COVID-19

Que doit retenir le cardiologue ?

Pr Atul PATHAK

MONACO

Pourquoi les cardiologues sont concernés?

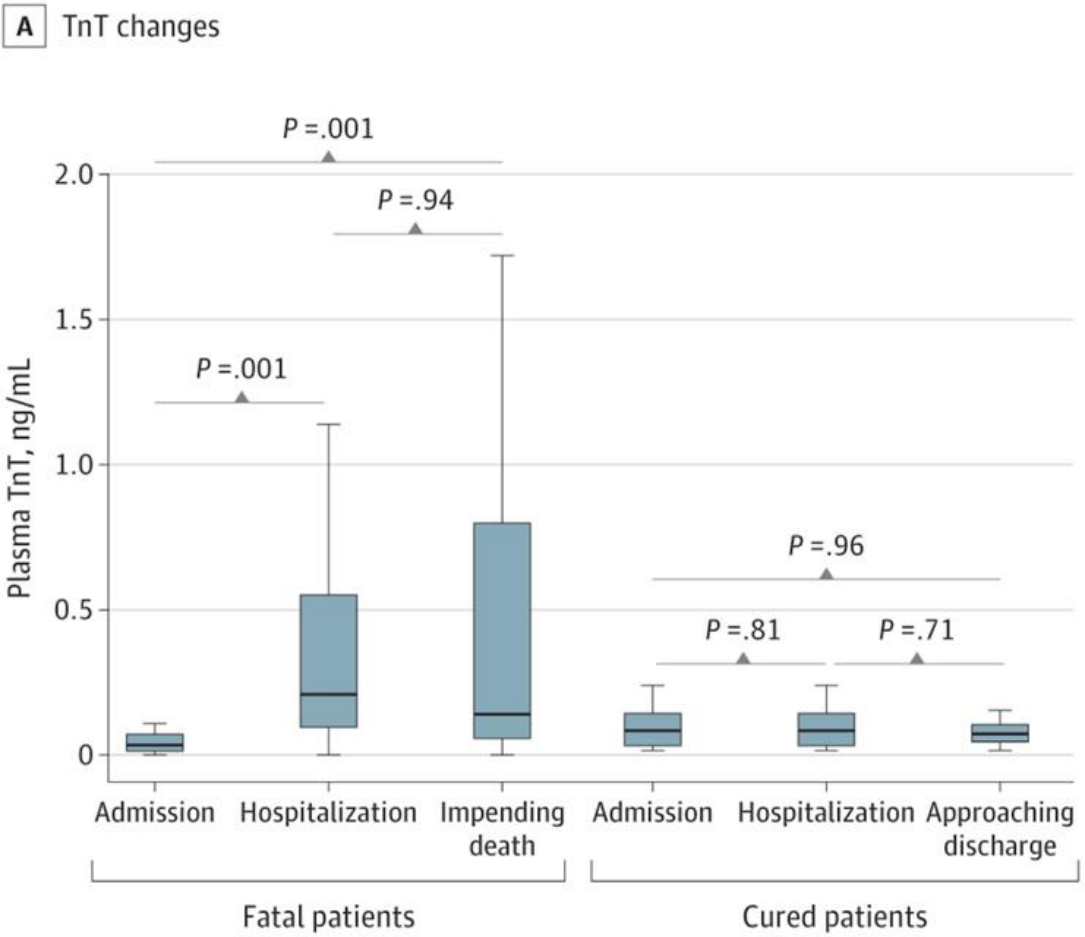
Pourquoi les Cardiologues sont concernés ?

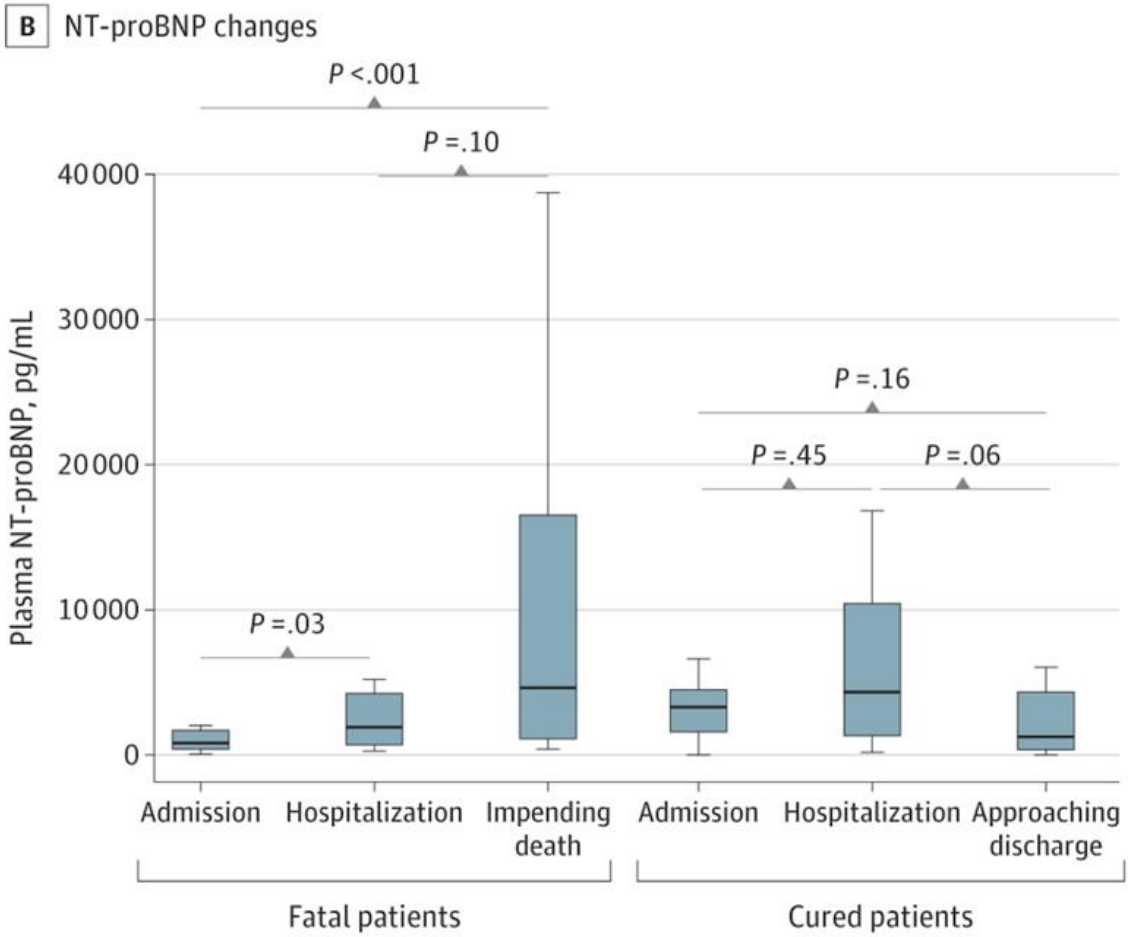
JAMA Cardiology | Original Investigation

27 mars 2020

Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19)

Tao Guo, MD; Yongzhen Fan, MD; Ming Chen, MD; Xiaoyan Wu, MD; Lin Zhang, MD; Tao He, MD; Hairong Wang, MD; Jing Wan, MD; Xinghuan Wang, MD; Zhibing Lu, MD





	No. (%)
Demographic information	
Total No.	5700
Age, median (IQR) [range], y	63 (52-75) [0-107]
Sex	
Female	2263 (39.7)
Male	3437 (60.3)
Comorbidities	
Total No.	5700
Cancer	320 (6)
Cardiovascular disease	
Hypertension	3026 (56.6)
Coronary artery disease	595 (11.1)
Congestive heart failure	371 (6.9)
Metabolic disease	
Obesity (BMI ≥30)	1737 (41.7)
No.	4170
Morbid obesity (BMI ≥35)	791 (19.0)
No.	4170
Diabetes[e]	1808 (33.8)
Never smoker	3009 (84.4)
No.	3567

Toujours pareil

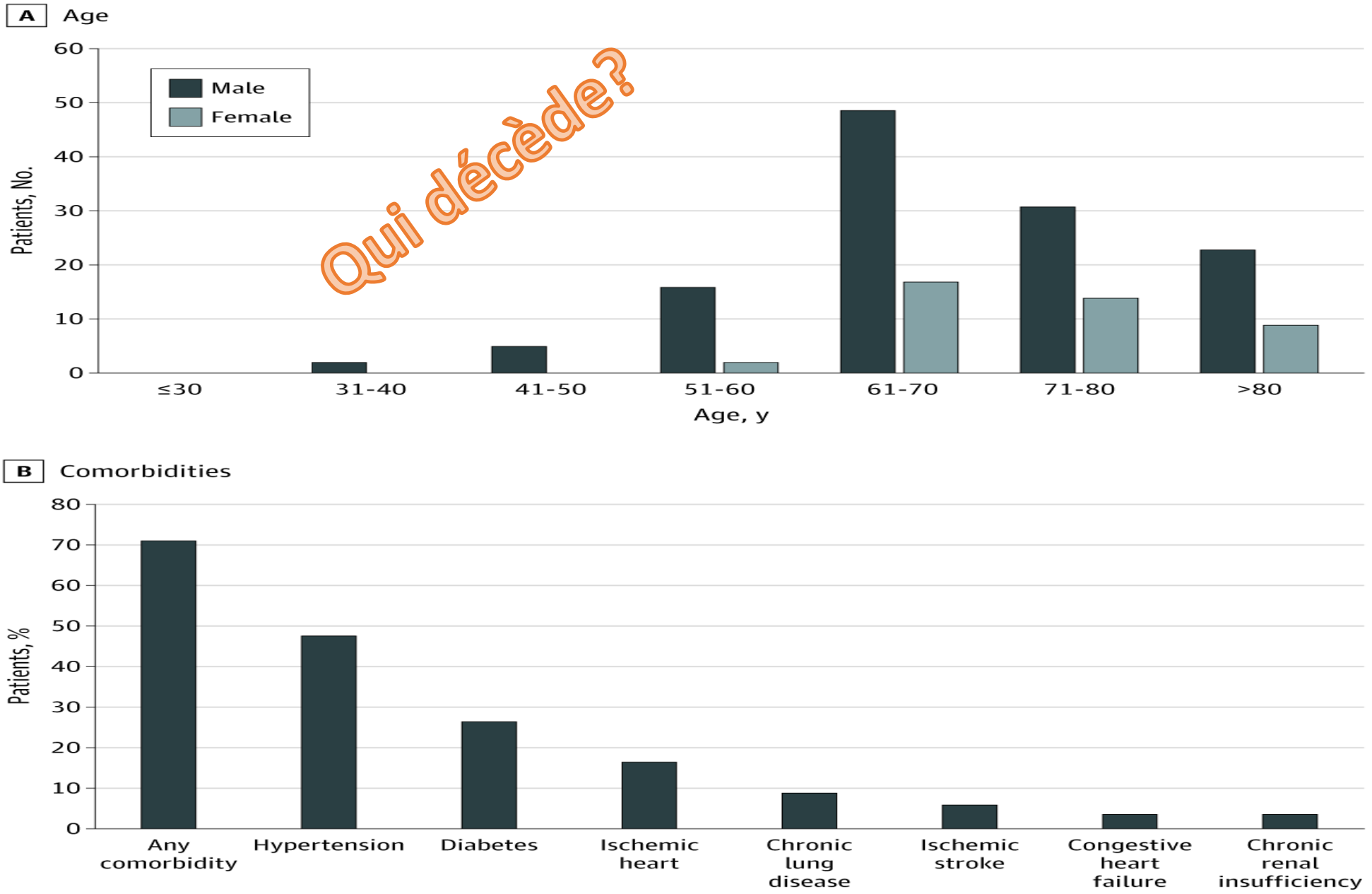
JAMA. Published online April 22, 2020.
doi:10.1001/jama.2020.6775

