KARIM
1.LF UK A VFN V PRAZE

Specifika těžkých forem Covid19

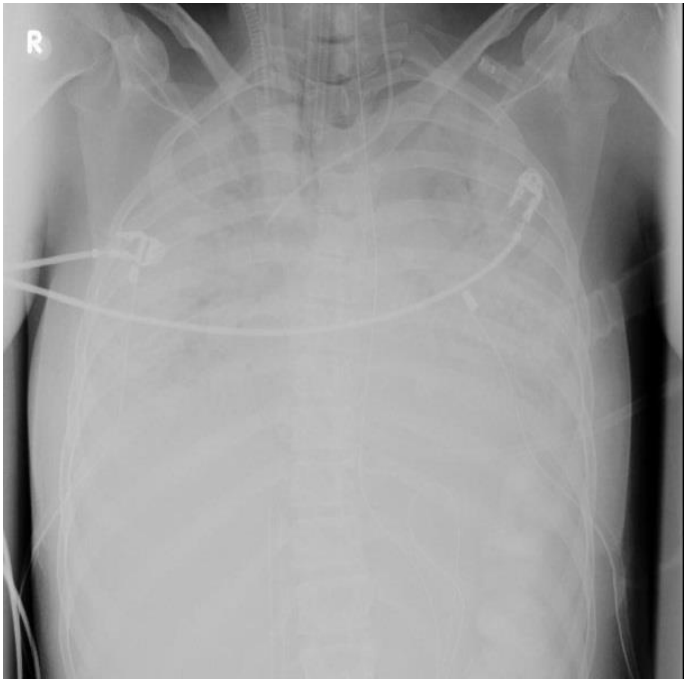
Martin Balík

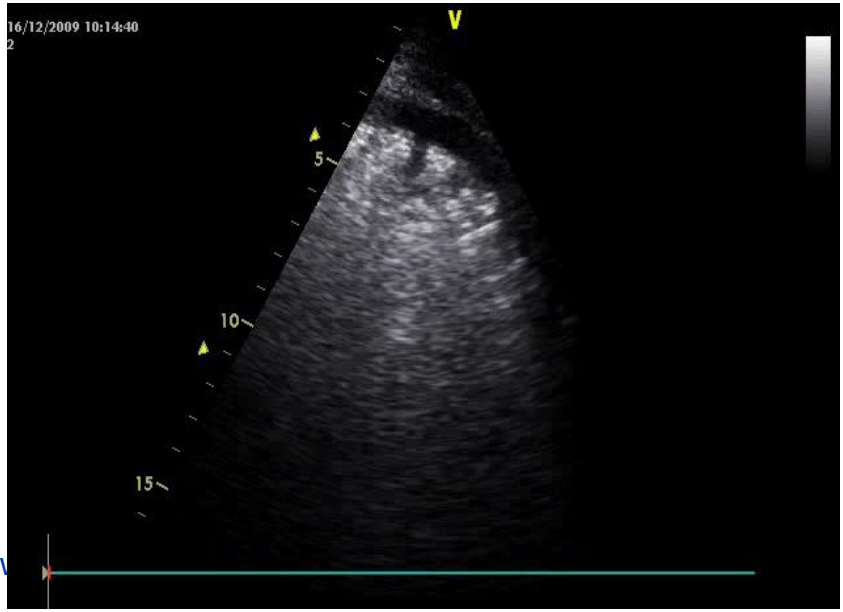
Intenzivista KARIM VFN a 1. LF UK Praha

Klinika anesteziologie, resuscitace a intenzivní medicíny
1. lékařské fakulty UK a Všeobecné fakultní nemocnice v Praze

Adresa: U nemocnice 2; 128 08 Praha 2
www.karim-vfn.cz

Těžké virové pneumonie/primární ARDS na KARIM VFN - od roku 2007……





KARIM
1.LF UK A VFN V PRAZE

www

ECLS Registry Report

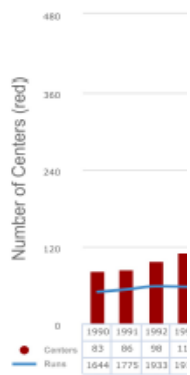
International Summary

January, 2020

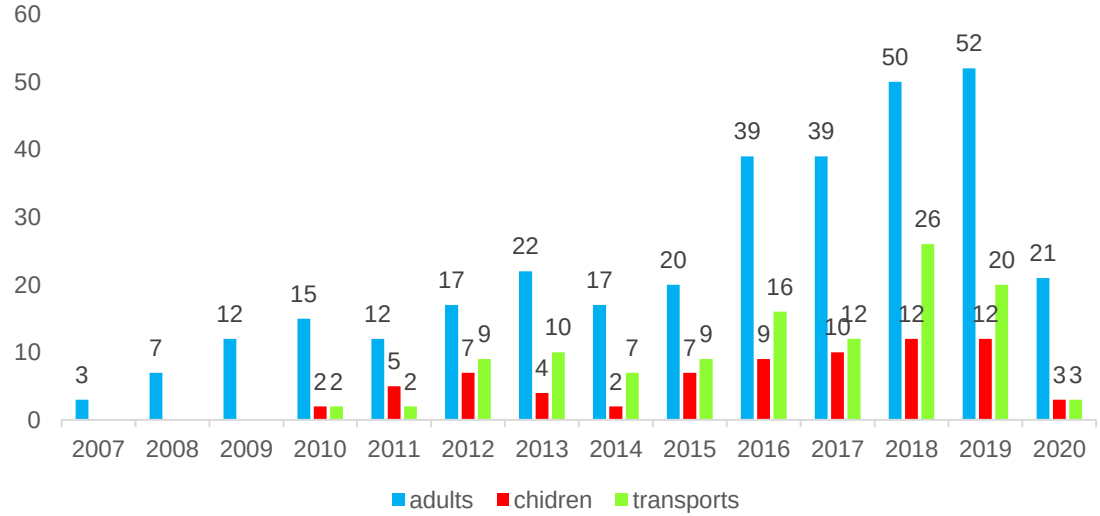
Extracorporeal Life Support Organization
2800 Plymouth Road
Building 300, Room 303
Ann Arbor, MI 48109

Overall Outcomes

	Total Runs	Survived ECLS		Survived to DC or Transfer	
Neonatal					
Pulmonary	32,385	28,417	87%	23,675	73%
Cardiac	8,830	6,097	69%	3,818	43%
ECPR	2,035	1,427	70%	861	42%
Pediatric					
Pulmonary	10,346	7,471	72%	6,199	59%
Cardiac	12,538	9,042	72%	6,667	53%
ECPR	4,945	2,940	59%	2,086	42%
Adult					
Pulmonary	24,395	16,971	69%	14,714	60%
Cardiac					
ECPR					
Total	[redacted]				



