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Comment ventiler un ARDS Covid-19 ?

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Lien d'intérêt

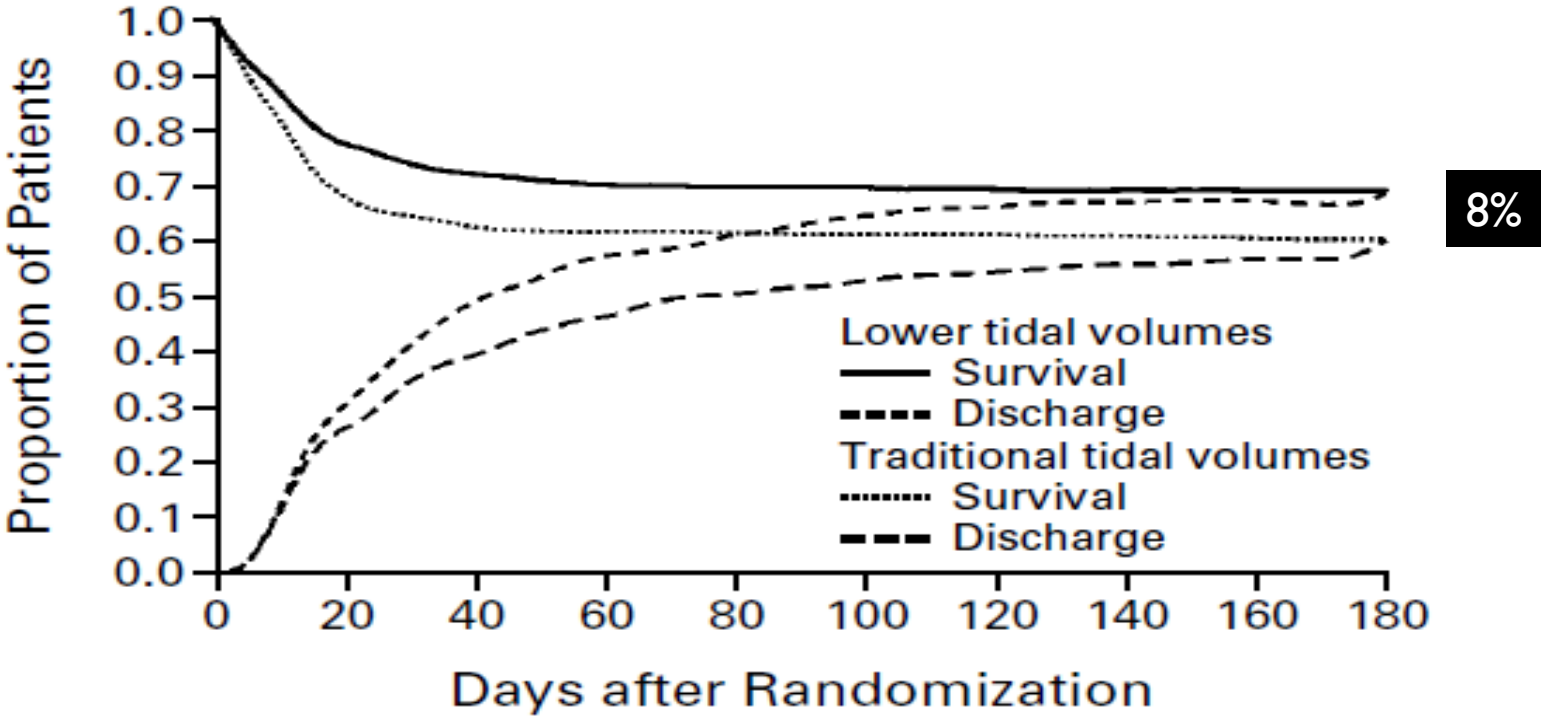
- Aucun en lien avec la présentation

- Conseil scientifique à Transgène SA

Est-ce un ARDS « comme les autres » ?