Les malades CV sont les plus graves

	No. (%)			
	Total (N = 138)	ICU (n = 36)	Non-ICU (n = 102)	*P* Value[a]
Age, median (IQR), y	56 (42-68)	66 (57-78)	51 (37-62)	<.001
Sex				
Female	63 (45.7)	14 (38.9)	49 (48.0)	.34
Male	75 (54.3)	22 (61.1)	53 (52.0)	
Huanan Seafood Wholesale Market exposure	12 (8.7)	5 (13.9)	7 (6.9)	.30
Infected				
Hospitalized patients	17 (12.3)	9 (25.0)	8 (7.8)	.02
Medical staff	40 (29)	1 (2.8)	39 (38.2)	<.001
Comorbidities	64 (46.4)	26 (72.2)	38 (37.3)	<.001
Hypertension	43 (31.2)	21 (58.3)	22 (21.6)	<.001
Cardiovascular disease	20 (14.5)	9 (25.0)	11 (10.8)	.04
Diabetes	14 (10.1)	8 (22.2)	6 (5.9)	.009
Malignancy	10 (7.2)	4 (11.1)	6 (5.9)	.29
Cerebrovascular disease	7 (5.1)	6 (16.7)	1 (1.0)	.001
COPD	4 (2.9)	3 (8.3)	1 (1.0)	.054
Chronic kidney disease	4 (2.9)	2 (5.6)	2 (2.0)	.28
Chronic liver disease	4 (2.9)	0	4 (3.9)	.57
HIV infection	2 (1.4)	0	2 (2.0)	>.99

JAMA. 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585

Clinical Characteristics of Patients Who Died of Coronavirus Disease 2019 in China



JAMA Netw Open. 2020;3(4):e205619. doi:10.1001/jamanetworkopen.2020.5619

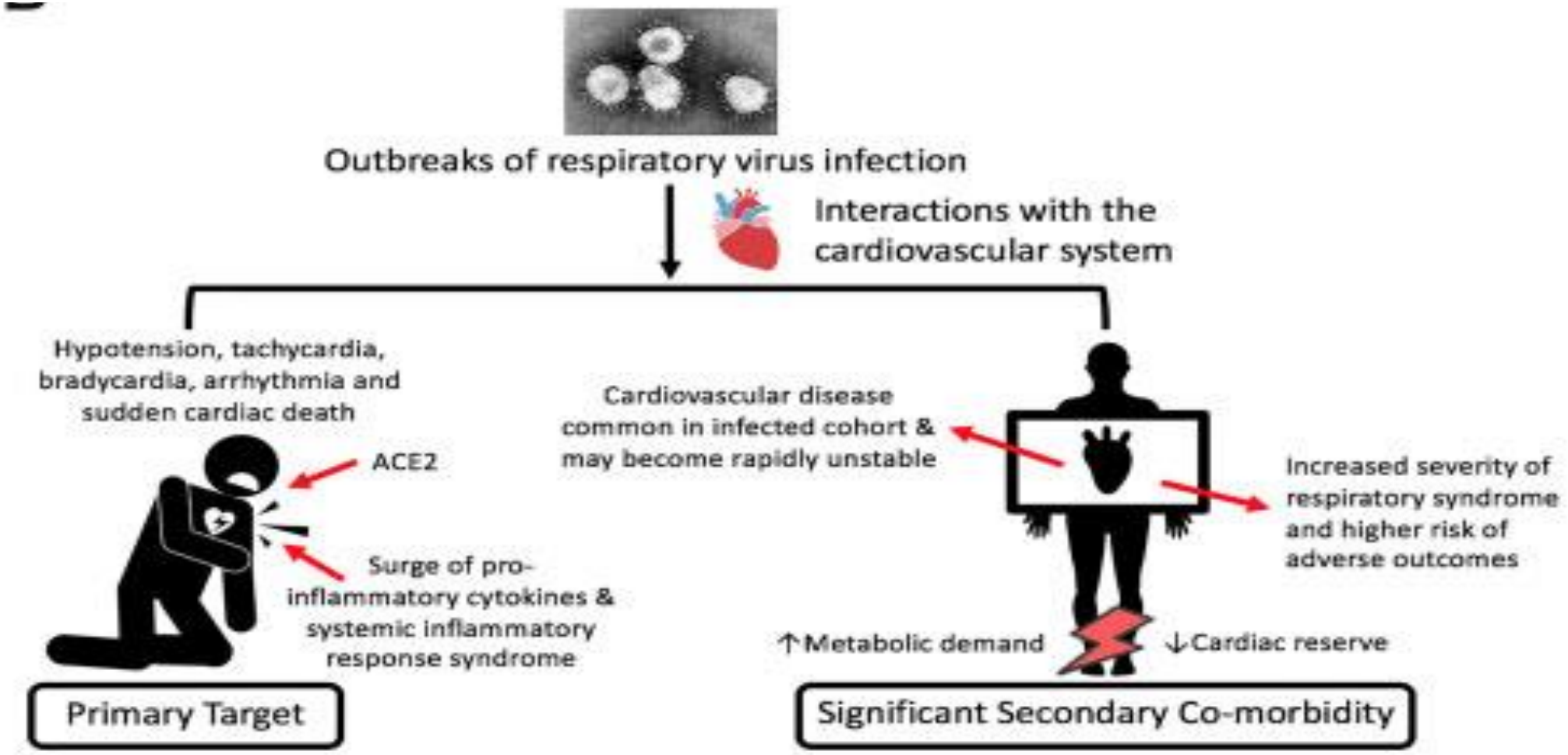
Qui dit HTA dit….

- Sujet âgé
- A risque de faire des pneumopathies
- Comorbidités (Diabète, SAS, Obesité..)
- Troubles de l'immunité cellulaire
- Traité par IEC ou ARA 2
- Donc à risque accru d'évènements CV

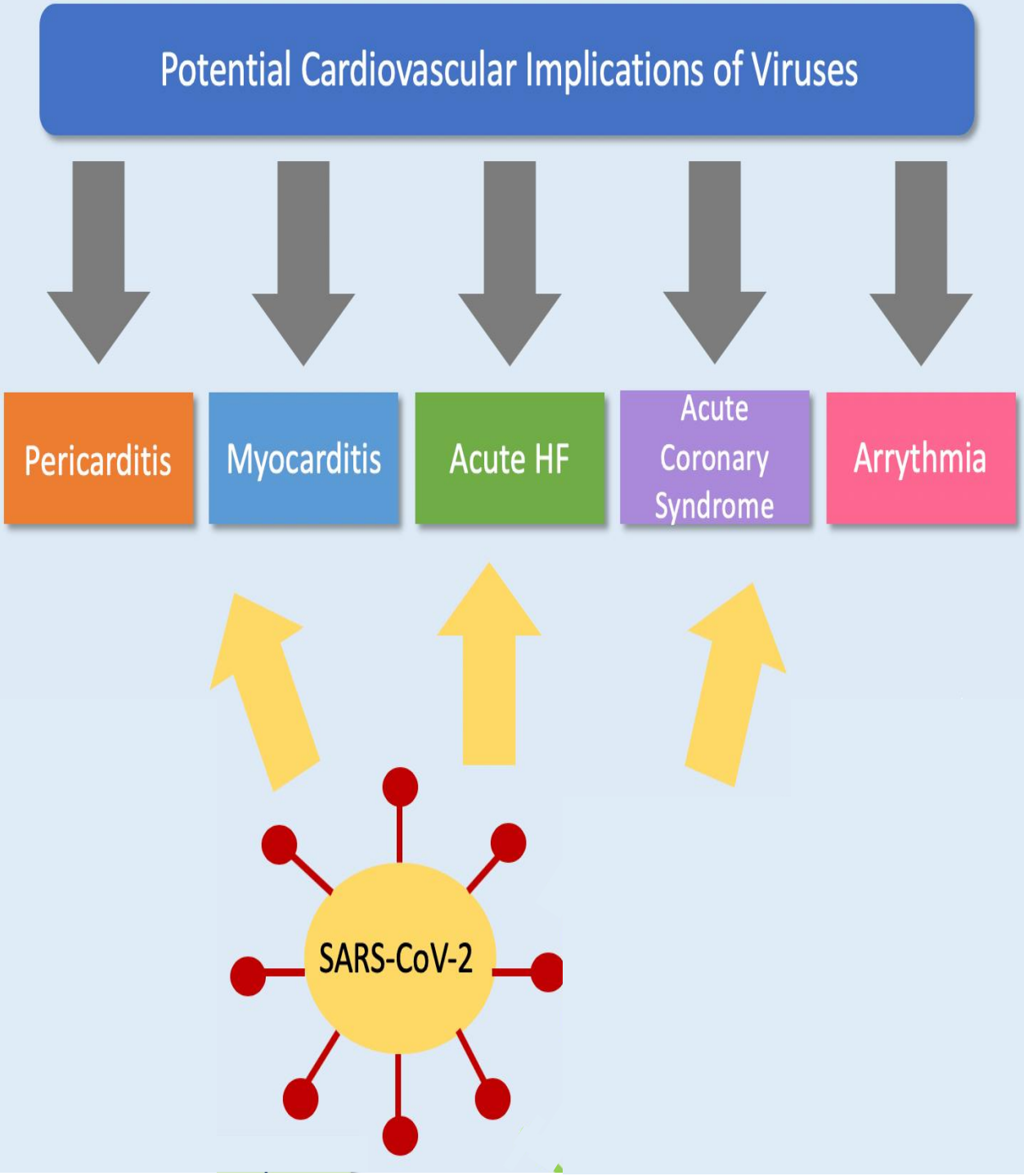
HTA marqueur intégratif d'une population à risque plus que facteur de susceptibilité à l'infection

Quelles manifestations le cardiologue doit reconnaître ?