ECMO 399 PATIENTS 2007-23.5.2020



KA
1.LF UK A

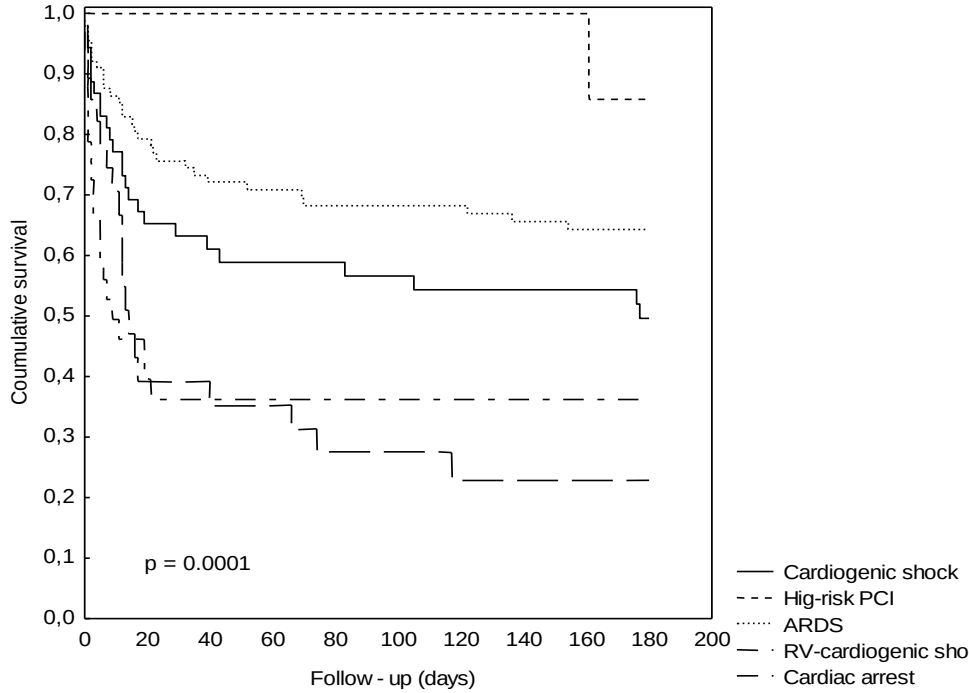
Výsledky ECMO centra VFN

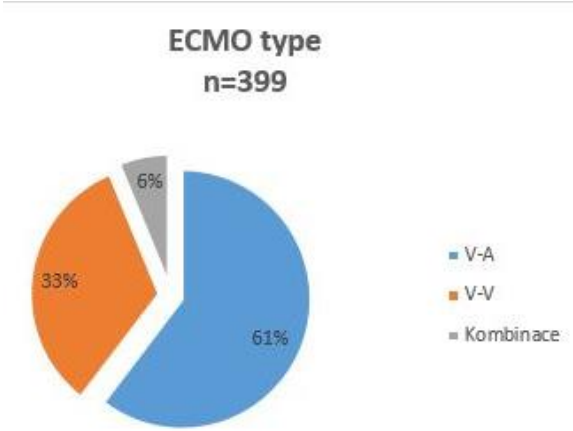
ECMO n=399 + 92 OHCA-H

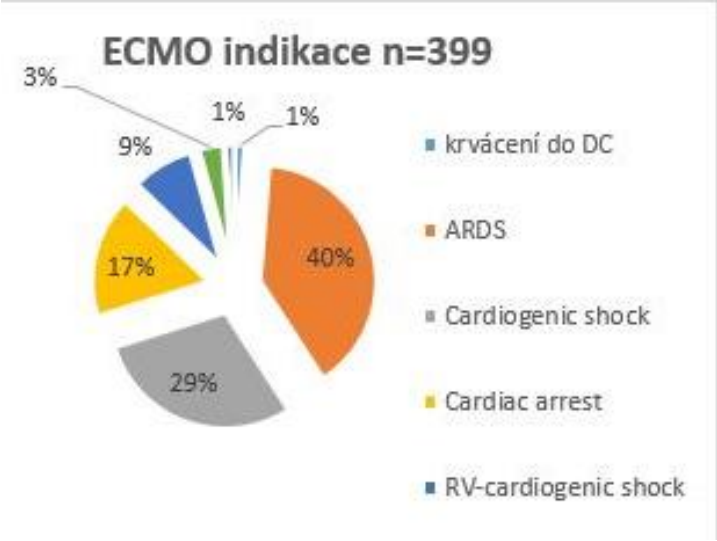
96% urg. kanylace

76% perkutánně intenzivista nebo kardiolog

24% chirurgicky







CRITICAL CARE PERSPECTIVE

Position Paper for the Organization of Extracorporeal Membrane Oxygenation Programs for Acute Respiratory Failure in Adult Patients

Alain Combes[1], Daniel Brodie[2], Robert Bartlett[3], Laurent Brochard[4], Roy Brower[5], Steve Conrad[6], Daniel De Backer[7],

AJRCCM 2014

ASAIO Journal Publish Ahead of Print

DOI: 10.1097/MAT.0000000000001173

Initial ELSO Guidance Document: ECMO for COVID-19 Patients with Severe Cardiopulmonary Failure

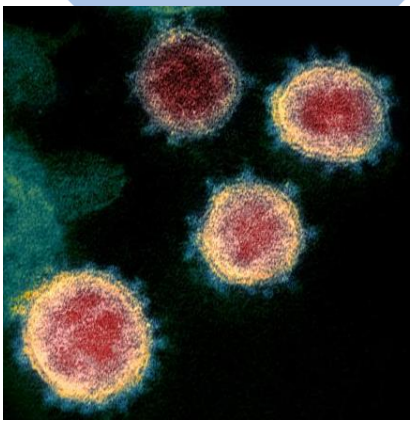
Robert H. Bartlett[1], Mark T. Ogino[2], Daniel Brodie[3], David M. McMullan[4], Roberto Lorusso[5], Graeme MacLaren[6], Christine M. Stead[1], Peter Rycus[1], John F. Fraser[7], Jan Belohlavek[8], Leonardo Salazar[9], Yatin Mehta[10], Lakshmi Raman[11], Matthew L. Paden[12]

ASAIO 2020

Darryl Abrams[1], A. Reshad Garan[2], Akram Abdelbary[3], Matthew Bacchetta[4], Robert H. Bartlett[5], James Beck[6], Jan Belohlavek[7], Yih-Sharng Chen[8], Eddy Fan[9,10], Niall D. Ferguson[9,11], Jo-anne Fowles[12], John Fraser[13], Michelle Gong[14], Ibrahim F. Hassan[15], Carol Hodgson[16,17], Xiaotong Hou[18], Katarzyna Hryniewicz[19], Shingo Ichiba[20], William A. Jakobleff[21], Roberto Lorusso[22], Graeme MacLaren[23,24], Shay McGuinness[25,26,27], Thomas Mueller[28], Pauline K. Park[5], Giles Peek[21], Vin Pellegrino[29], Susanna Price[30], Erika B. Rosenzweig[31], Tetsuya Sakamoto[32], Leonardo Salazar[33], Matthieu Schmidt[34,35], Arthur S. Slutsky[36,37], Christian Spaulding[38], Hiroo Takayama[39], Koji Takeda[39], Alain Vuylsteke[12], Alain Combes[34,35] and Daniel Brodie[1*] for The International ECMO Network (ECMONet) and The Extracorporeal Life Support Organization (ELSO)

ICM 2018

Covid19 ve VFN k 20.5. …..55 pacientů v A6 „Covid19 House“



KARIM RES UP + Pneumologie JIP + IV.int JIP

55 pacientů v intermediární a intenzivní péči

15 z nich na RES UP, 2 x VV-ECMO, 1 x VAV ECMO

LOS 8 (4-21) dní

5 zemřelých, 8 propuštěných z nemocnice, 2 dosud hospitalizováni,1 z nich již překládán (26.5.)