- Si oui, ventilons comme nous savons le faire

6 vs 12 mL/kg/IBW

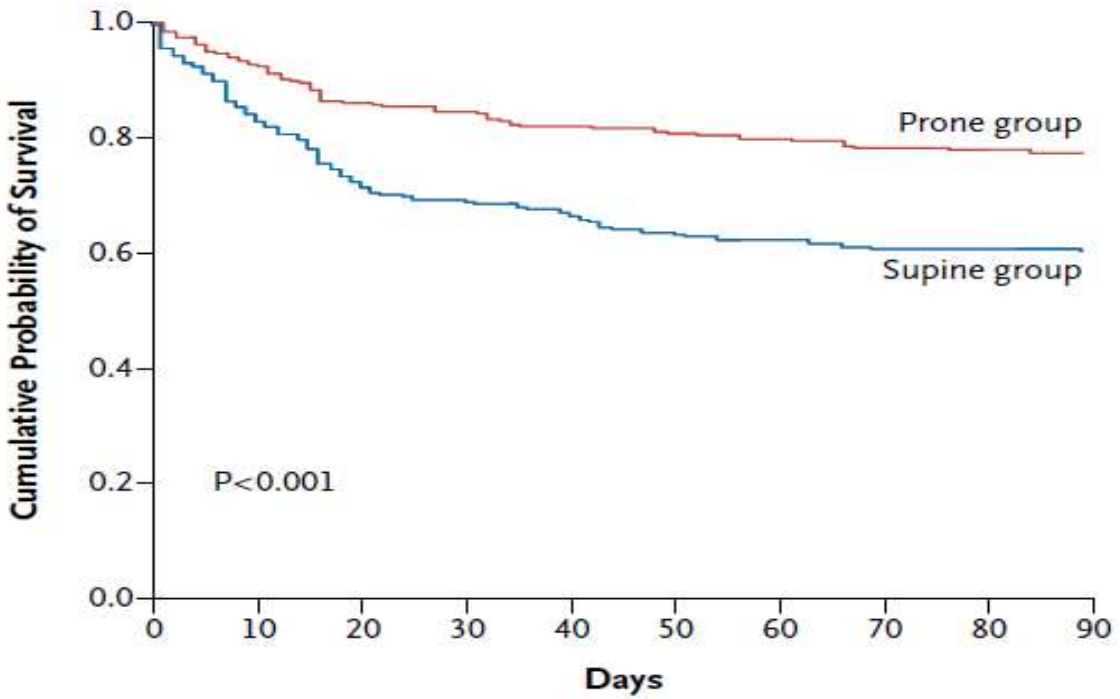


8%

- **Il faut connaître la taille des patients**

ARDS network NEJM 2000

Décubitus ventral



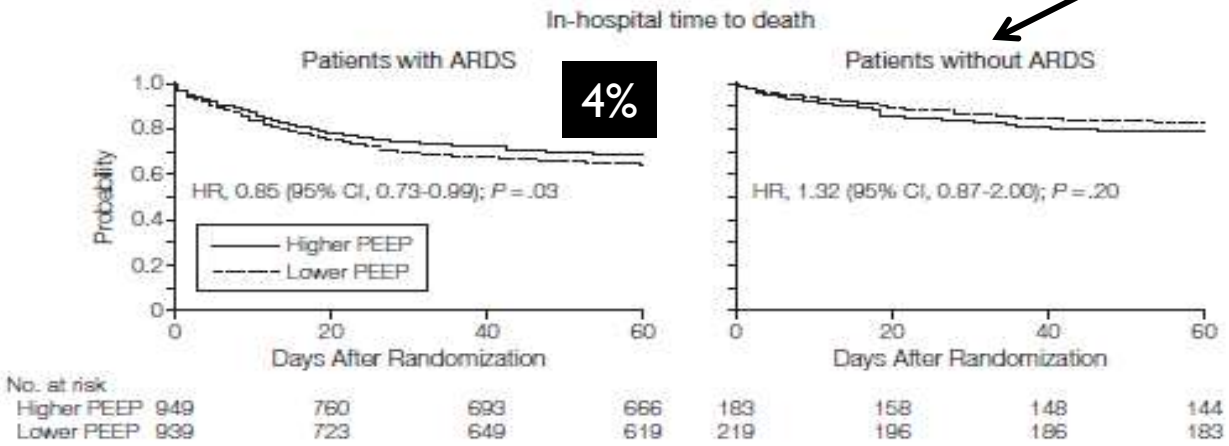
No. at Risk					
Prone group	237	202	191	186	182
Supine group	229	163	150	139	136

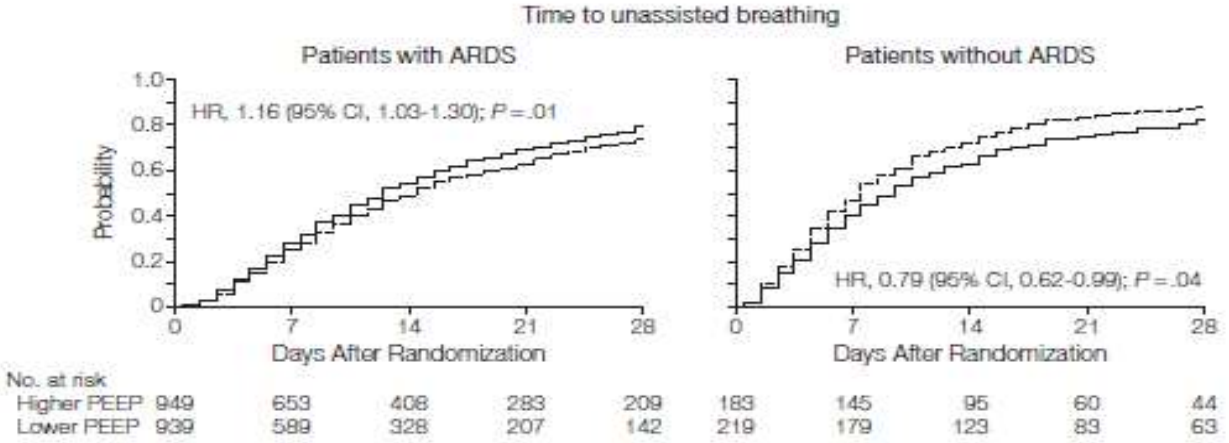
11%*

Guerin et al. NEJM 2013
** Bloomfield Cochrane 2015 PP > 16h*

PEEP

ARDS léger





- **Meta analyse**
  - **ARDS-net**
  - **LOV**
  - **Express**

Briel et al. JAMA 2010

Est-ce un ARDS « comme les autres » ?

- **Si oui, ventilons comme nous savons le faire**
- **Si non, faisons des études**

RCT Covid-19 & Ventilation mécanique

- Ventilation invasive: parent pauvre de la recherche Covid-19
- Pubmed: « invasive ventilation covid » :

  98 occurrences, 2 RCT multicentriques (non-invasif)

- Hydroxychloroquine, 24 RCTs
- Combien de patients ventilés pour Covid-19?
  - Le 05/10/2021: 85 000 « critical patients» sur worldometer
  - => plusieurs centaines de milliers
- Peu d'EBM dans ce que je vais vous dire …

L’ARDS est un syndrome

Pneumonie SARS-CoV-2: un ARDS ?

- **Images bilatérales, P/F < 300 mmHg, PEEP >5 cmH2O …**
- **L'ARDS-Covid19 répond à la définition**

- **Un ARDS oui mais un ARDS *spécial* *(Gattinoni, Marini)***
- **2 phénotypes dont 1 nécessite une prise en charge différente ?**
  - **Intubation précoce pour éviter la PSILI**
  - **VT jsq 8mL/kg/IBW car compliance élevée**
  - **Peu de PEEP car hypoxémie vasculaire**

Gattinoni et al. Crit care, AJRCCM, ICM, AIC 2020

graphics by RV Attorney

A model to approach ventilation in COVID-19 patients reflecting the phase of the disease induced by SARS-CoV-2 (pneumonia) that do these patients present from an hypoxemia perspective? Hypoxemia is mainly a V/Q dysregulation of pulmonary perfusion, really important; pulmonary micro-thrombosis it's a role according, more and more rationale). A "basic pulmonary edema ("ARDS like") COVID-19 patients could present with similar P/F ratio, but with completely different CXR appearance or CT scan patterns (remodeling or not ARDS and with different distribution of normal/consolidated lung).