Présentation clinique CV



European Heart Journal (2020) 0, 1–3


Potential Cardiovascular Implications of Viruses
Pericarditis
Myocarditis
Acute HF
Acute Coronary Syndrome
Arrythmia
SARS-CoV-2

Au début ……

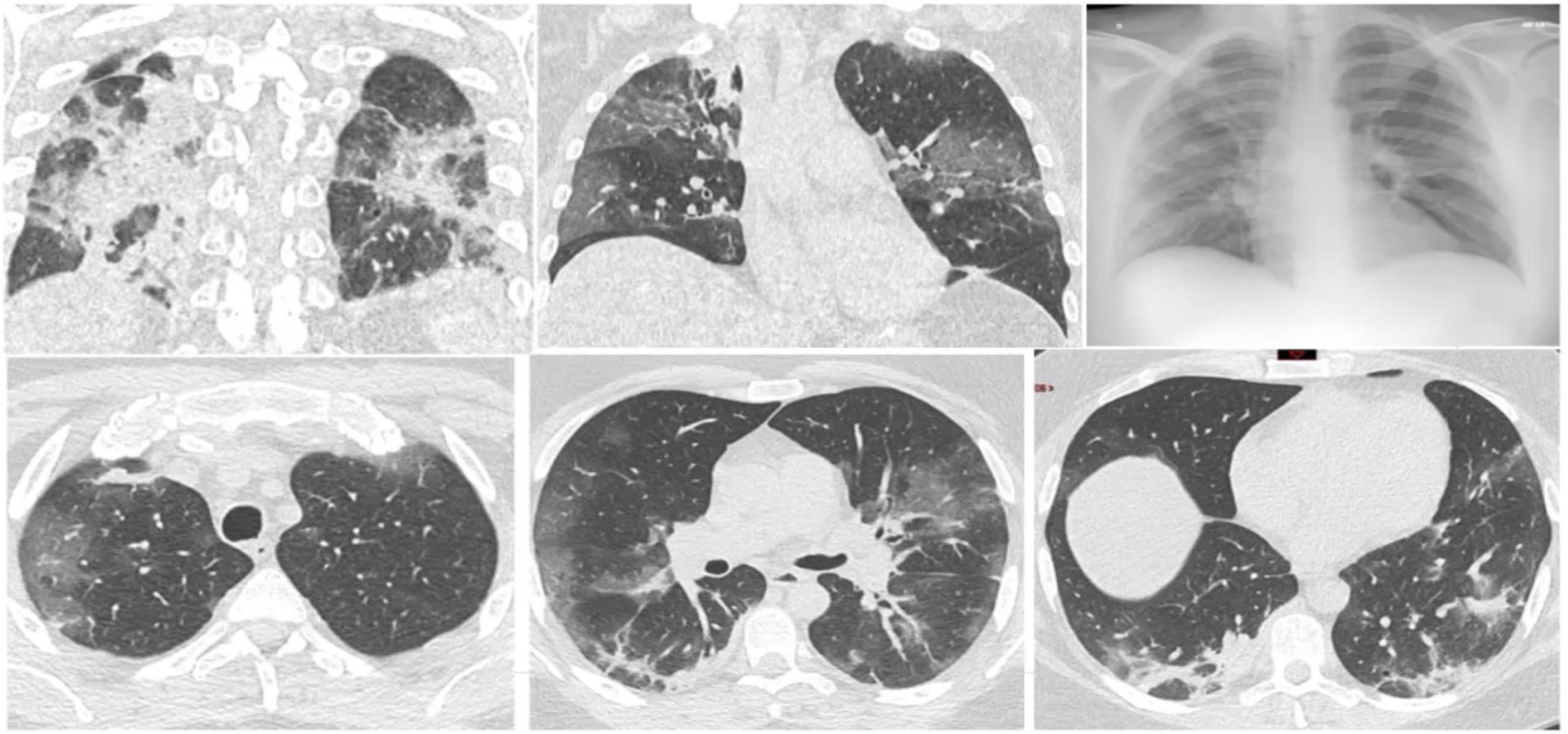
Les signes non CV sont les plus fréquents

Table 1. Baseline Characteristics of Patients Infected With 2019-nCoV

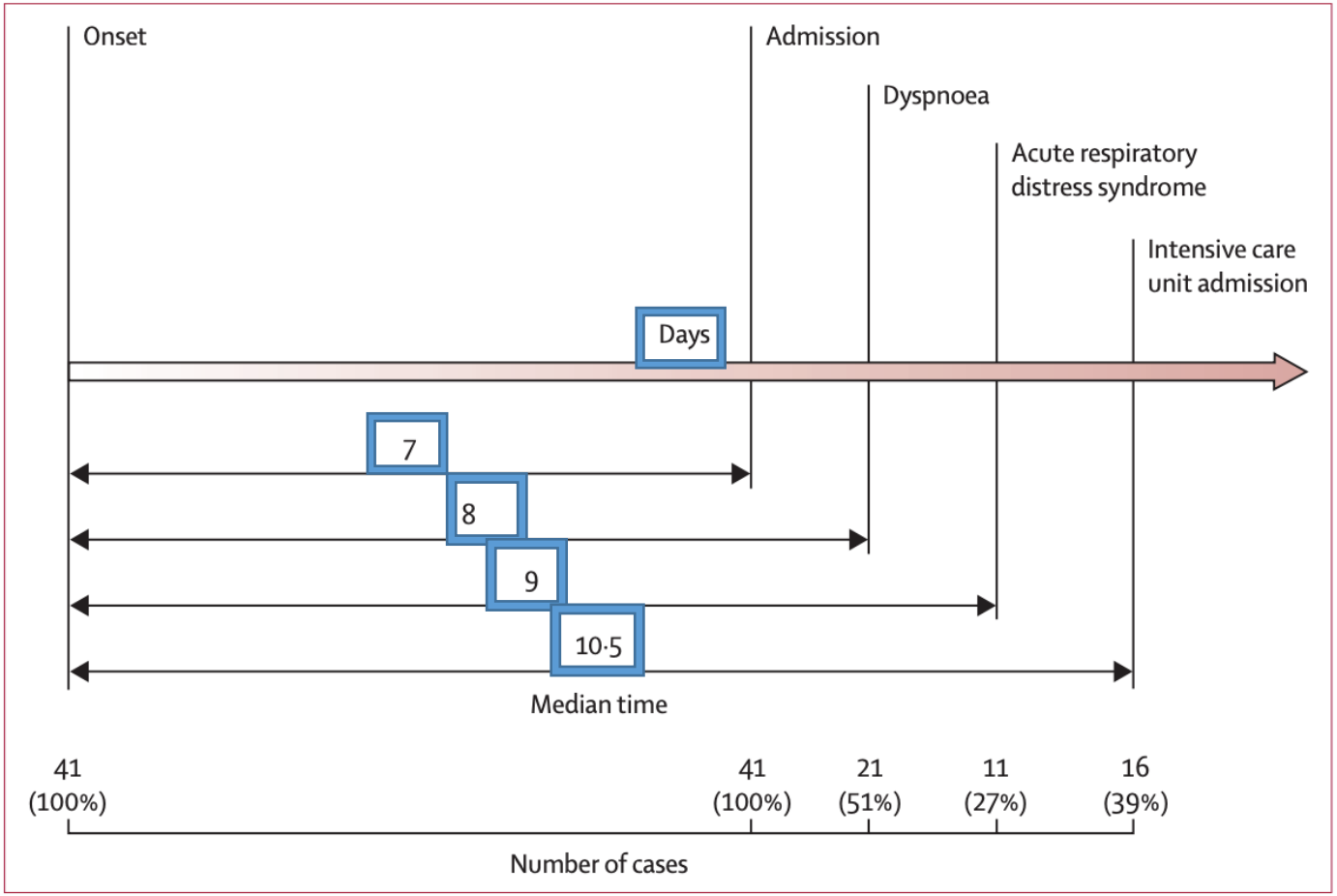
	No. (%)			
	Total (N = 138)	ICU (n = 36)	Non-ICU (n = 102)	*P* Value[a]
Signs and symptoms				
Fever	136 (98.6)	36 (100)	100 (98.0)	>.99
Fatigue	96 (69.6)	29 (80.6)	67 (65.7)	.10
Dry cough	82 (59.4)	21 (58.3)	61 (59.8)	.88
Anorexia	55 (39.9)	24 (66.7)	31 (30.4)	<.001
Myalgia	48 (34.8)	12 (33.3)	36 (35.3)	.83
Dyspnea	43 (31.2)	23 (63.9)	20 (19.6)	<.001
Expectoration	37 (26.8)	8 (22.2)	29 (28.4)	.35
Pharyngalgia	24 (17.4)	12 (33.3)	12 (11.8)	.003
Diarrhea	14 (10.1)	6 (16.7)	8 (7.8)	.20
Nausea	14 (10.1)	4 (11.1)	10 (9.8)	>.99
Dizziness	13 (9.4)	8 (22.2)	5 (4.9)	.007
Headache	9 (6.5)	3 (8.3)	6 (5.9)	.70
Vomiting	5 (3.6)	3 (8.3)	2 (2.0)	.13
Abdominal pain	3 (2.2)	3 (8.3)	0 (0)	.02
Onset of symptom to, median (IQR), d				
Hospital admission	7.0 (4.0-8.0)	8.0 (4.5-10.0)	6.0 (3.0-7.0)	.009
Dyspnea	5.0 (1.0-10.0)	6.5 (3.0-10.8)	2.5 (0.0-7.3)	.02
ARDS	8.0 (6.0-12.0)	8.0 (6.0-12.0)	8.0 (6.3-11.3)	.97
Heart rate, median (IQR), bpm	88 (78-97)	89 (81-101)	86 (77-96)	.14
Respiratory rate, median (IQR)	20 (19-21)	20 (16-25)	20 (19-21)	.57
Mean arterial pressure, median (IQR), mm Hg	90 (84-97)	91 (78-96)	90 (85-98)	.33

JAMA. 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585

Privilegier le TDM thoracique (low dose CT)



Cinétique d'évolution : tous les **jours** !



Lancet 2020; 395: 497–506

Les patients du cardiologue sont les plus à risque?