Hospital mortality 33%

Věk 54 (44-77), živí 53 (43-60) let

zemřelí: 77 (75-79) let:

všichni významné komorbidity

Covid19 na ICU je těžká virová pneumonitida s přechodem do ARDS – jako chřipka

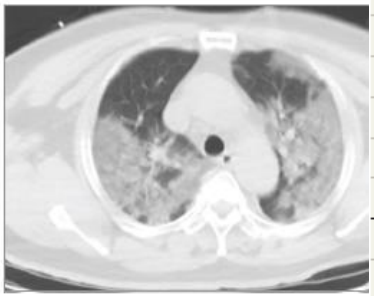
7. února 2020: single centre 138 pts….

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China

Dawei Wang, MD; Bo Hu, MD; Chang H
Zhenshun Cheng, MD; Yong Xiong, MD

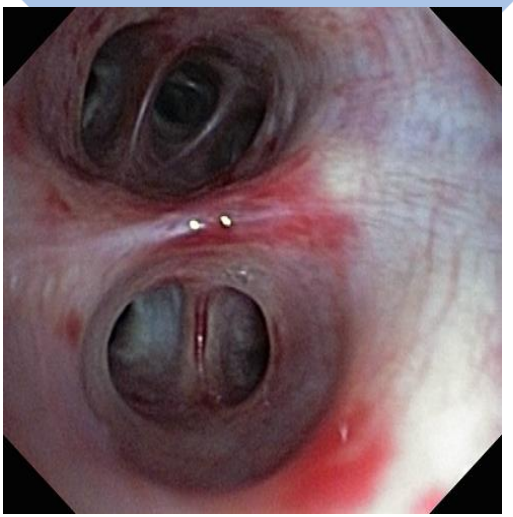
A Computed tomography images on day 5 af

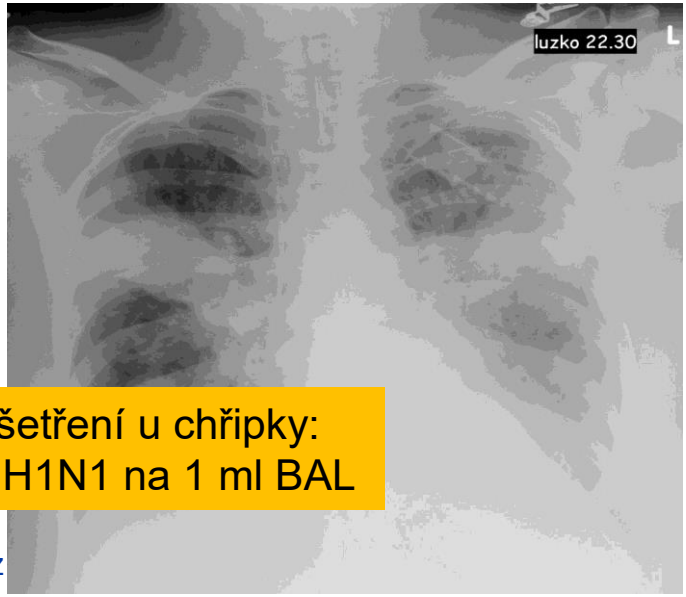


	No. (%)			
	Total (N = 138)	ICU (n = 36)	Non-ICU (n = 102)	*P* Value[a]
Complications				
Shock	12 (8.7)	11 (30.6)	1 (1.0)	<.001
Acute cardiac injury	10 (7.2)	8 (22.2)	2 (2.0)	<.001
Arrhythmia	23 (16.7)	16 (44.4)	7 (6.9)	<.001
ARDS	27 (19.6)	22 (61.1)	5 (4.9)	<.001
AKI	5 (3.6)	3 (8.3)	2 (2.0)	.11
Treatment				
Antiviral therapy	124 (89.9)	34 (94.4)	90 (88.2)	.36
Glucocorticoid therapy	62 (44.9)	26 (72.2)	36 (35.3)	<.001
CKRT	2 (1.45)	2 (5.56)	0	>.99
Oxygen inhalation	106 (76.81)	4 (11.11)	102 (100)	<.001
NIV	15 (10.9)	15 (41.7)	0	<.001
IMV	17 (12.32)	17 (47.22)	0	<.001
ECMO	4 (2.9)	4 (11.1)	0	.004

Covid19 diagnostika na ICU – jako u chřipky

- Pro umístění pacienta je rozhodující klinika
- + PCR pozitivita
- 30-33% negativit z nasopharyngu při pozitivitě z BAL
- Chřipka, H1N1: 27% negativit z nasofaryngu při pozitivitě z BAL
- Kontrolní odběr po pozitivním nejdéle za 14 dní a před propuštěním 2x

