Question 1
What are the pre-intubation options for patients with COVID-19?

Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy

Disease process:
-1,300 received respiratory support

-88% required invasive mechanical ventilation

-26% mortality

Table 1. Demographic and Clinical Characteristics of Patients in the First 24 Hours of ICU Admission for COVID-19 in Lombardy, Italy

	Patients by age, y, No. (%)								
	All	0-20	21-40	41-50	51-60	61-70	71-80	81-90	91-100
No. (%)	1591 (100)	4 (<1)	56 (4)	143 (9)	427 (27)	598 (38)	341 (21)	21 (1)	1 (<1)
Age, median (IQR), y	63 (56-70)	16 (14-19)	34 (31-38)	47 (44-49)	56 (54-59)	65 (63-68)	74 (72-76)	83 (81-84)	91
Males	1304 (82)	3 (75)	44 (79)	119 (83)	355 (83)	484 (81)	279 (82)	19 (90)	1 (100)
Females	287 (18)	1 (25)	12 (21)	24 (17)	72 (17)	114 (19)	62 (18)	2 (10)	0
Comorbidities, No. with data	1043	3	35	82	273	380	253	1	1
None	334 (32)	0	23 (66)	50 (61)	107 (39)	107 (28)	47 (19)	0	0
Hypertension	509 (49)	0	4 (11)	21 (26)	121 (44)	195 (51)	156 (62)	12 (75)	0
Cardiovascular disease[a]	223 (21)	0	1 (3)	4 (5)	43 (16)	87 (23)	81 (32)	6 (38)	1 (100)
Hypercholesterolemia	188 (18)	0	1 (3)	1 (1)	30 (11)	92 (24)	59 (23)	5 (31)	0
Diabetes, type 2	180 (17)	0	1 (3)	4 (5)	40 (15)	86 (23)	46 (18)	3 (19)	0
Malignancy[b]	81 (8)	0	0	2 (2)	10 (4)	33 (9)	33 (13)	3 (19)	0
COPD	42 (4)	0	1 (3)	0	8 (3)	12 (3)	20 (8)	1 (6)	0
Chronic kidney disease	36 (3)	0	0	2 (2)	10 (4)	17 (4)	7 (3)	0	0
Chronic liver disease	28 (3)	0	0	2 (2)	8 (3)	13 (3)	5 (2)	0	0
Obesity	205 (20)	3 (100)	6 (17)	10 (12)	49 (18)	77 (20)	53 (22)	5 (31)	0
Respiratory support, No.	1300	2	46	108	351	487	287	18	1
Invasive mechanical ventilation	1150 (88)	2 (100)	37 (80)	87 (81)	315 (90)	449 (92)	246 (86)	14 (78)	0
Noninvasive ventilation	137 (11)	0	8 (17)	16 (15)	33 (9)	36 (7)	39 (14)	4 (22)	1 (100)
Oxygen mask	13 (1)	0	1 (2)	5 (5)	3 (1)	2 (<1)	2 (1)	0	0
PEEP, cm H_2O									
No.	1017	2	33	81	278	377	234	11	1
Median (IQR)	14 (12-16)	9.5 (5-14)	14 (10-15)	14 (12-15)	14 (12-15)	14 (12-16)	14 (12-15)	12 (8-15)	10
FIO_2, %									
No.	999	2	31	81	270	375	228	11	1
Median (IQR)	70 (50-80)	40 (30-50)	60 (50-70)	60 (50-80)	65 (50-80)	70 (55-80)	70 (50-80)	60 (50-90)	60
PaO_2/FIO_2 ratio									
No.	781	2	26	58	213	306	169	7	0
Median (IQR)	160 (114-220)	259 (195-323)	201.5 (123-248)	168.5 (112-260)	163 (120-230)	152.5 (110-213)	163 (120-205)	150 (86-250)	NA
Prone position, No./total (%)	240/875 (27)	0/2	3/25 (12)	24/71 (34)	70/247 (28)	90/337 (27)	51/187 (27)	2/6 (33)	NA
ECMO, No./total (%)	5/498 (1)	NA	0/15	0/42	2/149 (1)	3/193 (2)	0/95	0/4	NA

Abbreviations: COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; FIO_2, Fraction of inspired oxygen; ICU, intensive care unit; IQR, interquartile range; NA, not applicable; PaO_2, arterial partial pressure of oxygen; PEEP, positive end-expiratory pressure.

[a] Cardiovascular disease includes cardiomyopathy and heart failure.

[b] Malignancy includes active neoplasia and neoplasia in remission.

[c] Other includes anemia, asthma, inflammatory bowel disease, epilepsy, chronic respiratory insufficiency, endocrine disorders, connective tissue diseases, neurologic disorders, chronic pancreatitis, immunocompromise, and organ transplant.

