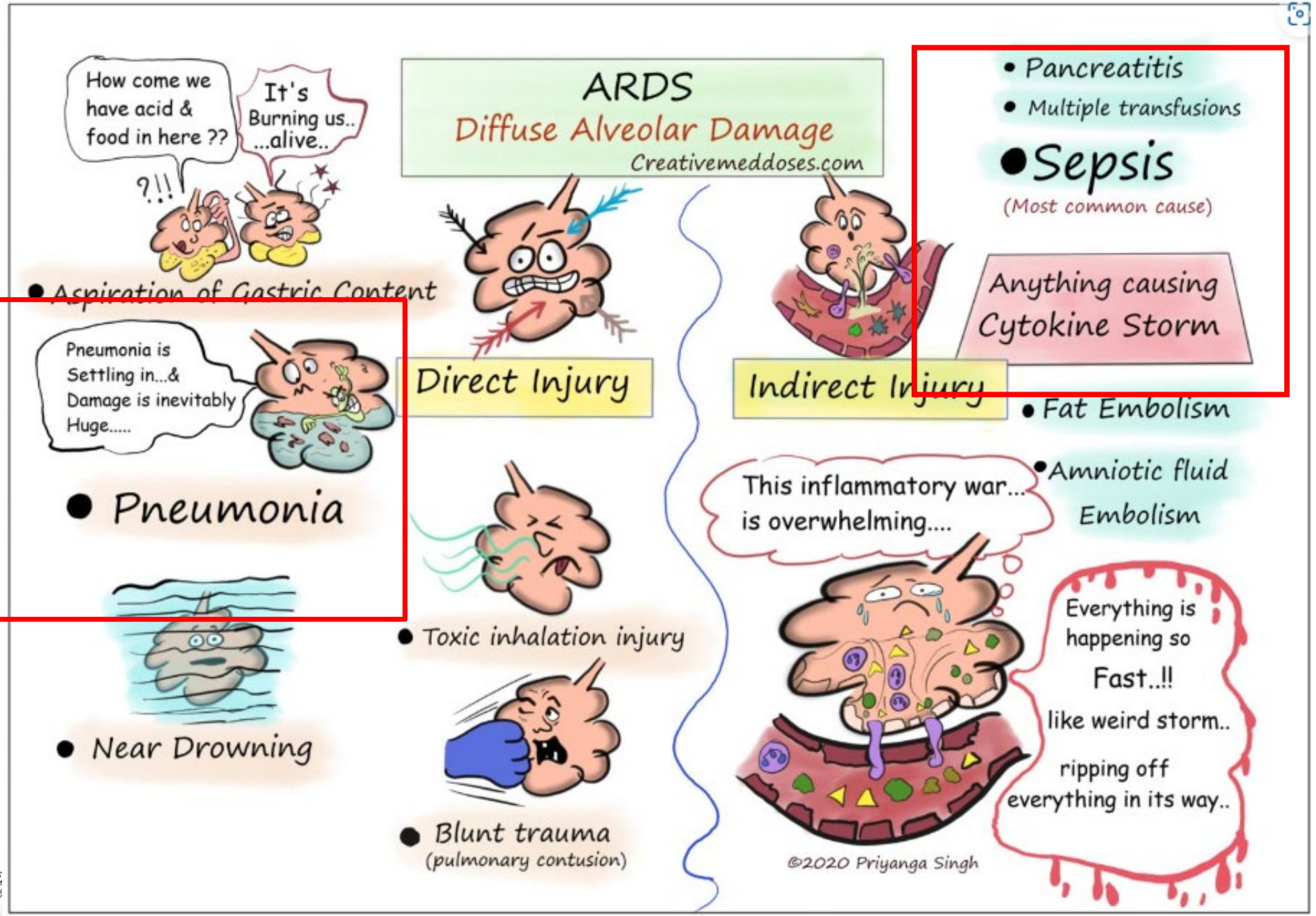
# Plíce a sepse

Pavel Dostál

Klinika anesteziologie, resuscitace a intenzivní medicíny
Univerzita Karlova, Lékařská fakulta v Hradci Králové
Fakultní nemocnice Hradec Králové

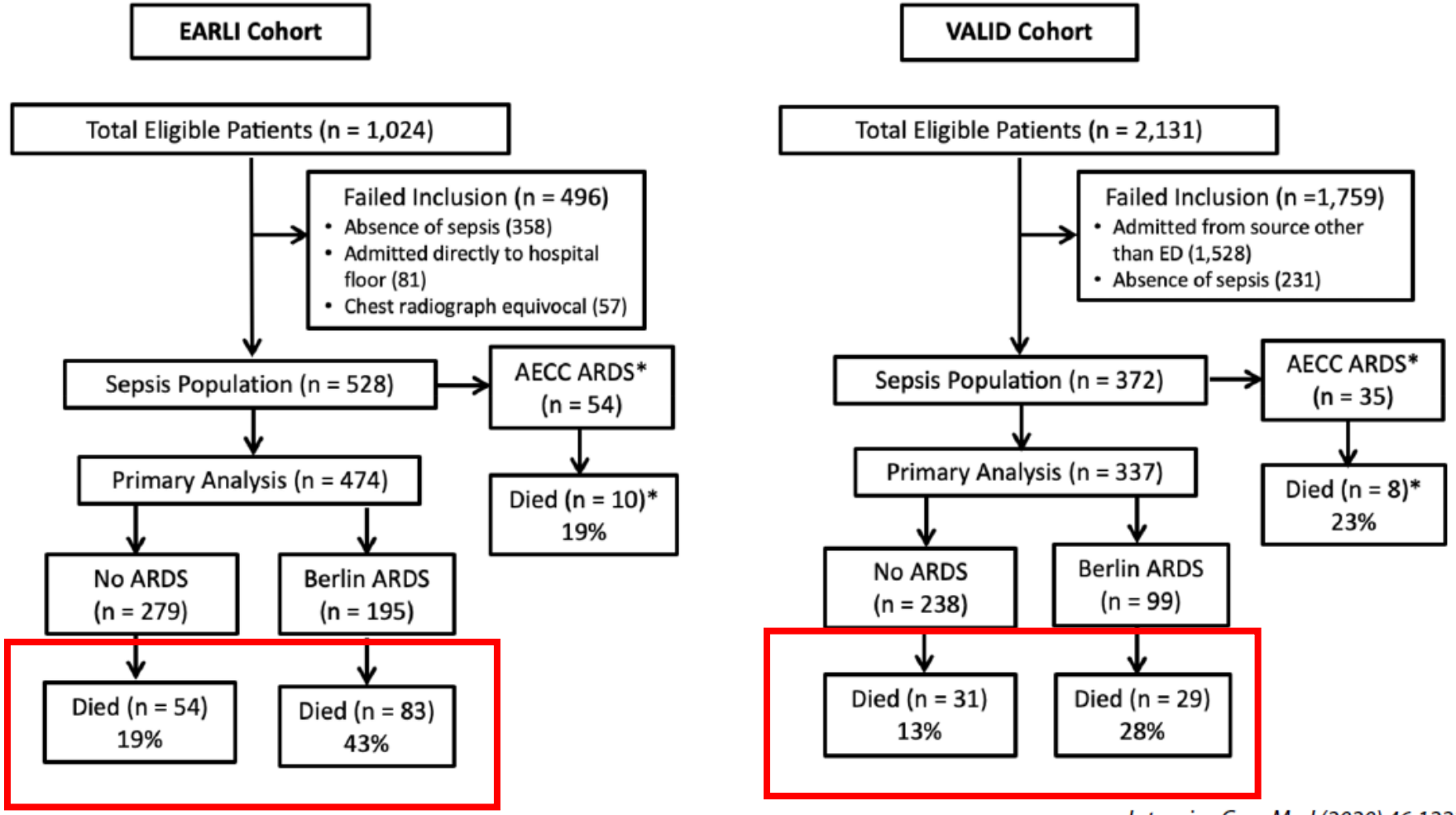

ARDS
Diffuse Alveolar Damage
Creativemeddoses.com
How come we have acid & food in here ??
It's Burning us.. ...alive..
?!!
• Aspiration of Gastric Content
Pneumonia is Settling in...& Damage is inevitably Huge.....
• Pneumonia
• Near Drowning
Direct Injury
• Toxic inhalation injury
• Blunt trauma
(pulmonary contusion)
• Pancreatitis
• Multiple transfusions
• Sepsis
(Most common cause)
Anything causing Cytokine Storm
Indirect Injury
• Fat Embolism
• Amniotic fluid Embolism
This inflammatory war... is overwhelming....
Everything is happening so Fast..!!
like weird storm..
ripping off everything in its way..
©2020 Priyanga Singh

# Epidemiologie

- 25-50% pacientů se sepsí má S-ALI se smrtností kolem 40%
  - Sevransky JE, Levy MM, Marini JJ. Mechanical ventilation in sepsis-induced acute lung injury/acute respiratory distress syndrome: an evidence-based review. Crit Care Med. (2004) 32:S548–53. doi: 10.1097/01.CCM.0000145947.19077.25
  - Rubenfeld GD, Caldwell E, Peabody E, Weaver J, Martin DP, Neff M, et al. Incidence and outcomes of acute lung injury. N Engl J Med. (2005) 353:1685–93. doi: 10.1056/NEJMoa050333

- 68,2% pacientů se sepsí mělo ALI s 90denní mortalitou 35,5%
  - Xie J, Wang H, Kang Y, Zhou L, Liu Z, Qin B, et al. The epidemiology of Sepsis in Chinese ICUs: a National Cross-Sectional Survey. Crit Care Med. (2020) 48:e209–18. doi: 10.1097/CCM.0000000000004155

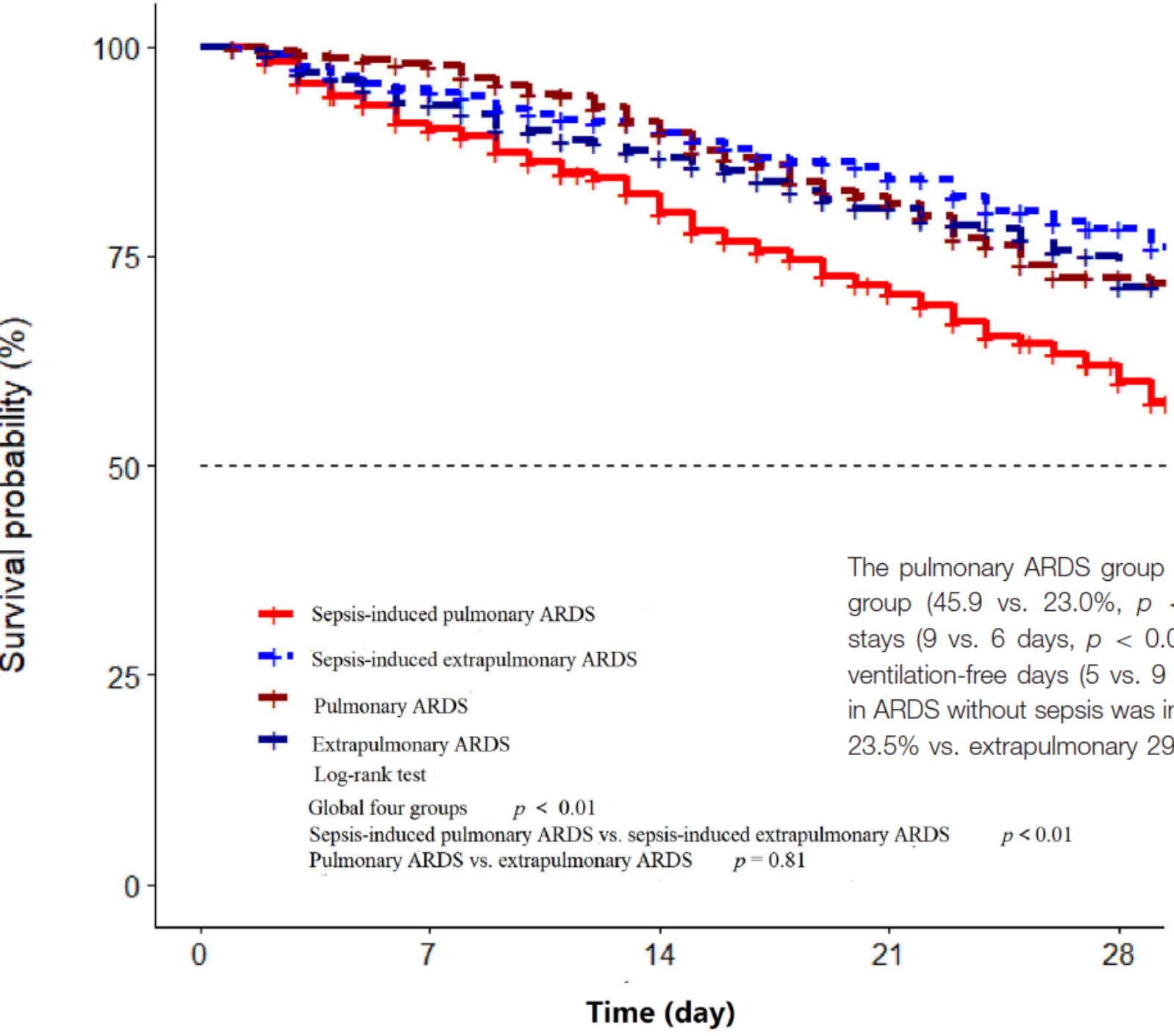
# Acute respiratory distress syndrome-attributable mortality in critically ill patients with sepsis




*Intensive Care Med (2020) 46:1222–1231*
https://doi.org/10.1007/s00134-020-06010-9

# The Association Between Etiologies and Mortality in Acute Respiratory Distress Syndrome: A Multicenter Observational Cohort Study

*Yan Wang[1], Linlin Zhang[1], Xiuming Xi[2]*, Jian-Xin Zhou[1]* and the China Critical Care Sepsis Trial (CCCST) Workgroup*