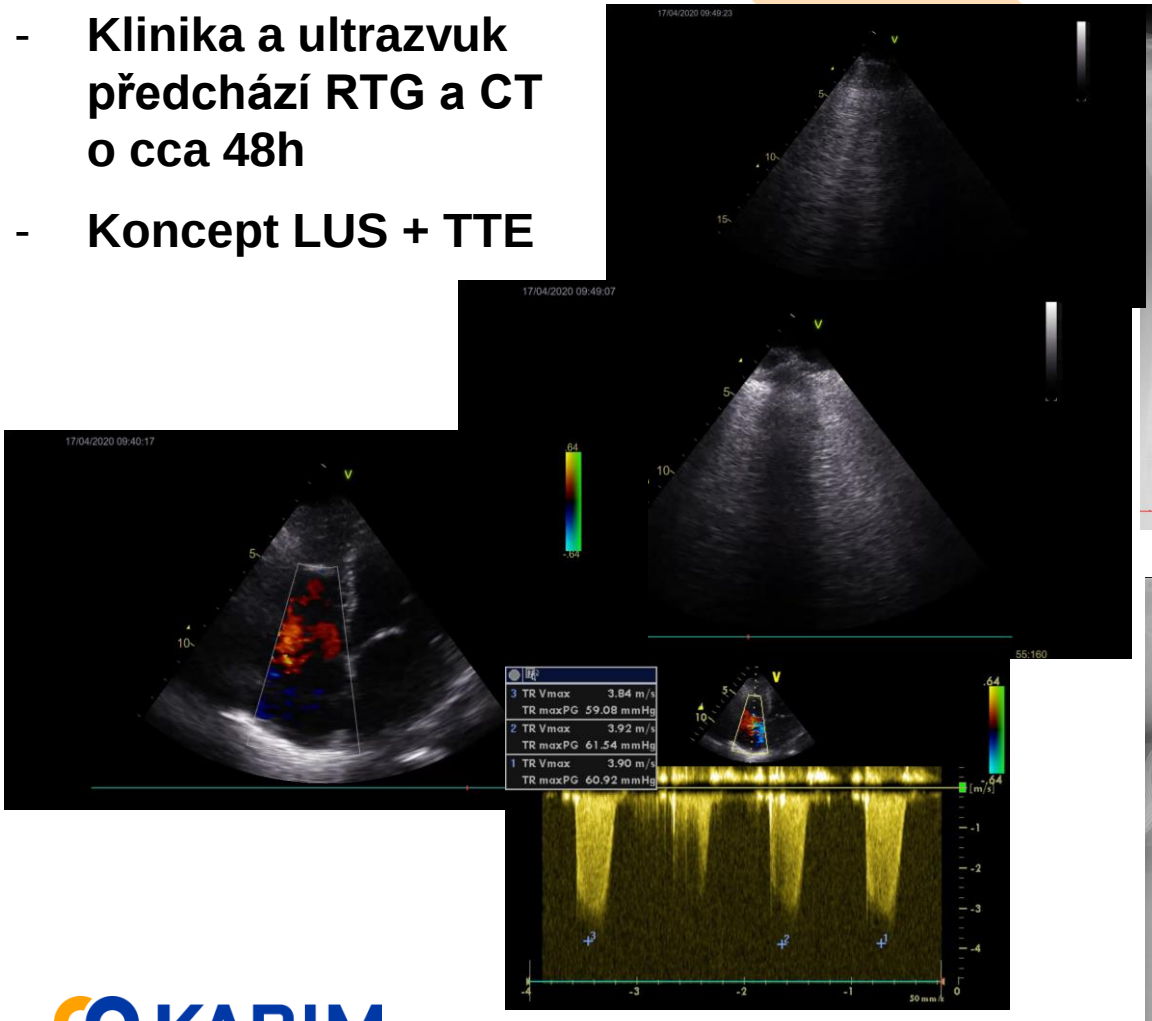


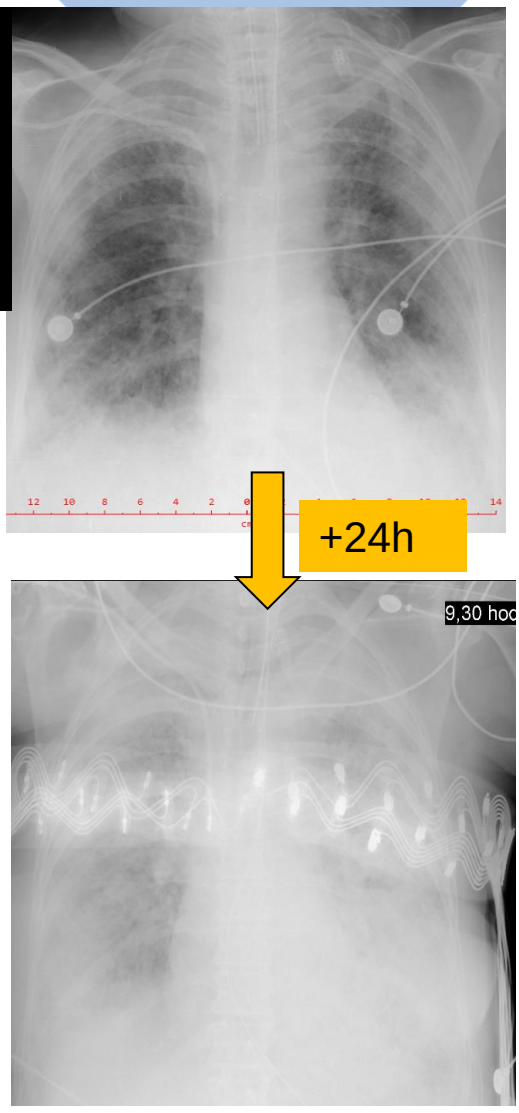


Kvantitativní vyšetření u chřipky:
….1.5 mil kopií H1N1 na 1 ml BAL

Covid19 a zobrazovací metody – jako u chřipky

- Klinika a ultrazvuk předchází RTG a CT o cca 48h
- Koncept LUS + TTE

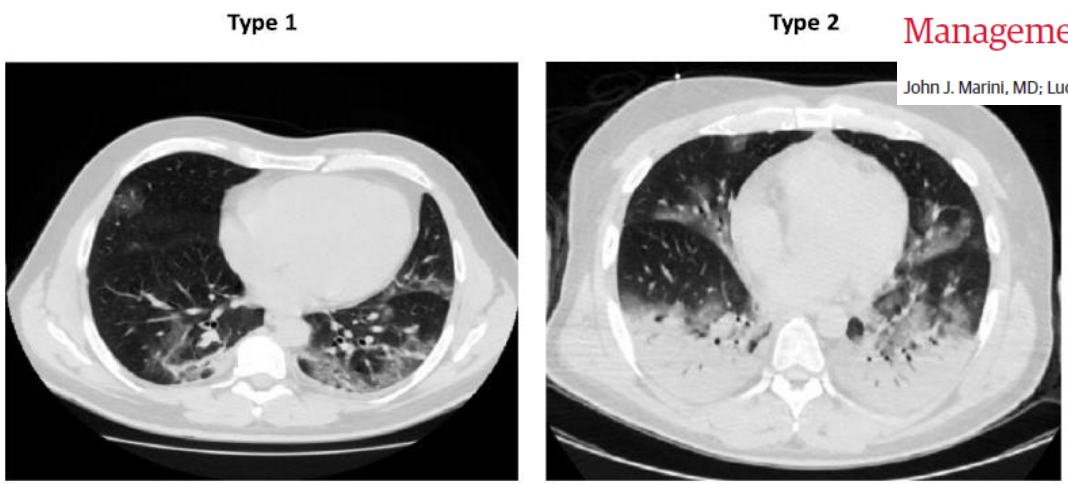




KARIM
1.LF UK A VFN V PRAZE

www.karim-vfn.cz

Plicní postižení odpovídá stupni V/Q nepoměru – kapilárního poškození plic



JAMA Insights | CLINICAL UPDATE

Management of COVID-19 Respiratory Distress

John J. Marini, MD; Luciano Gattinoni, MD

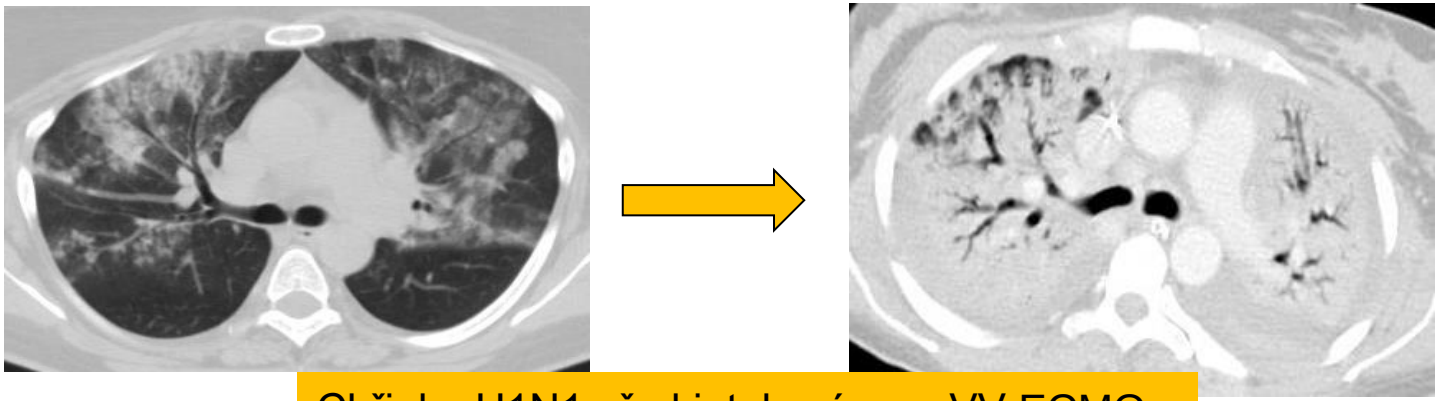
Gattinoni *et al. Critical Care* (2020) 24:154
https://doi.org/10.1186/s13054-020-02880-z

Typ 1 („L“): Kompliantní plíce, Cdyn 40-50 ml/mbar, dominuje perfuzní problém – nutná šetrná ventilace s kontrolou hemodynamiky (TTE), optimalizace V/Q v (semi) pronační poloze…

Typ 2 („H“): U déle trvajících prodromů/superinfekce/iatrogenního přístupu - distress se ztrátou FRC a VC, Cdyn klesá, zvýšení EWLV a hmotnosti plic – nutná agresivnější UPV s rizikem overinflace zachovaných plicních okrsků…..

