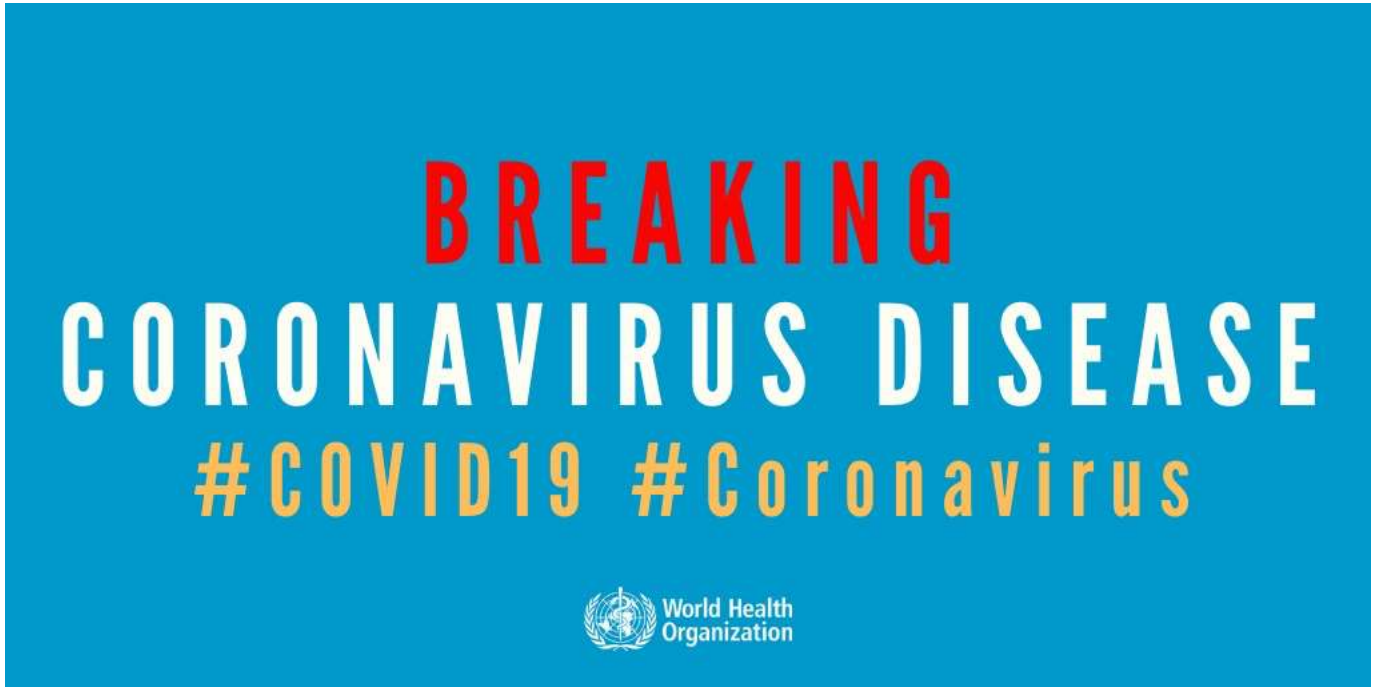
I – Bevezetés

Állapotfelmérés, intenzív osztályos felvétel és gépi lélegeztetés indikációi

Leiner Tamás, Ruszkai Zoltán, Tánczos Krisztián, Molnár Zsolt

TM KETLAK
KORONAVÍRUS
ELLENI TRANSZLÁCIÓS
LAKOSSÁGTÁMOGATÓ
AKCIÓ- ÉS KUTATÓCSOPORT

BEVEZETÉS- Idővonal – SARS CoV2- COVID 19



"We have therefore made the assessment that #COVID19 can be characterized as a pandemic"-@DrTedros #coronavirus

JAMA | Original Investigation

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

Giacomo Grasselli, MD; Alberto Zangrillo, MD; Alberto Zanella, MD; Massimo Antonelli, MD; Luca Cabrini, MD; Antonio Castelli, MD; Danilo Cereda, MD; Antonio Coluccello, MD; Giuseppe Foti, MD; Roberto Fumagalli, MD; Giorgio Iotti, MD; Nicola Latronico, MD; Luca Lorini, MD; Stefano Merler, MS; Giuseppe Natalini, MD; Alessandra Piatti, MD; Marco Vito Ranieri, MD; Anna Mara Scandroglio, MD; Enrico Storti, MD; Maurizio Cecconi, MD; Antonio Pesenti, MD; for the COVID-19 Lombardy ICU Network

JAMA. doi:10.1001/jama.2020.5394
Published online April 6, 2020.

Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China
Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention

Zunyou Wu, MD, PhD[1]; Jennifer M. McGoogan, PhD[1]

JAMA. Published online February 24, 2020. doi:10.1001/jama.2020.2648

- Enyhe, tünetmentes lefolyás ~ 80%
- Közepes- súlyos - 14-20.4 % - kórházi ellátást igényel
- ITO ellátás

Up through March 18, 2020, a total of 17 713 people had tested positive for the new SARS-CoV-2 coronavirus in Lombardy and 1593 (9%) had been admitted to the ICU. Information on the incidence and clinical characteristics of critically ill patients diagnosed with COVID-19 is still limited. Among hospitalized patients with COVID-19 in China, the percentage of patients who required ICU care has varied from 5% to 32%.[4,5]

COVID-19 ITO mortalitás (UK)

Table 3 Outcome, length of stay and organ support* for patients admitted to critical care with confirmed COVID-19

Critical care unit outcome	Patients with confirmed COVID-19 and critical care outcome reported (N=690)	Patients with viral pneumonia (non-COVID-19), 2017-19 (N=4434)
Outcome at end of critical care, n (%)		
Alive	344 (49.9)	3441 (77.6)
Dead	346 (50.1)	993 (22.4)
Length of stay		
Length of stay in critical care (days), median (IQR)		
Survivors	4 (2, 8)	6 (3, 12)
Non-survivors	5 (3, 8)	6 (2, 13)

icnarc intensive care national audit & research centre
25 years and counting...
Napier House
24 High Holborn
London WC1V 6AZ
email: COVID-19@icnarc.org
www.icnarc.org

ICNARC report on COVID-19 in critical care

04 April 2020

COVID-19 ITO mortalitás (Lombardia)

JAMA | Original Investigation

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

Giacomo Grasselli, MD; Albe... MD; Luca C...
Antonio Coluccello, M... Latro...
Giuseppe Natalini, M... MD;
Antonio Pesenti, MD...

61% !!!