The pulmonary ARDS group had higher mortality compared with the extrapulmonary group (45.9 vs. 23.0%, $p < 0.01$), longer intensive care unit (ICU) and hospital stays (9 vs. 6 days, $p < 0.01$, 20 vs. 18 days, $p = 0.01$, respectively), and fewer ventilation-free days (5 vs. 9 days) in the presence of sepsis. However, the mortality in ARDS without sepsis was inverted compared with extrapulmonary ARDS (pulmonary 23.5% vs. extrapulmonary 29.2%, $p = 0.04$). After adjusting for the Acute Physiology

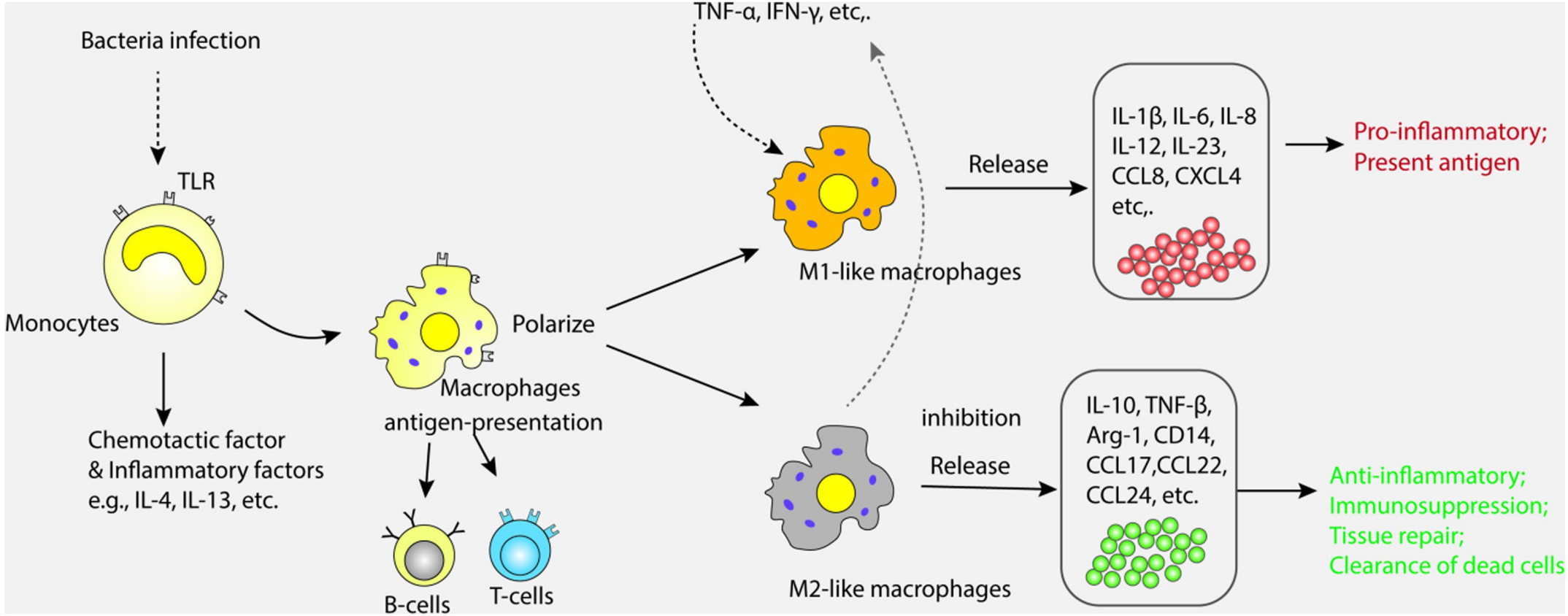
*Front. Med. 8:739596.*
*doi: 10.3389/fmed.2021.739596*

| | Sepsis-induced pulmonary ARDS *n* = 647 | Sepsis-induced extrapulmonary ARDS *n* = 396 | *p* | Pulmonary ARDS *n* = 536 | Extrapulmonary ARDS *n* = 559 | *p* |
|---|---|---|---|---|---|---|
| Gender, male, *n* (%) | 431 (66.6%) | 306 (66.7%) | 0.65 | 339 (63.2%) | 377 (67.4%) | 0.15 |
| Age, year, median (IQR) | 65 (50–78) | 63 (51–75) | <0.01 | 65 (53–77) | 58 (45–68) | <0.01 |
| BMI, kg/m$^2$ median (IQR) | 22.2 (20.2–24.2) | 22.7 (20.3–24.9) | <0.01 | 22.7 (20.2–24.9) | 22.5 (20.3–24.5) | 0.77 |
| APACHE II score, median (IQR) | 21 (16-27) | 17 (12-24) | <0.01 | 13 (8-19) | 13 (8-20) | 0.51 |
| SOFA median (IQR) | 7 (4-10) | 6 (2-10) | 0.01 | 2 (2-5) | 2 (1-5) | 0.96 |
| Admission to ARDS onset, days median (IQR) | 1 (1,2) | 1 (1-4) | <0.01 | 3 (1-4) | 3 (1-4) | 0.07 |
| $PaO_2/FiO_2$, mmHg, median (IQR) | 150 (124–198) | 151 (142–214) | 0.01 | 150 (150–200) | 150 (153–206) | 0.11 |
| **Outcomes** | | | | | | |
| No. organ failure, median (IQR) | 1(1-1) | 1(1-1) | 0.01 | 1(1-1) | 1(1-1) | 0.03 |
| Ventilation-free days within 28 days, days median (IQR) | 5 (5-13) | 9 (5-18) | <0.01 | 13 (11-26) | 12 (10-25) | 0.06 |
| Length of ICU stay, days median (IQR) | 9 (4-20) | 6 (3-12) | <0.01 | 4 (2-11) | 4 (2-12) | 0.18 |
| Length of hospital stay, days median (IQR) | 20 (11-31) | 18 (10-29) | 0.01 | 17 (11-27) | 17 (19-28) | 0.25 |

*Front. Med. 8:739596.*
*doi: 10.3389/fmed.2021.739596*

# Patogeneze

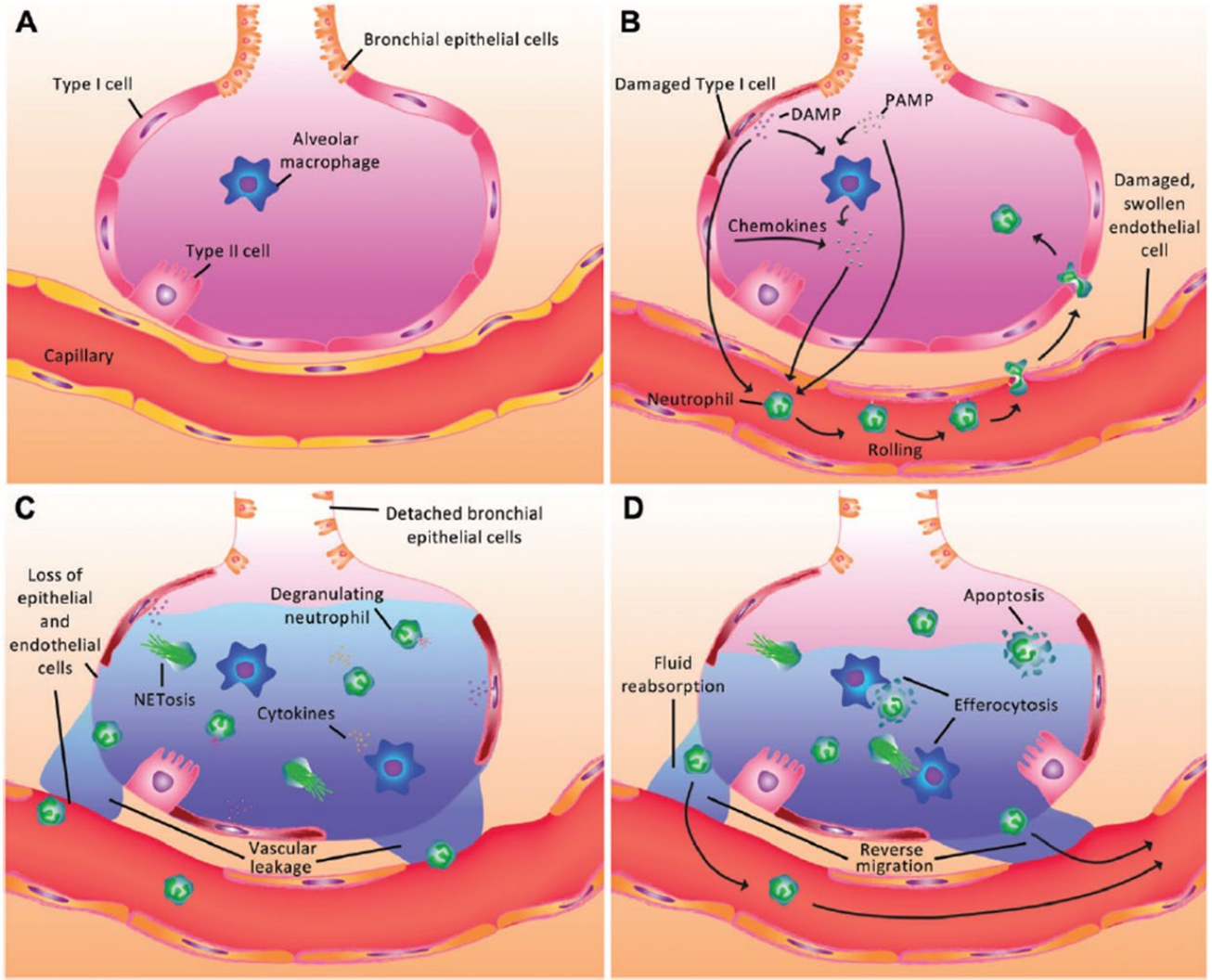
- Aktivace makrofágů




*Front. Med.* 10:1289194.
doi: 10.3389/fmed.2023.1289194

# Patogeneze

- Aktivace makrofágů
- Aktivace neutrofilů




Journal of Pathology
*J Pathol* 2019; **247**: 672–685
Published online 15 February 2019 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/path.5221

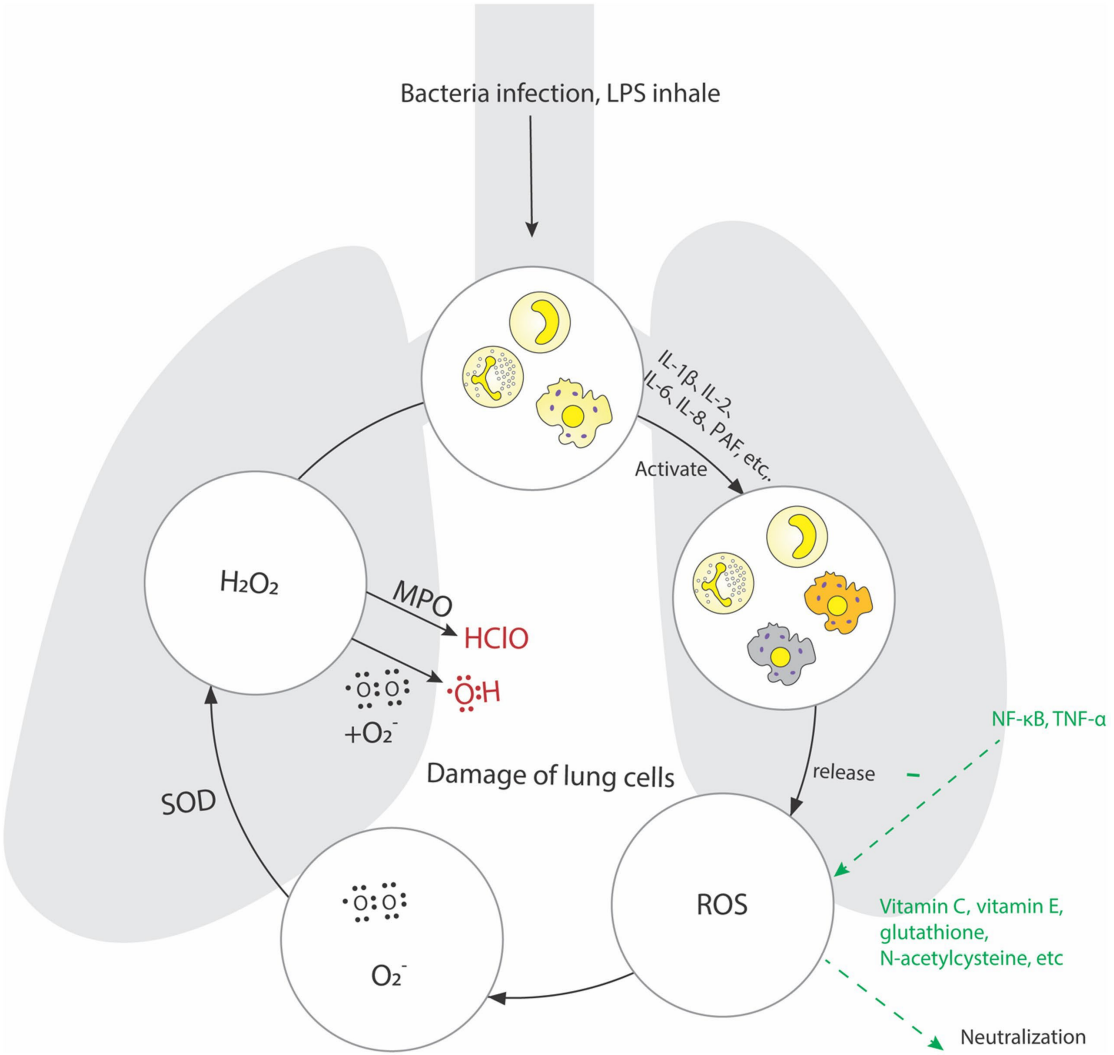
INVITED REVIEW

Neutrophils in the initiation and resolution of acute pulmonary inflammation: understanding biological function and therapeutic potential