Stupeň endotheliálního poškození Covid19

- **určuje ztrátu pulmonální vazoregulace a hypoxické plicní vazokonstrikce**
  - promítá se do ventilačně perfuzního nepoměru (V/Q)
  - stupně hypoxie
  - potencuje trombogenezu (nejen) v plicnicovém řečišti
- **endotheliálním poškozením se Covid19 vymezuje vůči myxovirovým pneumonitidám, které postihují primárně více alveoli a plicní parenchym – než cévní stěnu a endothel**



Chřipka H1N1 před intubací a na VV-ECMO

ORIGINAL

Ventilator-related causes of lung injury: the mechanical power

L. Gattinoni[1*], T. Tonetti[1], M. Cressoni[2], P. Cadringher[3], P. Herrmann[1], O. Moerer[1], A. Protti[3], M. Gotti[2], C. Chiurazzi[2], E. Carlesso[2], D. Chiumello[4] and M. Quintel[1]

IPPV = mechanická energie

Vt (exponential^2)

ΔPaw (Pplat-PEEP) (exponential^2)

Průtok (exponential^2)

PEEP (exponential$^{1.4}$)

RR (linear)

….mechanické poškození plic

Velikost plic (menší s nižším prahem..)

Edém, zánět

Nehomogenita postižení (hl. faktor VILI !)

Perfuze

pH, pCO_2, pO_2

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial

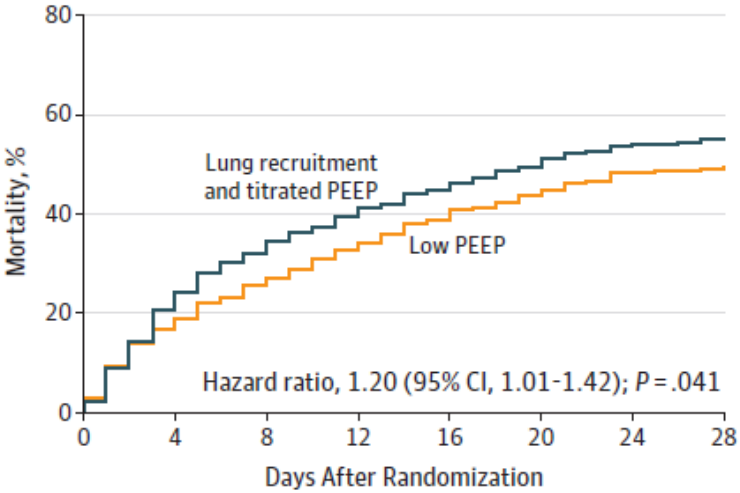
Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (

501 LRM vs 509 kontrol

Ppl 25-6, driving P 13.5, PEEP 12.5

15.6% LRM přerušeno pro hypotenzi neb desaturaci

3 resuscitace během LRM



Outcome	Lung Recruitment Maneuver With PEEP Titration Group (n = 501)	Low-PEEP Group (n = 509)	Type of Effect Estimate	Effect Estimate (95% CI)	P Value
Primary Outcome					
Death ≤28 d, No. of events/total No. (%)	277/501 (55.3)	251/509 (49.3)	HR	1.20 (1.01 to 1.42)	.041
Within 6 mo[a]	327/501 (65.3)	305/509 (59.9)	HR	1.18 (1.01 to 1.38)	.04
No. of ventilator-free d from d 1 to d 28, mean (SD), d	5.3 (8.0)	6.4 (8.6)	MD	-1.1 (-2.1 to -0.1)	.03
Median (IQR)	0.0 (0.0 to 11.0)	0.0 (0.0 to 14.0)			
Pneumothorax requiring drainage ≤7 d, No./total No. (%)	16/501 (3.2)	6/509 (1.2)	RD	2.0 (0.2 to 3.8)	.03
Barotrauma ≤7 d, No./total No. (%)	28/501 (5.6)	8/509 (1.6)	RD	4.0 (1.5 to 6.5)	.001

Bedside ultrazvuk u respiračního selhání: Koncept echokardiografie a hrudní sonografie

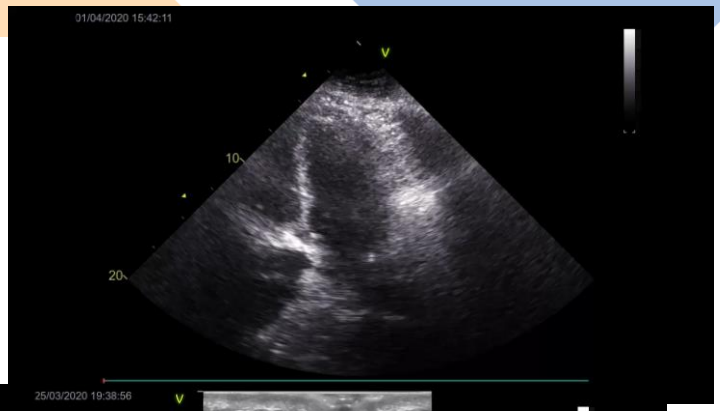
- LV funkce a LVEDP/LAP, mitrální chlopeň

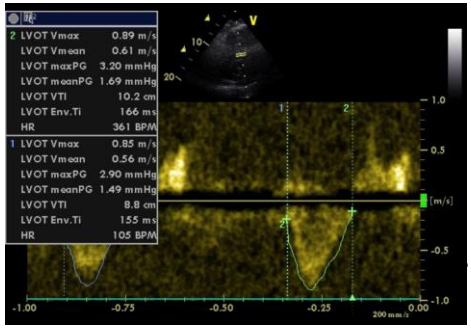
Publ. Feb.-Mar. 2020

- ECMO: rozhodnutí o VV nebo VA kanylaci

Covid 19 a postižení myokardu – podobné jako u chřipkového postižení

- **Možný větší podíl postižení endothelu věnčitých tepen**
- Chřipková myokarditida, perikarditida – virová replikace v srdečním svalu (Greaves K, et al: Arch Intern Med 2004), vztah k „náhlým srdečním selháním“ u H1N1
- **Stressová kardiomyopatie (…hypoxie, katecholaminy)**
- **Septická kardiomyopatie u superinfekcí**