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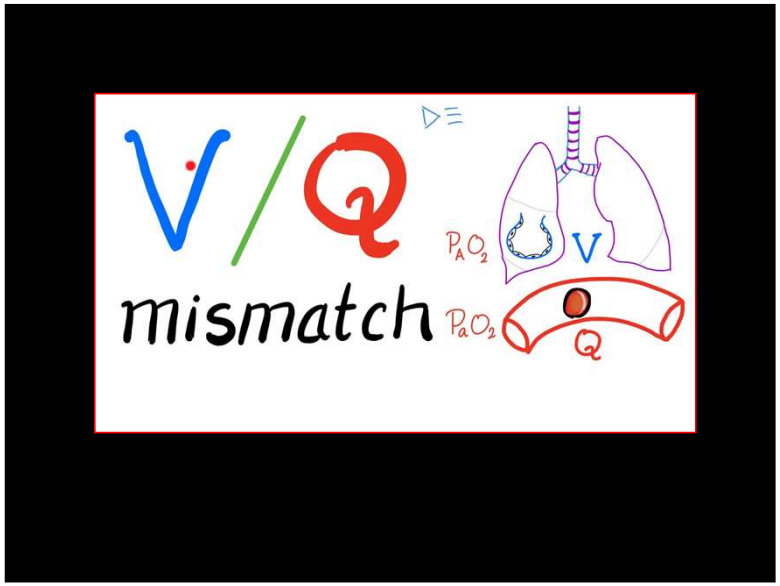
Disease burden seems severe…88% intubation rate. Mortality number doesn't match up.

Not all Pts have completed clinical course

If a virus destroys lungs 99% of the time to the need of mechanical support (invasive and non-invasive support); shouldn't it be more virulent?

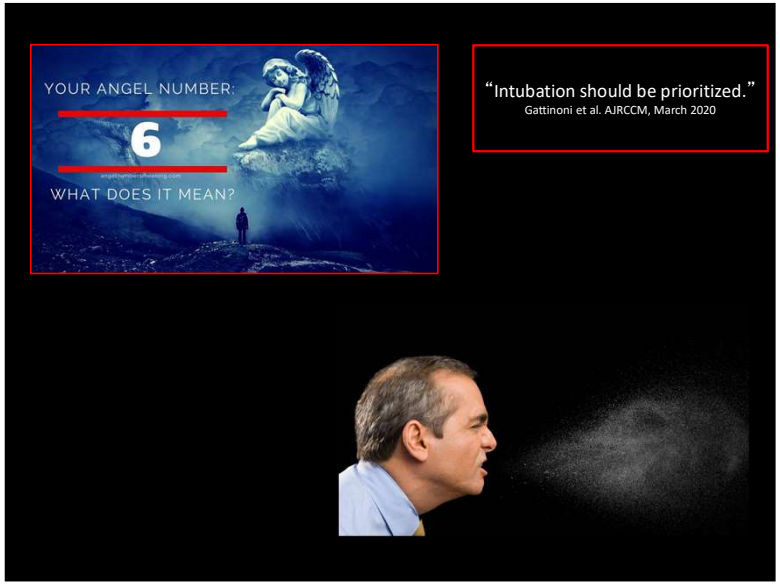
Do we need to intubate all of these patients?



Evolving paradigm of this viral process.

Compliant lungs, but very hypoxic. “Q” issue, hypoxic induced pulmonary vasoconstriction and blood flow redistribution. Pts look surprisingly good for level of hypoxia. Labeled the “Happy Hypoxic”; similar to altitude induced hypoxic state.

Different than a concomitant ventilation issue (with decreased compliance) which we typically see in ARDS. Our bodies don’t do well with alterations of paCO2 levels… hold your breath for a second… your medulla will get unhappy quickly. Strongest stimulus to breath is an increased concentration of CO2. Seen as tachypnea and accessory muscle usage.



Early protocols latched on to the number of 6L NC (and lots of early intubations)

Expressed concern of aerosol generating methods (NIPPV, HFNC)

Now reports showing multi-organ system failure with this early intubation practice; ? VILI, ?cytokine storm

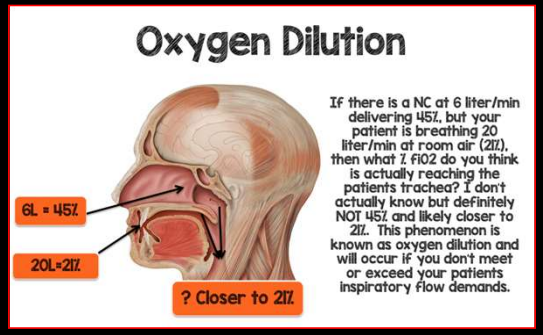
It appears this aggressive intubation pattern may have been wrong…