Philippe MD Potey, Adriano G Rossi, Christopher D Lucas and David A Dorward*

# Patogeneze

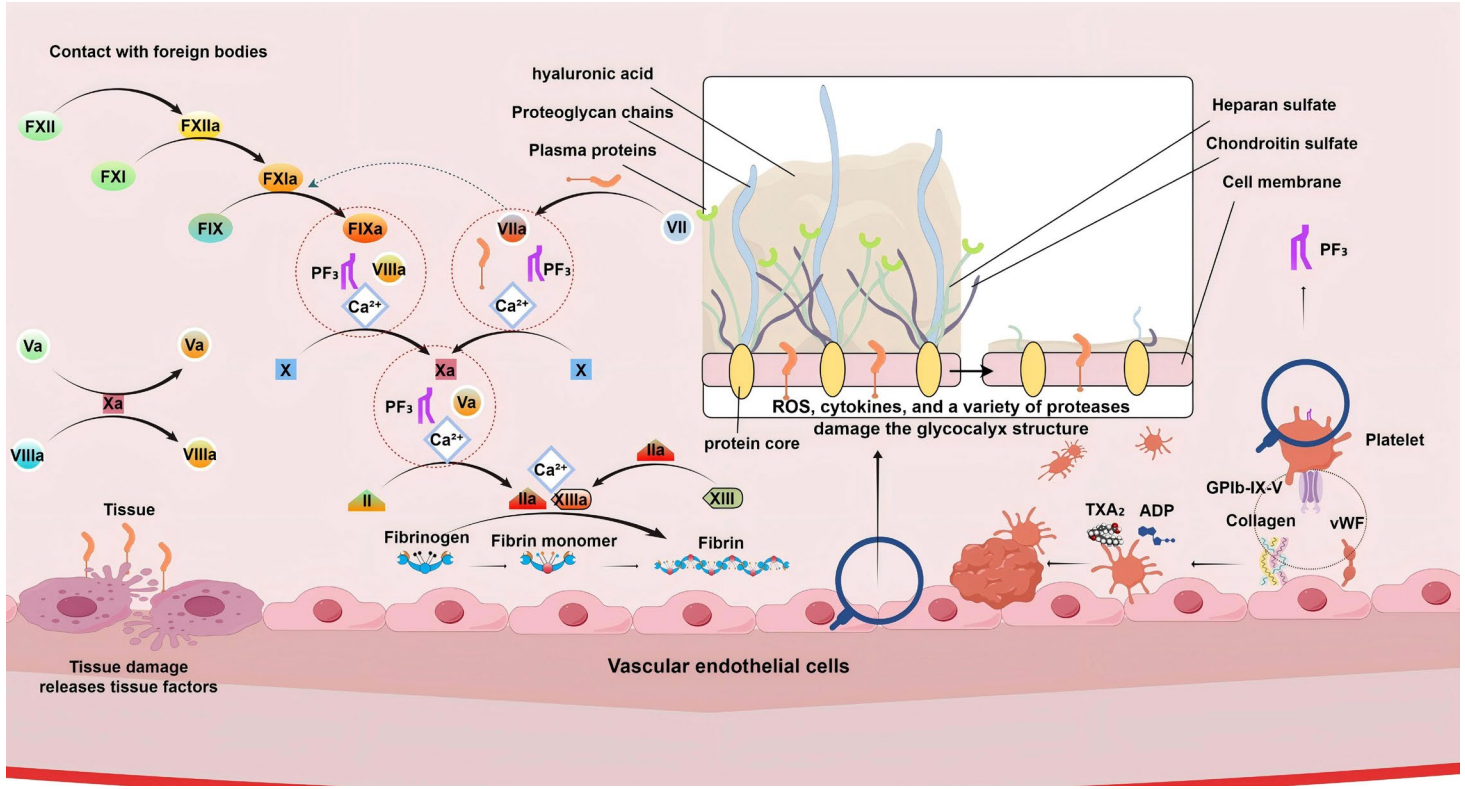
- Aktivace makrofágů
- Aktivace neutrofilů
- Oxidativní stres a ROS




*Front. Med.* 10:1289194.
doi: 10.3389/fmed.2023.1289194

# Patogeneze

- Aktivace makrofágů
- Aktivace neutrofilů
- Oxidativní stres a ROS
- Poškození glykokalyx
- Aktivace koagulace

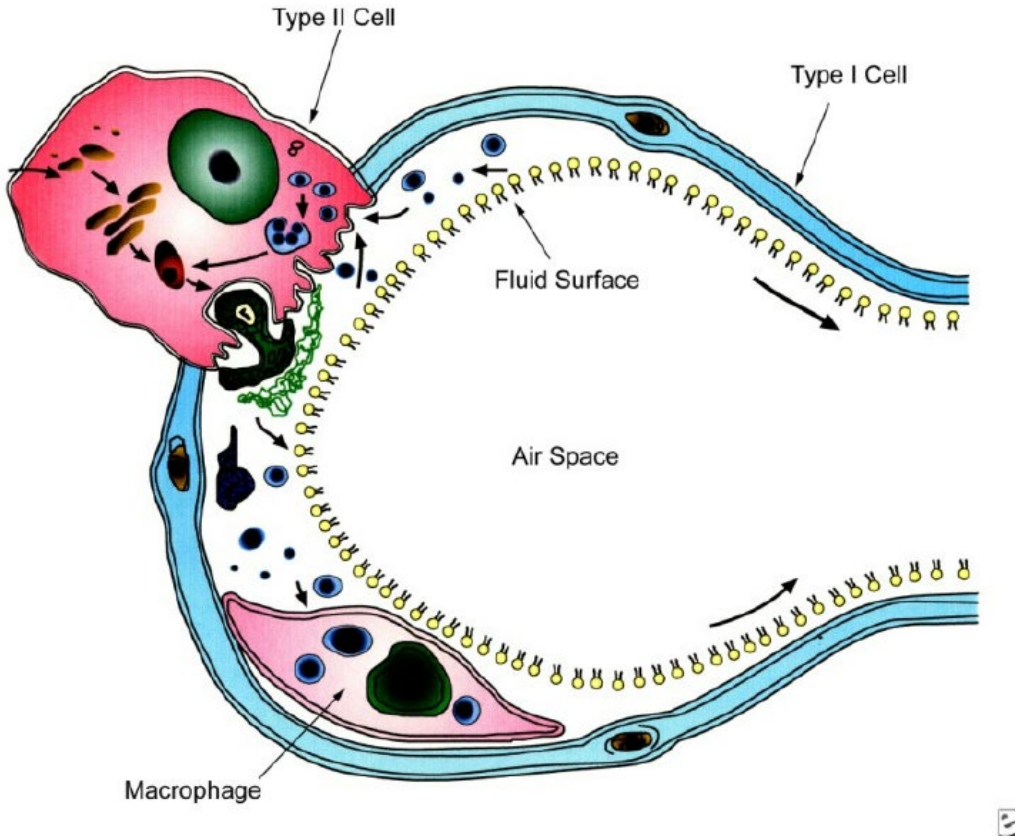



Journal of Inflammation Research 2025:18 1479–1495

# Patogeneze

- Aktivace makrofágů
- Aktivace neutrofilů
- Oxidativní stres a ROS
- Poškození glykokalyx
- Aktivace koagulace
- Dysfunkce surfaktantu

- Genetické faktory




Almstrand, Ann-Charlotte. Analysis of Endogenous Particles in Exhaled Air.

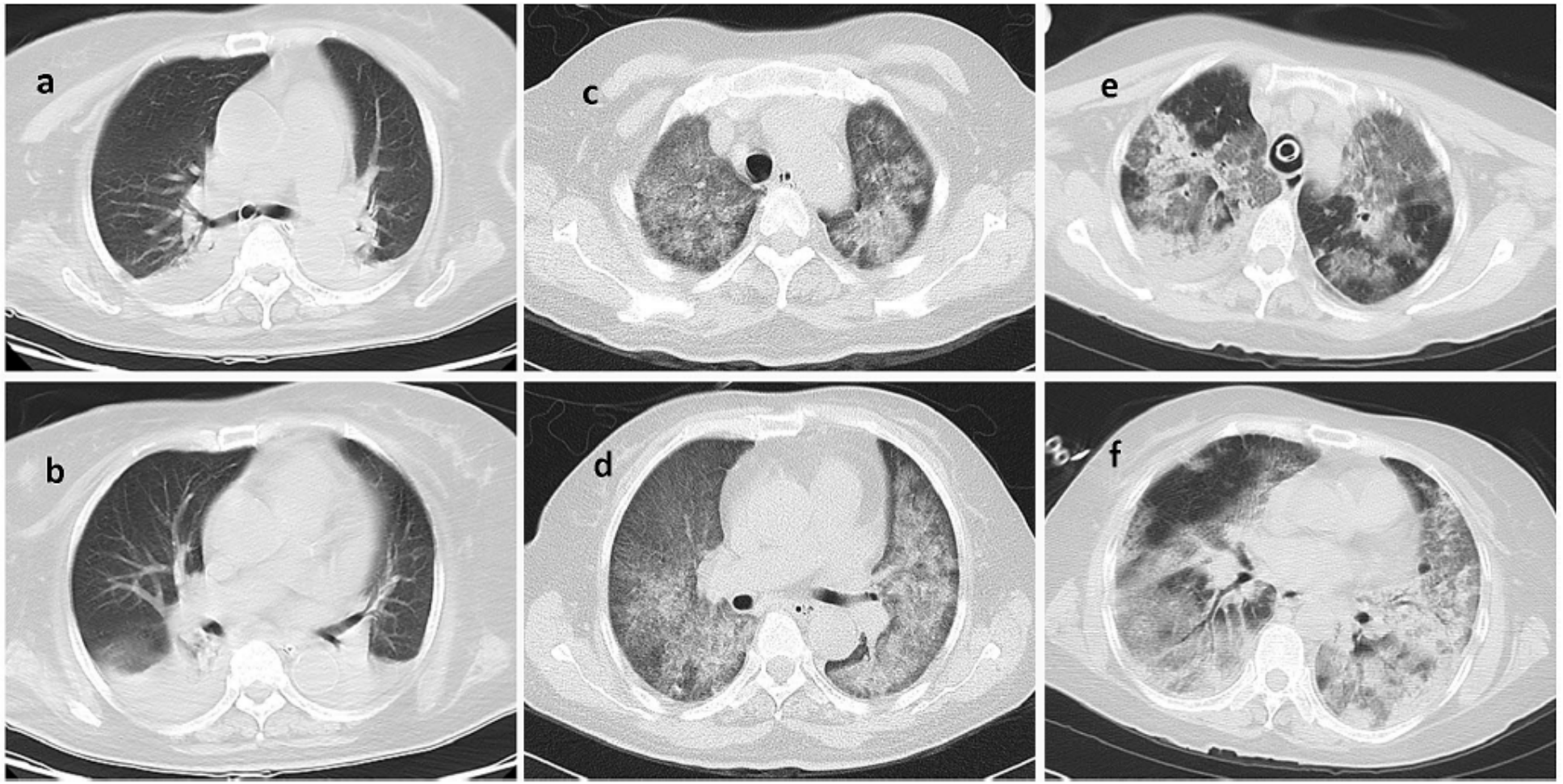
# Subfenotypy ARDS a potenciální terapie

# Příklady subfenotypizací

| Fyziologické | Klinické | Biologické |
|---|---|---|
| $PaO_2/FiO_2$ | Úrazový vs neurazový | Genomické |
| Poměr dechového objemu a mrtvého prostoru | Přímé vs nepřímé poškození | Transkriptomické |
| Hybný tlak | Fokální nebo difuzní poškození | Proteomické |
| | S nebo bez akutního poškození ledvin | Metabolomické |

# Advances in medical imaging to evaluate acute respiratory distress syndrome

Shan Huang[1] · Yuan-Cheng Wang[1,2] · Shenghong Ju[1]

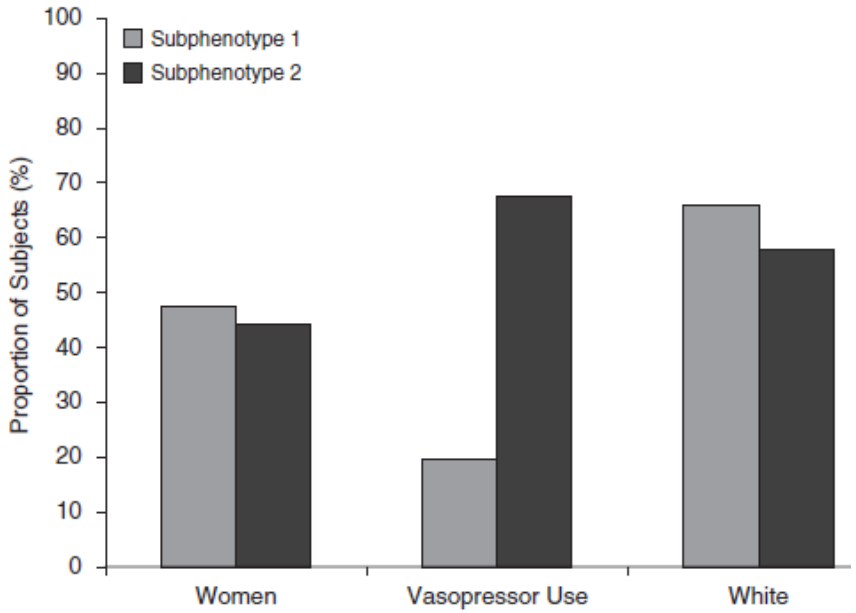


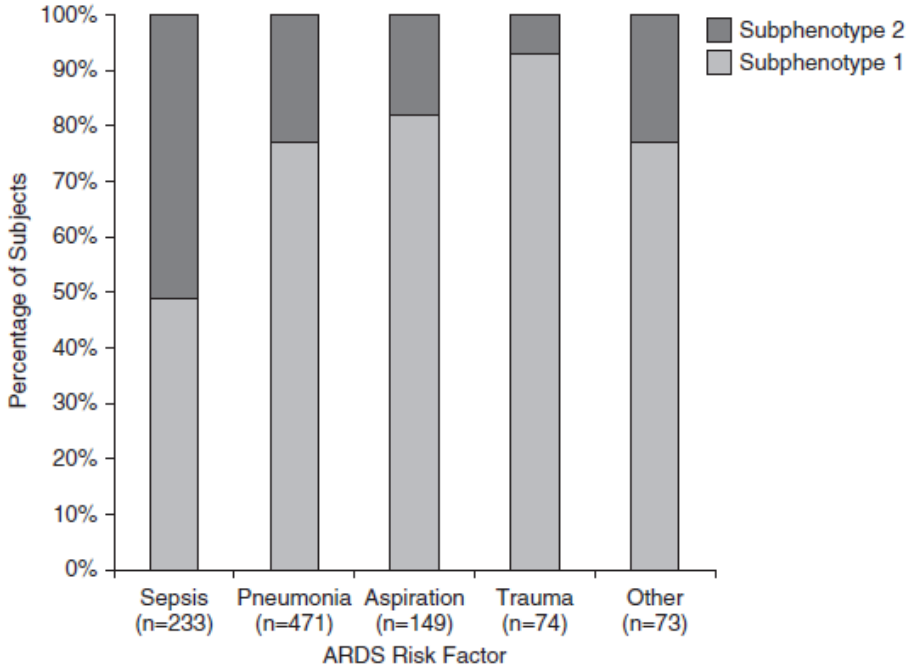

Chinese Journal of Academic Radiology (2022) 5:1–9
https://doi.org/10.1007/s42058-021-00078-y