Table 2. Patient Disposition From COVID-Only Intensive Care Units (ICUs), Total and Stratified by History of Hypertension

	Patients by age, y, No. (%)								
	All (N = 1591)	0-20 (n = 4)	21-40 (n = 56)	41-50 (n = 143)	51-60 (n = 427)	61-70 (n = 598)	71-80 (n = 341)	81-90 (n = 21)	91-100 (n = 1)
Overall									
Outcome, No. with data	1581	2	56	142	423	596	340	21	1
Died in ICU	405 (26)	0	4 (7)	16 (11)	63 (15)	174 (29)	136 (40)	11 (52)	1 (100)
Discharged from ICU	256 (16)	0	20 (36)	35 (25)	90 (21)	69 (12)	40 (12)	2 (10)	0
Still in ICU as of 3/25/2020[a]	920 (58)	2 (100)	32 (57)	91 (64)	270 (64)	353 (59)	164 (48)	8 (38)	0
Patients with hypertension[b]									
No.	509	0	4 (<1)	21 (4)	121 (24)	195 (38)	156 (31)	12 (2)	0
Outcome									
Died in ICU	195 (38)	0	0	4 (19)	24 (20)	82 (42)	78 (50)	7 (58)	0
Discharged from ICU	84 (16)	0	1 (25)	8 (38)	26 (21)	25 (13)	23 (15)	1 (8)	0
Still in ICU as of 3/25/2020[a]	230 (58)	0	3 (75)	9 (43)	71 (59)	88 (45)	55 (35)	4 (33)	0
Patients without hypertension[b]									
No.	526	1 (<1)	31 (6)	60 (11)	148 (28)	184 (35)	97 (18)	4 (1)	1 (<1)
Outcome									
Died in ICU	114 (22)	0	3 (10)	3 (5)	21 (14)	43 (23)	40 (41)	3 (75)	1 (100)
Discharged from ICU	128 (24)	0	17 (55)	19 (32)	47 (32)	33 (18)	12 (12)	0	0
Still in ICU as of 3/25/2020[a]	284 (54)	1 (100)	11 (35)	38 (63)	80 (54)	108 (59)	45 (46)	1 (25)	0

[a] Patients were admitted between 2/20/2020 and 3/18/2020, with follow-up through 3/25/2020.

[b] Hypertension status for those with outcome data was available for 1035 patients; hypertension status overall was available for 1043 patients.

COVID-19 SSC ajánlás: oxigénterápia

Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)

Authors

Waleed Alhazzani[1,2], Morten Hylander Møller[3,4], Yaseen M. Arabi[5], Mark Loeb[1,2], Michelle Ng Gong[6], Eddy Fan[7], Simon Oczkowski[1,2], Mitchell M. Levy[8,9], Lennie Derde[10,11], Amy Dzierba[12], Bin Du[13], Michael Aboodi[6], Hannah Wunsch[14,15], Maurizio Cecconi[16,17], Younsuck Koh[18], Daniel S. Chertow[19], Kathryn Maitland[20], Fayez Alshamsi[21], Emilie Belley-Cote[1,22], Massimiliano Greco[16,17], Matthew Laundy[23], Jill S. Morgan[24], Jozef Kesecioglu[10], Allison McGeer[25], Leonard Mermel[8], Manoj J. Mammen[26], Paul E. Alexander[2,27], Amy Arrington[28], John Centofanti[29], Giuseppe Citerio[30,31], Bandar Baw[1,32], Ziad A. Memish[33], Naomi Hammond[34,35], Frederick G. Hayden[36], Laura Evans[37], Andrew Rhodes[38]

COVID-19 SSC ajánlás: oxigénterápia

Recommendations:

23. In adults with COVID-19, we **suggest** starting supplemental oxygen if the peripheral oxygen saturation (SPO_2) is < 92% (weak recommendation, low quality evidence), and **recommend** starting supplemental oxygen if SPO_2 is < 90% (strong recommendation, moderate quality evidence).

24. In adults with COVID-19 and **acute hypoxemic respiratory failure on oxygen**, we **recommend** that SPO_2 be maintained no higher than 96% (strong recommendation, moderate quality evidence).

COVID-19 SSC ajánlás: High Flow Nasal Cannula (HFNC)

Recommendation:

25. For adults with COVID-19 and **acute hypoxemic respiratory failure** despite conventional oxygen therapy, we **suggest using** HFNC over conventional oxygen therapy (weak recommendation, low quality evidence).

Potenciális problémák:

1. Eszköz hiány
2. Aerosol képződés – rizikó az ellátószemélyzetre
3. Magas O2-felhasználás – nagyszámú beteg esetében ellátási gondot okozhat

COVID-19 SSC ajánlás: NIPPV

In a cohort of Middle East Respiratory Syndrome (MERS) patients, NIPPV was not associated with improved mortality or length of stay, compared with patients who were intubated without trying NIPPV [79]. However, NIPPV was associated with a high failure rate (92.4%), leading to intubation. Patients who received NIPPV prior to intubation had increased inhaled nitric oxide requirements and increased mortality

The balance between benefit and harm when using NIPPV in adults with COVID-19 is unclear. If, in certain COVID-19 patients, other forms of respiratory failure, such as acute hypercapnic respiratory failure or acute cardiogenic pulmonary edema, are known to be the cause of respiratory failure , NIPPV may be beneficial [88, 89]. However, because limited experience with NIPPV in pandemics suggests a high failure rate, we recommend that any patient receiving NIPPV be monitored closely and cared for in a setting where intubation can be facilitated in the event of decompensation [79, 80]. However, when resources become stretched, there may be insufficient ability to provide invasive ventilation, and even a moderate chance of success with NIPPV may justify its use.

HFNC vs NIPPV

Recommendation:

26. In adults with COVID-19 and **acute hypoxemic respiratory failure**, we **suggest** using HFNC over NIPPV (weak recommendation, low quality evidence).

Rationale:

In adults with COVID-19 and acute respiratory failure, we suggest the use of HFNC over NIPPV. In an RCT comparing HFNC with NIPPV in patients with acute hypoxic respiratory failure, HFNC resulted in reduced mortality at 90 days (HR 2.50, 95% CI 1.31 to 4.78), but did not significantly affect the need for intubation (50% failure rate in NIPPV vs 47% in conventional oxygen and 40% in HFNC groups; p=0.18) [71]. Another meta-analysis comparing HFNC with NIPPV showed HFNC to decrease the need for intubation of patients, yet without significantly reducing mortality or ICU length of stay [72]. Additionally, patients may find HFNC more comfortable than NIPPV [71]. Given the evidence for a decreased risk of intubation with HFNC compared with NIPPV in acute hypoxemic respiratory failure, and studies suggesting that NIPPV may carry a greater risk of nosocomial infection of healthcare providers, we suggest HFNC over NIPPV. However, any patients receiving HFNC or NIPPV should be monitored closely and cared for in a setting where intubation can be f n an unco