Nasal Cannula

High Flow NC

Non -rebreather

Optiflow/Airvo



We can provide O2 to patients… but will mix with ambient air (nose and oral pharynx)

Dependent on patients inspiratory flow rate/drive (oxygen dilution)

NC… maybe 44% max

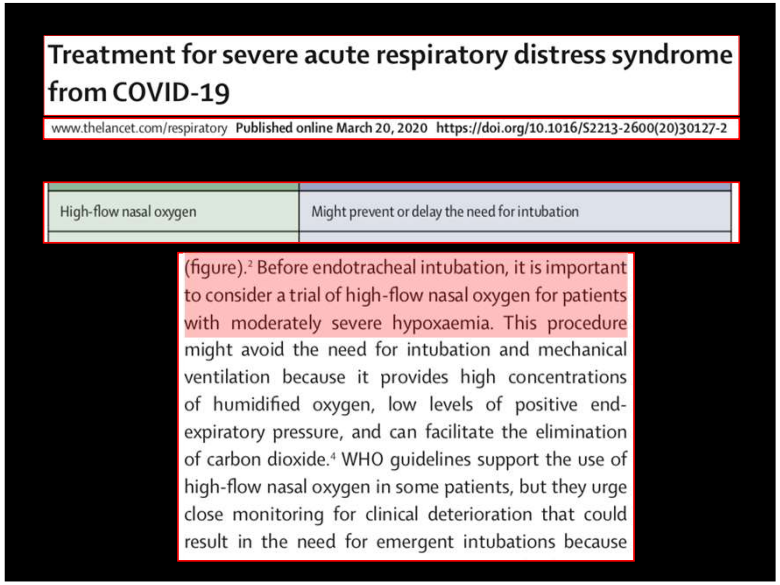
HFNC… may dry mucus membranes/uncomfortable

NRB… even though"100%"… may only deliver 60% FiO2 to pts flow rate/mixing

Optiflow…humidified, 60L rate (max patient inspiratory flow rate), thicker nasal prongs +flow (small amount of PEEP)

Provide oxygen, match their inspired flow rate.

Of these options… Optiflow might be the most supportive to correct the "Q"



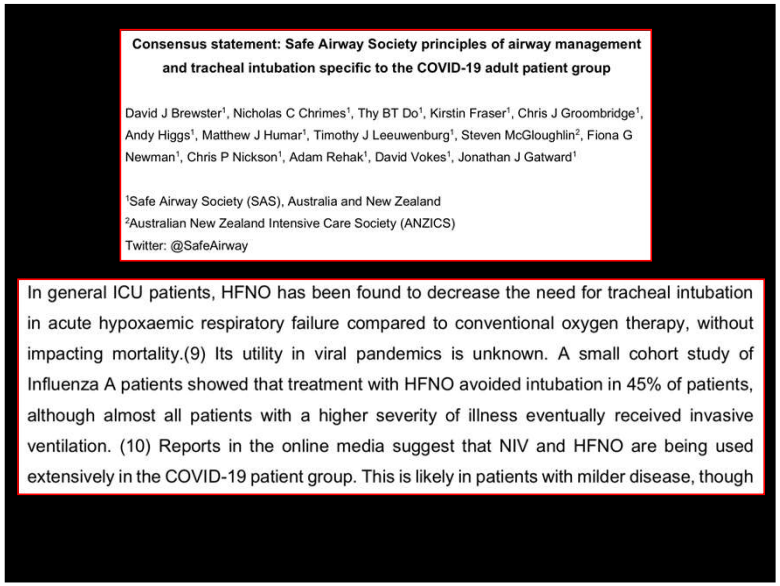
Treatment for severe acute respiratory distress syndrome from COVID-19

www.thelancet.com/respiratory **Published online March 20, 2020 https://doi.org/10.1016/S2213-2600(20)30127-2**

High-flow nasal oxygen	Might prevent or delay the need for intubation

(figure).[2] Before endotracheal intubation, it is important to consider a trial of high-flow nasal oxygen for patients with moderately severe hypoxaemia. This procedure might avoid the need for intubation and mechanical ventilation because it provides high concentrations of humidified oxygen, low levels of positive end-expiratory pressure, and can facilitate the elimination of carbon dioxide.[4] WHO guidelines support the use of high-flow nasal oxygen in some patients, but they urge close monitoring for clinical deterioration that could result in the need for emergent intubations because

Lancet recommendations for trial of HFNO (prior to moving to intubation).