Les complications les plus graves sont CV

Table 4. Complications and Treatments of Patients Infected With 2019-nCoV

	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

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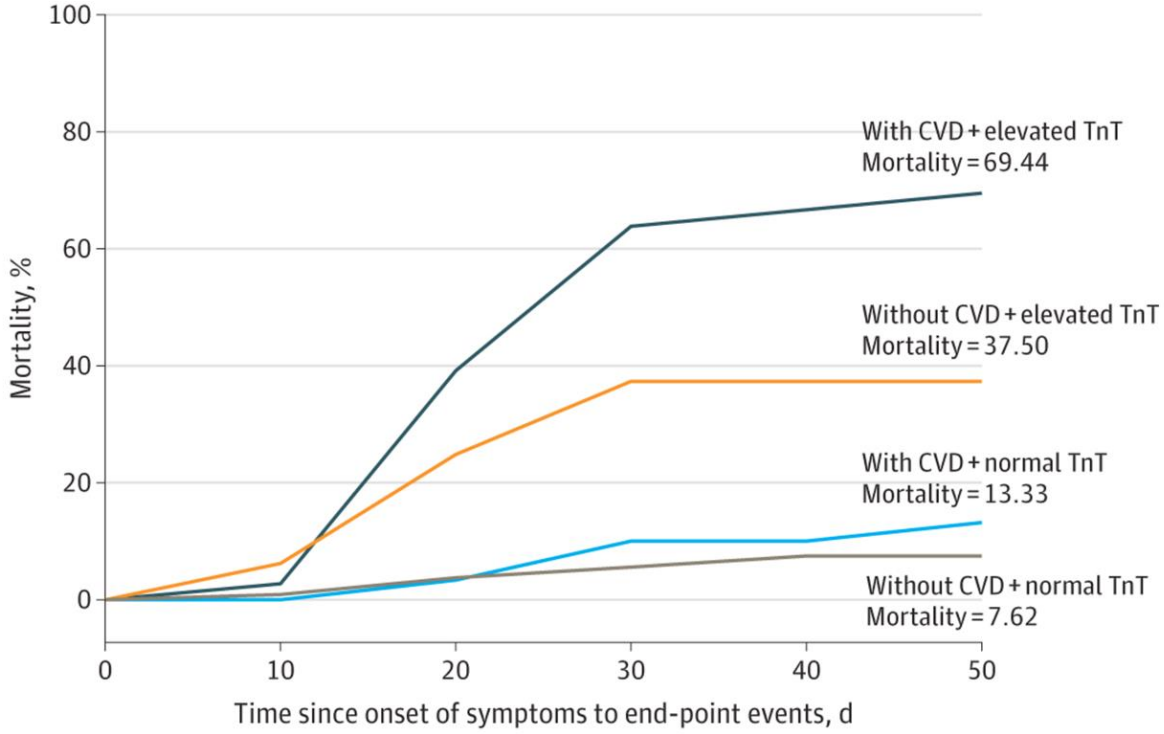
27 mars 2020



No. at risk

Without CVD + normal TnT (n = 105)	102	86	41	10	0
Without CVD + elevated TnT (n = 16)	15	12	7	1	0
With CVD + normal TnT (n = 30)	29	25	10	4	0
With CVD + elevated TnT (n = 36)	34	20	8	2	0

	All patients (n=41)	ICU care (n=13)	No ICU care (n=28)	p value
Duration from illness onset to first admission	7·0 (4·0–8·0)	7·0 (4·0–8·0)	7·0 (4·0–8·5)	0·87
Complications				
Acute respiratory distress syndrome	12 (29%)	11 (85%)	1 (4%)	<0·0001
RNAaemia	6 (15%)	2 (15%)	4 (14%)	0·93
Cycle threshold of RNAaemia	35·1 (34·7–35·1)	35·1 (35·1–35·1)	34·8 (34·1–35·4)	0·35
Acute cardiac injury*	5 (12%)	4 (31%)	1 (4%)	0·017
Acute kidney injury	3 (7%)	3 (23%)	0	0·027
Secondary infection	4 (10%)	4 (31%)	0	0·0014
Shock	3 (7%)	3 (23%)	0	0·027

Lancet 2020; 395: 497–506

Characteristic	Patients, No. (%)			
		Cardiac injury		
	All (n = 416)	With (n = 82)	Without (n = 334)	*P* value
Time from symptom onset to admission, edian (range), d	10 (1-30)	10 (1-30)	10 (1-28)	.27
Treatment				
Oxygen inhalation	316 (76.0)	26 (31.7)	290 (86.8)	<.001
Noninvasive ventilation	51 (12.3)	38 (46.3)	13 (3.9)	<.001
Invasive mechanical ventilation	32 (7.7)	18 (22.0)	14 (4.2)	<.001
Continuous renal replacement therapy	2 (0.5)	2 (2.4)	0	.04
Antiviral treatment	403 (96.9)	82 (100)	321 (96.1)	.08
Glucocorticoids	304 (73.1)	72 (87.8)	232 (69.5)	<.001
Intravenous immunoglobulin therapy	259 (62.3)	68 (82.9)	191 (57.2)	<.001
Antibiotic treatment	235 (56.5)	68 (82.9)	167 (50)	<.001
Complications				
ARDS	97 (23.3)	48 (58.5)	49 (14.7)	<.001
Acute kidney injury	8 (1.9)	7 (8.5)	1 (0.3)	<.001
Electrolyte disturbance	30 (7.2)	13 (15.9)	17 (5.1)	.003
Hypoproteinemia	27 (6.5)	11 (13.4)	16 (4.8)	.01
Anemia	13 (3.1)	4 (4.9)	9 (2.7)	.30
Coagulation disorders	12 (2.9)	6 (7.3)	6 (1.8)	.02
Clinical outcome				
Remained in hospital	319 (76.7)	38 (46.3)	281 (72.2)	<.001
Discharged	40 (9.6)	2 (2.4)	38 (23.4)	
Died	57 (13.7)	42 (51.2)	15 (4.5)	<.001

JAMA Cardiol. doi:10.1001/jamacardio.2020.0950

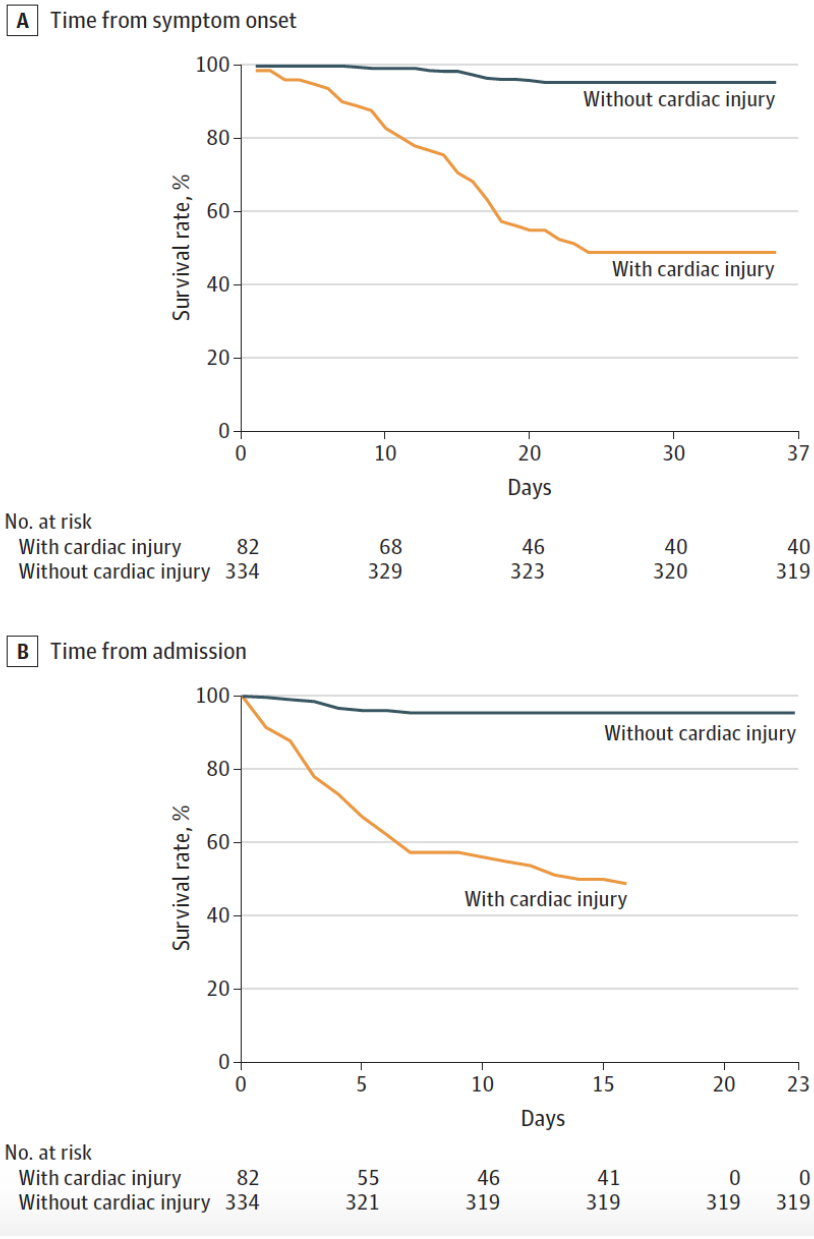


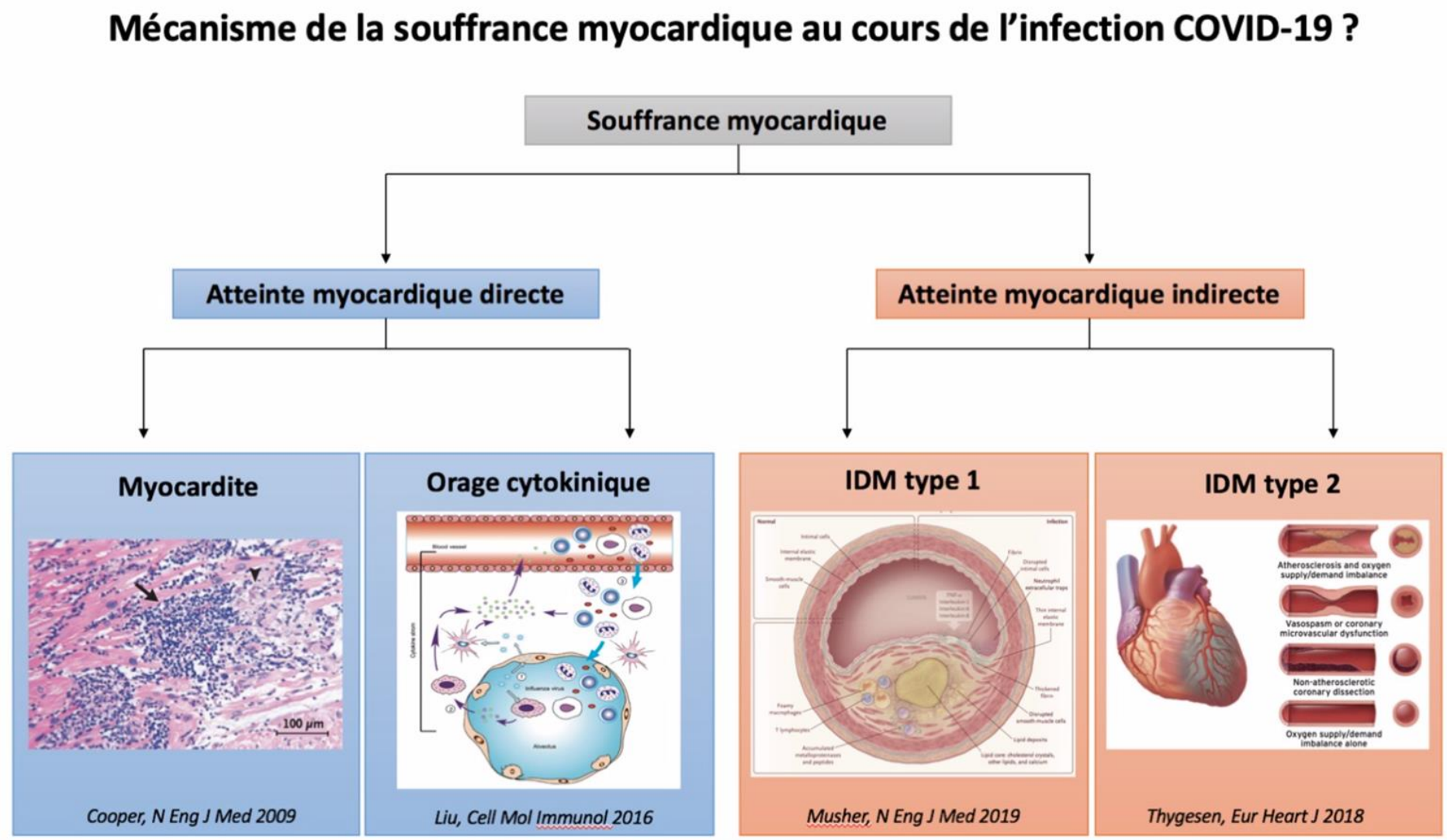
Table 3. Multivariate Cox Regression Analysis on the Risk Factors Associated With Mortality in Patients With COVID-19