# Hyperinflamatorní vs hypoinflamatorní fenotyp

# Acute Respiratory Distress Syndrome Subphenotypes Respond Differently to Randomized Fluid Management Strategy

Katie R. Famous[1], Kevin Delucchi[2], Lorraine B. Ware[3,4], Kirsten N. Kangelaris[5], Kathleen D. Liu[6,7], B. Taylor Thompson[8], and Carolyn S. Calfee[1,7]; for the ARDS Network




Am J Respir Crit Care Med Vol 195, Iss 3, pp 331–338, Feb 1, 2017

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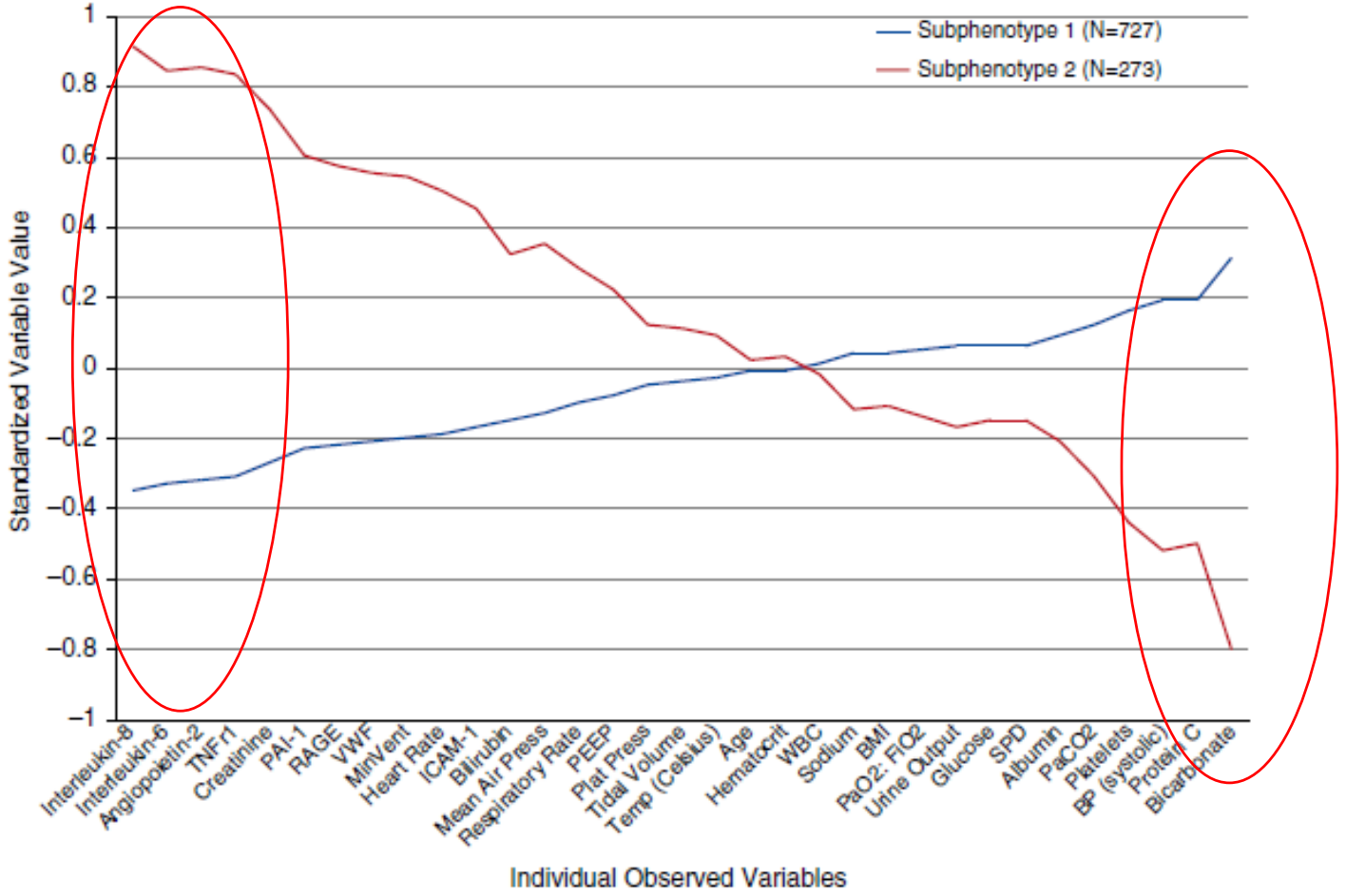
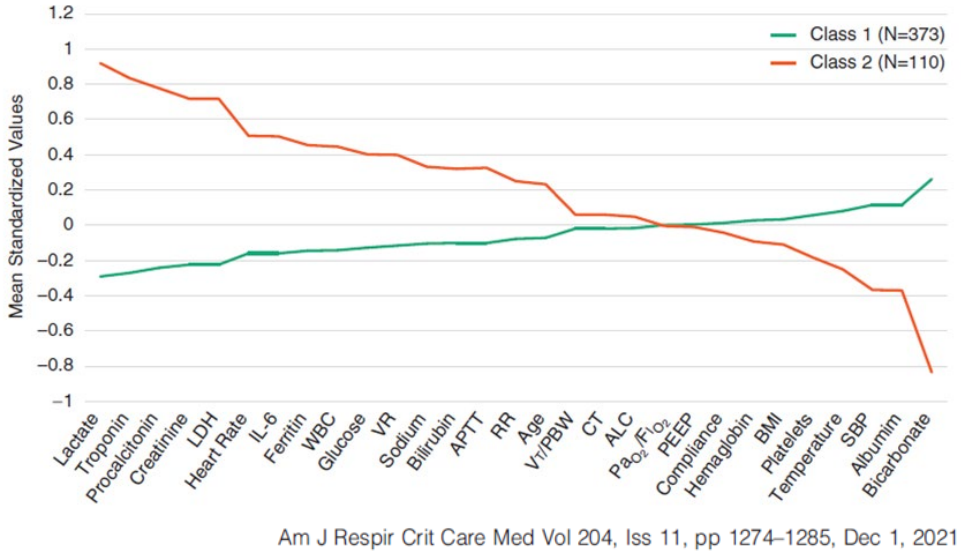



Am J Respir Crit Care Med Vol 195, Iss 3, pp 331–338, Feb 1, 2017

# Hypoinflamatorní fenotyp




Am J Respir Crit Care Med Vol 204, Iss 11, pp 1274–1285, Dec 1, 2021

- Nízká/žádná podpora oběhu
- Normální bikarbonát
- Normální nebo jen mírně snížený albumin
- Normální laktát
- Bez výrazné trombocytopenie
- Nižší IL-6 (cca do 500), Nízké PCT

# Statiny

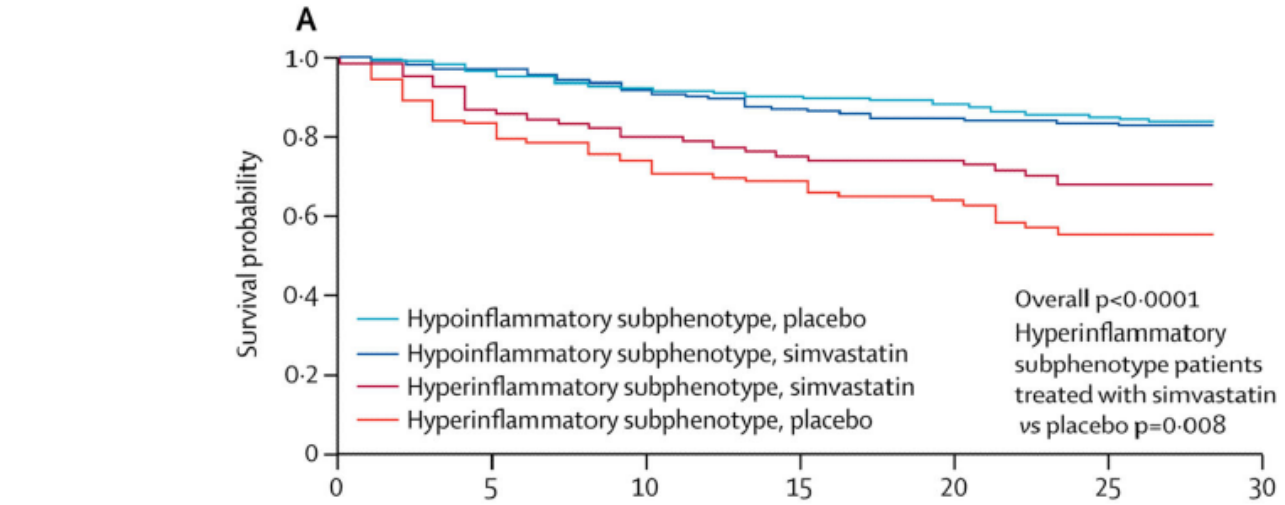
20

Simvastatin 80 mg/d do 48 h od dg. ARDS, max 28 dní

*Lancet Respir Med.* 2018 September ; 6(9): 691–698. doi:10.1016/S2213-2600(18)30177-2.

# ARDS Subphenotypes and Differential Response to Simvastatin: Secondary Analysis of a Randomized Controlled Trial

**Carolyn S. Calfee, MD[1,2,3], Kevin L. Delucchi, PhD[4] [Professor], Pratik Sinha, PhD[1], Michael A. Matthay, MD[1,2,3] [Professor], Jonathan Hackett, MBBCh[5], Manu Shankar-Hari, PhD[6,7], Cliona McDowell, MSc[8], John G. Laffey, MD[9,10,11] [Professor], Cecilia M. O'Kane, PhD[5], Daniel F. McAuley, MD[5,12] [Professor], and Irish Critical Care Trials Group**




| Number at risk | | | | | | |
|---|---|---|---|---|---|---|
| Hypoinflammatory subphenotype, placebo | 178 | 172 | 164 | 161 | 157 | 151 |
| Hypoinflammatory subphenotype, simvastatin | 175 | 170 | 161 | 152 | 148 | 146 |
| Hyperinflammatory subphenotype, simvastatin | 84 | 73 | 67 | 63 | 62 | 57 |
| Hyperinflammatory subphenotype, placebo | 102 | 85 | 75 | 70 | 65 | 56 |

Systematic Review and Meta-Analysis

Medicine®

OPEN

# The effects of statin therapy on mortality in patients with sepsis

## A meta-analysis of randomized trials

Mengyan Chen, MSc, Mingxia Ji, MSc*, Xiaoshui Si, BS

**Abstract**

**Background:** Much controversy persists regarding the role of statins therapy in patients with sepsis. This systematic review and meta-analysis of randomized trials aimed to evaluate the clinical efficacy of statin therapy on mortality from sepsis.

**Methods:** We comprehensively searched PubMed, Embase, and Cochrane controlled trials register for relevant clinical studies. Randomized controlled trials reporting the effect of statin therapy on mortality in septic patients were included. Pooled risk estimates were calculated with a fixed-effects model. Heterogeneity was determined by Cochran chi-square test and the $I^2$ statistic.

**Results:** Nine trials with a total of 2333 patients were included. Seven randomized trials were eligible for the in-hospital mortality analysis. There were 257 deaths among 1078 individuals in the statin treatment group and 268 deaths among 1081 individuals in the control group. There was no statistically significant difference (RR, 0.96; 95% CI, 0.83–1.11). Five randomized trials reported data on 28 day-hospital mortality. There were 123 deaths among 613 individuals in the statin treatment group and 141 deaths among 633 individuals in the control group. There was no statistically significant difference (RR, 0.90; 95% CI, 0.73–1.11).

**Conclusion:** This systematic review and meta-analysis of randomized trials indicates that statin therapy has no effect on mortality outcomes in patients with sepsis compared with placebo.

**Abbreviations:** CI = confidence interval, ICU = intensive care unit, RR = relative risk, SIRS = systemic inflammatory response syndrome.

