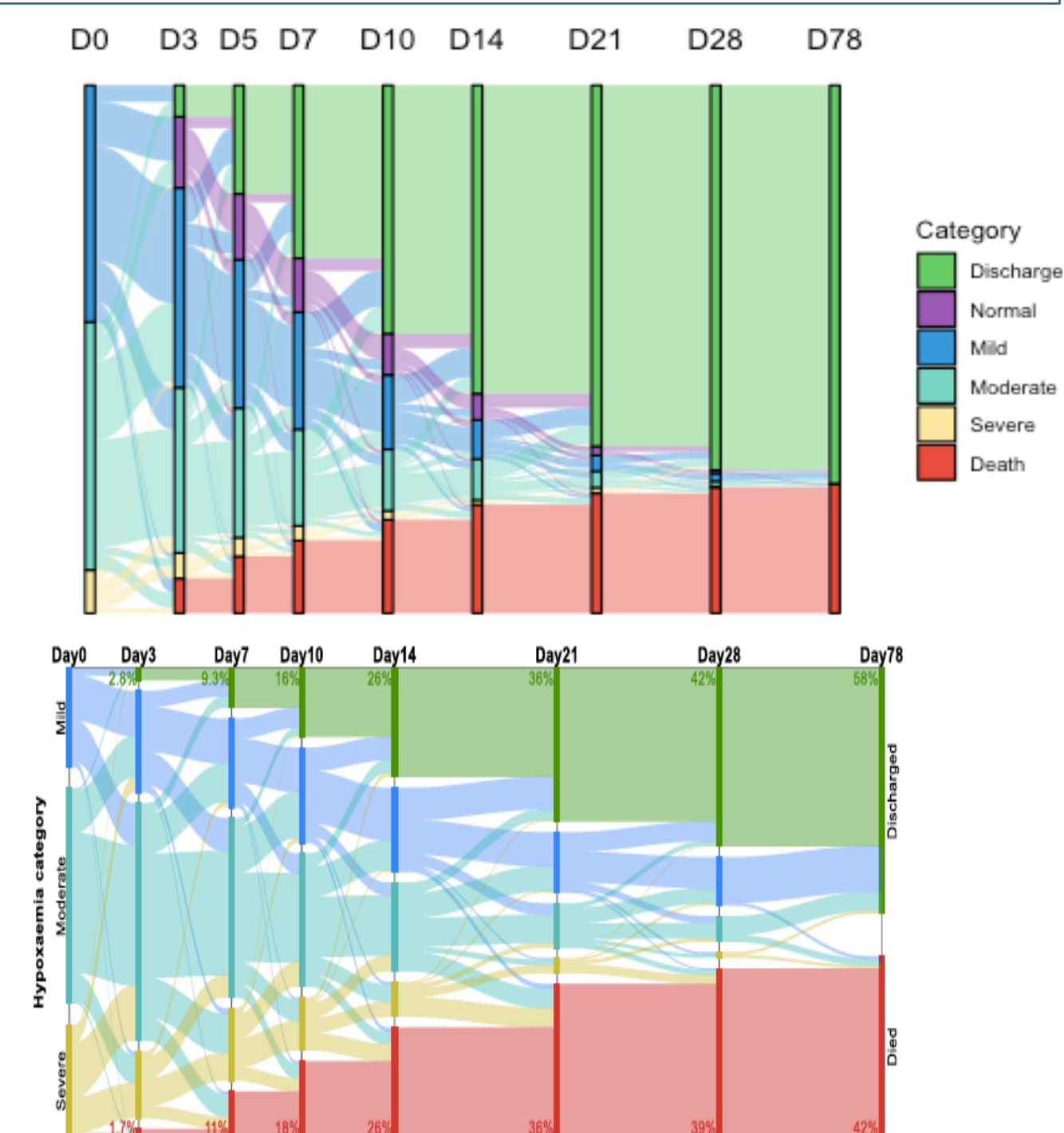


Figure 1 Alluvial plot showing the progression of hypoxia from intubation to discharge or death in MIMIC (top) and COVID (bottom) patients.