1 HYPOXEMIA

- ★ dysregulation of pulmonary perfusion with
- ★ + pulmonary micro-thrombosis creating difficulty in lung perfusion/hypoxemia & dead space (increased CO2)

low Elastance, low V/Q matching, low recruitability, do & limited "PEEP response" = named as **PHENOTYPE L**

L = Low everything.

- ★ pulmonary edema - collapse ARDS-like with

High lung compliance, & compared to the other type higher recruitability higher R→L shunt higher "PEEP response" = **PHENOTYPE H**

H = high everything.

(Gattinoni et al. ICM 2020 in press)

Early categorizing these patients according to the 2 phenotypes could be really important, as therapeutic approach, or at least management, could be quite different. Moreover, consider that patients may progress from phenotype L to phenotype H, due to disease progression, but also due to early management. SARS-CoV-2 has an important effect on ACE2 receptor, impacting on pulmonary perfusion, with differential effects on ANG2 receptors' profusion vasodilation prevails at the beginning, and on later on inflammation, vasoconstriction and fibrosis.

COVID-19 ≠ ARDS

Comparing COVID-19 pneumonia to the conventional ARDS definition, it is clear that COVID-19 does not fits all the criteria of Berlin definition does not fit timing very well, with some late presentations in these patients about chest imaging, at least for phenotype L (opacity of patchy at presentation). Oxygenation criteria remains relevant. COVID-19 pneumonitis may not similar or equal to ARDS.

2 RESPIRATORY DRIVE

Respiratory drive could have different sources: hypoxemia drives increase in VT, therefore increasing tubing in esophageal and pleural pressures, impacting on lung stress/strain. The other important point is the pulmonary edema, leading to elastin wet and increased RR. Also consider the metabolic drive: some of these patients have incredibly high intubation/tachypnea and O2 consumption/demand is increased, leading to respiratory drive. Also is becoming clear a neuropsychiatric for SARS-CoV-2, particularly around midbrain, influencing respiratory/cardiovascular control (with some patient of the extreme presenting with sudden unexplained cardiac arrest). Subjective dyspnea may be less pronounced, with patients not fully perceiving work. FIO_2 is an important first measure: improve V/Q matching, prone positioning may work really well. On the other side, for the elastic work mechanical support & maybe pharmacological support may be needed to control RR so stress/strain of the lung.

- ★ hypoxemia → tidal volume ↓ ΔPtot = stress-strain → FIO_2 improve V/Q
- ★ neurotropism of SARS-CoV-2 (ACE2?) → cardio-respiratory control: delirium, cognition, anosmia
- ★ pulmonary edema → elastic work, respiratory rate → mechanical support, control of RR
- ★ metabolic drive

This can lead to a perpetuating vicious circle, where:

modified Brochard/Patient ATS2020

WHAT'S NEXT ?

what to do next? we have a series of options: NIV, HFNO, CPAP... intubation?? and some clinical/organizational considerations need to be made:

- infection control: big issue... in some hospitals, HFNO not allowed in COVID-19 positive patient because of the potential risk for spreading the infection
- adequate support: what kind of support does the patient actually require?
  - work of breathing
  - failure rate: how likely will patient fail?
  - degree of hypoxemia
  - tolerance to the interface
  - control of transPulmonary Pressure
- duration of the disease: This is not a disease likely to be easily reversible in few days. It is less responsive to short term positive pressure HV as in cardiogenic pulmonary edema.
- resources: it is really resources demanding:
  - ICU beds
  - Staffing
  - availability of ventilators
  - oxygen: HFNO/CPAP may take incredibly high quantities

Use of CPAP may be associated with decreased CO (Gattinoni et al Chest 1980) and as CO goes down, then the shunt fraction goes down, with an apparent increase in P/F ratio, exclusively related to a change in shunt fraction. In COVID-19 population, moreover, use of NIV may lead to delayed intubation. CPAP or NIV may decrease the work of breathing, but work need to be monitored (use of esophageal pressure is the gold standard): if excessive, this dictates immediate intubation. CPAP alone may not be very effective/efficient in decreasing elastic work, despite the fact it may improve P/F ratio. Keep in mind with some devices may not be easily measure VTE ↑ if ↓9-9.5 ml/kg, this may be associated to NIV failure and increased mortality.

HYPERACUTE DISEASE

severe hypoxemia and breathlessness leading to immediate intubation

INDOLENT

(even improving) moderate or severe hypoxemia but only moderate work of breathing; patient may be on NIV or often NIV for days

BIPHASIC

initial isolated caustic followed, typically after 5-7 days, by (very) acute deterioration with hyper-inflammation, worsening respiratory failure with bilateral infiltrates & consolidation, and patients requiring multiple organ support

severity

ASSESSMENT

named as the 2 different initial phenotypes (treatment of respiratory failure (mainly hypoxemic) may be really different. First stage of management of respiratory failure is non-invasive assessment of "shunt fraction"/severity of hypoxemia

Assess very early (ICU) patient may have very aggressive/fulminant disease. If WOB (& low, who HIV/O2 may be prolonged but time limited & with strict monitoring. If SpO2 does not increase (& above 95%) on oxygen, shunt fraction is likely elevated, with moderate-severe hypoxemia, which may not be easily reversed with O2 therapy alone.