**Keywords:** meta-analysis, mortality, sepsis, statins

# Hodnocení

- Potenciální benefit u hyperinflammatorního fenotypu
- Nejasný efekt při kombinaci s dalšími imunomodulačními postupy (kortikoidy)
- Potenciální závažné NÚ
- Pragmatický závěr: ponechat, ale nenasazovat z této indikace

# Kortikoidy

Moderate to severe ARDS
20 mg of dexamethason per day (1st to 5th day)
10 mg of dexamethrasion per day (6th to 10th day)

Systematic Review and Meta-Analysis

Medicine

OPEN

# Dexamethasone for the treatment of acute respiratory distress syndrome

## A systematic review and meta-analysis

Long-hua Feng, MM[a,*], Xiao-dan Li, MM[a,*], Xiao-yu Zhang, MM[b], Peng-jiang Cheng, MB[a], Zheng-yun Feng, MB[a,*]

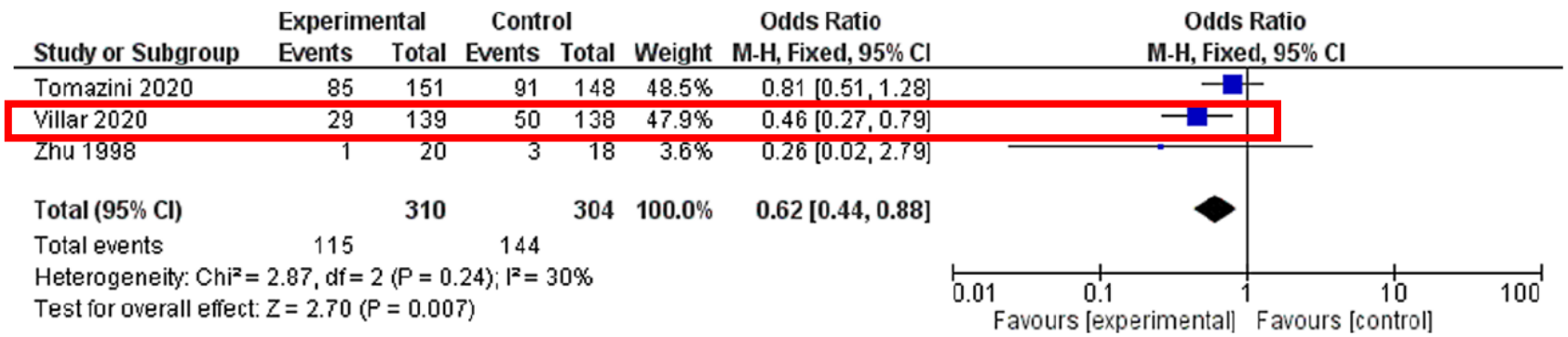
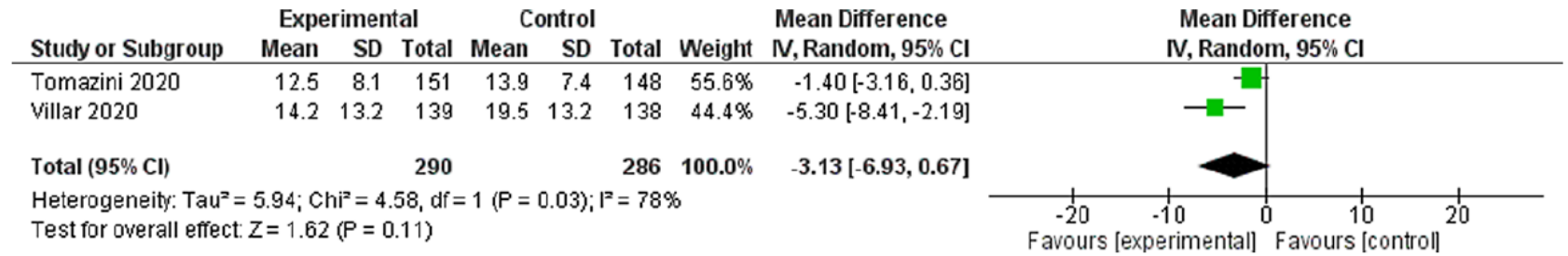
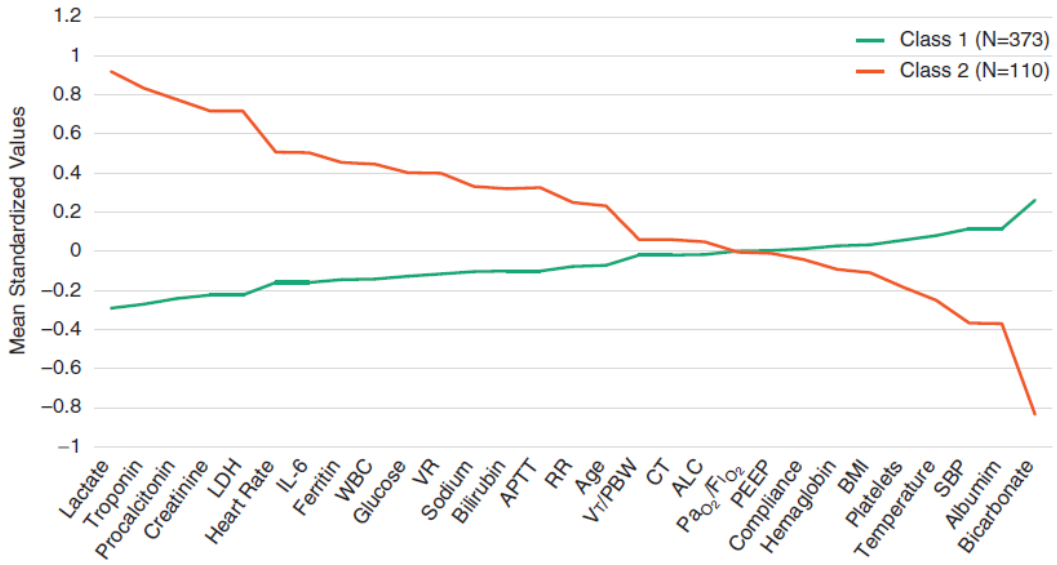


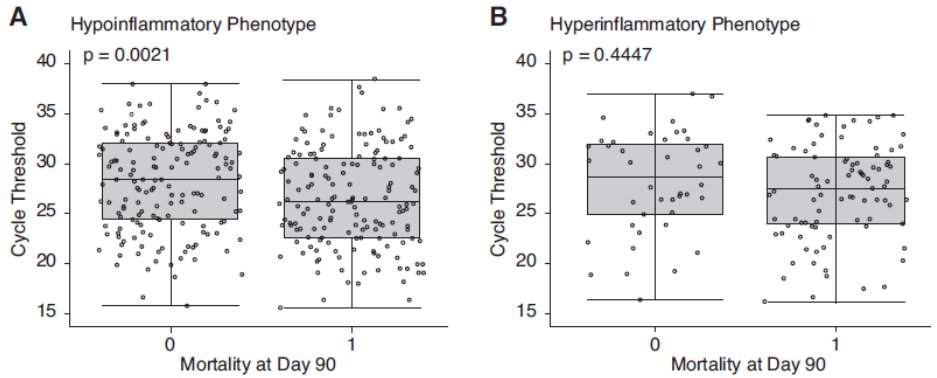

Figure 3. Meta-analysis of all-cause mortality.






# Latent Class Analysis Reveals COVID-19–related Acute Respiratory Distress Syndrome Subgroups with Differential Responses to Corticosteroids

Pratik Sinha[1*], David Furfaro[2*], Matthew J. Cummings[2], Darryl Abrams[2], Kevin Delucchi[3], Manoj V. Maddali[4], June He[1], Alison Thompson[2], Michael Murn[2], John Fountain[5], Amanda Rosen[5], Shelief Y. Robbins-Juarez[6], Matthew A. Adan[6], Tejus Satish[6], Mahesh Madhavan[7], Aakriti Gupta[7], Alexander K. Lyashchenko[8], Cara Agerstrand[2], Natalie H. Yip[2], Kristin M. Burkart[2], Jeremy R. Beitler[2], Matthew R. Baldwin[2], Carolyn S. Calfee[9,10,11‡], Daniel Brodie[2‡], and Max R. O'Donnell[2,12‡]




| Corticosteroid Use | ARDS Subphenotype: Hypoinflammatory | ARDS Subphenotype: Hyperinflammatory | *P* Value |
|---|---|---|---|
| Yes | 115/226 (51%) | 57/94 (61%) | 0.0295 |
| No | 51/113 (45%) | 37/48 (77%) | |

| Corticosteroid Use | COVID-19–related ARDS Class: Class 1 | COVID-19–related ARDS Class: Class 2 | *P* Value |
|---|---|---|---|
| Yes | 120/244 (49%) | 52/76 (68%) | 0.0273 |
| No | 58/127 (46%) | 30/34 (88%) | |

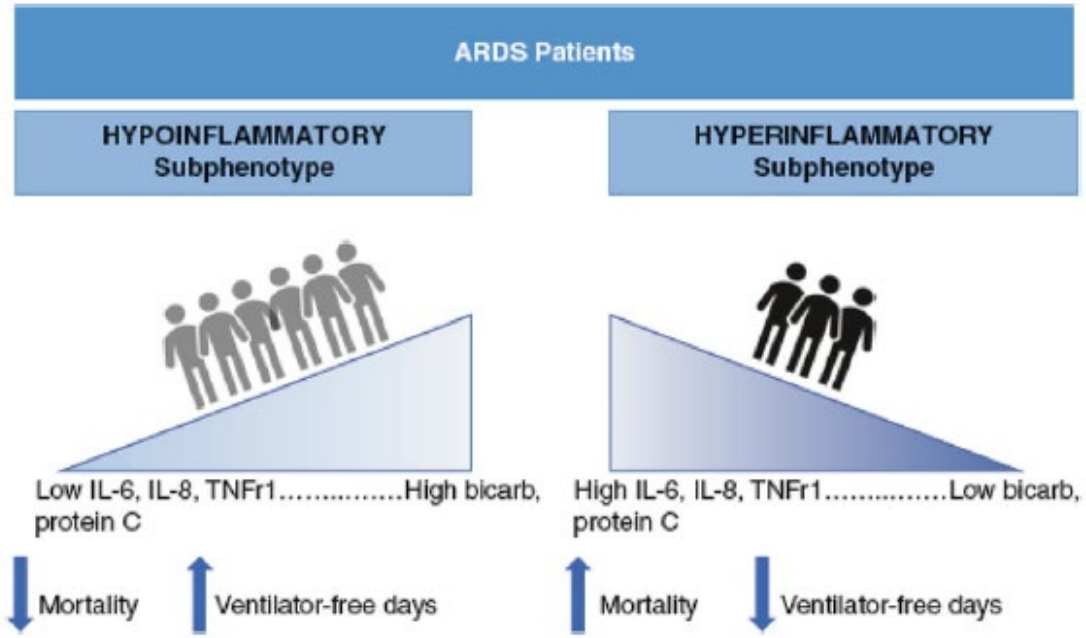
Am J Respir Crit Care Med Vol 204, Iss 11, pp 1274–1285, Dec 1, 2021

# Hodnocení

- **Septická dávka hydrocortisonu** u pacientů se septických šokem
- **Časný ARDS (+ hyperinflamatorní subfenotyp)** – Dexamethason
- **CAP** (+hyperinflamatorní subfenotyp?)
  - Hydrokortison 200 mg iv bolus následovaný infuzí 10 mg/h na 7 dní
  - nebo
  - Methylprednisolon 0,5 mg/kg iv každých 12 h po 7 dní (zahájení do 36 h od přijetí do nemocnice, C reaktivní protein >150 mg/l
  - nebo
  - Methylprednisolon 40 mg iv bolus, poté
    - Dny 1–7: 40 mg/d
    - Dny 8–14: 20 mg/d
    - Dny 15–17: 12 mg/d
    - Dny 18–20: 4 mg/d


- Chaudhuri D, Nei AM, Rochwerg B, Balk RA, Asehnoune K, Cadena R, Carcillo JA, Correa R, Drover K, Esper AM, Gershengorn HB, Hammond NE, Jayaprakash N, Menon K, Nazer L, Pitre T, Qasim ZA, Russell JA, Santos AP, Sarwal A, Spencer-Segal J, Tilouche N, Annane D, Pastores SM. 2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia. Crit Care Med. 2024 May 1;52(5):e219-e233. doi: 10.1097/CCM.0000000000006172.

# Tekutinová terapie




Wilson and Calfee *Critical Care* (2020) 24:102
https://doi.org/10.1186/s13054-020-2778-x

Critical Care

REVIEW Open Access

# ARDS Subphenotypes: Understanding a Heterogeneous Syndrome

Jennifer G. Wilson[1] and Carolyn S. Calfee[2,3*]

| Intervention/trial cohort analyzed | Outcome | Hypoinflammatory subphenotype response | | Hyperinflammatory subphenotype response | |
|---|---|---|---|---|---|
| | | Intervention | Control | Intervention | Control |
| High vs. low PEEP/ ALVEOLI* [27] | 90-day mortality | 24% high PEEP | 16% low PEEP | 42% high PEEP | 51% low PEEP |
| Conservative vs. liberal fluid strategy/ FACCT* [29] | 90-day mortality | 18% conservative fluid strategy | 26% liberal fluid strategy | 50% conservative fluid strategy | 40% liberal fluid strategy |
| Simvastatin/ HARP-2 [40] | 28-day survival | No difference | | Improved survival with simvastatin ($p$ = 0.008) | |
| Rosuvastatin/SAILS [41] | 90-day mortality | No difference | | No difference | |

*PEEP* positive end-expiratory pressure; *$p$ value <0.05 for interaction between treatment and subphenotype

