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 - Antibody responses to SARS-COV-2 in patients of novel coronavirus disease 2019

Articles reviewed:

- Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China (JAMA Internal Medicine)
- Fair Allocation of Scarce Medical Resources in the Time of Covid-19 (NEJM)

ACC 10 points to remember: Coronaviruses and the cardiovascular system

<https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2020/03/20/08/56/coronaviruses-and-the-cardiovascular>

Original article: <https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa231/5809453>

Case report: Coronavirus fulminant myocarditis saved with glucocorticoids and human immunoglobulin

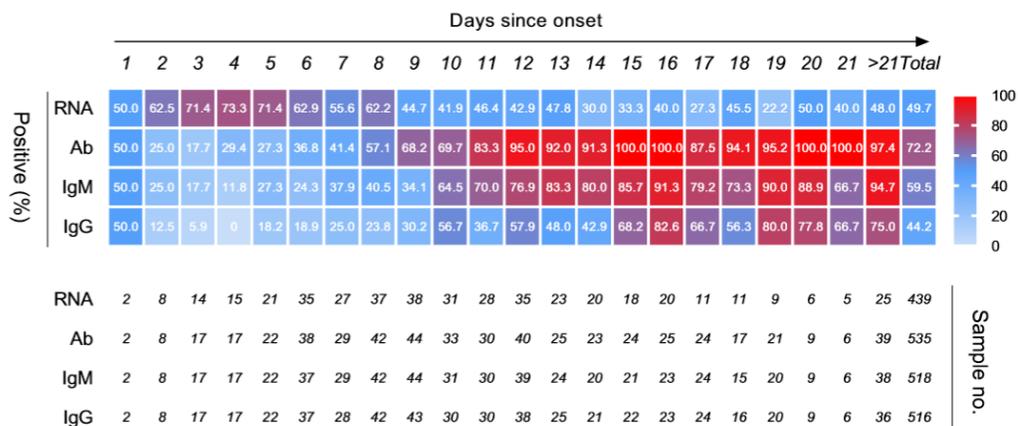
<https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa190/5807656>

Summary:

- 37y M with chest pain and dyspnea developed respiratory failure and cardiogenic shock with LVEF 27%
- Early steroids with IVIg given in addition to supportive care (pressors, diuretics) led to recovery (LVEF 66%)

Lastest in immunology research (not yet peer-reviewed)

- Reinfection could not occur in SARS-CoV-2 infected rhesus macaques
 - Rhesus monkeys, who have similar clinical syndrome to humans when infected with COVID-19, were not reinfected when exposed to the virus again after recovering from their initial illness
 - Conclusion: immunity to the virus may come after infection, lending optimism to vaccine development
 - <https://www.biorxiv.org/content/10.1101/2020.03.13.990226v1.full.pdf>
- Antibody responses to SARS-COV-2 in patients of novel coronavirus disease 2019
 - Viral load (PCR), total antibody (Ab), IgM, and IgG were serially measured in 173 patients
 - Within first 7 days of illness, PCR had higher sensitivity (66.7%) compared to Ab (38.3%)
 - After day 8 Ab better sensitivity, reaching 90% on day 12
 - At 15 days, sensitivity was 100.0%, 94.3%, and 79.8% for Ab, IgM, IgG respectively
 - Conclusion: serologic testing is likely an important adjunct to PCR
 - <https://www.medrxiv.org/content/10.1101/2020.03.02.20030189v1.full.pdf+html>



Article Title:	Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China
Authors:	Wu C, Chen X, Cal Y et al
Full Citation:	Wu C, Chen X, Cal Y et al, (2020). Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China, <i>JAMA Intern Med.</i> Published online 13 March 2020 at www.jamanetwork.com

Study Question:

What clinical characteristics are associated with developing ARDS in COVID19 patients? With progression from ARDS to death?

Methods:

Retrospective cohort study of 201 patients at a single center in Wuhan, China with confirmed COVID-19 pneumonia over a one month period from 12/2019-1/2020. Patient characteristics, lab values, and in-hospital treatments were reviewed. Primary outcomes were development of ARDS and progression to in-hospital death.