Consensus statement: Safe Airway Society principles of airway management and tracheal intubation specific to the COVID-19 adult patient group

David J Brewster[1], Nicholas C Chrimes[1], Thy BT Do[1], Kirstin Fraser[1], Chris J Groombridge[1], Andy Higgs[1], Matthew J Humar[1], Timothy J Leeuwenburg[1], Steven McGloughlin[2], Fiona G Newman[1], Chris P Nickson[1], Adam Rehak[1], David Vokes[1], Jonathan J Gatward[1]

[1]Safe Airway Society (SAS), Australia and New Zealand
[2]Australian New Zealand Intensive Care Society (ANZICS)
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In general ICU patients, HFNO has been found to decrease the need for tracheal intubation in acute hypoxaemic respiratory failure compared to conventional oxygen therapy, without impacting mortality.(9) Its utility in viral pandemics is unknown. A small cohort study of Influenza A patients showed that treatment with HFNO avoided intubation in 45% of patients, although almost all patients with a higher severity of illness eventually received invasive ventilation. (10) Reports in the online media suggest that NIV and HFNO are being used extensively in the COVID-19 patient group. This is likely in patients with milder disease, though

Australian/New Zealand Inten Care Society Consensus statement… role of HFNO2 supported

Assessment of the potential for pathogen dispersal during high-flow nasal therapy

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[b] Kirby Neurobiology Center, Boston Children's Hospital, Harvard Medical School, Boston, USA
[c] Surgical Center, University of Yamanashi Hospital, University of Yamanashi, Yamanashi, Japan

Journal of Hospital Infection 104 (2020) 534–537

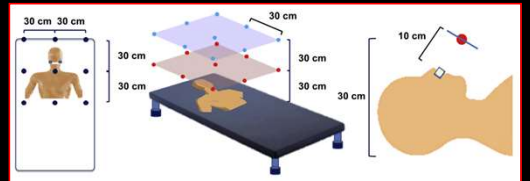
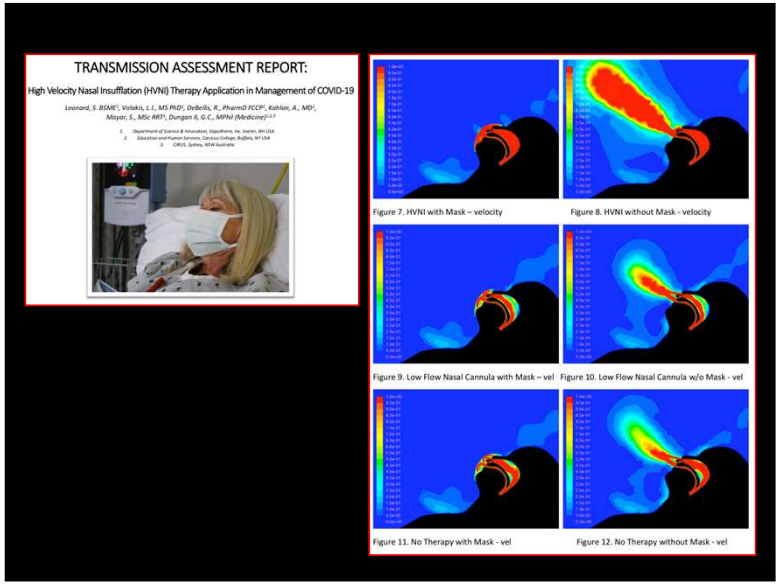


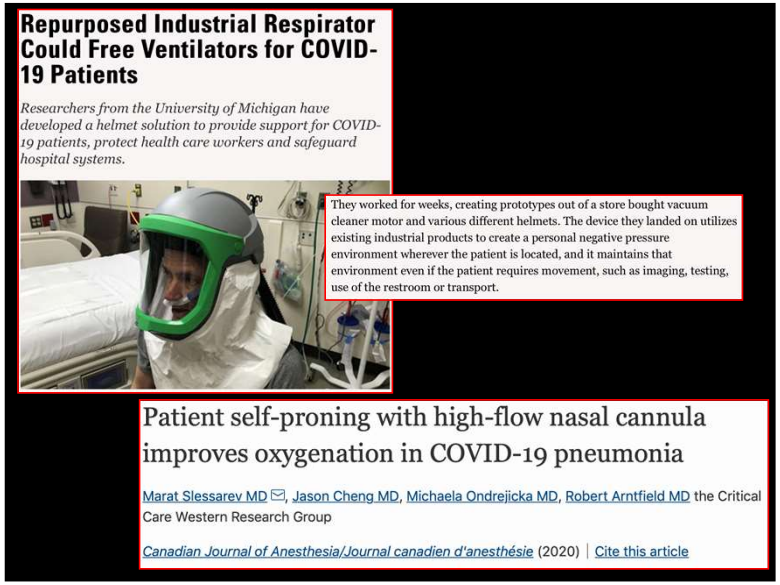
Figure 1. Experimental design for assessing the dispersal of water and yeast.

areas >60 cm away from the face. These results suggest that use of high-flow nasal canula does not increase the risk of droplet infection because coughing or sneezing may generate droplets that can travel farther [6].