	From symptom onset		From admission	
Factor	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Age, y	1.02 (0.99-1.05)	.07	1.02 (0.99-1.04)	.18
Cardiovascular diseases	1.51 (0.70-3.30)	.30	1.40 (0.65-3.03)	.39
Cerebrovascular diseases	1.12 (0.46-2.70)	.80	1.71 (0.71-4.09)	.25
Diabetes	0.79 (0.41-1.52)	.48	0.75 (0.38-1.50)	.42
Chronic obstructive pulmonary disease	0.37 (0.04-3.50)	.38	0.39 (0.04-3.68)	.41
Renal failure	1.10 (0.49-2.44)	.82	0.66 (0.29-1.46)	.30
Cancer	1.75 (0.43-7.16)	.44	0.82 (0.18-3.65)	.79
Acute respiratory distress syndrome	7.89 (3.73-16.66)	<.001	7.11 (3.31-15.25)	<.001
Cardiac injury	4.26 (1.92-9.49)	<.001	3.41 (1.62-7.16)	.001
Creatinine ≥1.50 mg/dL	0.59 (0.29-1.23)	.16	1.22 (0.60-2.50)	.58
N-terminal pro-B-type natriuretic peptide ≥900 pg/mL	1.16 (0.54-2.47)	.70	1.52 (0.74-3.10)	.25

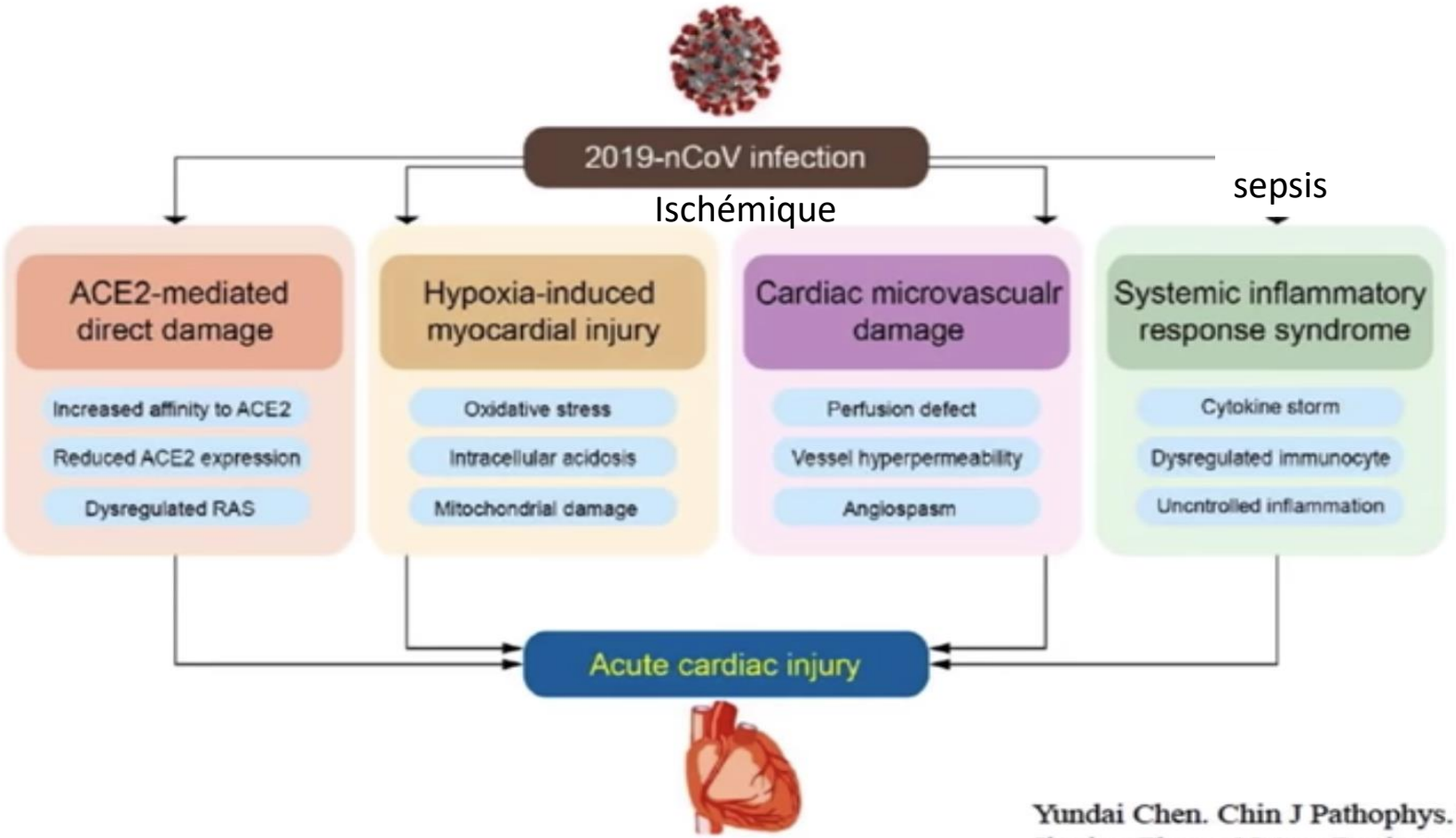
JAMA Cardiol. doi:10.1001/jamacardio.2020.0950

Troponine élevée de manière isolée?

“Atteinte cardiaque”



Mécanismes?