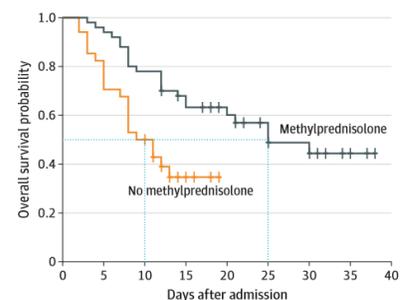
Results:

- For all pts with COVID PNA: median age 51 (IQR 43-60), 63.7% male, 76.6% presented with fever and cough
- Median time from admission to ARDS was 2 days (IQR 1-4)
- 41.8% developed ARDS (n=81) with 26.4% (n=53) admitted to ICU and 33.3% (n=67) requiring mechanical ventilation
- Of those who required mechanical ventilation, 65.7% (n=44/67) died
- Patients with ARDS were: older, had higher fevers, were more likely to present with dyspnea, were more likely to have a comorbidity (including HTN: +13.7%); had higher bilirubin, BUN, IL-6, D-dimer and lower lymphocytes
- Patients with ARDS who died were: older, less likely to have high fever, more likely to have underlying HTN; had higher bilirubin, BUN, IL-6, D-dimer and lower lymphocytes, CD8 counts
- On Bivariate Cox analysis, higher IL-6 levels were statistically significantly associated with death while higher fever was negatively associated with death
- Patients who developed ARDS were more likely to receive methylprednisolone than those who did not, but the drug was associated with lower risk of death within the ARDS subgroup

Table 4. Bivariate Cox Regression of Factors Associated With ARDS Development or Progression From ARDS to Death

Patient characteristics and findings	ARDS		Death	
	HR (95% CI)	P value	HR (95% CI)	P value
Clinical characteristics				
Age (≥65 vs <65), y	3.26 (2.08-5.11)	<.001	6.17 (3.26-11.67)	<.001
Gender (male vs female)	1.47 (0.92-2.36)	.11	0.56 (0.30-1.05)	.07
Highest patient temperature (≥39 °C vs <39 °C)	1.77 (1.11-2.84)	.02	0.41 (0.21-0.82)	.01
Comorbidities				
Hypertension (yes vs no)	1.82 (1.13-2.95)	.01	1.70 (0.92-3.14)	.09
Diabetes (yes vs no)	2.34 (1.35-4.05)	.002	1.58 (0.80-3.13)	.19

Figure. Survival Curve in Patients With Acute Respiratory Distress Syndrome Who Did and Did Not Receive Methylprednisolone Treatment



No. at risk	0	5	10	15	20	25	30	35	40
No methylprednisolone	50	48	39	29	20	14	11	4	0
Methylprednisolone	34	28	17	4	0	0	0	0	0

Conclusions:

- Older age was associated with higher risk of both ARDS and death – potentially due to decreased immune response
- Fever was associated with ARDS but with better outcomes after ARDS developed
- Several other RFs for ARDS were RFs for death once ARDS developed
- Methylprednisolone was associated with survival in those who had ARDS

Perspective:

Overall, this was a small retrospective study which confirmed that older age and comorbidities are risk factors for ARDS. On a hopeful note, not all RFs for development of ARDS were RFs for death, suggesting there is an important role for therapeutic intervention in rescuing critically ill patients. There is a signal towards positive outcomes with the use of steroids in ARDS, but it was a very small, non-randomized sample.

Summary Written by:

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Topic Areas: ARDS, pneumonia, COVID-19

Article Title:	Fair Allocation of Scarce Medical Resources in the Time of Covid-19
Authors:	Emanuel EJ, Persad G, Upshur R et al
Full Citation:	Emanuel EJ, Persad G, Upshur R et al. (2020). Fair Allocation of Scarce Medical Resources in the Time of Covid-19. <i>New Eng J Med</i> . Published online 23 March 2020 at www.nejm.org

Key points:

- Even conservative estimates show COVID pandemic-related health care needs will exceed U.S. hospital capacity
- Rationing is already happening – diagnostic tests, N95 and other PPE for health care providers
- Anticipated shortages in beds, ICU beds, ventilators, and likely doctors and nurses (due to illness and/or quarantine)
- Key ethical principles should be considered ahead of time in planning for allocation: “maximizing the benefits produced by scarce resources, treating people equally, promoting and rewarding instrumental value, and giving priority to the worst off”
- 6 summary ethical recommendations presented:
 - (1) the value of maximizing benefits is the most important – maximizing lives and/or maximizing life-years
 - (2) front-line health care workers should be prioritized for interventions (testing, PPE, ICU beds, treatments, vaccines) to keep critical infrastructures operating – without them all patients will suffer
 - (3) for patients with similar prognoses, random allocation is preferred to first-come first-served
 - (4) prioritization guidelines should be considered for each intervention and respond to new science i.e. therapeutics likely prioritized to younger, healthier patients and preventatives (ie vaccines) likely prioritized to more frail
 - (5) people in research into therapeutics and preventatives (vaccines) should receive priority for their work
 - (6) Covid-19 patients and those with other medical conditions should receive equal priority regarding scarce resources
- Multiple ethical issues must be considered by clinicians, patients, public officials to devise and implement allocation – individual physicians should not be forced to decide alone which patients should receive life-saving care and which should not

Summary written by:

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Topic Areas: medical ethics, scarcity, rationing, COVID-19