O_2 therapy (15 l/) with target SpO2 90-95%

- If FIO_2 > 0.5 and no ceiling of escalation → palliative care
- ceiling of escalation → work of breathing: low / high

INTUBATION

Intubation + HV (ideal HR?11) volume control ventilation to monitor driving P V_T 5 ml/Kg, PEEP (not super-low thanks) PEEP 5 cmH2O RR - initially to $EtCO_2$ 4-5 kPa

- Is driving pressure > 15 cmH_2O?
  - no → reduce V_T to 6 ml/Kg PBW
  - yes → if not shocked at presentation, low dose vasoconstrictors, minimize fluids; keep V_T 8 ml/Kg PBW

targets on HV: SpO2 90-96% / PaO_2 8 kPa / $PaCO_2$ - 6 or pH >7.30 / P_{plat} < 25 cmH_2O

SpO2 < 90% with FIO_2 > 0.7 → NIMA

uptitrate PEEP in 2 cmH_2O steps up to 15 cmH_2O if required (but characterizing phenotype needed before optimizing HV)

targets on HV: SpO2 90-96% / PaO_2 8 kPa / $PaCO_2$ - 6 or pH >7.30 / P_{plat} < 30 cmH_2O / ΔP < 13 cmH_2O

SpO2 < 90% with FIO_2 > 0.7

obtain echo as soon as possible

IDENTIFY PHENOTYPES

compliance < 40ml/cmH_2O

- no: consider switch to APRV to improve recruitment and improve alveolar stability; PEEP/FIO_2; RR (ΔO_2 x 10-15?)
  - ARDS-Like Phenotype H: High Elastance, PEEP responsive, Prone responsive
- yes: aim to combine if targets not achieved → near normal compliance: first strategy is prone positioning, with mean HV settings
  - COVID-19 pneumonitis Phenotype L: Low elastance, Prone responsive, (NO - (upon? biological rationale) pulmonary vascular reactivity test

FAILURE & ESCALATION

If refractory hypoxemia (< 6h, earlier if life threatening)

ECMO candidate ?

- no → review targets & strategy
- yes → VV-ECMO

4 QUESTIONS

- pt selection
  - 4 questions to consider thinking about ECLS particularly in a pandemic
  - is the pathology reversible (maybe not the case hyperinflammation or HOT)
  - is the patient able to recover? frailty, comorbidities, ability to sustain
  - prolonged ECMO/rehab particularly in a limited resources setting
- timing/indications
  - is the gas exchange so severe that is life-threatening? (+ patient selection)
  - is mechanical ventilation injurious?!

Early recognition of hyper-acute disease: need for immediate intubation and high risk of cardiovascular events, some related to the myocardial dysfunction (some centrally mediated impact of the virus in midbrain-central control)

Short and judicious use of CPAP/NIV for hemodynamically stable patients with moderate hypoxemia: low respiratory drive and low inflammatory phenotype, beware of biphasic course of the disease in some patients, who may fail late.

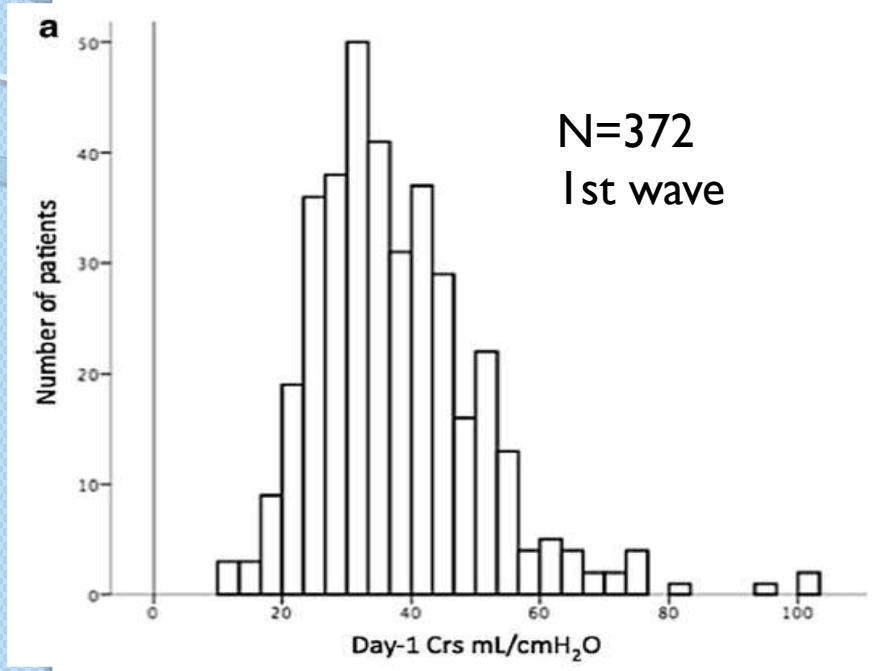
Early differentiation of L Phenotype (preserved compliance, dysregulated pulmonary perfusion). Need to balance PEEP with perfusion. Do not use high PEEP or PEEP/FIO2 ratios. This is not ARDS!

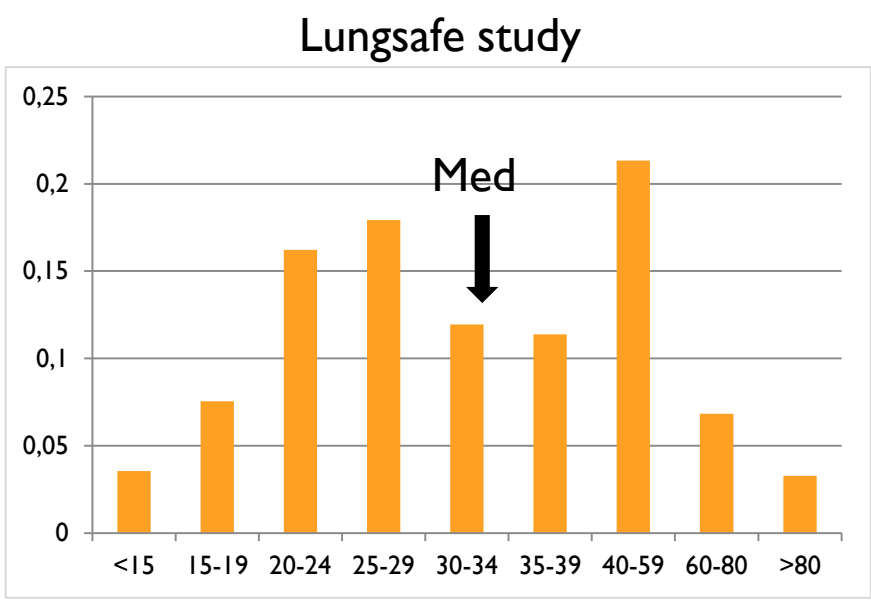
Un syndrome, des maladies (Claude Bernard)