NB: HFNC és NIV elérhetősége széles körben korlátozott

Egy érdekes és fontos megfigyelés…

PRELIMINARY OBSERVATIONS ON THE VENTILATORY MANAGEMENT

EXPERIENCE FRO
March 2020

Redacted from notes

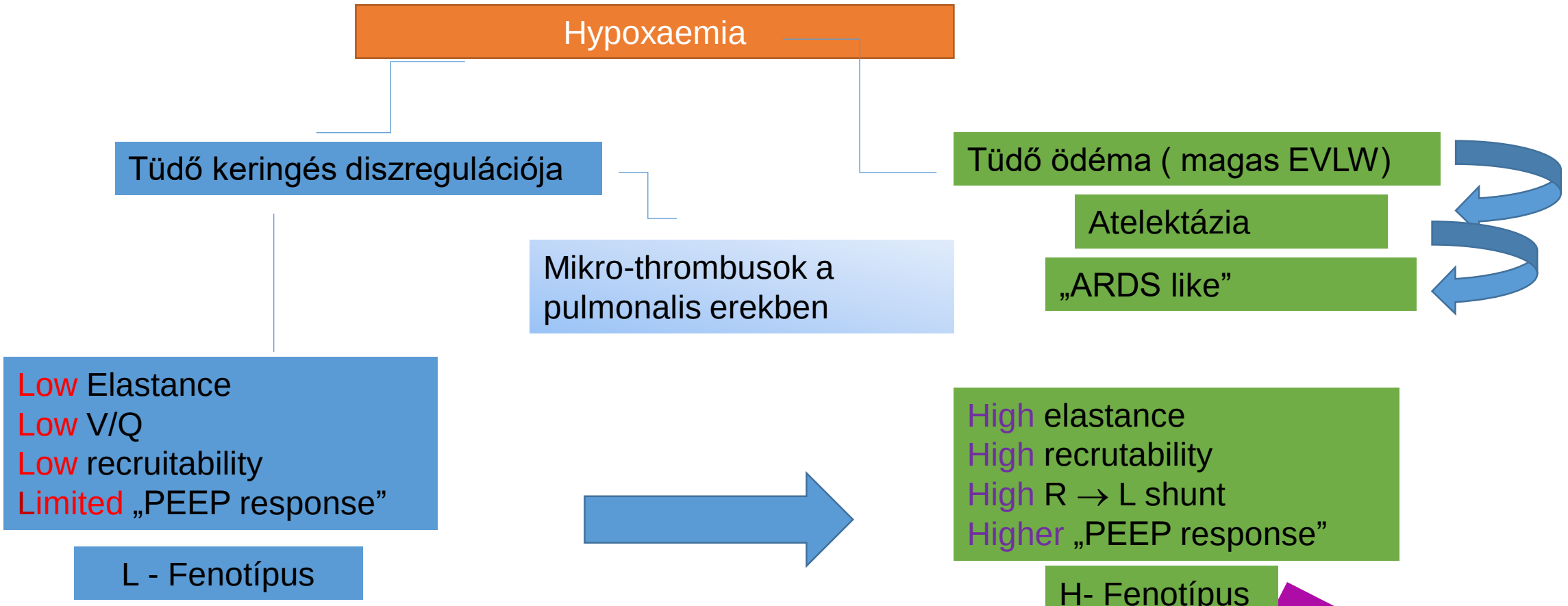
In Covid-19 ICU patients the pulmonary pattern is **NOT similar to ARDS**, as hypoxia is prevalent and pulmonary compliance is generally high. In general, **two categories of patients may be identified**:

a. **High-pulmonary compliance patients with isolated viral pneumonia.** The main finding is hypoxic vasoconstriction, explaining the observed severe hypoxemia. In those patients, the major issue is related to perfusion, as lungs are inflated and increasing PEEP does not help. High PEEP and prone positioning do not lead to recruitment of collapsed areas, but they only adjust pulmonary perfusion. Lung CT scans in those patients confirm that there are not significant areas to recruit, and a 50% shunt is present. Moreover, PEEP levels at 15 cmH20 and beyond may compromise right cardiac filling and an increase of the need for fluid intake and/or norepinephrine. A PaO_2 level around 60 mmHg (8 kPa), and patients should be mildly sedated, or paralyzed.

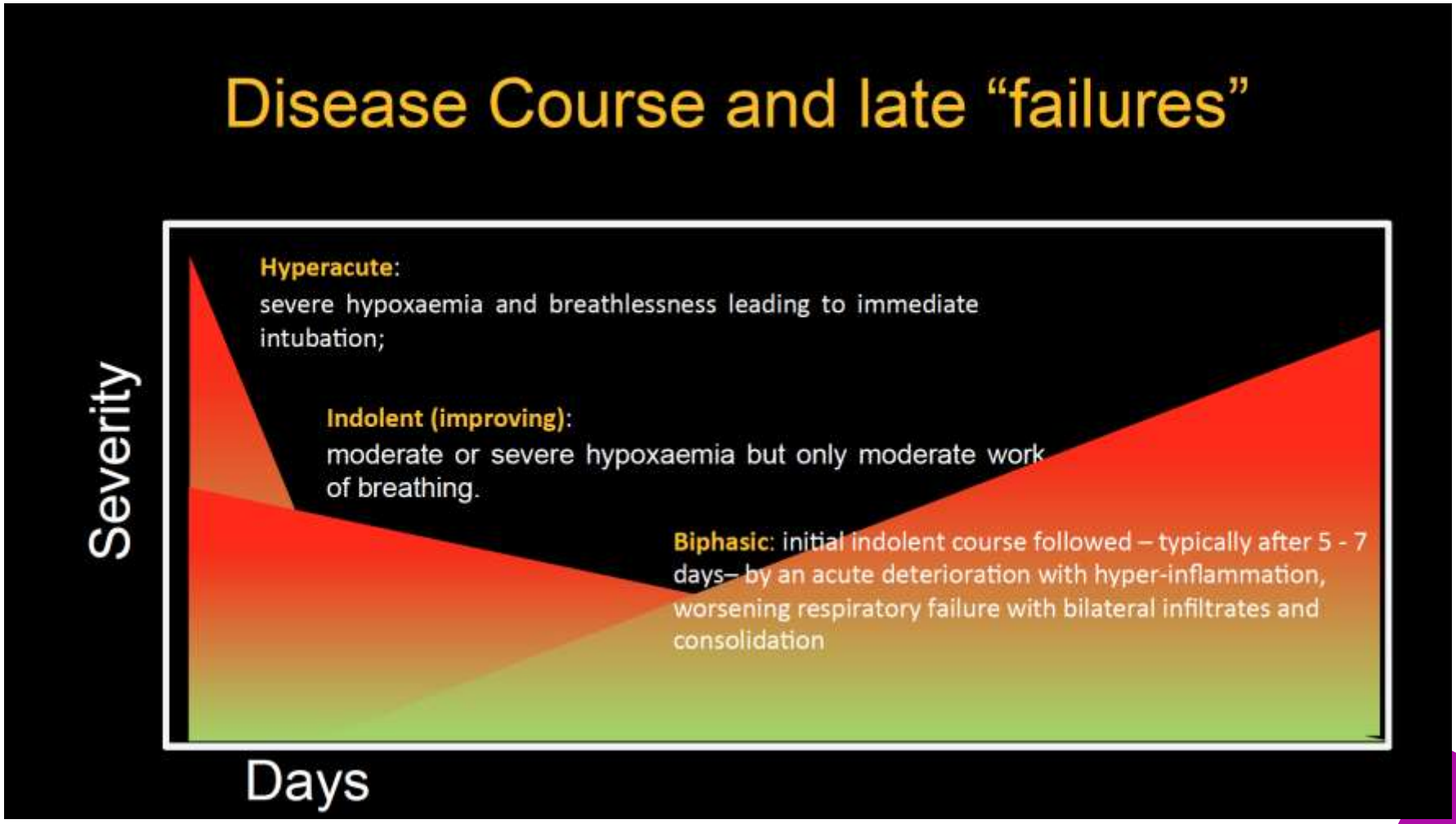
Patients who have been treated with CPAP helmet [in Italy the use of helmet facemask is more prevalent than facemask, but findings may apply for both] show high inspiratory efforts and highly negative intrathoracic pressure. In addition to viral pneumonia, those patients likely have also self-inflicted ventilator induced lung-injury with subsequent decrease in compliance (values lower than 50 ml/cmH_2O) and edema in the lower lobes, as seen in CT scans. Those patients present a pattern similar to ARDS and they benefit of PEEP and prone positioning, paying attention in variations of $ScVO_2$ and $PaCO_2$