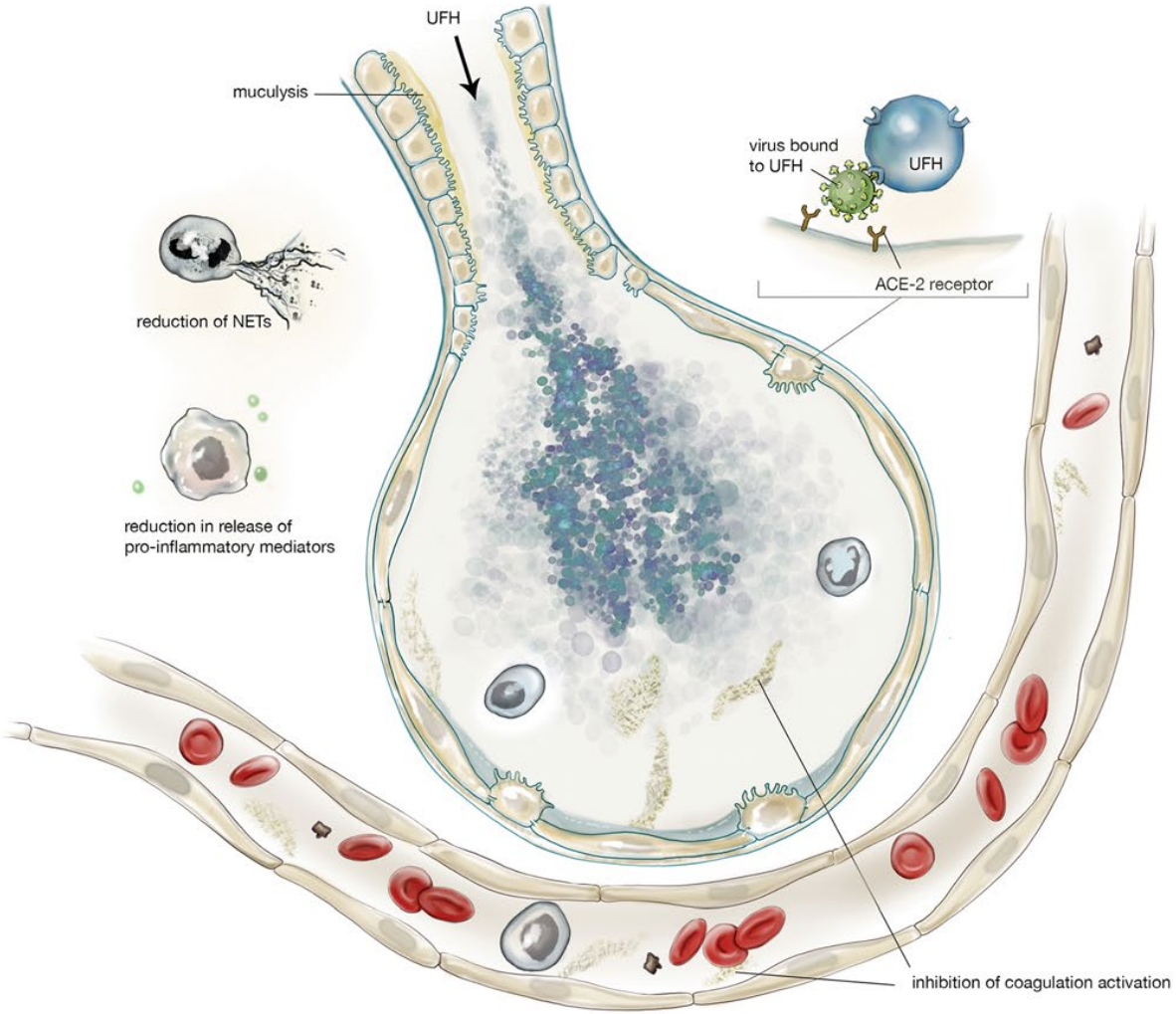
# Co ještě máme (klinicky k dispozici)?

# Další

- ASA, aprotinin, heparin,  ..
- Albumin
- Anti-endothelin 1 (bosentan)
- Sildenafil
- Epoprostenol
- Sivelestat
- Dornása alfa
- Přípravky tradiční čínské medicíny
- …

# Inhalační aplikace heparinu

B




# Nebulised heparin as a treatment for COVID-19: scientific rationale and a call for randomised evidence

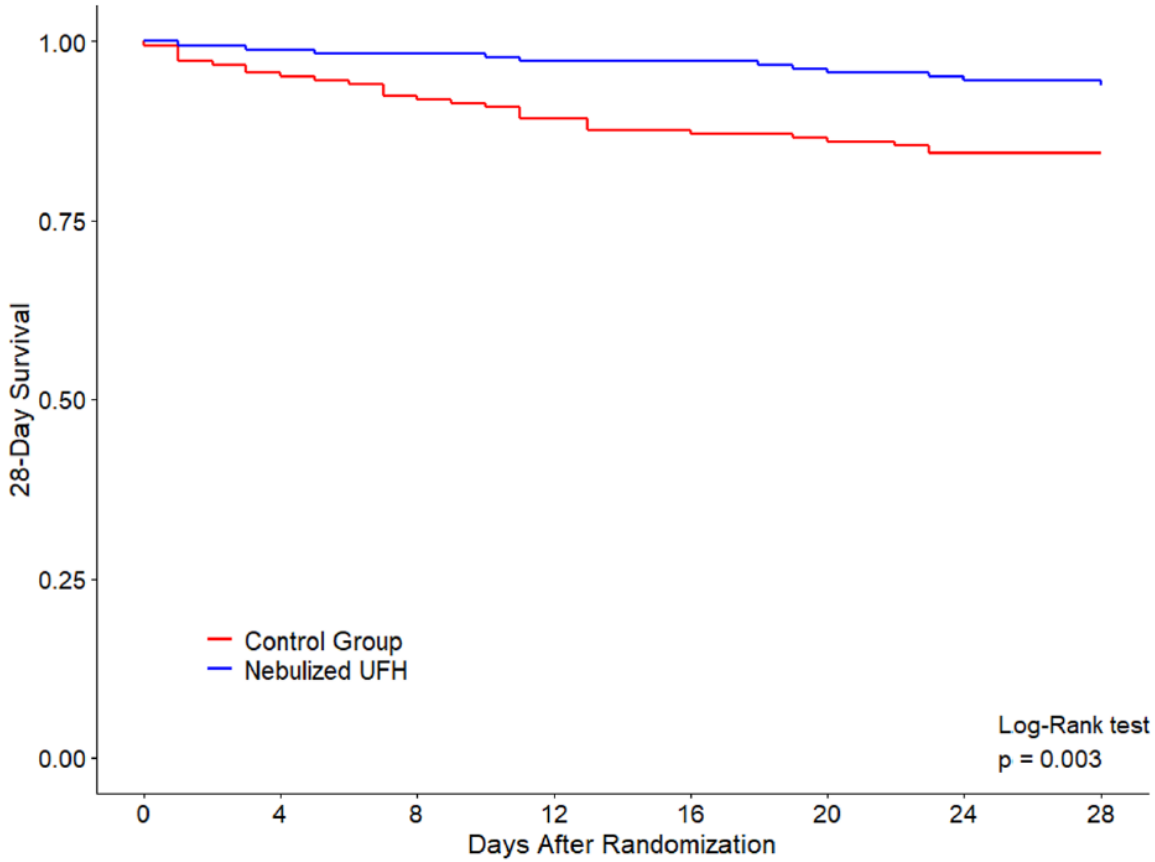
Frank M. P. van Haren[1,2*], Clive Page[3], John G. Laffey[4,5], Antonio Artigas[6], Marta Camprubi-Rimblas[7], Quentin Nunes[8], Roger Smith[9], Janis Shute[10], Mary Carroll[11], Julia Tree[12], Miles Carroll[12], Dave Singh[13], Tom Wilkinson[11] and Barry Dixon[9]

- Vazba SARS-CoV2 na ACE-2 receptor alveolárních buněk
- Tvorba hyalinních membrán
- Mikrovaskulární trombóza
- Antiinflamatorní vlastnosti
- Snížení tvorby NETs
- Sekretolytické vlastnosti

van Haren *et al. Critical Care* (2020) 24:454
https://doi.org/10.1186/s13054-020-03148-2

# Efficacy of inhaled nebulised unfractionated heparin to prevent intubation or death in hospitalised patients with COVID-19: an investigator-initiated international meta-trial of randomised clinical studies

Frank M. P. van Haren,[a,b,*] Sarah J. Valle,[b] Ary Serpa Neto,[c,d] Marcus J. Schultz,[e,f] John G. Laffey,[g,h] Antonio Artigas,[i] Barry Dixon,[j] Alicia B. Vilaseca,[k] Ruben A. Barbera,[k] Tarek I. Ismail,[l] Rabab S. Mahrous,[m] Mohamed Badr,[n] Gilberto DeNucci,[o,p] Carlos Sverdloff,[o,q] Marta Camprubi-Rimblas,[i] David W. Cosgrave,[g,h] Bairbre McNicholas,[g,h] Catriona Cody,[r] Gerard Curley,[s] Thomas L. Smoot,[t] Sabrina Staas,[t] Khine Sann,[t] Caitlin Sas,[t] Anusha Belani,[t] Christopher Hillman,[t] Sidharta Kusuma Manggala,[u] Dita Aditianingsih,[u,v] Adhrie Sugiarto,[u] Mira Yulianti,[u] Herikurniawan Herikurniawan,[u] Robert Sinto,[u] Aino Nindya Auerkari,[v] Septian Adi Permana,[w] Ashley Woodcock,[x] Mary Carroll,[y] Tom Wilkinson,[y] Dave Singh,[z] Janis Kay Shute,[aa] Miles Carroll,[ab] and Clive Page[ac]




10000 - 25000j (5 ml) á 6-8 h

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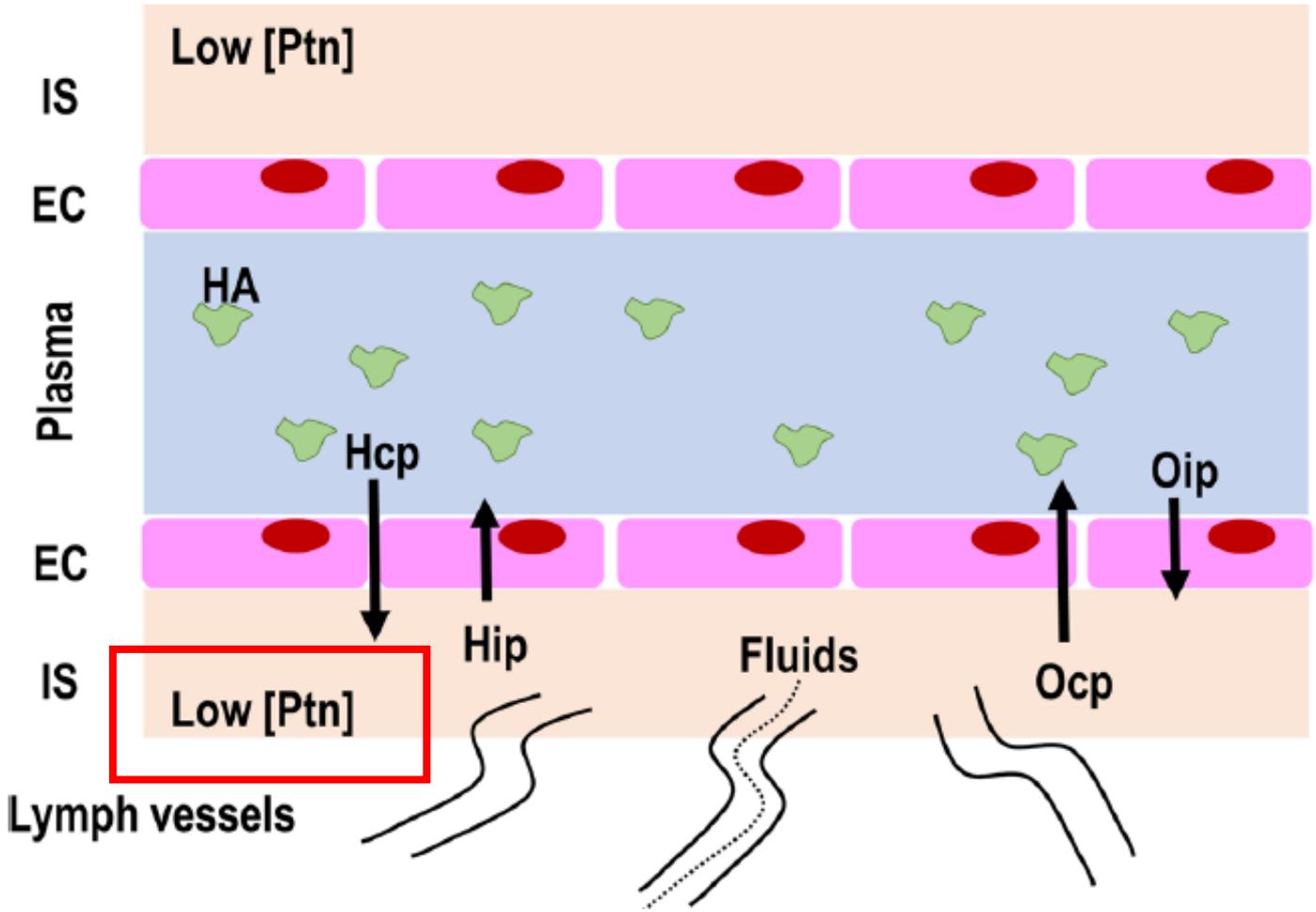
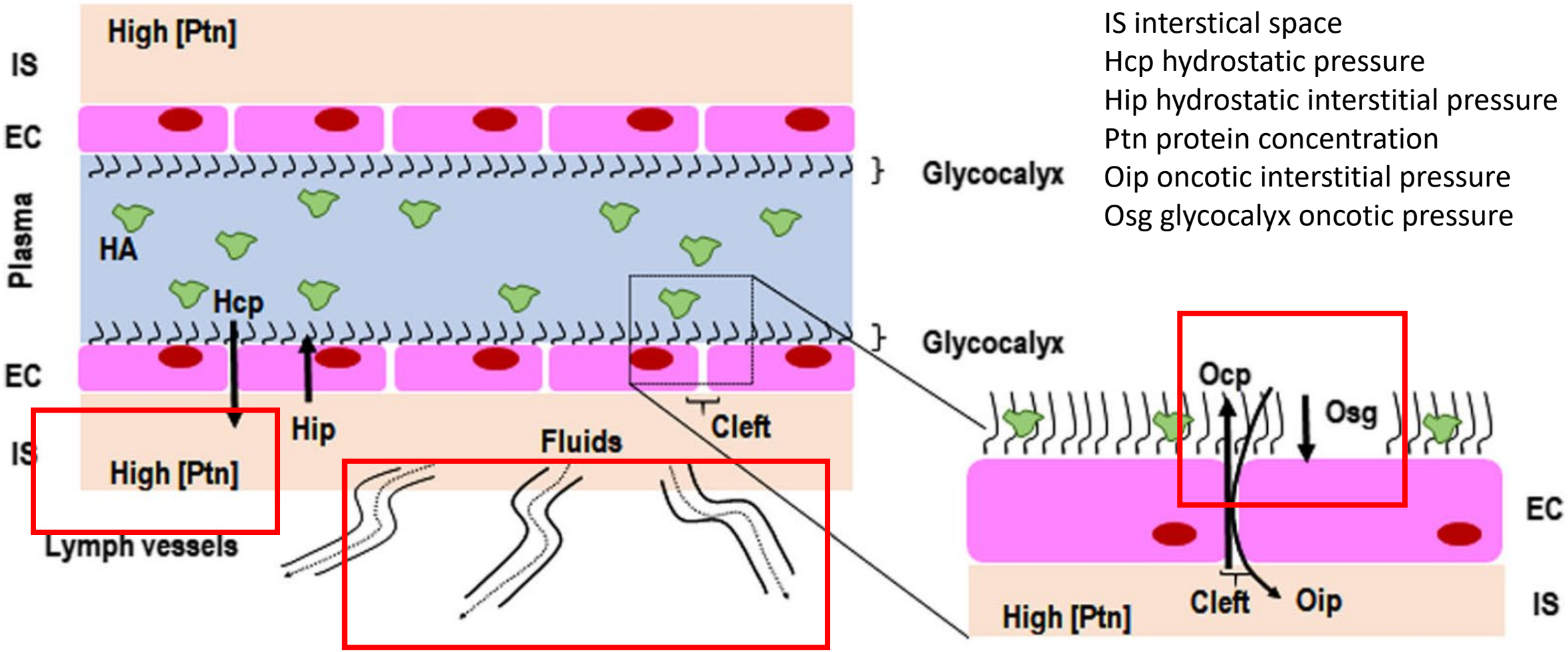
# Závěry