>70% RCTs ARDS

- **Pneumonie bactérienne** (inhomogène, choc +++, ATB ++)
- **Inhalation/noyade** (évolution rapidement favorable)
- **ARDS grippal** (CPK élevées, cortico délétère, antiviraux marginaux)
- **Extra-pulmonaire** (homogène, choc, évolue avec la patho extra-respi)
- **Hémorragies intra-alvéolaires** (du sang dans le tube)
- **Pneumocystose…** (verre dépoli, compliance rapidement effondrée)
- **… et l'ARDS Covid-19** (verre dépoli, atteinte vasculaire, mais Crs idem)

La compliance de l'ARDS Covid-19



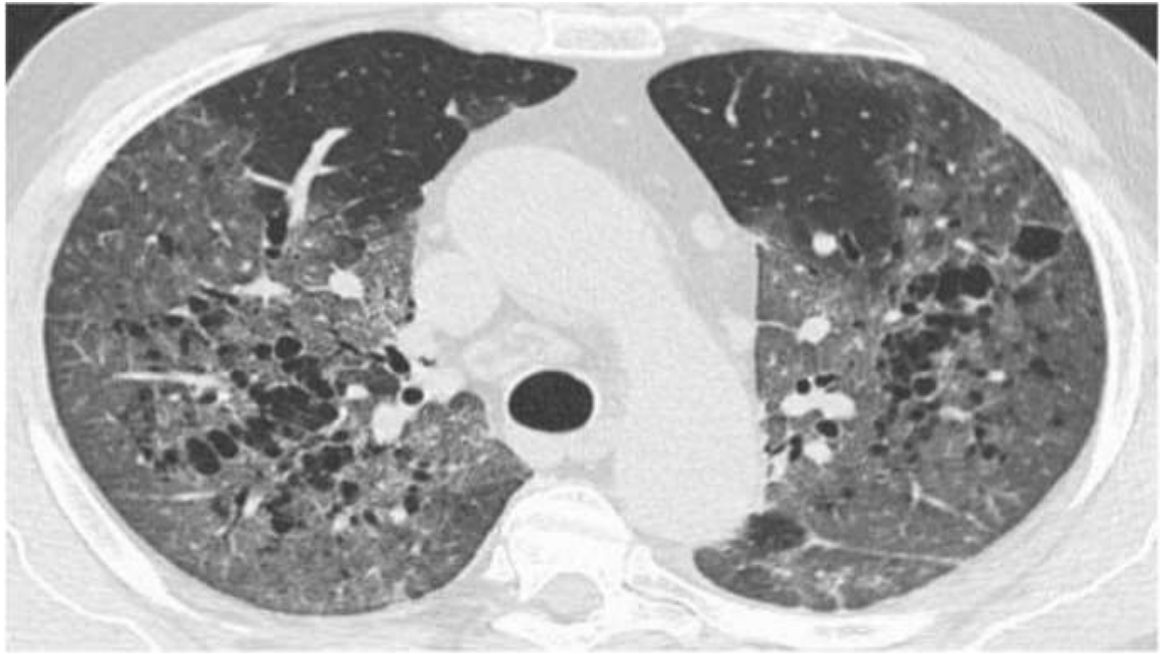


- **Crs médiane 35.4 mL/cmH_2O ;**
- **Spain 35 mL/cmH_2O**
- **Min Netherlands: 31.9mL/cmH_2O**
- **Max 41 mL/cmH_2O (Italy)**

Vandenbunder et al. Crit Care 2021
LUNGSAFE supp data JAMA 2016
Ferrando et al. ICM 2020
Grasselli Lancet Resp Med 2020
Botta Lancet Resp Med 2021

Un risque supérieur de VILI ?

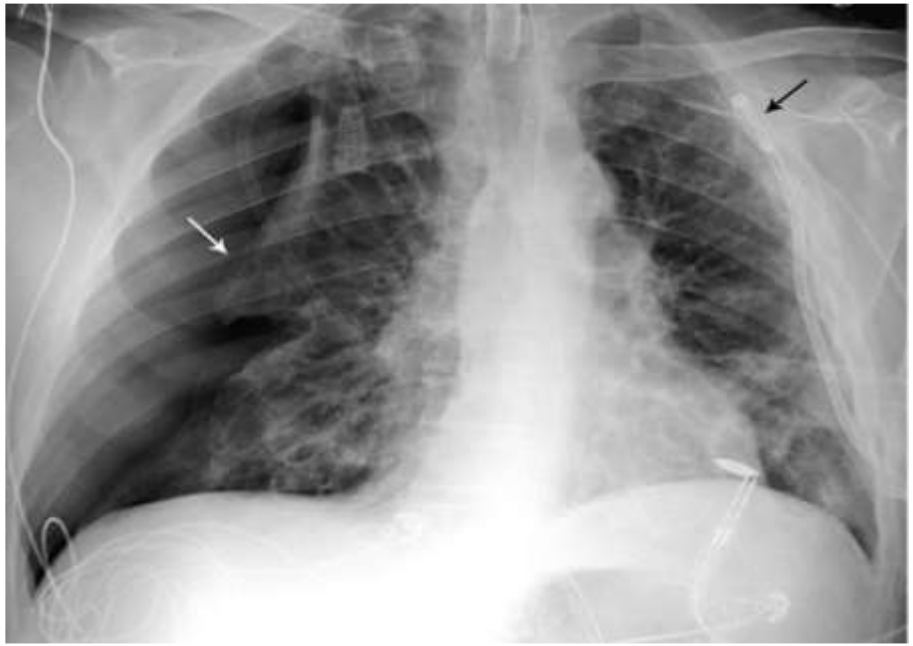
- **News from China – « evolution to cyst & enphysema »**



Shi Lancet Inf Dis 2020

Un risque supérieur de VILI ?