High IL1-beta,
IL-6,
IFN gamma
IL1-inhibitors

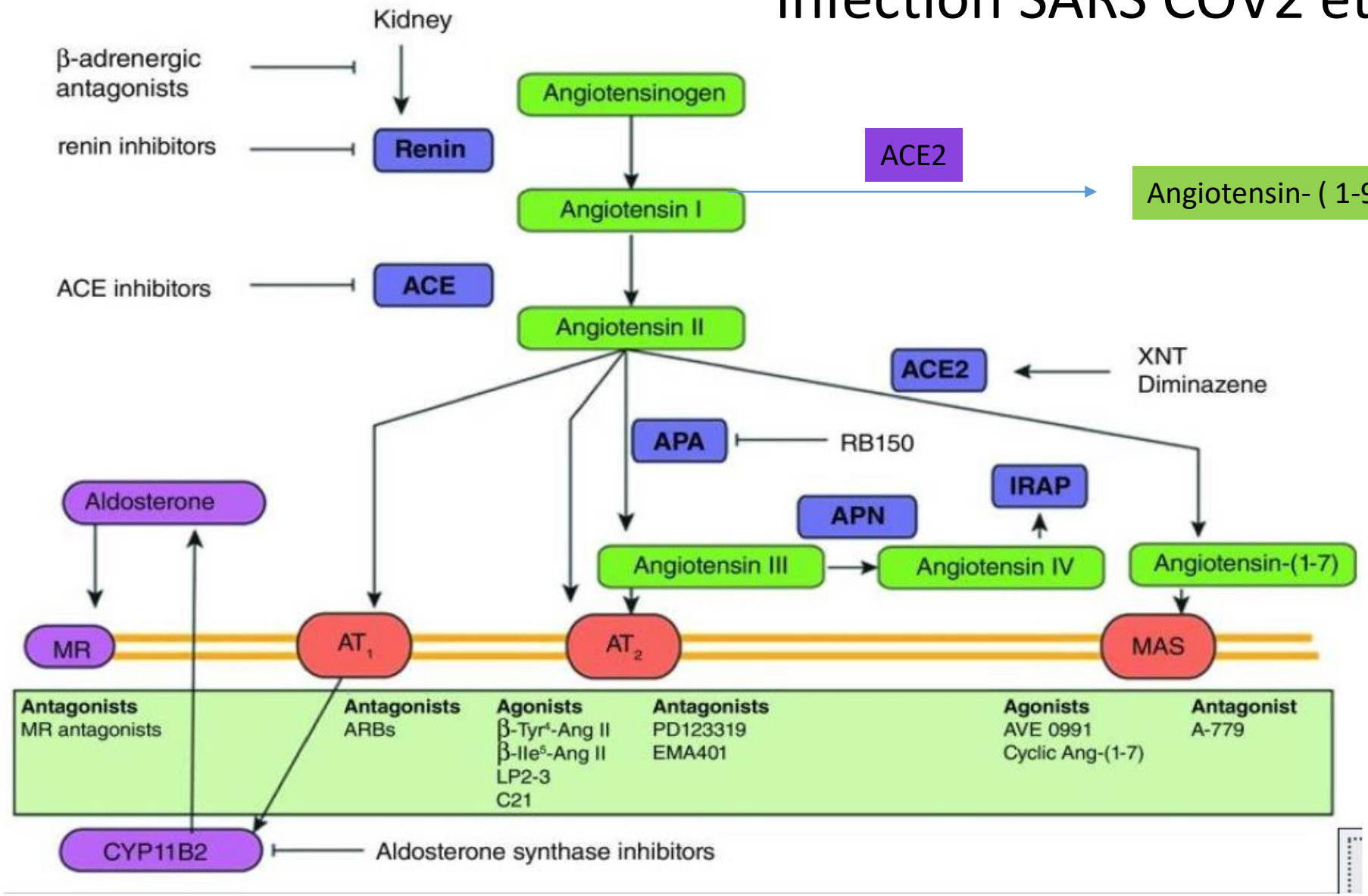
IL6-inhibitors
JAK-inhibitors

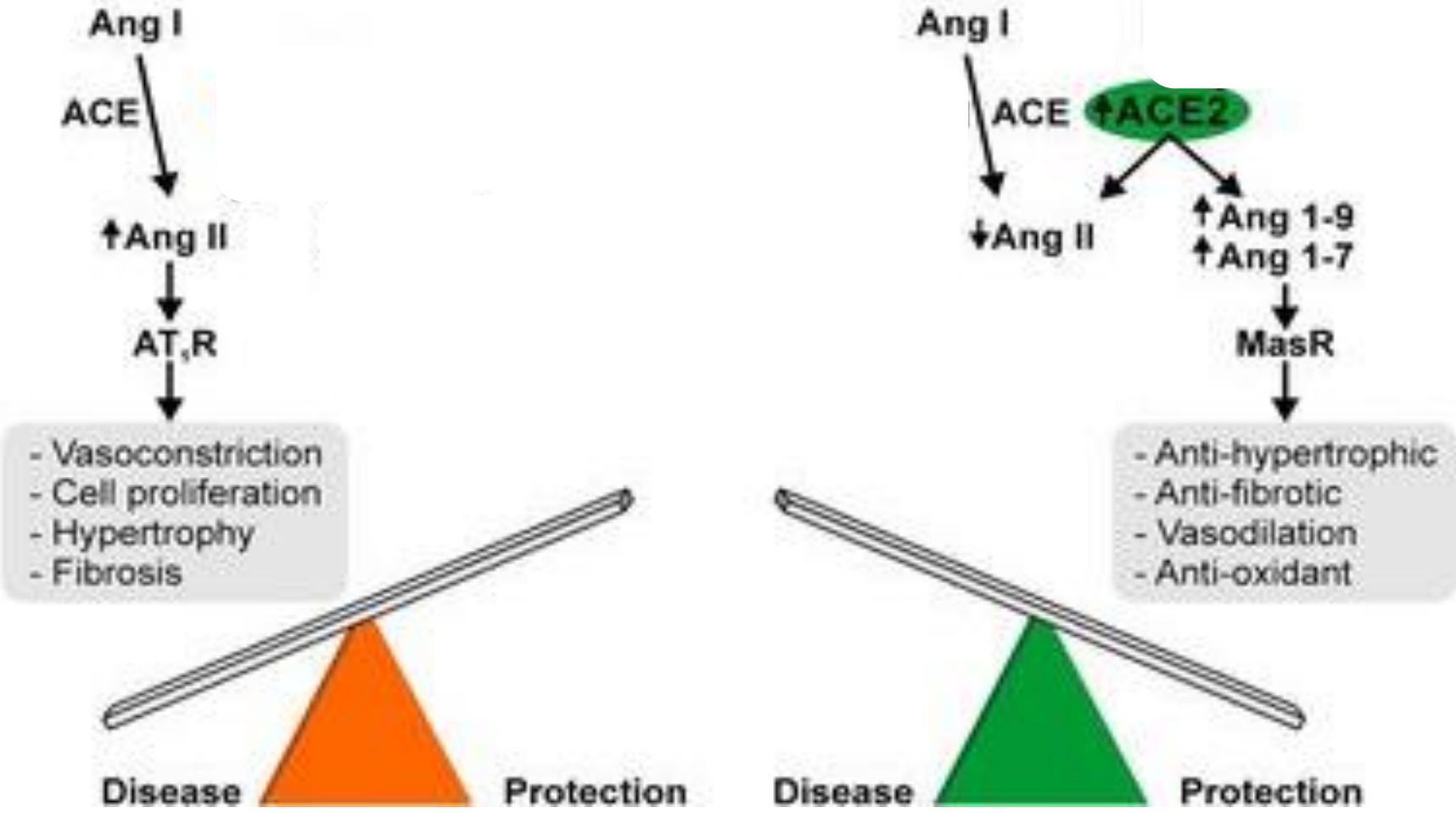
Augmentation de la Troponine

Yundai Chen. Chin J Pathophys. 2020;
Jinying Zhang. Nature Reviews. 2020

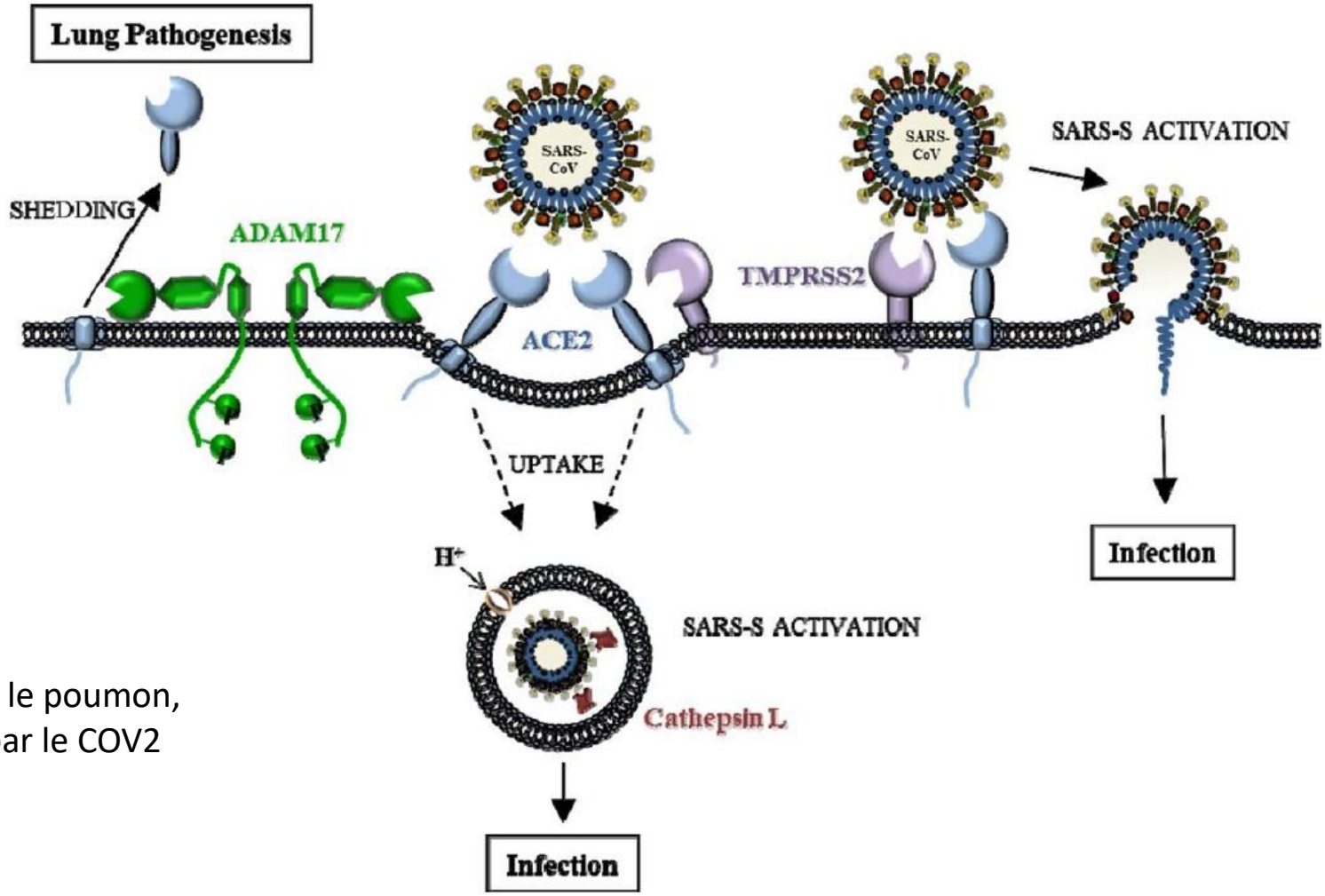
COVID 19 : quel rôle pour le SRAA?

Infection SARS COV2 et SRAA




Ang I
ACE
↑Ang II
AT1R
- Vasoconstriction
- Cell proliferation
- Hypertrophy
- Fibrosis
Disease
Protection
Ang I
ACE
↑ACE2
↓Ang II
↑Ang 1-9
↑Ang 1-7
MasR
- Anti-hypertrophic
- Anti-fibrotic
- Vasodilation
- Anti-oxidant
Disease
Protection

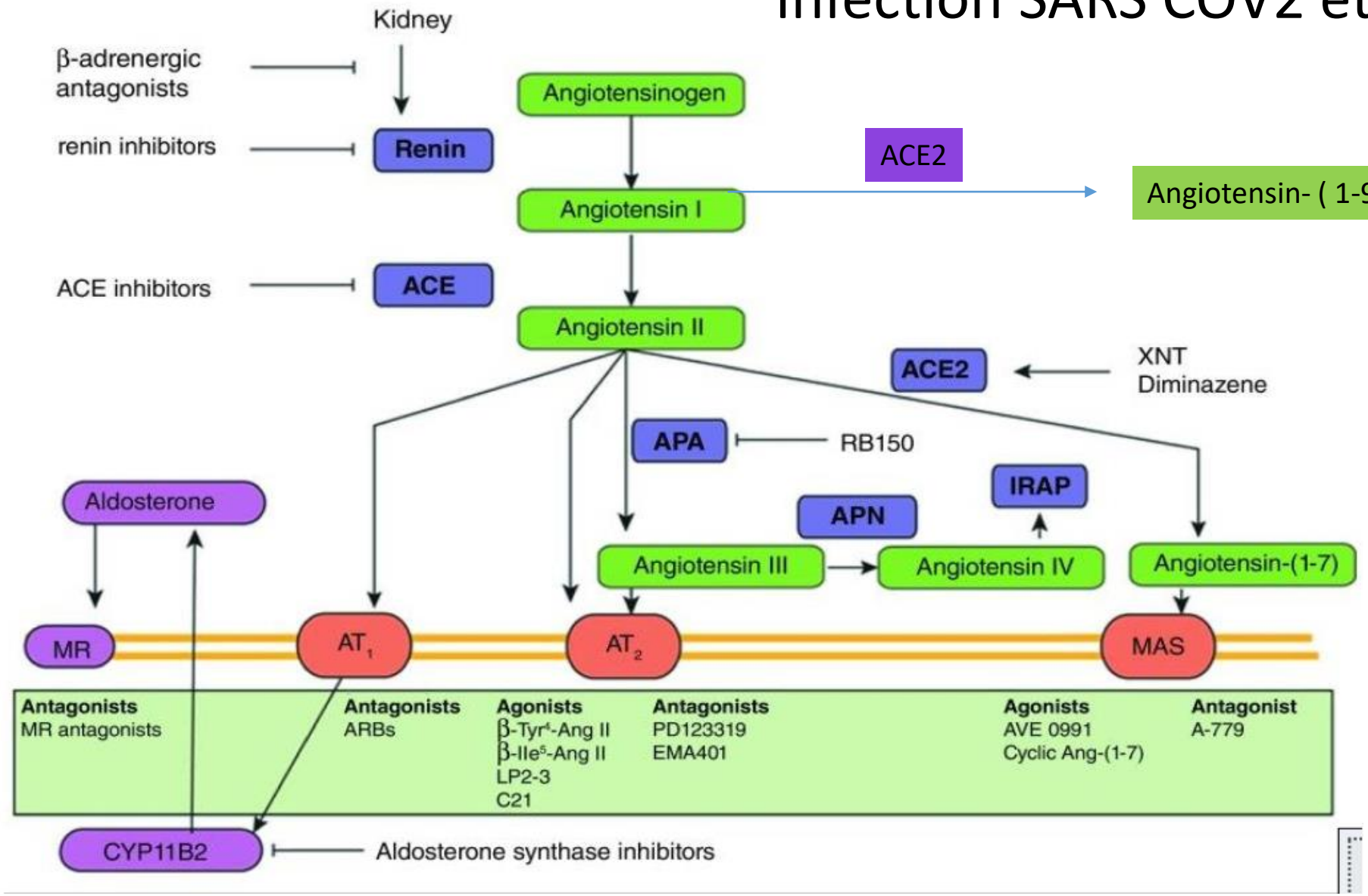
Pneumocytes et Enterocytes expliquent donc la sémiologie clinique