- Základem je řešení příčiny + podpůrná terapie
- Pacienti tvoří heterogenní populaci, efekt intervencí pravděpodobně závisí na konkrétní subpopulaci
- Ke zvážení je časné použití kortikoidů a/nebo simvastatinu
- Nepřiměřená/předčasná restrikce tekutin může být riziková i nemocných s hyperinflamatorním fenotypem
- Řada nových intervencí testovaných při COVID-19, není ale jasný vztah k ostatním nemocných s plicní infekcí

pavel.dostal@fnhk.cz

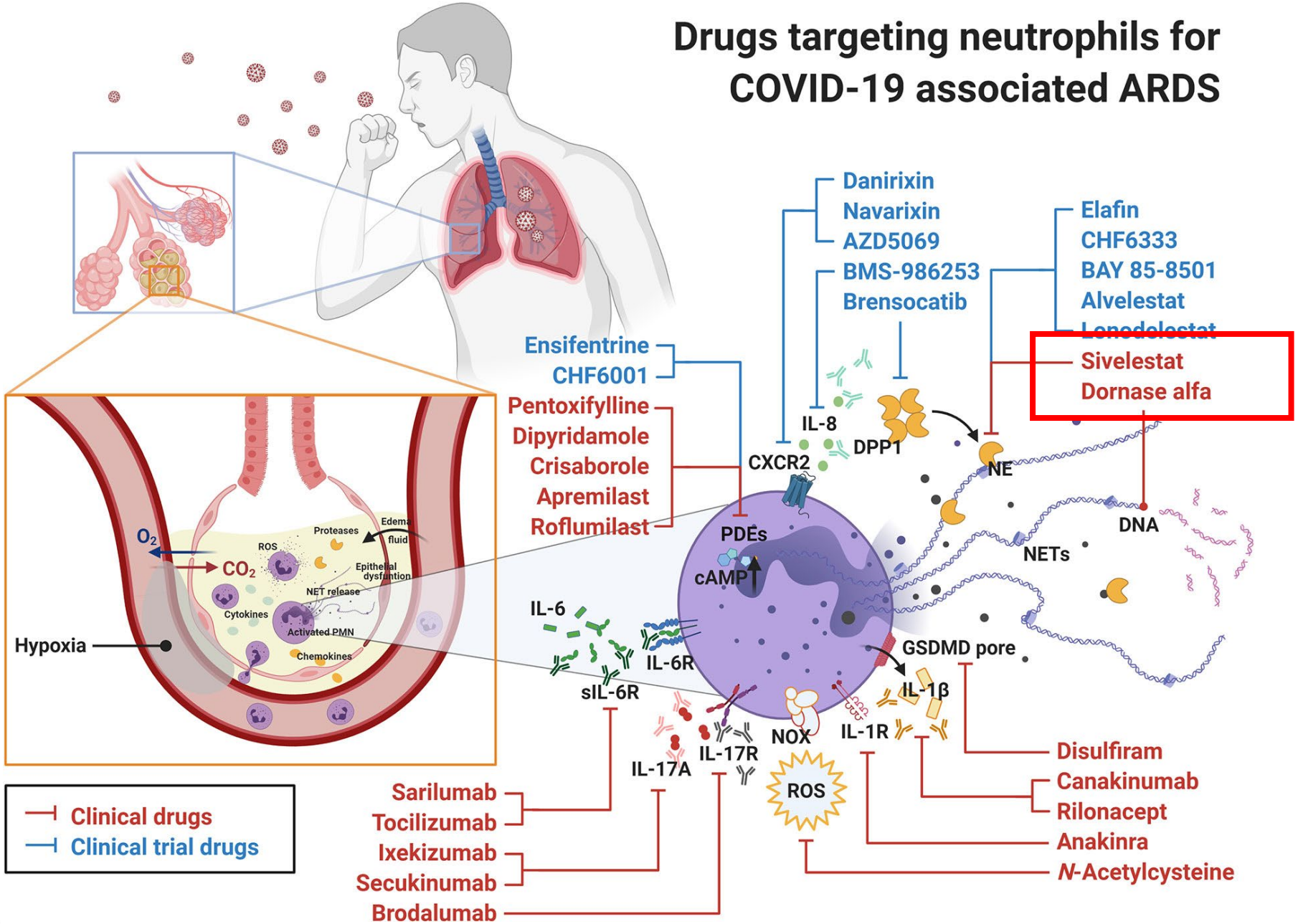
$$\text{Fluid Flow} = K\,[(Hcp - Hip) - \sigma\,(Ocp - Oip)]$$






IS interstical space
Hcp hydrostatic pressure
Hip hydrostatic interstitial pressure
Ptn protein concentration
Oip oncotic interstitial pressure
Osg glycocalyx oncotic pressure

# Drugs targeting neutrophils for COVID-19 associated ARDS




Front. Pharmacol. 11:572009.
doi: 10.3389/fphar.2020.572009

# *Sivelestat*

# Effect of sivelestat sodium in patients with acute lung injury or acute respiratory distress syndrome: a meta-analysis of randomized controlled trials

Shenglan Pu[1], Daoxin Wang[1*], Daishun Liu[2], Yan Zhao[1], Di Qi[1], Jing He[1] and Guoqi Zhou[1]

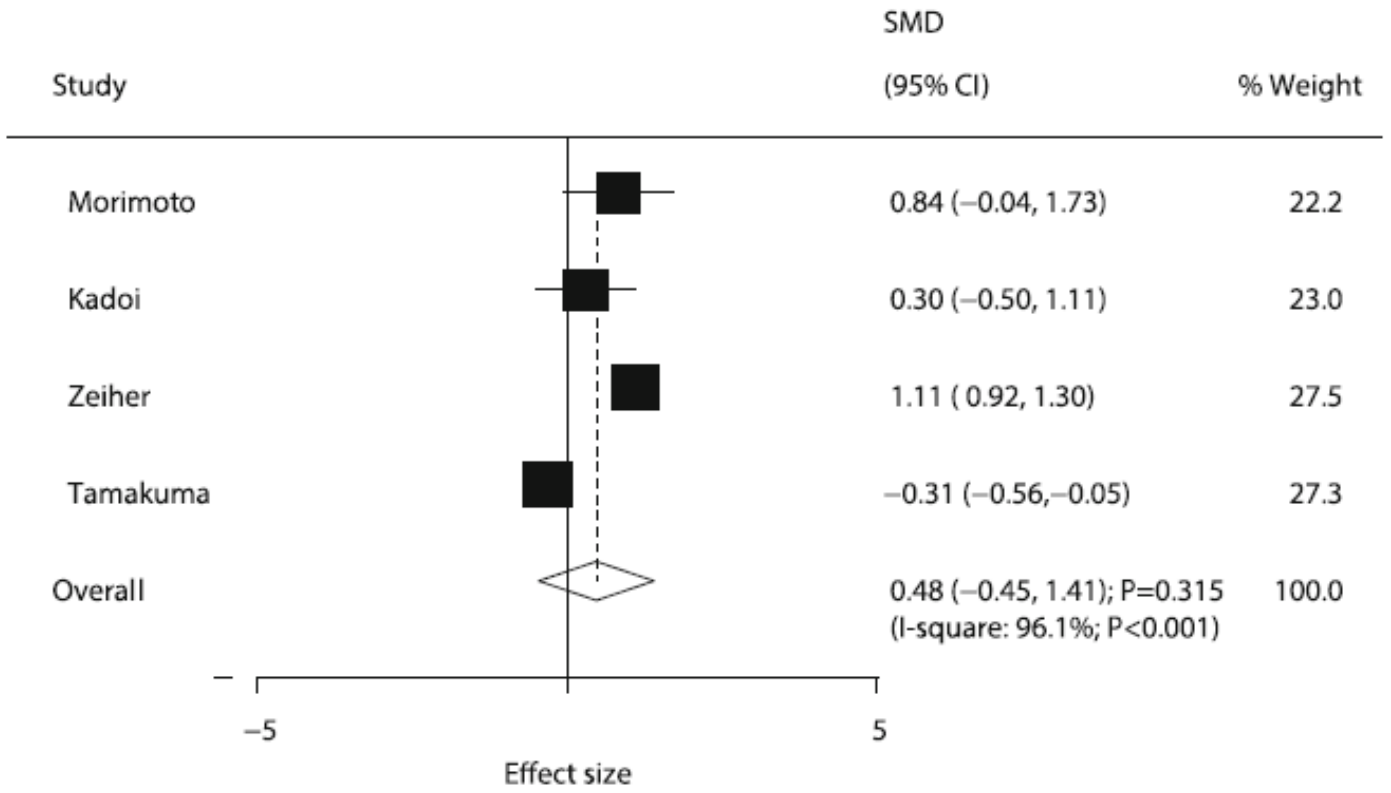


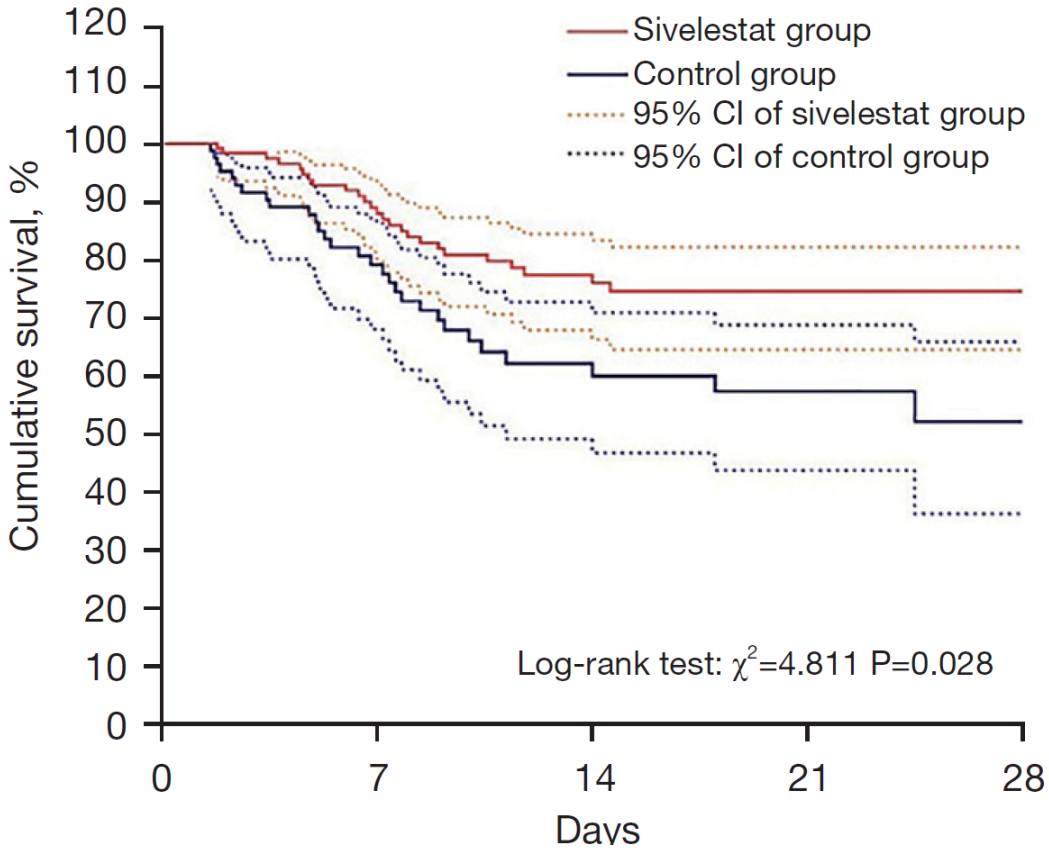

**Fig. 4** Effect of sivelestat therapy on $PaO_2/FiO_2$

Pu *et al. BMC Pulmonary Medicine* (2017) 17:148
DOI 10.1186/s12890-017-0498-z

Sivelestat (Elaspol) has been approved for clinical use in Japan and the Republic of Korea.