What about aerosolization risk… study looked at that. Used droplet paper to measure spread (used water and yeast in their model). No worse than a cough or sneeze.



Industry sponsored by Vapotherm (makers of Optiflow)…. But showed minimal dispersal with Optoflow and mask in place.

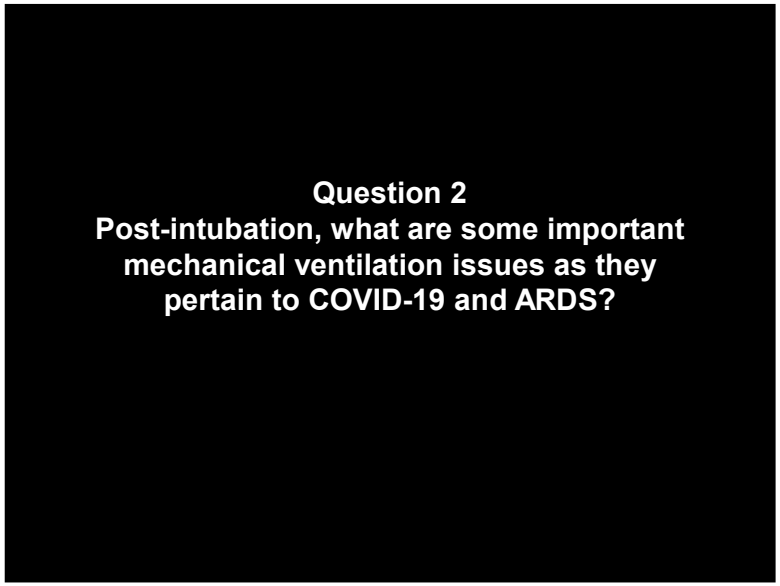


Univ of Michigan solution (one of our EM/CCM colleagues: Ben Bassin). Allows the negative pressure room to become portable and transport with the patient (note the HFNC on this patient).

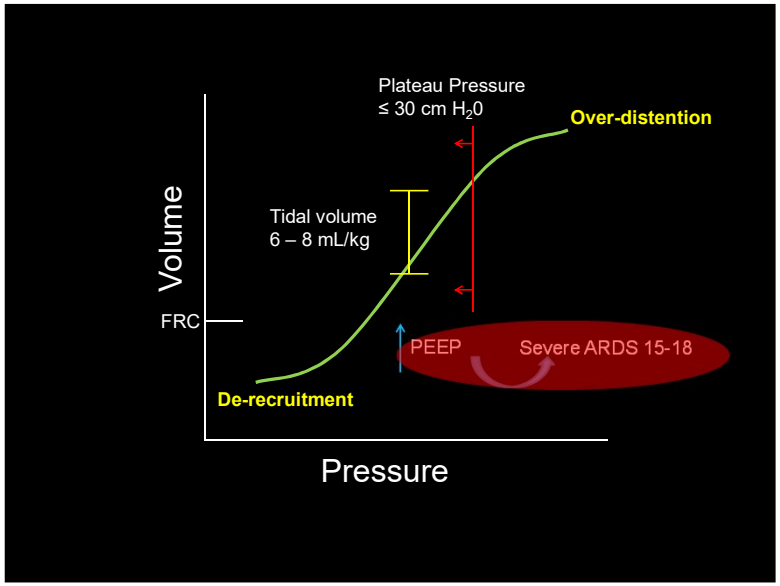
Also may be some benefit of awake proning/positioning…. “tummy time”.

Recommendation…

And watch work of breathing (P-SILI risk) and mental status closely…..like normal basically.



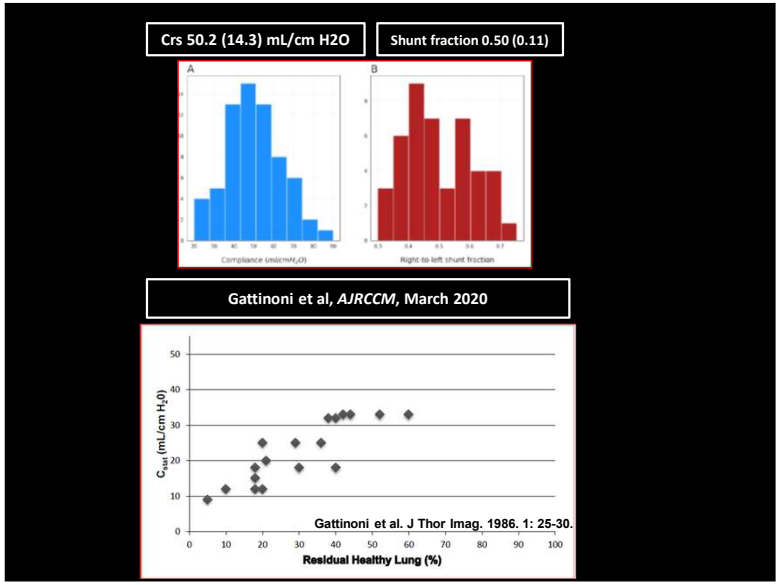
So I think we have high variability in reported outcomes for these patients. Timing of intubation, and yes/no, intubation I think has contributed to that. Also, the wide variation in mortality rates across different intensive care units raises the possibility that the approach to ventilator management could be contributing to outcome as well. Lombardi Italy, 26%; Washington State, 67% (small study);