COVID-19 – fenotípusok

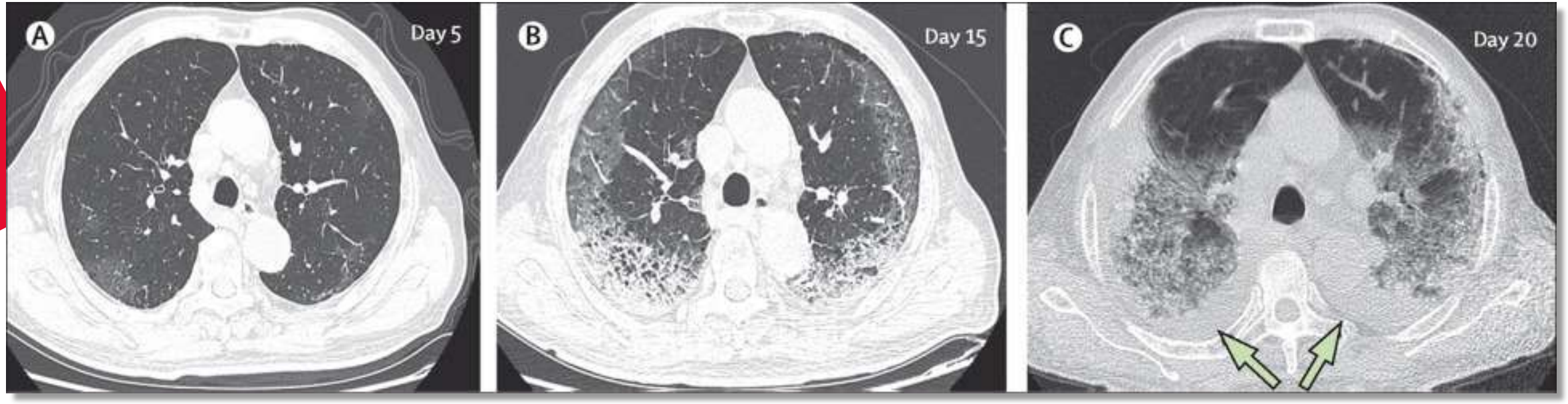
Gattinoni L. et al. COVID-19 pneumonia: different respiratory treatment for different phenotypes? (2020) Intensive Care Medicine; DOI: 10.1007/s00134-020-06033-2



Betegség lefolyás az intenzív osztályon(L. Camporota)



Radiológiai progresszió



Heshui Shi et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020; **20**: 425–34