KARIM
1.LF UK A VFN V PRAZE

CZ

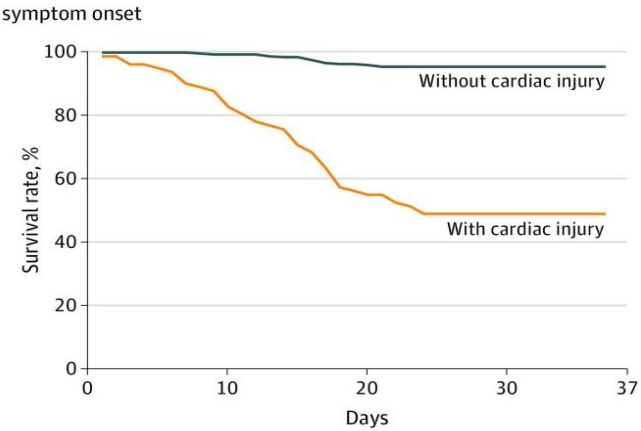
Srdeční selhání a Covid19

- 19.7% ze 417 pts mělo elevaci hsTnI – vztah k mortalitě
- ST elevace cca v 2/3 pozit SKG, vždy D-dimer X 64% pozitivita D-dimer u kontrolních STEMI
- Arytmie (SV) u 18.5-44% na ICU
- Vazopressory 95% na IPPV

JAMA Cardiol. 2020 Mar 25;e200950. doi: 10.1001/jamacardio.2020.0950. Online ahead of print.

Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China

Shaobo Shi [1 2 3], Mu Qin [4], Bo Shen [1 2 3], Yuli Cai [5], Tao Liu [1 2 3], Fan Yang [6], Wei Gong [7], Xu Liu [4], Jinjun Liang [1 2 3], Qinyan Zhao [1 2 3], He Huang [1 2 3], Bo Yang [1 2 3], Congxin Huang [1 2 3]



The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

BMJ Open Efficacy and safety of 1C class antiarrhythmic agent (propafenone) for supraventricular arrhythmias in septic shock compared to amiodarone: protocol

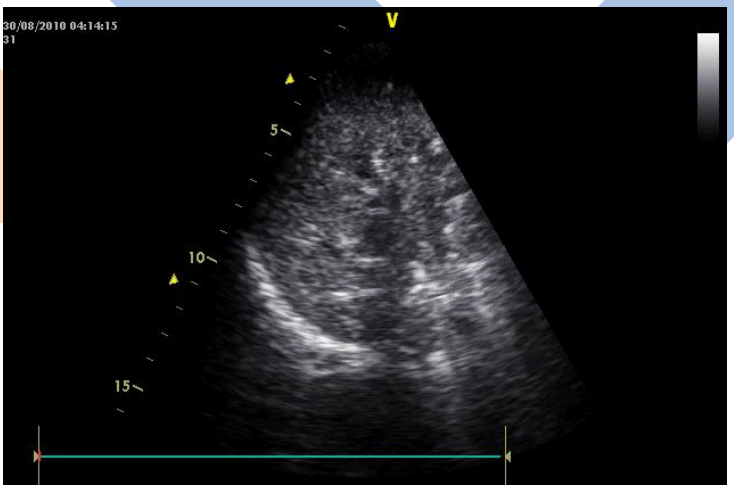
Γ-Segment Elevation in Patients with Covid-19 — A Case Series

Propafenone vs Amiodarone in Septic Shock, ClinicalTrials.gov ID: NCT03029169

Martin Balik,[1] Petr Waldauf,[2] Michal Maly,[1] Vojtech Matousek,[1] Tomas Brozek,[1] Jan Rulisek,[1] Michal Porizka,[1] Robert Sachl,[1] Michal Otahal,[1] Petr Brestovansky,[1] Eva Svobodova,[1] Marek Flaksa,[1] Zdenek Stach,[1] Jaroslav Pazout,[2] Frantisek Duska,[2] Ondrej Smid,[3] Martin Stritesky[1]

KARIM VFN: 5 pac z 15 Covid19 (33%) zařazeno do studie SV arytmií v sept. šoku

Covid19 a ECMO – když standardní postupy nefungují…..Náhrada plic nebo srdce a plic ?



Incidence ECMO 0.3-0.5% všech případů (National Coordination & Experience in Italy, https://www.esicm.org/resources/coronavirus-public-health-emergency/)
W. Guan, Z. Ni, Yu Hu, W. Liang, et al: Clinical Characteristics of Coronavirus Disease 2019 in China, NEJM 2020, DOI: 10.1056/NEJMoa2002032

Echocardiography in extracorporeal life support: A key player in procedural guidance, tailoring and monitoring

Perfusion
1–11
© The Author(s) 2018
Reprints and permissions:
sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/0267659118766438
journals.sagepub.com/home/prf
SAGE

Dirk W. Donker,[1] Christiaan L. Meuwese,[2] Sue A. Braithwaite,[3]
Michael Broomé,[4,5,6] Joris J. van der Heijden,[1]
Jeannine A. Hermens,[1] Marc Platenkamp,[1] Michel de Jong,[7]
Jacqueline G.D. Janssen,[1] Martin Balík[8] and Jan Bělohlávek[9]

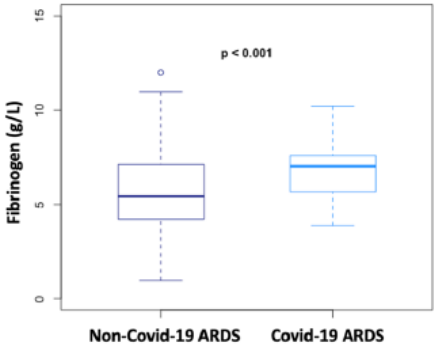
Covid 19 a specifické postižení endothelu

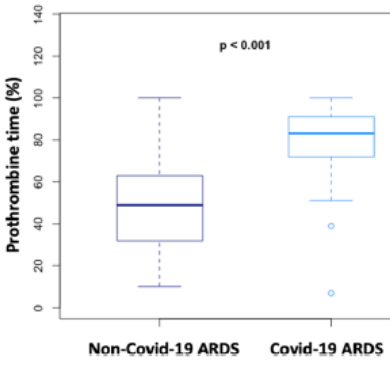
Intensive Care Med
https://doi.org/10.1007/s00134-020-06062-x

ORIGINAL

High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study

Julie Helms[1,2], Charles Tacquard[3], François Severac[4], Ian Leonard-Lorant[5], Mickaël Ohana[5], Xavier Delabranche[3]





- **Endothelitis - kapiláry parenchymových orgánů (plíce, srdce, mozek, ledviny, játra….), akra, Kawasaki-like, doprovázená prokoagulačním stavem**
- **150 pts, PE in 11.2%, elevace D-dimer, fib, vWf_Ag, fVIII, IIa, PAI-1, lupus coagulans in 88% (membránové fosfolipidy…)**
- **Absence DIC….**
- **Potenciace hypoxií…..alveolární mikrotrombotizace„vicious circle“**
- **DVT u 14.8%-22%, asociace se subsegm PE**

Intensive Care Med
https://doi.org/10.1007/s00134-020-06040-3

LETTER

Thrombotic events in SARS-CoV-2 patients: an urgent call for ultrasound screening

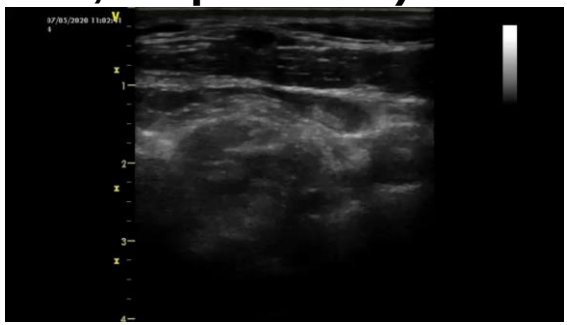
Guido Tavazzi[1,2*], Luca Civardi[2], Luca Caneva[2], Silvia Mongodi[2] and Francesco Mojoli[1]