This is the traditional sort of schema related to lung-protection

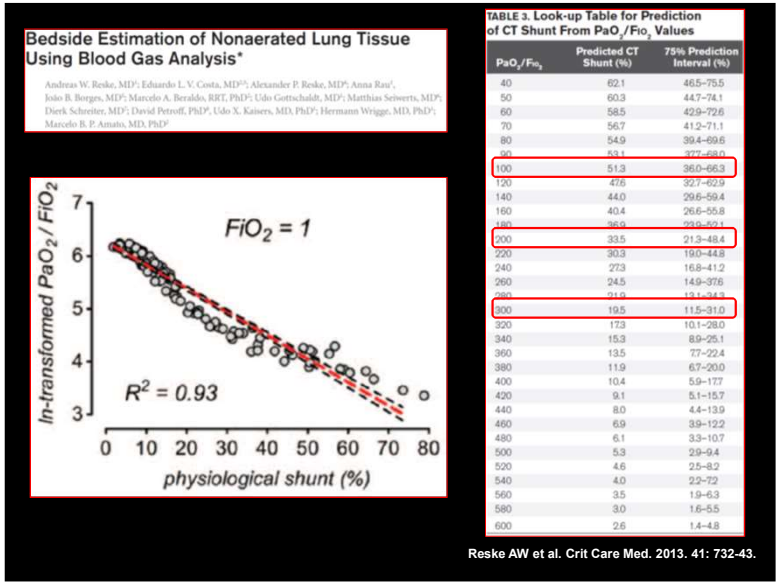
Traditional thought process behind lung protection and prevention of high volume lung injury and low volume lung injury.

Why do we do these things? Set 6-8 because that is normal mammalian tidal volume and RCTs show consistent mortality difference in ARDS; limit plateau to less than 30 because that is a normal level in humans (if chest wall not stiff) and data shows outcome difference at 29; set PEEP to prevent end-expiratory de-recruitment to prevent low volume lung injury (atelectrauma). In severe ARDS that usually settles out around 15-18 (should at least, many times higher). This is the biggest issue people have seen with respect to COVID-19 and the potential that we may be harming some people if the ventilator is not individualized (like in all patients really). **COVID 19 seems to be a disease of the vascular endothelium, and seeing quite profound hypoxia, yet with unremarkable pulmonary mechanics.**



But this isn't what is always seen in COVID-19 patients. Report from 16 patients early on in Northern Italy. Despite a shunt fraction of 50%, which would likely lead to P:F ratio in the severe ARDS range, these patients had compliance that was normal. Such a wide discrepancy is virtually never seen in most forms of ARDS. Relatively high compliance indicates well preserved lung gas volume in this patient cohort, in sharp contrast to expectations for severe ARDS. These patients would be expected to have a compliance in the 20-30 range, and therefore a great loss in lung gas volume (i.e. baby lung is very small).

As an example, a compliance of 50 in a 70kg man of average height, will yield a plateau pressure of 21 and driving pressure of 11.



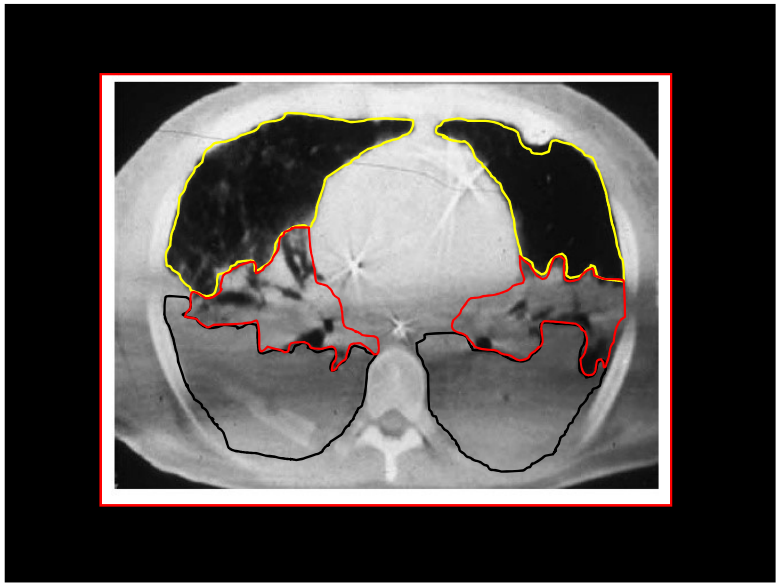
What is more typical is the following……

So interesting study looking at ARDS patients given FiO2 of 1.0 (so pure shunt assessment), CT scans. And then looked at correlation between CT scan predicted shunt/non-aerated tissue and P:F. Strong linear relationship where you can see a strong relationship between an increasing shunt (ever smaller baby lung) and P:F.