Hypoxaemia súlyosságának megítélése

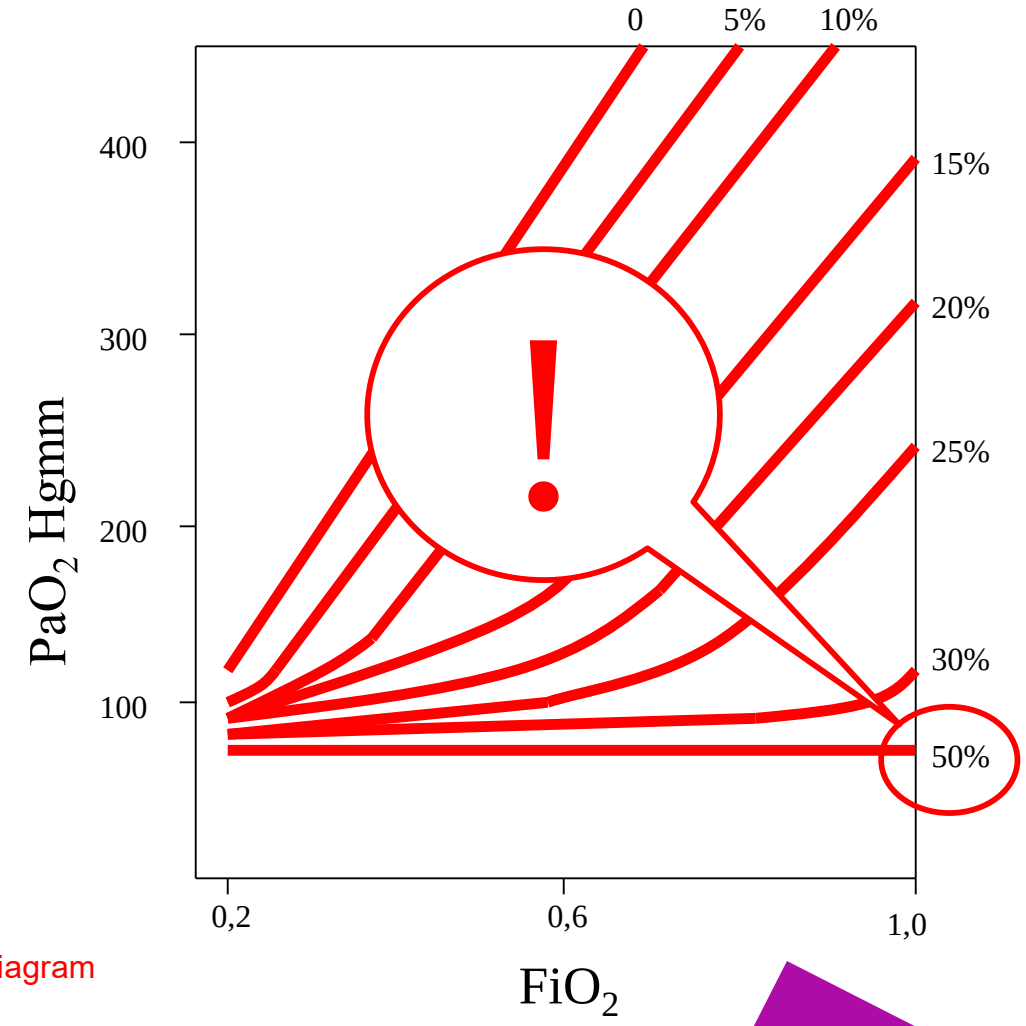
O_2 :15 L/ perc

$SpO_2 \geq 95\%$

IGEN — NEM

ENYHE — KÖZEPES

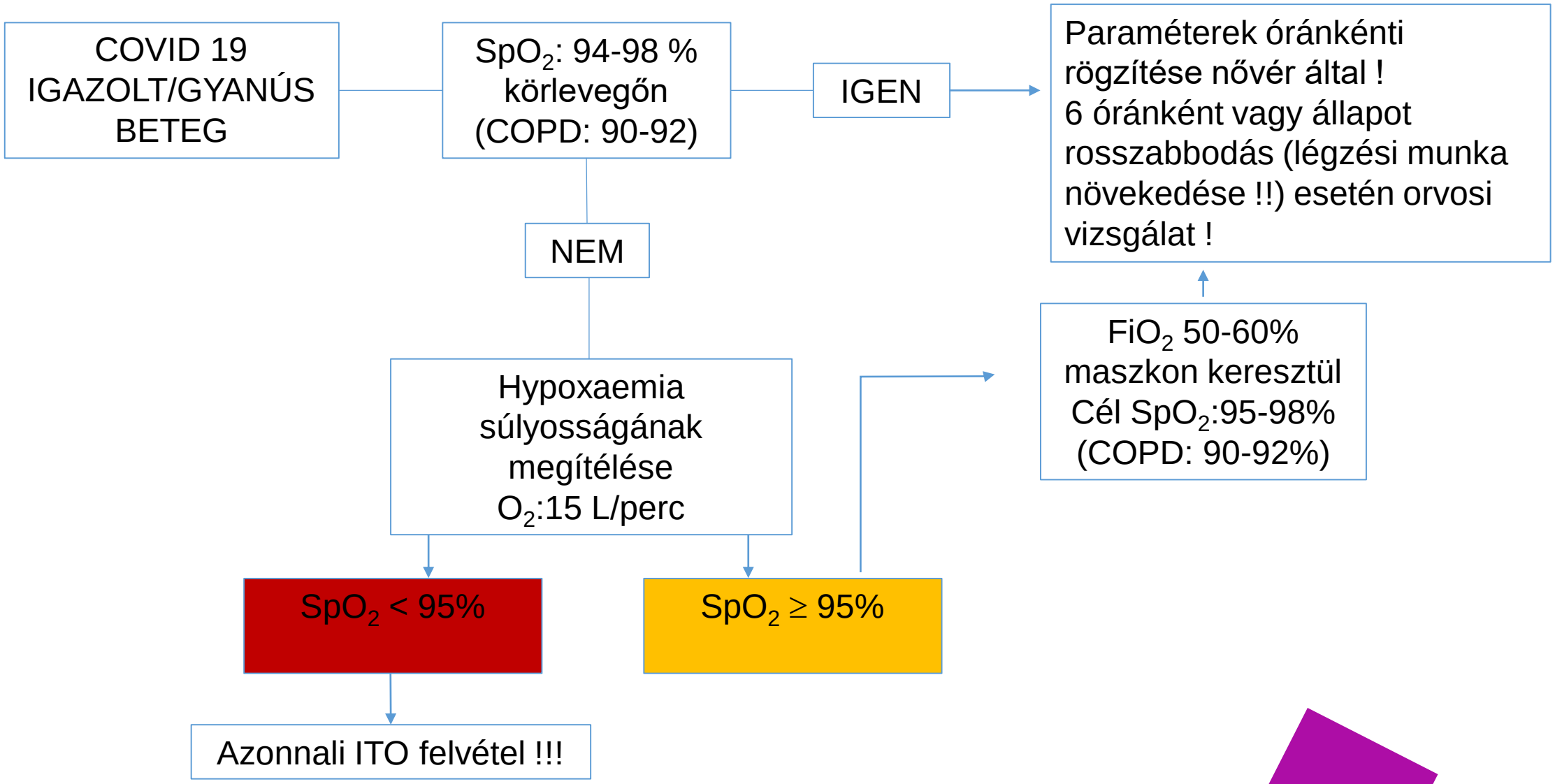
SÚLYOS



„Iso-shunt" diagram

Nunn JF. Appl. Resp Physiol., 1993

Egy lehetséges döntési algoritmus ITO felvétel előtt



Intubációs ellenőrző lista : COVID-19 módosított

TRANSLATIONAL MEDICINE

Védelem

Előkészület - ellenőrzés

Intubáció

Szerepek

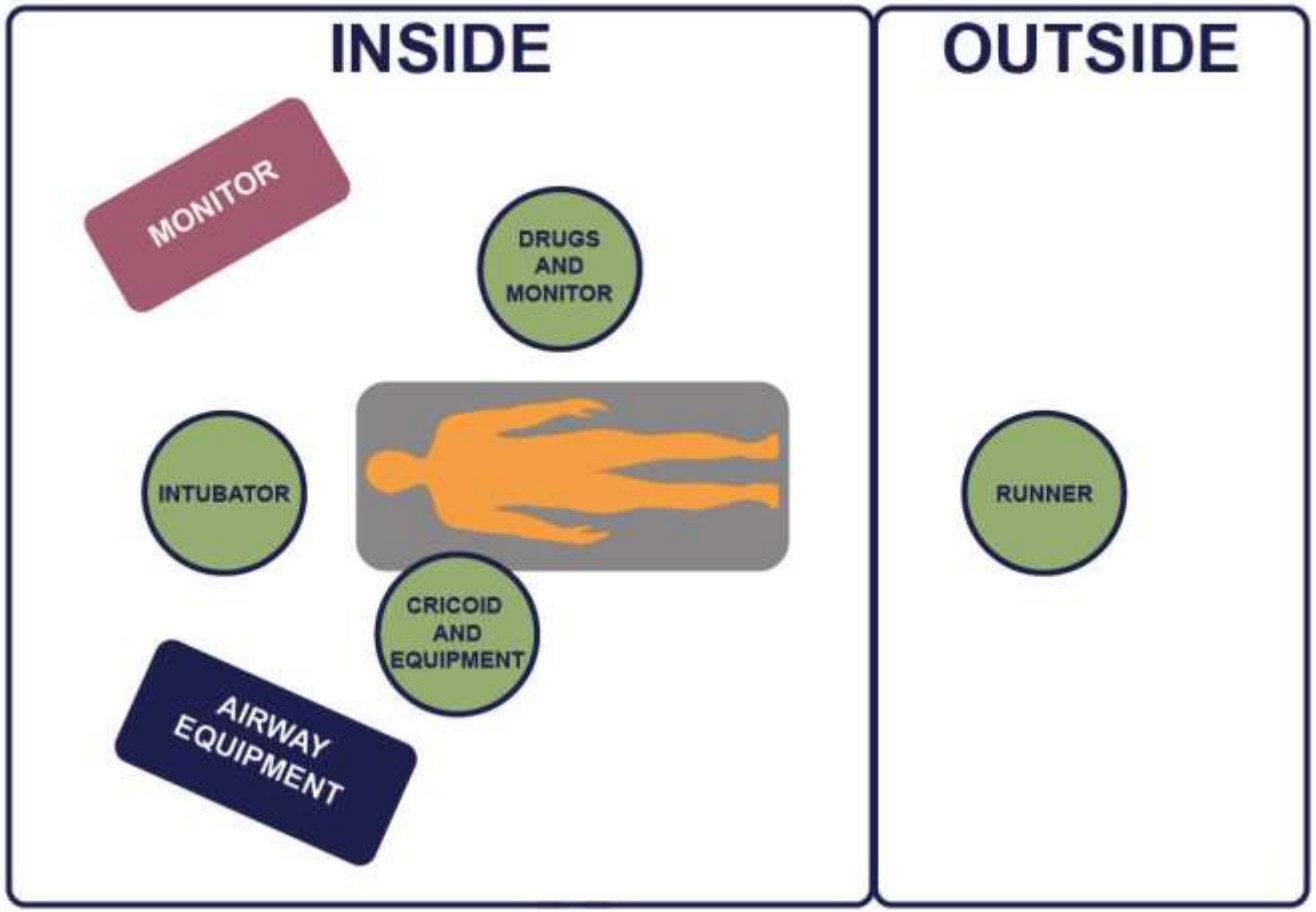
Gyógyszerek

Terv minden eshetőségre

Dekonta-miináció

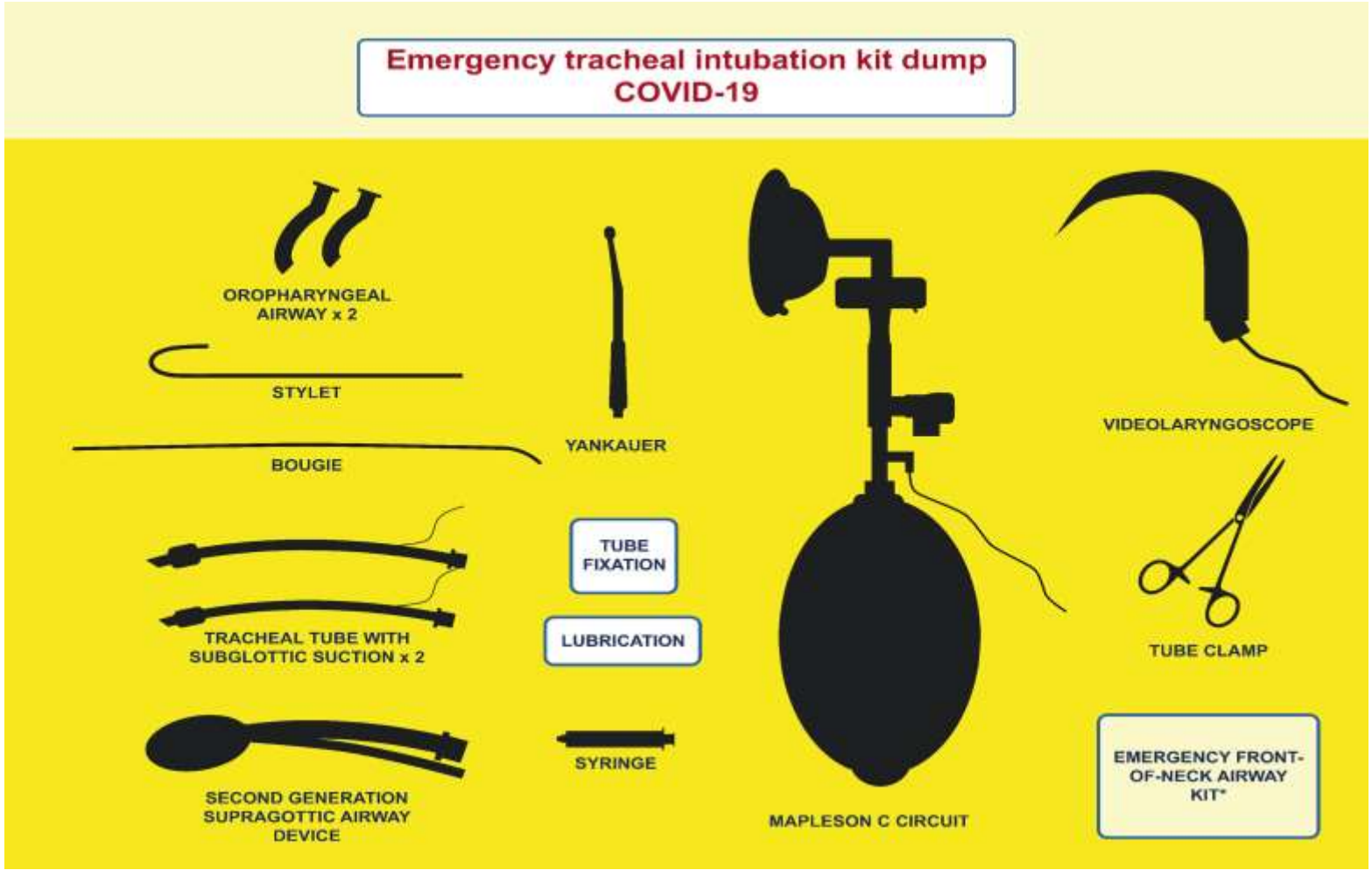
M. Cook, K. El-Bog… A. Pate… .10.1111/anae.15054

Intubációs algoritmus: COVID-19 módosított- Elhelyezkedés



Consensus guidelines for managing the airway in patients with COVID-19
Guidelines from the Difficult Airway Society, the Association of Anaesthetists the Intensive Care Society, the Faculty of Intensive Care Medicine and the Royal College of Anaesthetists