Endocytose

ACE2 sert à protéger le poumon,
mécanisme bloqué par le COV2

Infection SARS COV2 et SRAA



Modulation ACE 2 : downregulation

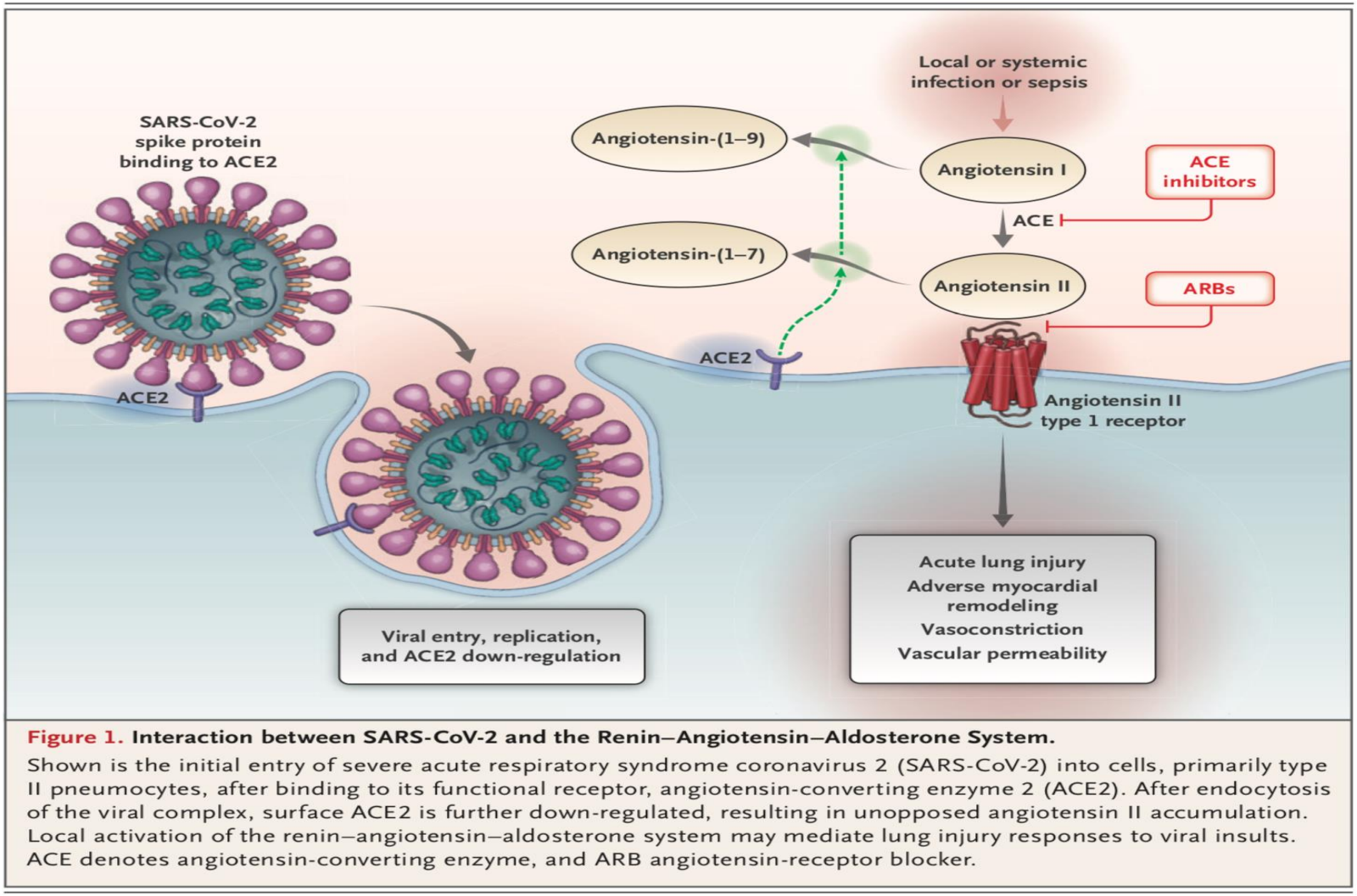
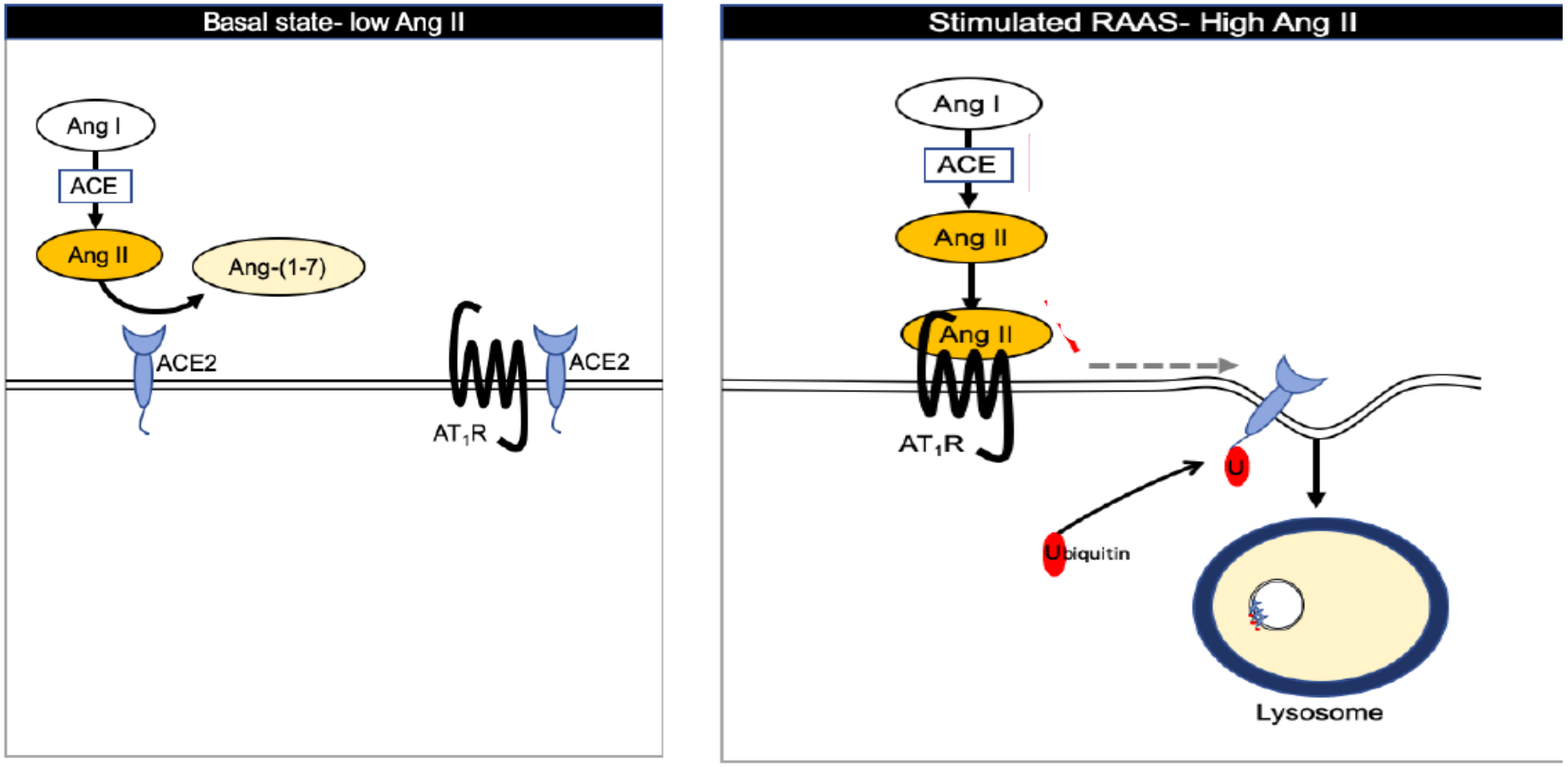