They then tabled these findings, so you can see the in severe ARDS patients, they will have a shunt between 36 and 66%.

And you can see that the less aerated tissue that exists (i.e. smaller baby lung), the greater the shunt. So that a severe ARDS patient will have a shunt between 36% and 66%.

These patients will have low compliance read out on the ventilator.

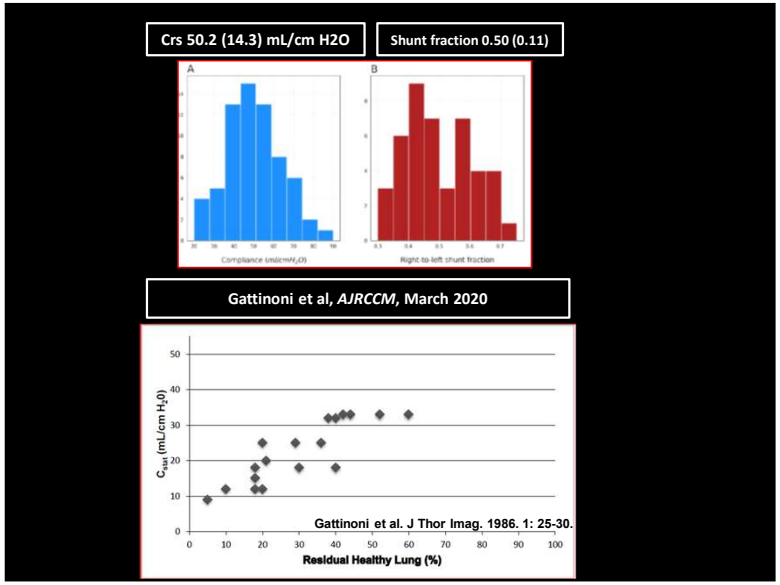


This is heterogeneity at the macroscopic level……

So what does this create? Putting it all together: it creates **maldistribution of ventilation**. But what this heterogeneous distribution of ventilation creates are areas that are prone to **volume overdistention (the baby lung)** and areas that are prone to **cyclic collapse at end-expiration and re-opening at end-inspiration (what is termed atelectrauma**, or shear stress).

And this model shows nicely why it is a disastrous approach to use high volumes and pressure to ventilate a small lung. **A 12-15mL/kg tidal volume in a child will destroy that lung.**

It also shows why even though you have set your tidal volume to the holy grail of 6 mL/kg PBW, fitting that into a very small baby lung may STILL be injurious.



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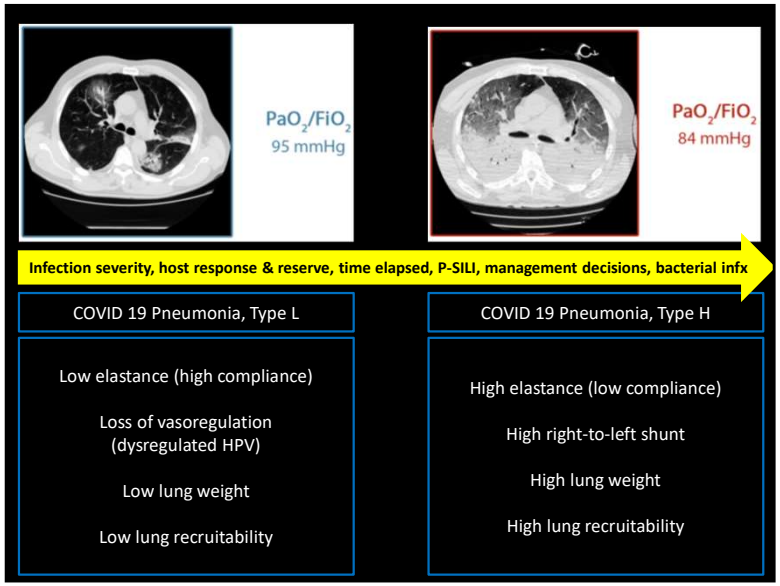


CT scan in spontaneously breathing patient at presentation to ED; CT scan after 7 days of non-invasive support. The first CT scan is congruent with those patients that were being intubated very early despite looking quite good.