T. M. Cook, K. El-Boghdadly, B. McGuire, A. F. McNarry, A. Patel and A. Higgs, Anaesthesia 2020 doi:10.1111/anae.15054

Intubációs algoritmus: COVID-19 módosított- Eszközök



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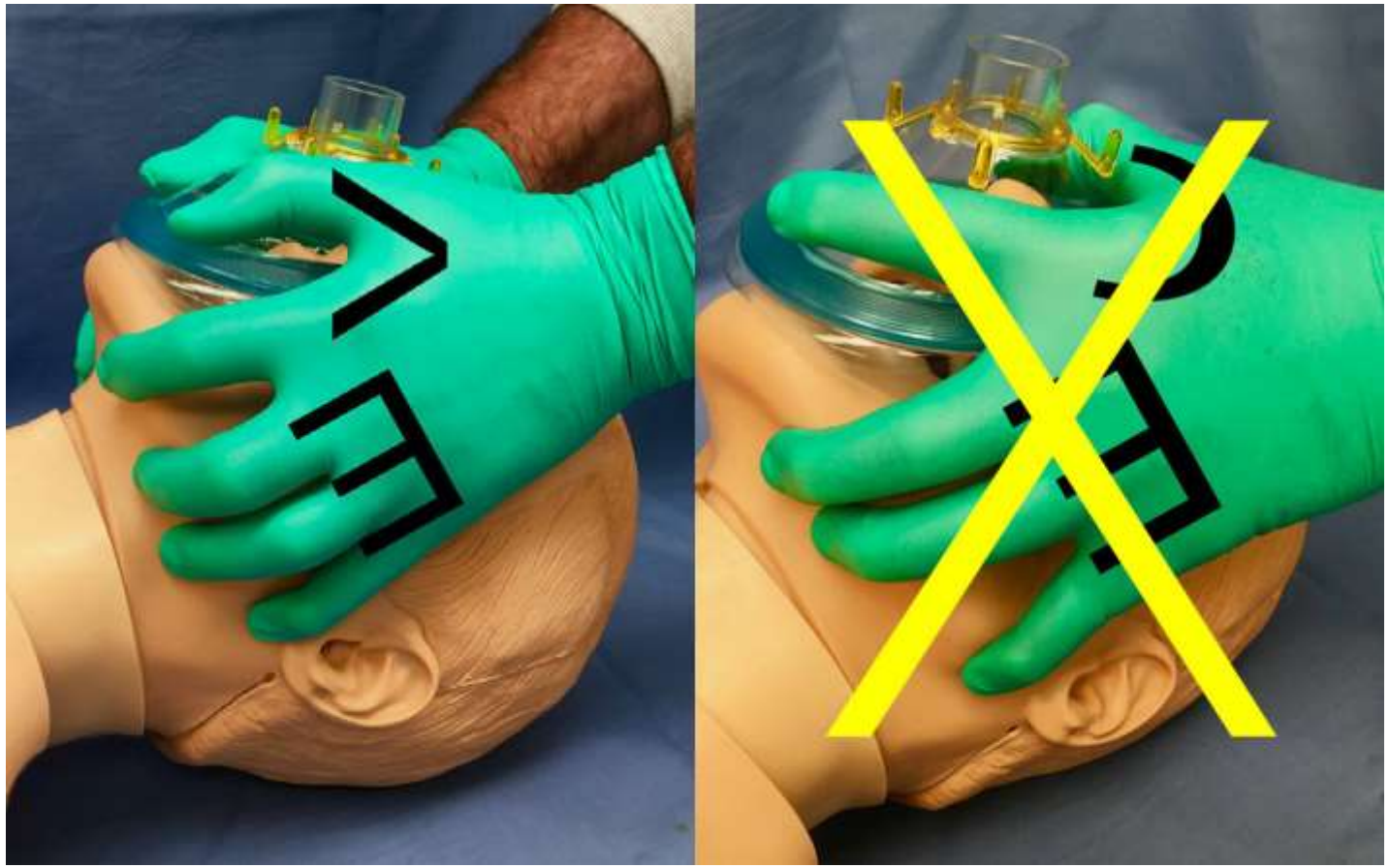
T. M. Cook, K. El-Boghdadly, B. McGuire, A. F. McNarry, A. Patel and A. Higgs, Anaesthesia 2020 doi:10.1111/anae.15054

Intubációs algoritmus: COVID-19 módosított- Kéztartás



Consensus guidelines for managing the airway in patients with COVID-19
Guidelines from the Difficult Airway Society, the Association of Anaesthetists the Intensive Care Society, the Faculty of Intensive Care Medicine and the Royal College of Anaesthetists
T. M. Cook, K. El-Boghdadly, B. McGuire, A. F. McNarry, A. Patel and A. Higgs, Anaesthesia 2020 doi:10.1111/anae.15054