- **News from New-York – 15% barotrauma !**



Survival 22%
Still ICU 21%
VT ?
Pplat ?

COVADIS group: 8% (48/586), hosp survival 51,2%
VT : 6.2 ±0.8 mL/kg
Pplat : 23 ±4cmH2O

McGuiness et al. Radiology 2020
Serck N Annoni F Lascarrou JB in revision

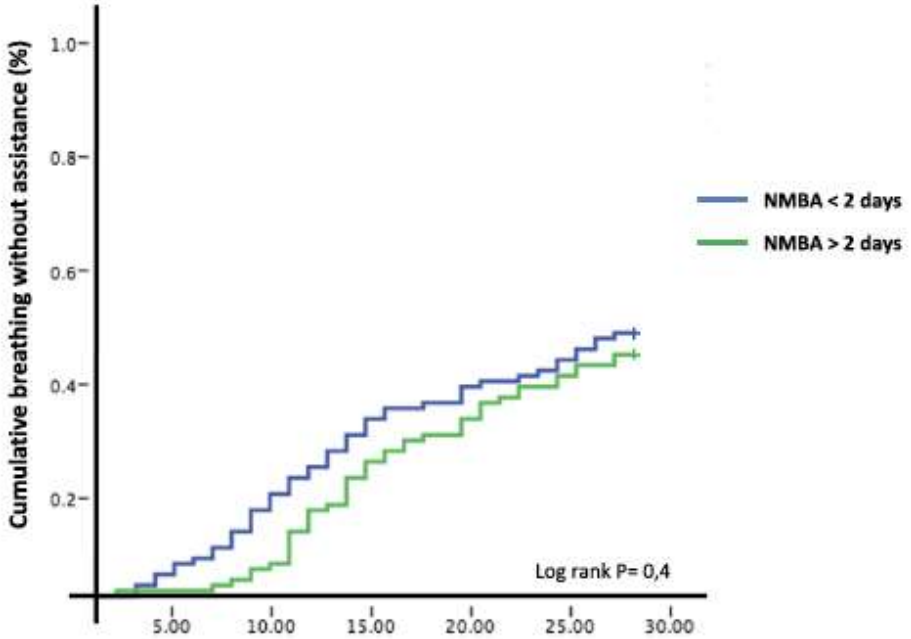
Ventilation protectrice & COVID-19

- **Décubitus Ventral (pas de données)**
- **Vt 6mL/kg IBW (pas de données)**

Quelle utilisation des paralysants ?

- 407 Covid-19
- 241 curares > 2d
- Matching score de prop

- Pas de différence
  - Survie
  - Durée ventilation

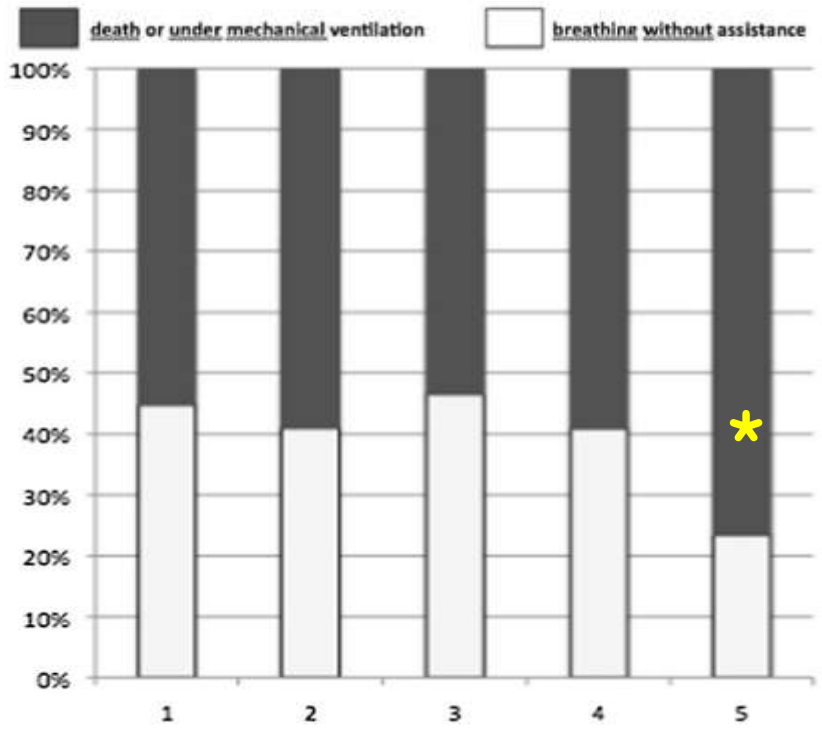


No. At risk

Day	0	5	10	15	20	25	28
NMBA < 2 days	103	96	81	68	63	57	52
NMBA > 2 days	103	102	91	76	68	60	58

Courcelle et al. Crit Care 2021

Quelle pression de plateau ?