The nearly normal compliance indicates that the amount of gas in the lung is nearly normal.

Since the gas volume is nearly normal, hypoxemia may be best explained by the loss of regulation of perfusion and by loss of hypoxic vasoconstriction. The pulmonary vasoconstriction that normally occurs in response to hypoxia fails to occur because of an endothelial assault that mismatches perfusion to ventilation and may result in profound hypoxemia.

Only ground-glass densities are present on CT scan, signifying interstitial rather than alveolar edema. Consequently, lung weight is only moderately increased.

The amount of non-aerated tissue is very low, consequently the recruitability is low.

The decrease of gas volume due to increased edema accounts for the increased lung elastance.

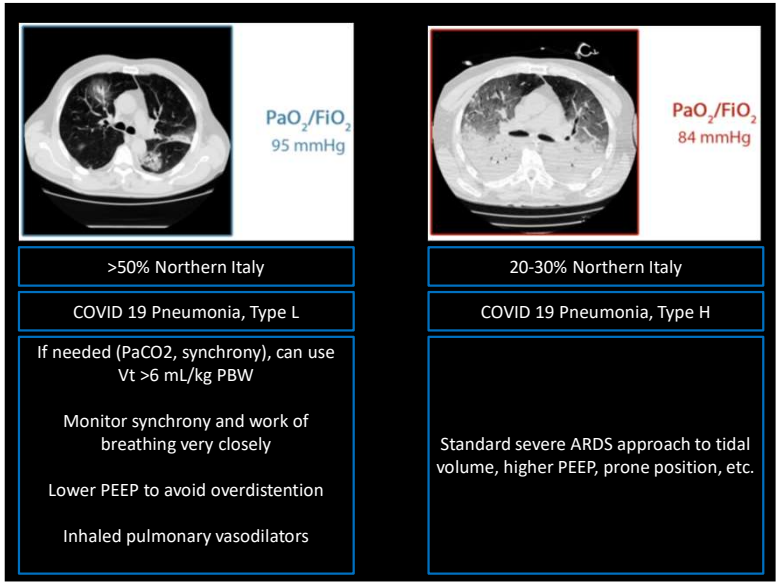
This is due to the fraction of cardiac output perfusing the non-aerated tissue which develops in the dependent lung regions due to the increased edema and superimposed pressure.

Quantitative analysis of the CT scan shows a remarkable increase in lung weight (> 1.5 kg), on the order of magnitude of severe ARDS.

The increased amount of non-aerated tissue is associated, as in severe ARDS, with increased recruitability.

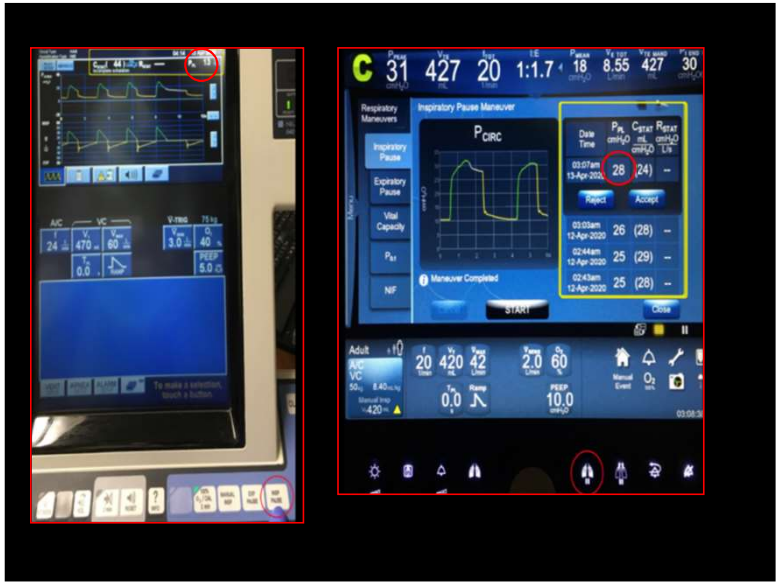
THESE ARE CONCEPTUAL EXTREMES OF A SPECTRUM

Patient self-inflicted lung injury: vigorous spontaneous efforts reduce pleural pressure and therefore increase transalveolar pressure. This increases lung volume/tidal volume in spontaneous breathing. This, combined with increased lung permeability and inflammation, leads to increased edema. This will increase lung weight over time, superimposed pressure, and increase atelectasis. Also increases tissue stress and raises pulmonary transvascular pressures and vascular flow, both of which can promote edema.



High compliance results in tolerable strain without commensurate increase risk of VALI. But you have to watch the evolution closely.

Higher PEEP in more compliant lungs will also more adversely affect hemodynamics.



The logistics of how to check inspiratory plateau pressure, and therefore figure out what compliance is.