KARIM
1.LF UK A VFN V PRAZE

Covid 19 jako generalizovaný trombofilní stav

7.2.2020: single centre 138 pts

- **D-dimery, trombofilie…..**
- **LDH implik. mikroangiopatii**
- **KARIM VFN – všichni terap. <u>i.v.</u> antikoagulace (APTT 45-55s, resp. 55-70s)**



JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China

Dawei Wang, MD; Bo Hu, MD; Chang Hu, MD; Fangfang Zhu, MD; Xing Liu, MD; Jing Zhang, MD; Binbin Wang, MD; Hui Xiang, MD; Zhenshun Cheng, MD; Yong Xiong, MD; Yan Zhao, MD; Yirong Li, MD; Xinghuan Wang, MD; Zhiyong Peng, MD

		Median (IQR)			
	Normal Range	Total (N = 138)	ICU (n = 36)	Non-ICU (n = 102)	*P* Value[a]
D-dimer, mg/L	0-500	203 (121-403)	414 (191-1324)	166 (101-285)	<.001
Lactate dehydrogenase, U/L	125-243	261 (182-403)	435 (302-596)	212 (171-291)	<.001

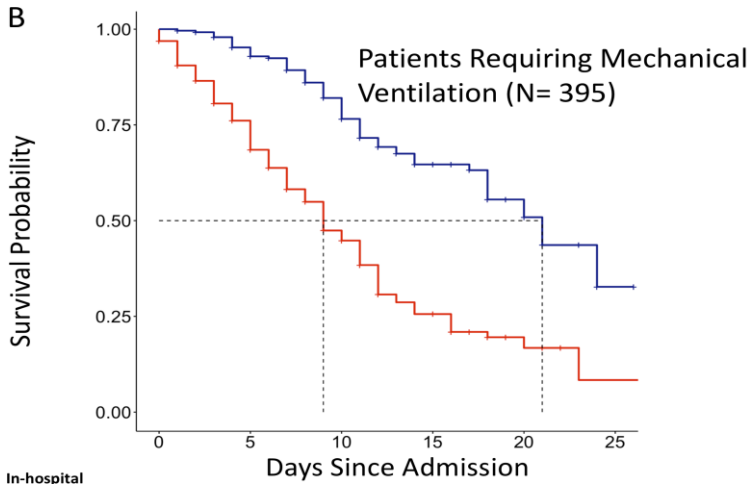
Journal Pre-proof

JACC

Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19

Ishan Paranjpe, BS, Valentin Fuster, MD, PhD, Anuradha Lala, MD, Adam Russak,

Received treatment-dose anticoagulation during hospitalization



5.2020, JACC: Antikoagulovaní na UPV: LOS 9 dní, přežití 63% vs LOS 21 dní a přežití 29%, HR 0.86 per day, p<0.001

Covid 19 a afinita k ACE2 receptorům v GIT a ledvinách – jako AKI asociované s chřipkou, zvl. H1N1

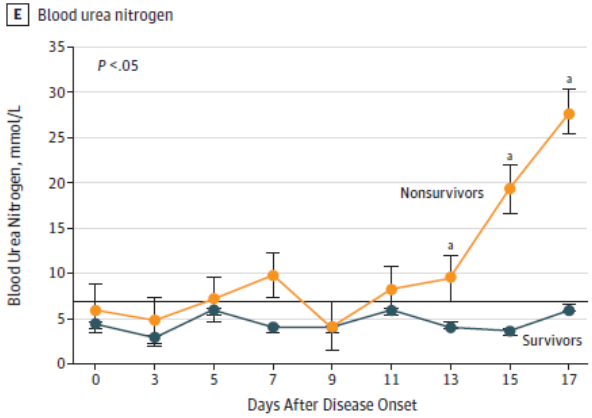
7.2.2020: Single centre 138 pts

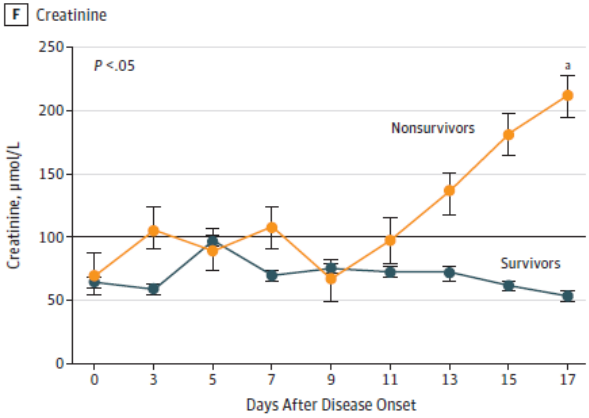
AKI 8.3% …..

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China

Dawei Wang, MD; Bo Hu, MD; Chang Hu, MD; Fangfang Zhu, MD; Xing Liu, MD; Jing Zhang, MD; Binbin Wang, MD; Hui Xiang, MD; Zhenshun Cheng, MD; Yong Xiong, MD; Yan Zhao, MD; Yirong Li, MD; Xinghuan Wang, MD; Zhiyong Peng, MD





Italská databáze: 25% AKI

Hirsch JS, Kidney Int 2020: 36% AKI, z nich 13.6% RRT

ACE2 + mikrotrombotizace + anamnéza + crit. illness

Nové možnosti ovlivnění ACE2 a AT receptorů v intenzivní péči ?

ACE1 a plicní zánět…redukce ATII

Koronavirus a ACE2…možnost ovlivnění exogenním ATII ?