> 26 cmH₂O

quintiles de Pplat
P for trend =0,03

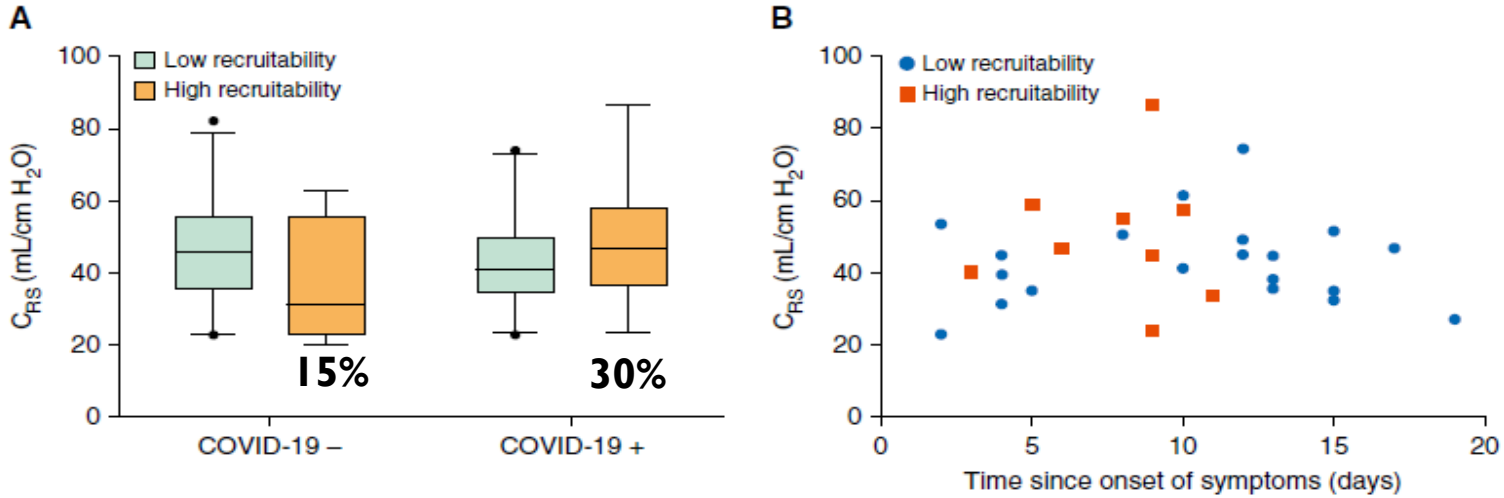
Table 3 Factors associated with breathing without assistance at day-28

	Adjusted OR[a]	CI 95%[a]
Age, per year	0.95	0.93–0.97
Gender, men	0.5	0.3–0.8
PaO_2/FiO_2 per mmHg	1.006	1.002–1.01
Plateau pressure per cmH_2O	0.93	0.88–0.99
Model using absolute values of Crs		
Crs per mL/cmH_2O	1.0	0.98–1.02

Vandenbunder et al. Crit Care 2021

Quelle PEEP ? Regarder la recrutabilité

- **Quelle PEEP ? Regarder la recrutabilité**



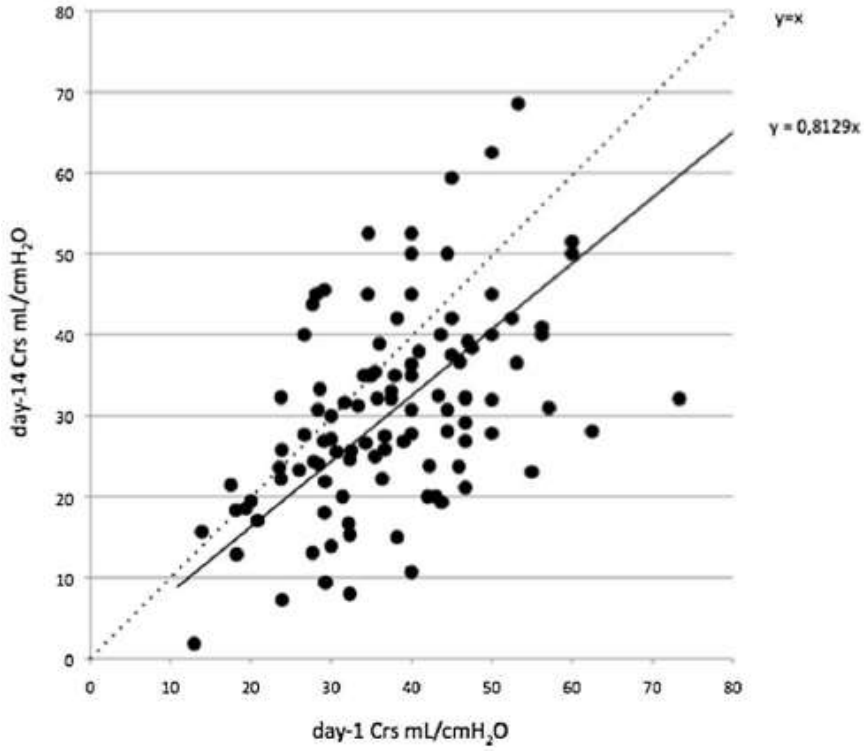
- **Aucun lien avec la Crs**
- **Aucun lien Crs et durée**
- **Autres études recrutabilité 64 et 73%**