HOW TO VENTILATE COVID-19 PATIENTS?

freely based on talk by Luigi Camporota during ESICM webinar on Apr 2 2020 moderated by Prof. Claude Guerin
graphics by MV Antonini @FOAMecmo

A model to approach ventilation in COVID-19 patients reflecting the phase of the disease induced by SARS-CoV-2 Coronavirus. How do these patients present from an hypoxemia perspective? Hypoxemia is mainly 3 fold: dysregulation of pulmonary perfusion, really important; pulmonary micro-thrombosis (it's role becoming more and more relevant), & frank pulmonary edema ("ARDS like"). COVID-19 patients could present with similar P/F ratio, but with completely different CXR appearance or CT scan patterns (resembling 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, So a limited "PEEP response"
= named as **PHENOTYPE L**
L = Low everything

- pulmonary edema - collapse ARDS-like with

High elastance, & 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 AKAP receptors: profound 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 (majority of patients 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 swing in esophageal and pleural impacting on lung stress/strain. The other important point is the pulmonary edema, leading to elastin WOB, and increased RR. Also consider drive: some of these patients have incredibly high inflammatory/febrile status and O_2 consumption/demand is increased, leading to respir becoming clear a neurotropism for SARS-CoV-2, particularly around midbrain, influencing respiratory/cardiovascular control (with extreme presenting with sudden unexplained cardiac arrest). Subjective dispnea may be less pronounced, with patients not fully important first measure: improve V/Q matching: prone positioning may work really well. On the other side, for the elastic WOB pharmacological support may be needed to control RR so stress/strain of the lung.

- hypoxemia → tidal volumes/Δ Pes = stress-strain → FIO_2, improve V/Q
- neurotropism of SARS-CoV-2 (ACE2) → cardio-respiratory centres, delirium, cognition, anosmia
- pulmonary edema → elastic WOB, respiratory rate → mechanical support, control of RR
- metabolic drive

This can lead to a perpetuating vicious circle.

Brochard/Pulenti ATS2020

WHAT'S NEXT

what to do next? We have a
and some clinical/organiz

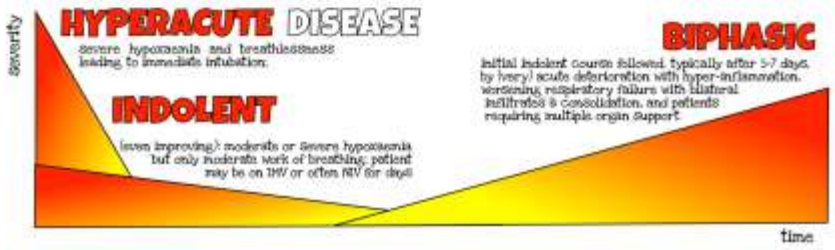
- Infection control
- adequate

allowed in
for spreading
as the patient actually
patient fail?

face
Pulmonary Pressure
This is not a disease likely to be easily
ays, it is less responsive to short term positive
cardiogenic pulmonary edema

It is really resources demanding:
ICU beds
Staffing
availability of ventilators
oxygen: NIMO/CPAP may use incredibly high quantities

Use of CPAP may be associated with decreased CO (Dantzker 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 WOB 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 WOB, 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.



ASSESSMENT

based on 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 WOB: patient may have very aggressive/fulminant disease. If WOB is low, use NIV/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 (Is it) with target
If FIO2 > 0.4 and no
ceiling of escalation
palliative care

INTUBATION

targets on MV:
SpO_2 90-94%
PaO_2 > 8 KPa
$PaCO_2$
Pplat

to measure driving P
per-low tidals!
HCO_3 4-5 KPa
driving pressure < 15 cmH_2O?
if not shocked at presentation
low dose vasoconstrictors
minimize fluids!
yes
no
acute V_T to 6 ml/Kg PBW
keep V_T 8 ml/Kg PBW

IDENTIFY PHENOTYPES

targets on MV:
SpO_2 90-94%
PaO_2 > 8 KPa
$PaCO_2$ < 6 or pH >7.30
Pplat ≤ 30 cmH_2O
ΔP < 15 cmH_2O

SpO2 > 90% with FIO_2 > 0.7
NMBA
uptitrate PEEP in 2 cmH_2O steps up to 15 cmH_2O if required
(but characterizing phenotype needed before optimizing MV)
SpO2 > 90% with FIO_2 > 0.7
obtain echo as soon as possible
compliance > 40ml/cmH_2O
no
yes
consider switch to APRV to improve recruitment and improve alveolar stability
PEEP/FIO_2
RM (40 x 10-15?)
aim to combine if targets not achieved
near normal compliance: first strategy is prone positioning, with same MV settings
ARDS-Like Phenotype H
High Elastance
PEEP responsive
Prone Responsive
COVID-19 pneumonitis Phenotype L
Low elastance
Prone responsive
iNO - Iloprost (biological rationale)
pulmonary vascular reactivity test

FAILURE & ESCALATION

if refractory hypoxemia (> 4h, earlier if life threatening)
ECMO candidate *
no
yes
review targets & strategy
VV-ECMO

4 QUESTIONS

pt selection
- 4 questions to consider thinking about ECLS particularly in a pandemics:
- is the pathology reversible (maybe not the one hyperinflammation or MOF)?
- 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 myocarditis. Some centrally mediated (effect 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 fall 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 scales. This is not ARDS!

graphics by MV Antonini @FOAMecmo
CCM/CCP, MS - 1st ICU University Hospital of Parma, Italy

SARS-CoV , SARS-CoV-2

SARS- CoV-2 and SARS-CoV spike proteins share 76.5% identity in amino acid sequences and, importantly, the SARS- CoV-2 and SARS-CoV spike proteins have a high degree of homology.

This similarity with SARS-CoV is critical because ACE2 is a functional SARS-CoV receptor in vitro and in vivo.