## Sivelestat improves clinical outcomes and decreases ventilator-associated lung injury in children with acute respiratory distress syndrome: a retrospective cohort study

Yi Wang[1,2#], Min Wang[2#], Hua Zhang[2], Ying Wang[2], Yanqiang Du[2], Zhangyan Guo[2], Le Ma[2], Yong Zhou[2], Huiping Zhang[3], Li Liu[1]

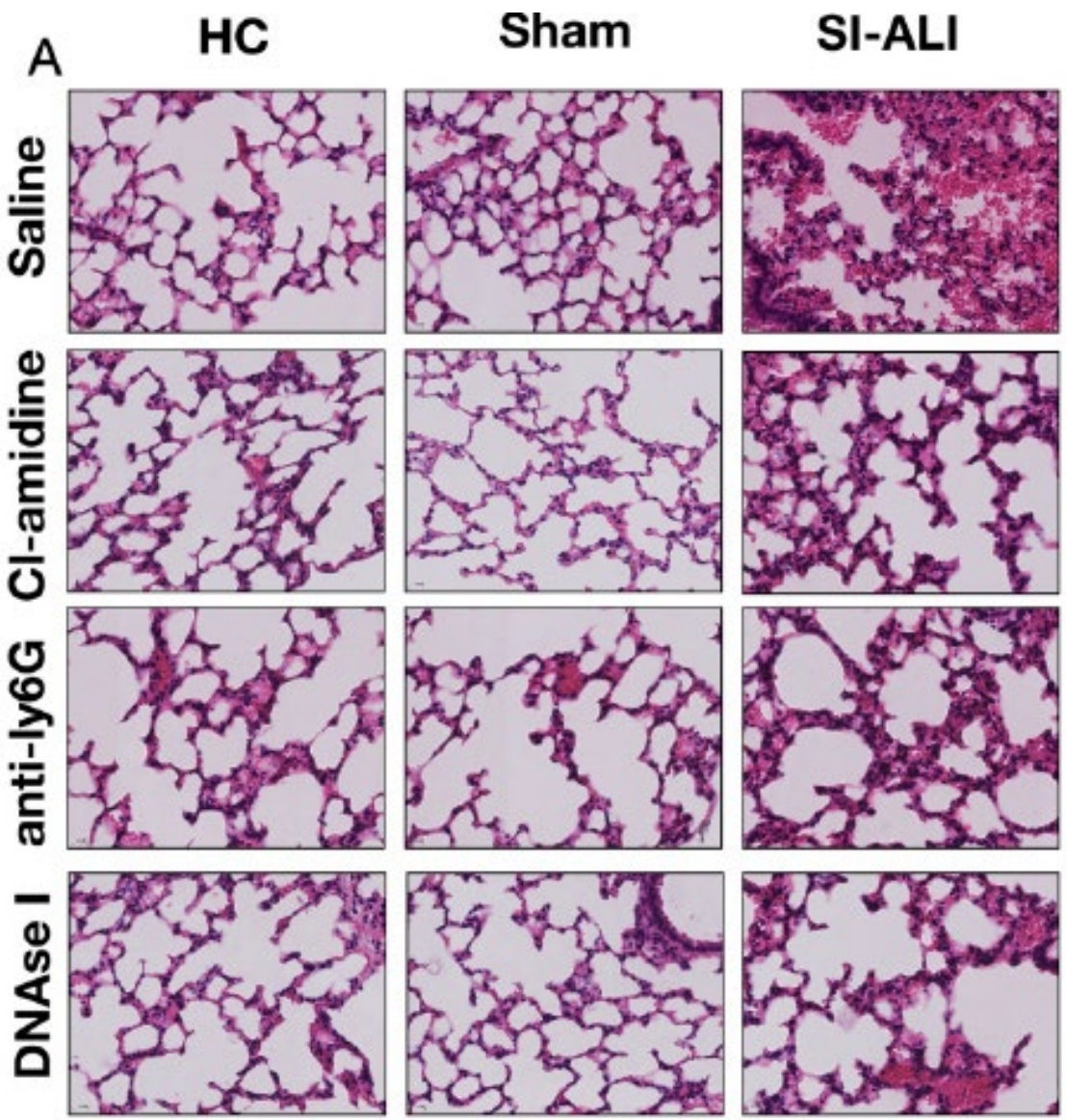



*Transl Pediatr* 2022;11(10):1671-1681 | https://dx.doi.org/10.21037/tp-22-441

# *DNAse*

# Neutrophil extracellular traps mediate m$^6$A modification and regulates sepsis-associated acute lung injury by activating ferroptosis in alveolar epithelial cells

Hao Zhang, MD, PhD[1,3,11*]; Jinlong Liu, PhD[2*]; Yilu Zhou[8*]; Mengdi Qu, PhD[1]; Yanghanzhao Wang, MD[1]; Kefang Guo, MD, PhD[1]; Ruling Shen, PhD[7]; Zhirong Sun, MD, PhD[4]; Juan P. Cata, MD[5,6]; Shuofei Yang, MD, PhD[10]✉; Wankun Chen, MD, PhD[1,2,9]✉ and Changhong Miao, MD, PhD[1,3,9,11]✉




Inhibition of NETs formation

Neutrophil depletion

NETs degradation

**NETs contribute to the progression of sepsis-associated ALI by inducing ferroptosis in alveolar epithelial cells**

**NETs promote METTL3 upregulation by activating the TLR9/MyD88/NF-kβ pathway in alveolar epithelial cells**

**METTL3 knockout inhibits NETs-induced ferroptosis in alveolar epithelial cells and protects mice against sepsis-associated ALI**

*International Journal of Biological Sciences*
2022; 18(8): 3337-3357. doi: 10.7150/ijbs.69141

# Nebulized in-line endotracheal dornase alfa and albuterol administered to mechanically ventilated COVID-19 patients: a case series

Andrew G. Weber[1], Alice S. Chau[2], Mikala Egeblad[3*], Betsy J. Barnes[4*] and Tobias Janowitz[3,5]

## Pulmozyme

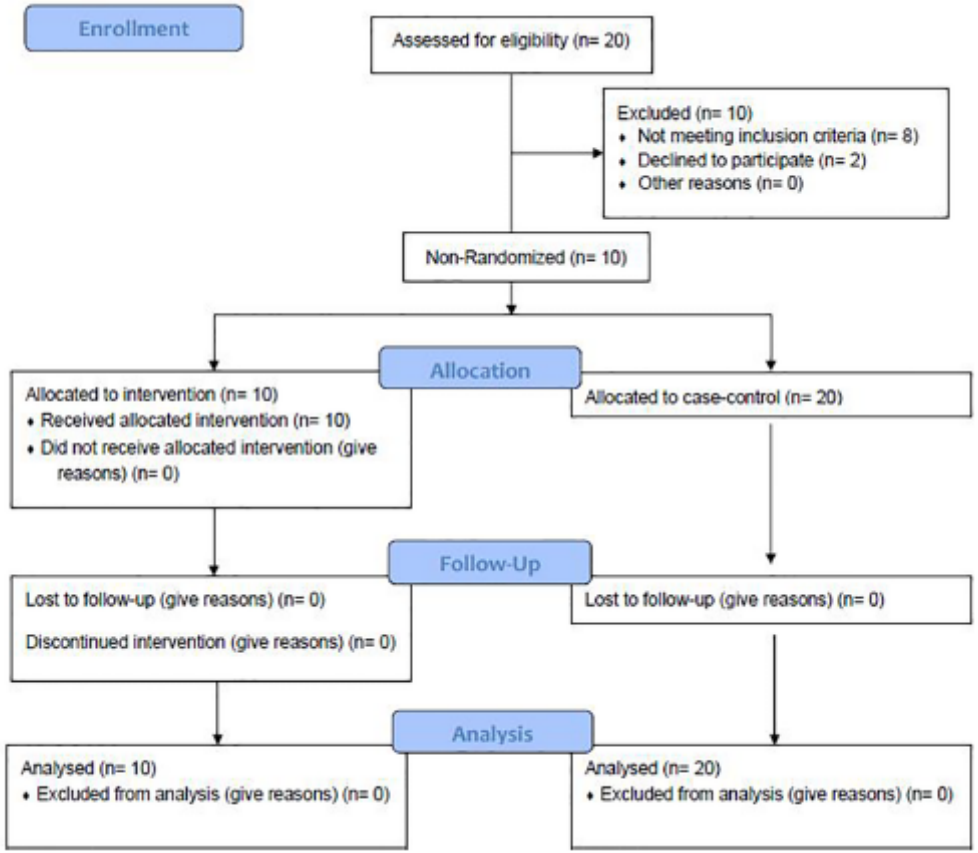
mands. All patients received the same treatment doses: nebulized dornase alfa (2.5 mg) co-administered twice daily with the short-acting $\beta_2$-agonist albuterol (2.5 mg) to improve delivery to the alveoli (referred to as nDA + A). Of note, $\beta_2$-adrenoreceptor agonism may also inhibit NET formation by direct action on neutrophils (Marino et al. 2018). The treatment was administered with an Aerogen® Solo in-line nebulizer to avoid open aerosol generation, which would place staff at risk of exposure to SARS-CoV-2.

ır Medicine (2020) 26:91
https://doi.org/10.1186/s10020-020-00215-w

# Non-Randomized Trial of Dornase Alfa for Acute Respiratory Distress Syndrome Secondary to Covid-19

*Zachary M. Holliday[1*], Alexander P. Earhart[2], Mohammed M. Alnijoumi[1], Armin Krvavac[1], Lee-Ann H. Allen[3] and Adam G. Schrum[3,4,5]*

Patients in the treatment group received nebulized dornase alfa (2.5mL) *via* vibrating mesh through the ventilator circuit twice daily for three days after enrollment. Control group patients

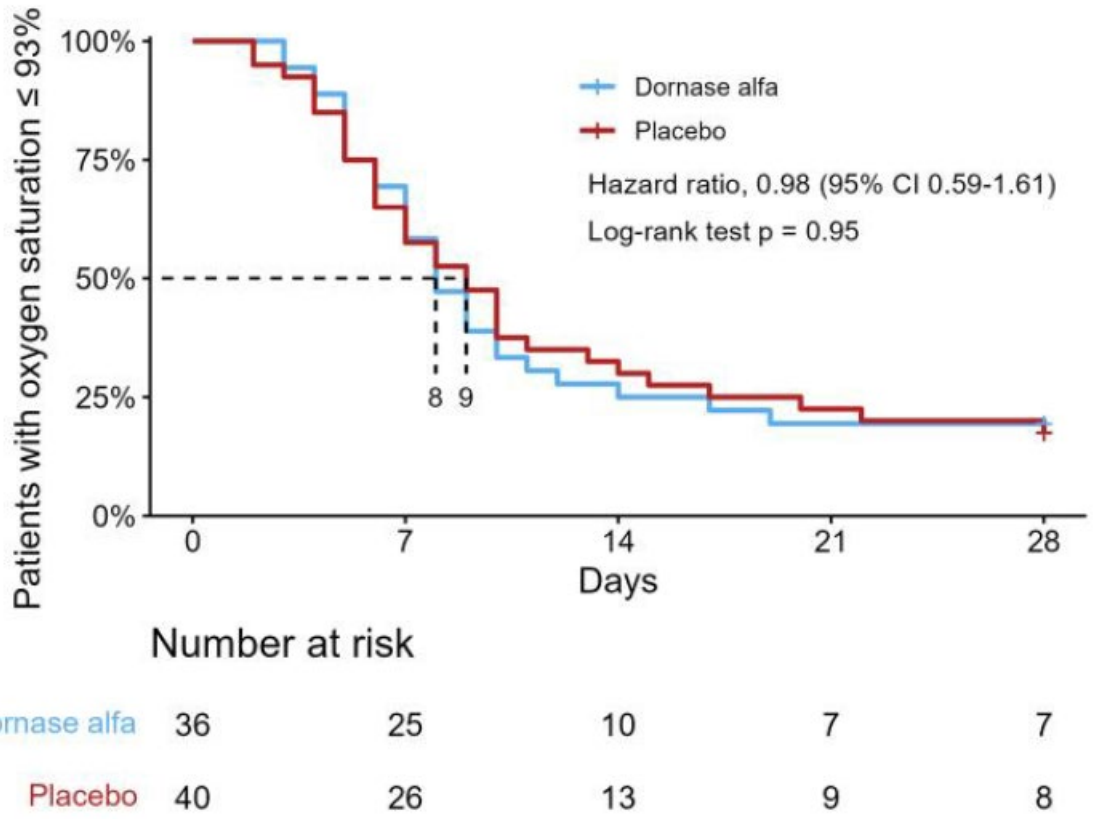



| | | | |
|---|---|---|---|
| Δ Lung compliance from Day 0 (95% CI) | | | |
| Day 1 (mL/cm$H_2O$) | -4.2 to 3.9 | -1.7 to 7.9 | 0.28 |
| Day 2 | -3.1 to 2.3 | -1 to 9 | 0.08 |
| Day 3 | -9.8 to -1.6 | -0.8 to 13.3 | **<0.01** |
| Day 4 | -9.4 to -1.8 | -3.2 to 11.3 | **<0.01** |
| Day 5 | -8.4 to -1.3 | -1.8 to 16.6 | **<0.01** |
| Day 14 | -17.9 to -2.4 | -16.3 to 17.8 | 0.09 |
| Δ PEEP from Day 0 (95% CI) | | | |
| Day 1 (cm$H_2O$) | -0.7 to 1.7 | -0.8 to 1.2 | 0.74 |
| Day 2 | -0.8 to 1.7 | -1.7 to 0.9 | 0.34 |
| Day 3 | -1.1 to 2.4 | -3.1 to 1.3 | 0.27 |
| Day 4 | -1.6 to 2.2 | -4.5 to 1.6 | 0.28 |
| Day 5 | -1.4 to 3.1 | -5.5 to 2 | 0.19 |
| Days on Mechanical Ventilation* | 18.2 (8-38) | 15.2 (5-29) | 0.47 |
| Days in ICU* | 22.1 (11-47) | 16.5 (7-30) | 0.23 |
| Days of Hospitalization* | 28.7 (15-60) | 22.5 (8-52) | 0.61 |
| Secondary Pulmonary Infections** | 5 (25%) | 3 (30%) | 0.78 |
| Mortality, 28-day** | 9 (45%) | 4 (40%) | 0.8 |
| Mortality, 90-day** | 11 (55%) | 4 (40%) | 0.46 |

*Front. Immunol. 12:714833.*
*doi: 10.3389/fimmu.2021.714833*

# Aerosolized Dornase Alfa (DNase I) for the Treatment of Severe Respiratory Failure in COVID-19: A Randomized Controlled Trial

Per Åkesson,[1,2] Lisa Mellhammar,[1,2] Magnus Rasmussen,[1,2] Malin Inghammar,[1,2] Sara Jesperson,[3] Fredrik Månsson,[4] Elin Economou Lundeberg,[5] John Walles,[5,6] Martin Wallberg,[7] Attila Frigyesi,[8] and Adam Linder[1]




https://doi.org/10.1093/ofid/ofaf246