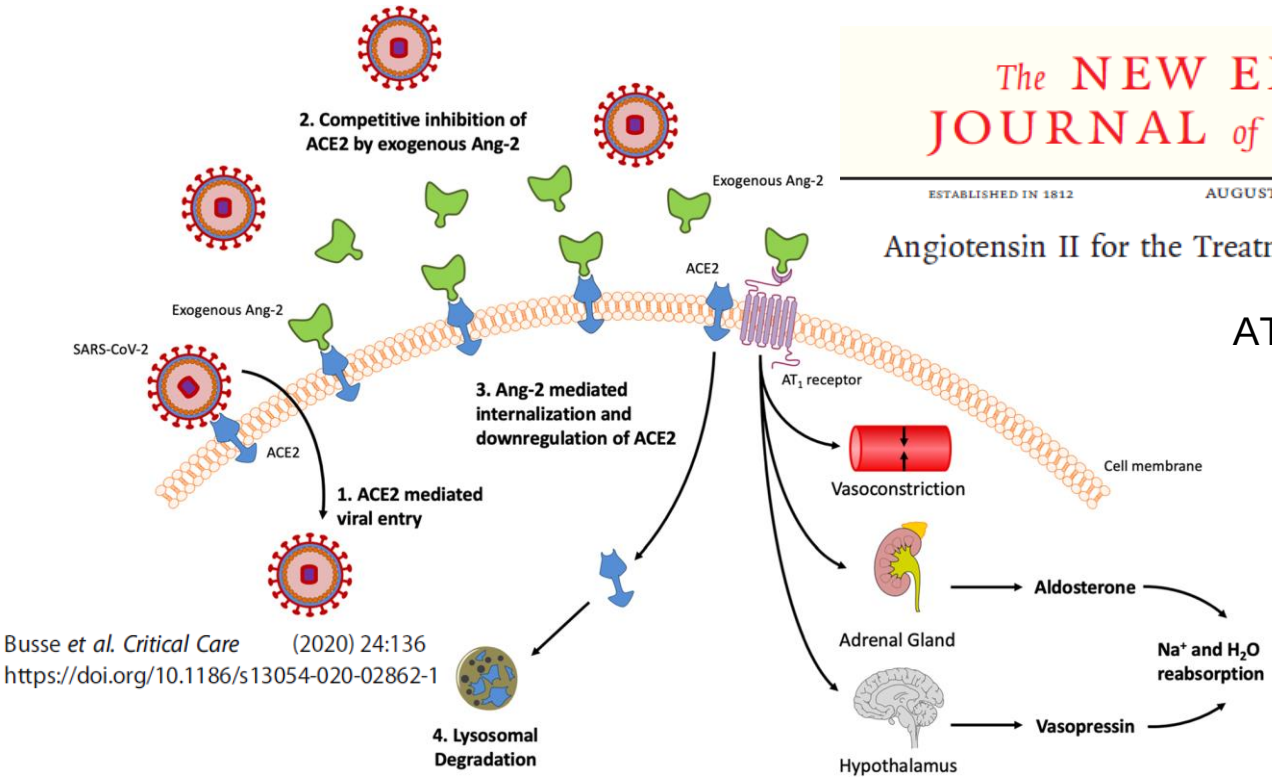
ESC European Society of Cardiology
European Heart Journal (2020) 41, 1810–1817
doi:10.1093/eurheartj/ehaa373
FASTTRACK CLINICAL RESEARCH
Heart failure/cardiomyopathy

Circulating plasma concentrations of angiotensin-converting enzyme 2 in men and women with heart failure and effects of renin–angiotensin–aldosterone inhibitors

Iziah E. Sama[1], Alice Ravera[1,2], Bernadet T. Santema[1], Harry van Goor[3],

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 AUGUST 3, 2017 VOL. 377 NO. 5

Angiotensin II for the Treatment of Vasodilatory Shock



Busse *et al. Critical Care* (2020) 24:136
https://doi.org/10.1186/s13054-020-02862-1

AT II (Giapreza) registrace FDA 21.12.2017 jako rescue terapie pro refrakterní septický nebo distribuční šok

Neexistuje souvislost mezi používáním ACE inh a ATII blokátorů a epidemiol či závažností onemocnění Covid19

- Lékové skupiny jsou stejně rizikové jako protektivní

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19

Mandeep R. Mehra, M.D., Sapan S. Desai, M.D., Ph.D., SreyRam Kuy, M.D., M.H.S., Timothy D. Henry, M.D., and Amit N. Patel, M.D.

JAMA Cardiology | Original Investigation

Association of Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers With Testing Positive for Coronavirus Disease 2019 (COVID-19)

Neil Mehta, MBBS; Ankur Kalra, MD; Amy S. Nowacki, PhD; Scott Anjewierden, BS; Zheyi Han, BS;

Ankit B. Patel, MD, PhD
Renal Division, Brigham and Women's Hospital, Boston, Massachusetts.

Ashish Verma, MBBS
Renal Division, Brigham and Women's Hospital, Boston, Massachusetts.

VIEWPOINT

COVID-19 and Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers
What Is the Evidence?

Covid19 NENÍ cytokinová bouře (…definice ?)

- **endothelitida, vaskulární dysfunkce, trombóza…..a imunitní dysregulace s lymfopenií….riziko iatrogenní imunosuprese**
- **HLH (sekundární haemophagocytická lymphohistiocytoza) jako vzácná indikace k supresi makrofágů (MAS)**
- **kortikoidy potencují šíření viru a asociují s mortalitou – s výjimkou prim indikací (MP<0.2 mg/kg.den) a reparativní fáze ARDS (fibrotizace…)**
- **ferritin typicky ve stovkových hodnotách, elevace IL6, IL8 a IL1β málo signifikantní X jiné ARDS, CRS**

Covid19 mean IL6: 7-125 pg/mL (Qin C, Clin Infect Dis. 2020)

ARDS mean IL6: 282 (111–600) pg/mL u “hypoinflammatory” ARDS a 1618 (517–3205) pg/mL in hyperinflammatory ARDS (Sinha P, Lancet 2020)

CRS – IL6 i CAR-Tcell 10.000 pg/mL (Maude SL N Engl J Med 2014)

The Journal of Rheumatology

The Rheumatologist's Role in Covid-19

Randy Q. Cron and W. Winn Chatham

DOI: 10.3899/jrheum.200334
http://www.jrheum.org/content/early/2020/03/24/jrheum.200334

Intensive Care Medicine

GUIDELINES **Un-edited accepted proof***

Recommendation

50. There is insufficient evidence to issue a recommendation on the use of tocilizumab in critically ill adults with COVID-19.

Covid19 je velmi infekční

- virulence podobná chřipce, ale cca dvojnásobná kontagiozita
- vývoj českých ochranných pomůcek (Compotech Sušice, FZÚ AV)

ANZICS

The Australian and New Zealand Intensive Care Society (ANZICS)

COVID-19 Guidelines

Version 1

16 March 2020

rim

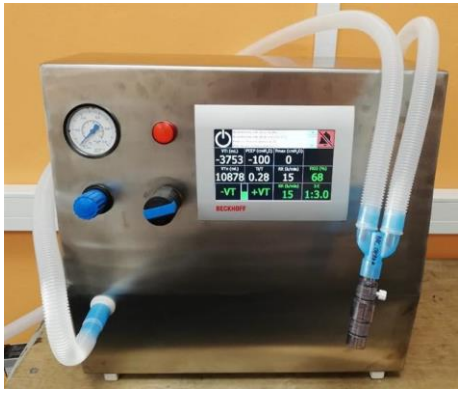
Intensive Care Med
https://doi.org/10.1007/s00134-020-06042-1

LESS IS MORE IN INTENSIVE CARE

ICU beds: less is more? Yes

Thomas S. Valley[1,2,3*] and Danilo T. Noritomi[4,5]

- **Intenzivní medicína jako nejdražší medicínský obor**
- **Příležitost k zavádění rapid response systems, advanced care planning, critical care outreach v nemocnicích…..a efektivního ICU servisu při menším počtu lůžek**
- **Investice do postgraduálního systému vzdělávání lékařů a sester v IM žádoucí – standardizace dle EU diplomů (….EDIC)**
- **Překotný nákup přístrojové techniky nežádoucí a nehospodárný - povede ke zhoršení kvality zdravotní péče v ČR – viz improvizované ICUs v Itálii a USA**
- **Podpora domácích výrobců ochranných pomůcek…….a <u>exportních</u> snah domácích výrobců ventilátorů**



Děkuji za pozornost !

Komplexní kardiovaskulární centrum
1. LF UK a VFN

U nemocnice 2; 128 08 Praha 2
T: +420 224 963 366
F: +420 224 962 118
E: martin.balik@vfn.cz
www.karim-vfn.cz