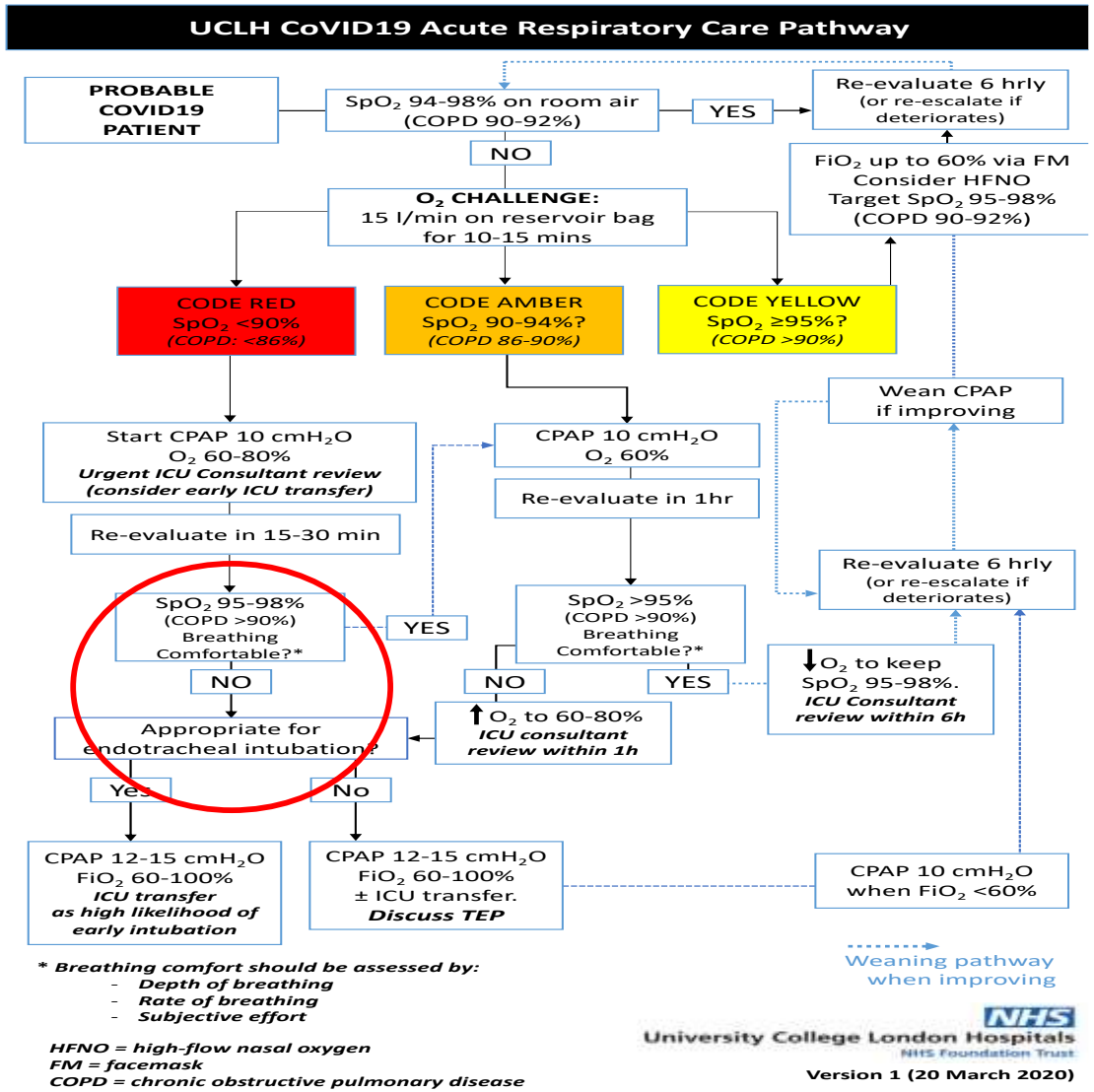
For SARS-CoV pathogenesis, ACE2 is not only the entry receptor of the virus but also protects from lung injury. We therefore previously suggested that in contrast to most other coronaviruses, SARS-CoV became highly lethal because the virus deregulates a lung protective pathway.

A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus–induced lung injury

Keiji Kuba1,7, Yumiko Imai1,7, Shuan Rao2,7, Hong Gao3, Feng Guo2, Bin Guan2, Yi Huan2, Peng Yang2, Ya Zhang2, Wei Deng3, Linlin Bao3, Binlin Zhang3, Guang Liu2, Zhong Wang4, Mark Chappell5, Yanxin Liu2, Dexian Zheng2, Andreas Leibbrandt1, Teiji Wada1, Arthur S Slutsky6, Depei Liu2, Chuan Qin3, Chengyu Jiang2 & Josef M Penninger1

NATURE MEDICINE VOLUME 11 | NUMBER 8 | AUGUST 2005
Published online 7 July 2005; doi:10.1038/nm1267

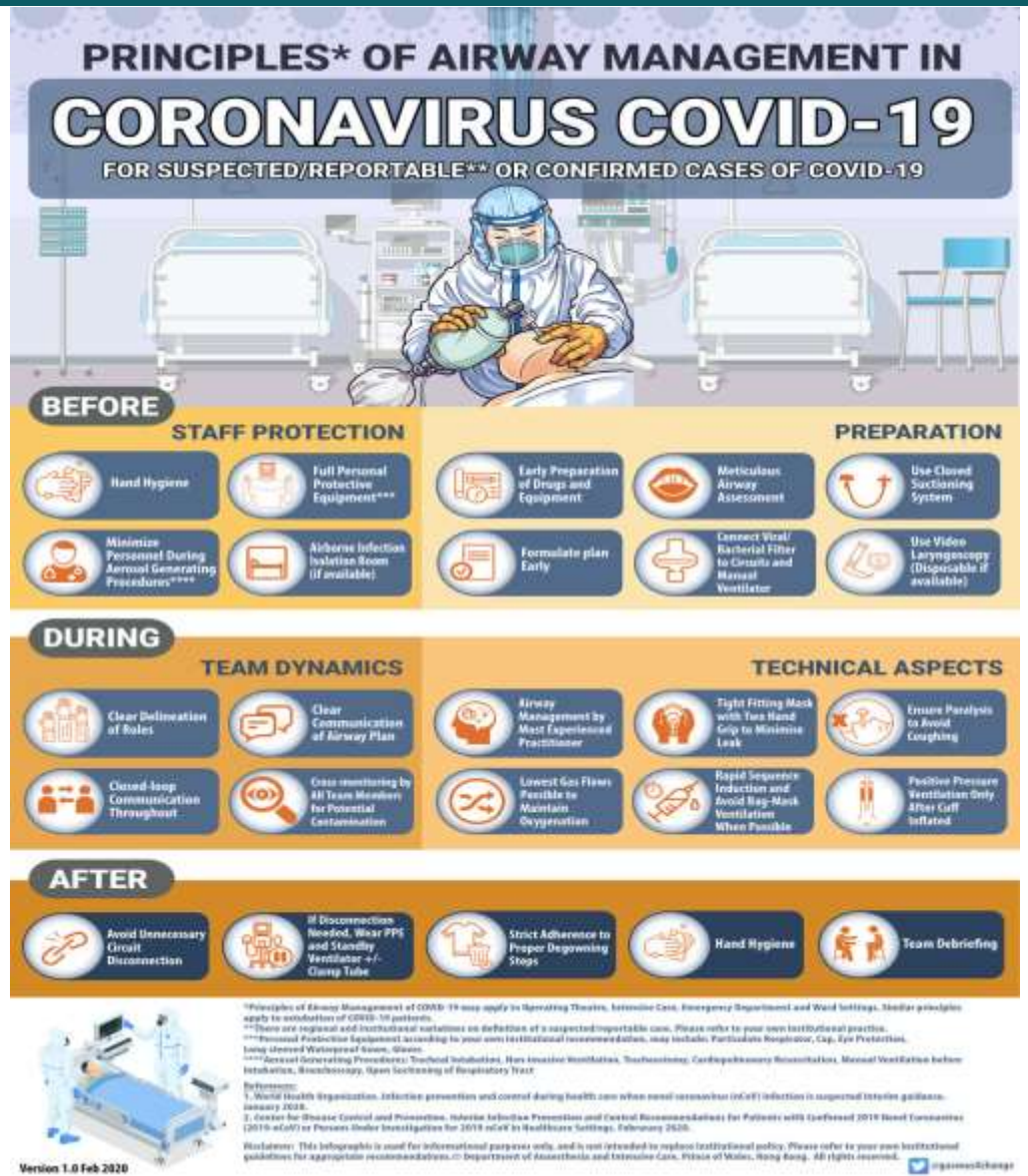
Döntési algoritmus az ITO felvétel előtt (UCL)



- SpO_2
- O_2 („100-as” maszk)
- Hatékonyság?
- CPAP/NIV
- ITO?

Intubációs algoritmus: COVID-19 módosított

Fegyelmezett szervezés



6 technikai elem betartása