Haudebourg et al. AJRCCM 2020
Grieco Crit Care 2020
Beloncle AIC 2020

Evolution au cours du temps

Table 4 Change in respiratory system mechanics from day-1 to day-14

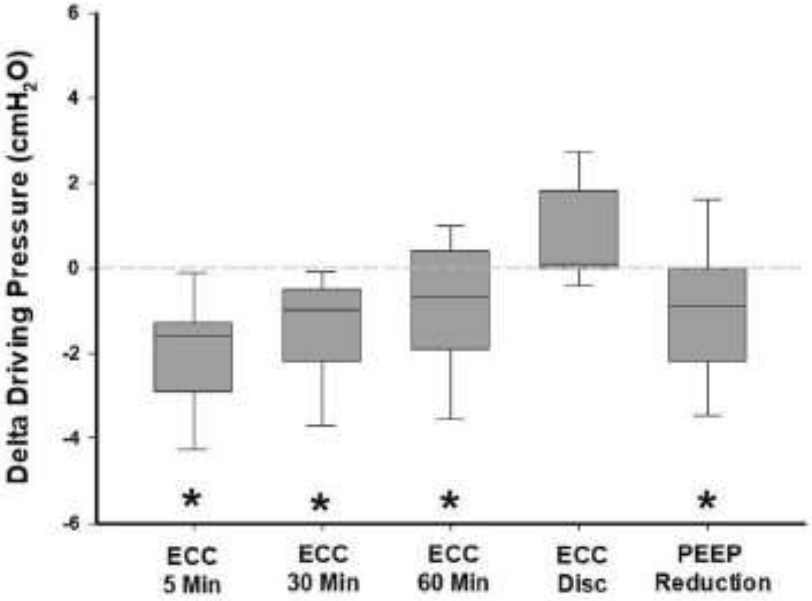
n = 108	Day 1	Day 14	*P* value[a]
Positive end expiratory pressure (cmH_2O), mean ± SD	11.8 ± 2.7	10.3 ± 2.8	< 0.001
Plateau pressure (cmH_2O), median (IQR)	23.5 (21–27)	23.5 (20–26.5	0.49
Driving pressure (cmH_2O), median (IQR)	11 (9–14)	13 (10–16)	< 0.001
Tidal volume (ml/kg IBW), mean ± SD	6.2 ± 0.8	5.6 ± 1.5	< 0.001
Crs (mL/cmH_2O), mean	37.8 ± 11.4	31.2 ± 14.4	< 0.001

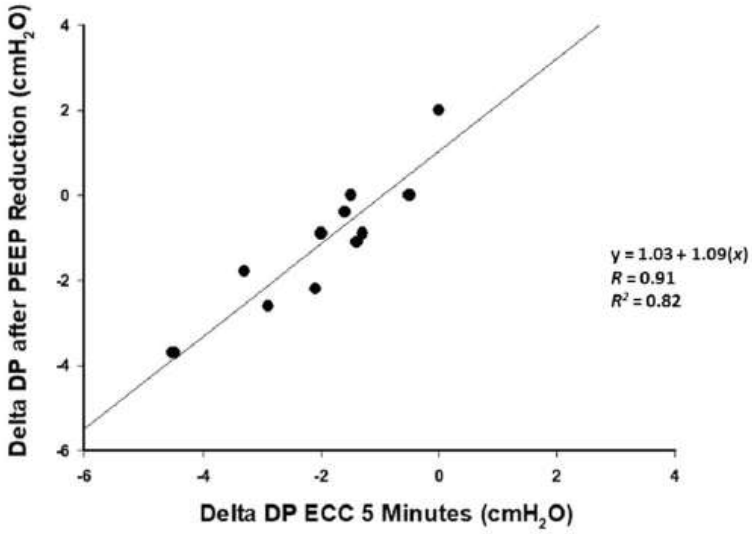


- **A J14 108 pts en VAC**
- **Baisse de compliance**
- **Association non significative avec mortalité**

Vandenbunder et al. Crit Care 2021

Quand la compliance s'effondre ...





- **Pose d'un sac de 5L sur le thorax => amélioration compliance**
- **Annule la surdistension créée par la PEEP => baisser la PEEP**
- **A ZEEP cela marche encore (obs pers) = PtP négative !**

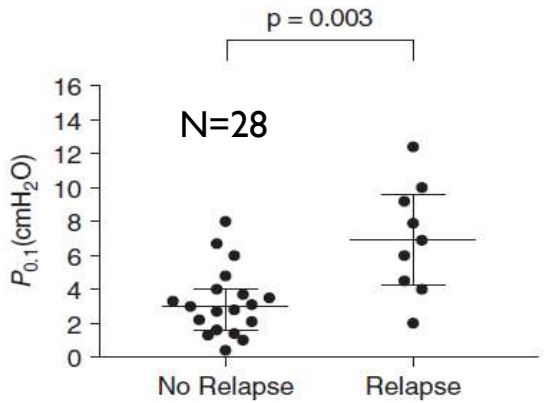
Bastia et al. Annals Intensive Care 2022

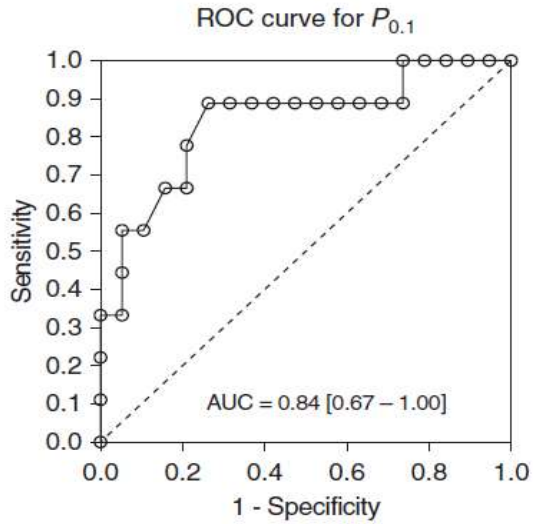
Sevrage ventilatoire & Covid-19

- **Drive + Sensibilité VILI = P-SILI +++**
- **Manque de données …**

- **P0.1 (<4) prédicteur du succès VS-AI !**

- **Mais aussi Plateau en VS-AI** ***(Bellani ICM)***
- **Paralysie partielle** ***(Doorduin AJRCCM 2017)***
- **« Impressions » …**





Esnault et al. AJRCCM 2021

Conclusion

- **ARDS Covid = un ARDS plus hpoxémique**
- **Appliquer la ventilation protectrice phase initiale**
  - **Paralysie**
  - **Recrutement**
  - **DV**
  - **VT 6mL/kg IBW**
- **Baisse de compliance : baisser PEEP et Vt**
- **Sevrage difficile avec risque de PSILI**
- **Apprendre à être patient et humble**
- **Effet des variants, des traitements ?**

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de Louvain

Merci au groupe COVADIS !

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