MIMIC		P/F Day 7			Total
		>26.7	13.3-26.6	<13.3	
P/F Day 0	>26.7	76.3%	11.9%	11.8%	18.9%
	13.3 - 26.6	59.5%	22.8%	17.7%	
	<13.3	36.4%	27.1%	36.4%	
		33.1%			47.9%

COVID		P/F Day 7			Total
		>26.7	13.3-26.6	<13.3	
P/F Day 0	>26.7	36.4%	50.7%	12.9%	31.8%
	13.3 - 26.6	20.6%	51.3%	28.1%	
	<13.3	7.4%	53.7%	38.9%	
		23.5%			44.7%

Table 1. Table comparing hypoxia at Day 0 and Day 7 of intubation. The percentage of patients whose hypoxia worsened (red), stayed the same (orange) or improved (blue) is outlined for MIMIC (top) and COVID (bottom) populations.

Results

Comparison of outcomes

The overall survival in this study was significantly higher than seen in the COVID-19 study (70.2% vs 57.7% respectively). Table two compares the outcomes for resolvers and non-resolvers in the two populations. Length of stay (LOS) and length of invasive mechanical ventilation (IMV) was significantly lower in this study regardless of resolver status. Interestingly, the survival for non-resolvers was similar in both this study and the COVID-19 study.

Parameter	Resolvers		Non-Resolvers	
	MIMIC	COVID	MIMIC	COVID
Proportion (%)	67.4	42.2	32.6	57.9
Initial P/F ratio	26.7	17.9	22.4	18.9
Mortality (%)	15.8	17.6	58.6	60.4
LOS (days)	7.8	13.0	8.7	15.0
IMV length (days)	4.5	12.0	5.7	14.0

Table 2. Comparison of outcomes between MIMIC and COVID patients, grouped by resolver status

Discussion

This study supports previous evidence that non-COVID ARDS patients have overall better trajectories and outcomes than COVID-19 ARDS patients. In addition, our study helps show that hypoxia progression accounts for a large proportion of the differences in outcomes between these two populations.

Non-COVID patients have a two-factor advantage in that, on average, they have less severe hypoxia initially and are more likely to improve their hypoxia status, when compared to COVID patients.

However, the similar survival rates of non-resolvers in the two populations shows overall survival differences between COVID and non-COVID population can be accounted for by the larger proportion of non-resolvers in the COVID-19 cohort, rather than a survival difference between the non-resolvers in the two populations.

Initial PF ratios in this study showed a significant difference between resolvers and non-resolvers and hence were a better predictor of overall survival. In contrast, PF ratios in the COVID-19 ARDS population were not significantly different between the two resolver groups, suggesting that previous Berlin Criteria¹ and Lung Safe study² guidelines of PF ratios used to predict survival are less applicable.

LOS and IMV length were much smaller in this ARDS population compared to the COVID ARDS population, regardless of resolver status, a critical factor affecting resource management in ICUs globally.

Conclusions

Non-COVID ARDS patients have a more predictable natural history and trajectory compared to COVID-19 ARDS patients. Respiratory failure occurs less frequently and is more likely to resolve, resulting in a lower proportion of hypoxia non-resolvers. However hypoxia non-resolvers of both populations have similar survival outcomes. Despite this, COVID ARDS patient have much longer ICU length of stay and length of ventilation which has significant implications for provision of critical care resources. Further analysis of the impact of COVID-19 therapies on these outcomes is needed.

References

- Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome: The Berlin definition. JAMA - J Am Med Assoc [Internet]. 2012 Jun 13 [cited 2021 Jun 17];307(23):2526–33. Available from: <https://jamanetwork.com/journals/jama/fullarticle/1160659>
- Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. JAMA [Internet]. 2016 Feb 23 [cited 2021 Aug 4];315(8):788–800. Available from: <https://jamanetwork.com/journals/jama/fullarticle/2492877>
- Johnson, A., Bulgarelli, L., Pollard, T., Horng, S., Celi, L. A., and Mark R. MIMIC-IV (version 1.0). PhysioNet. 2021.
- Patel B V., Haar S, Handlip R, Auepanwiriayakul C, Lee TM-L, Patel S, et al. Natural history, trajectory, and management of mechanically ventilated COVID-19 patients in the United Kingdom. Intensive Care Med [Internet]. 2021 May [cited 2021 Jun 17];47(5):549–65. Available from: [/pmc/articles/PMC8111053/](https://pmc/articles/PMC8111053/)