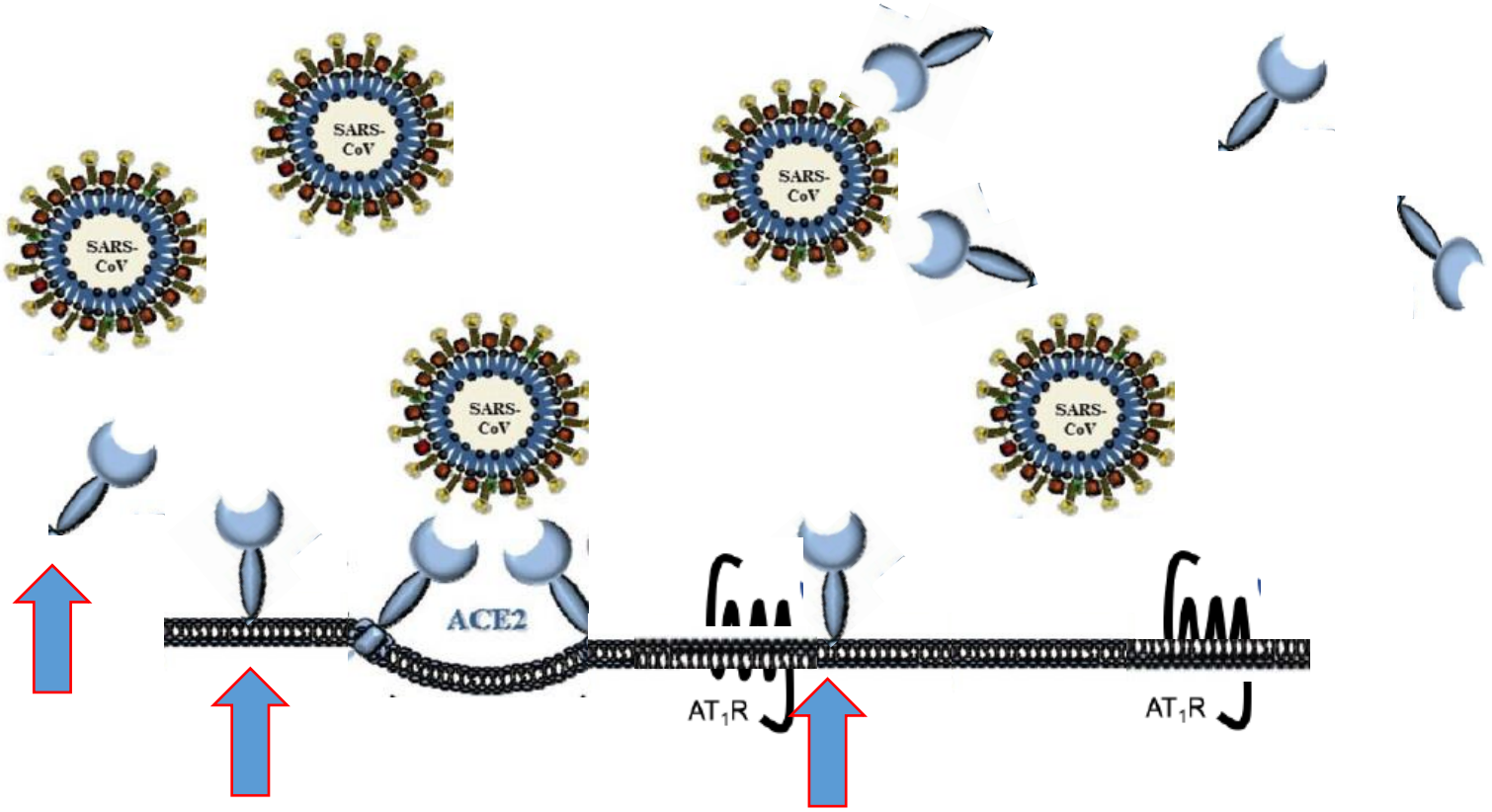
Figure 1. Interaction between SARS-CoV-2 and the Renin–Angiotensin–Aldosterone System.

Shown is the initial entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into cells, primarily type II pneumocytes, after binding to its functional receptor, angiotensin-converting enzyme 2 (ACE2). After endocytosis of the viral complex, surface ACE2 is further down-regulated, resulting in unopposed angiotensin II accumulation. Local activation of the renin–angiotensin–aldosterone system may mediate lung injury responses to viral insults. ACE denotes angiotensin-converting enzyme, and ARB angiotensin-receptor blocker.

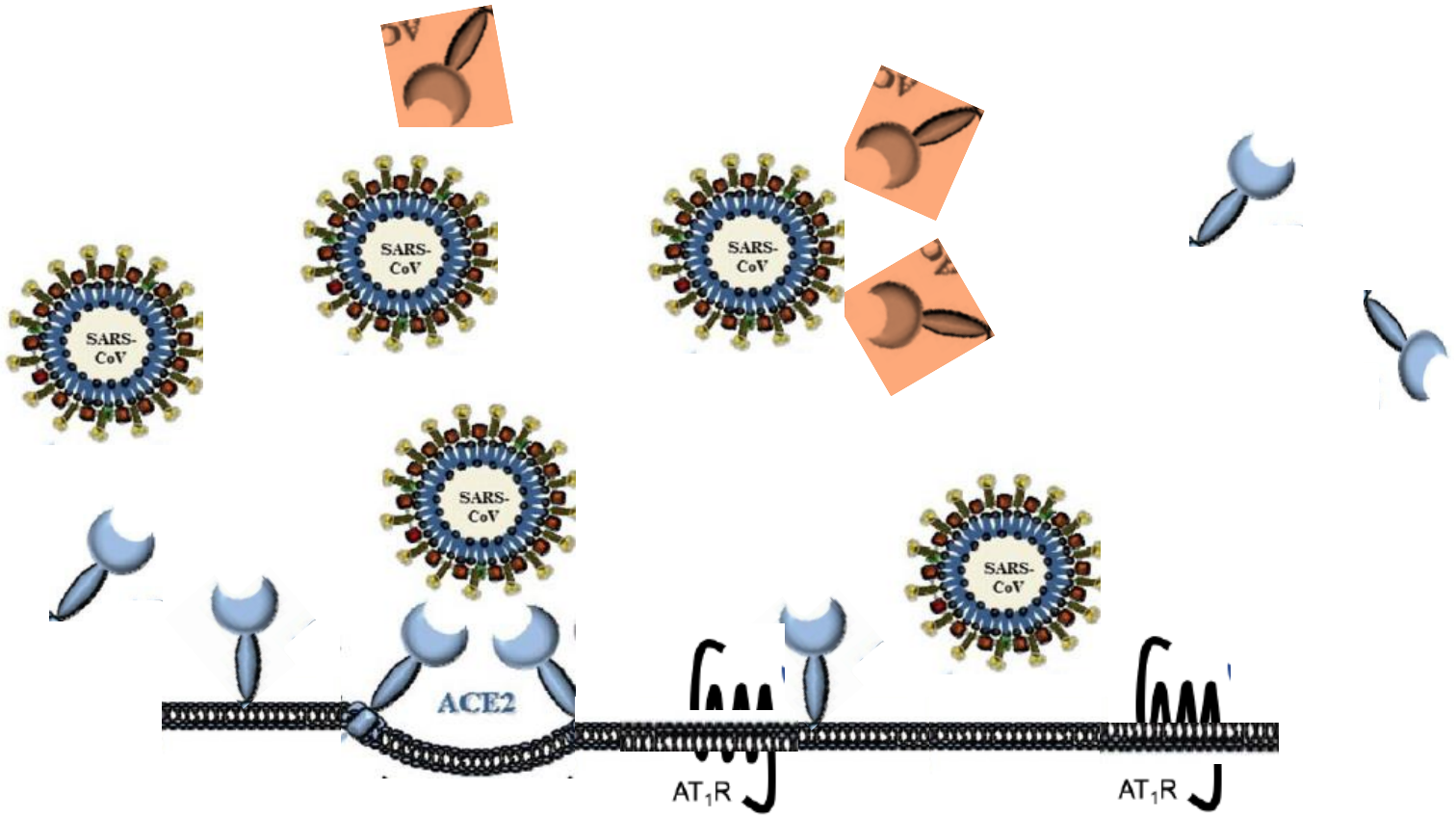
Modulation ACE 2 : recepteurs de reserve



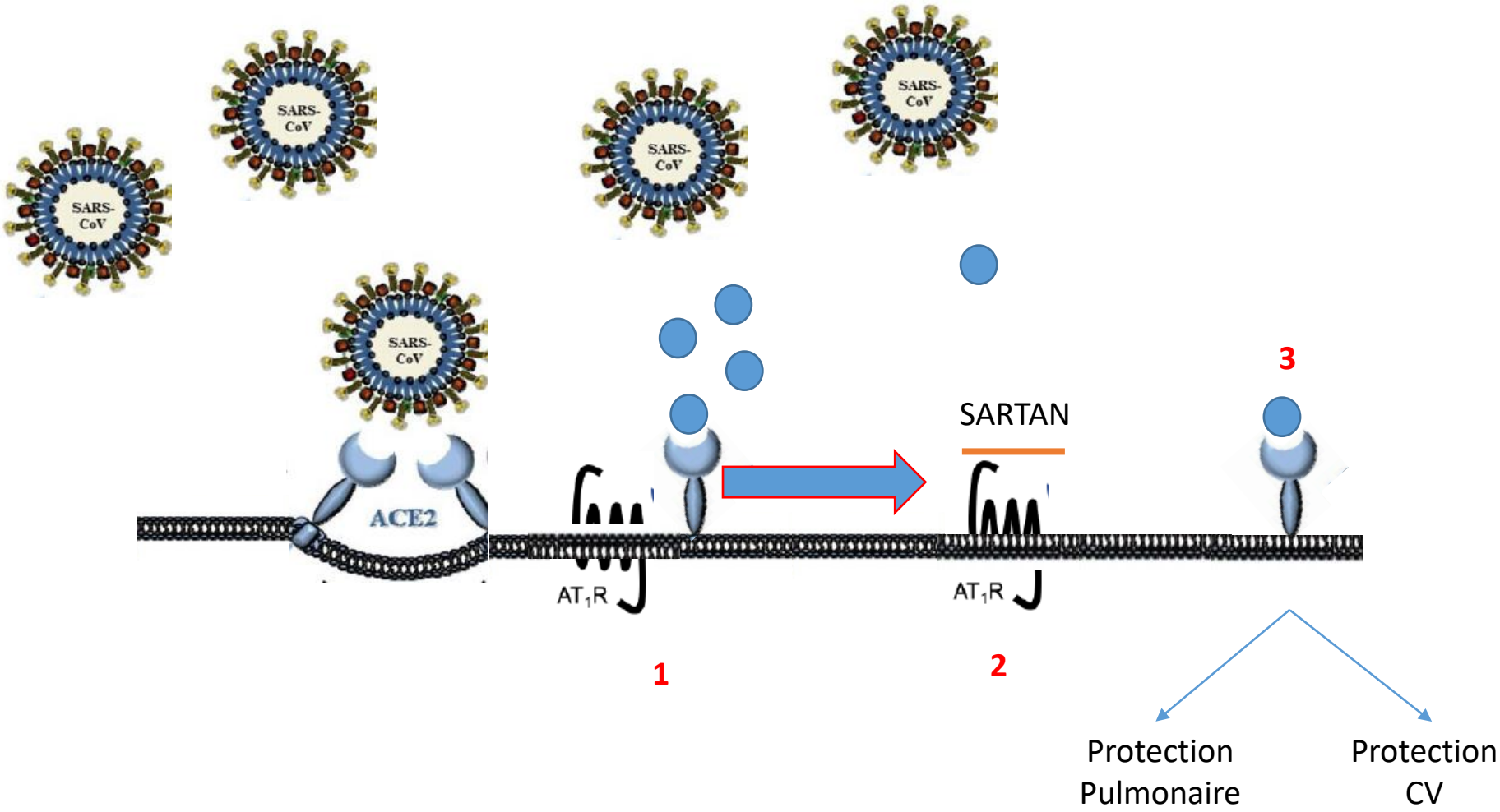
3 ACE2 : transmembranaire, solubles , couplés, 3 cibles ?



ACE2 recombinant



ARA 2 augmentent Angiotensine 2



Les IEC (non) et les ARA2 (oui) augmentent l'expression de ACE2?

- Chez l'animal oui et non.
- Chez l'homme non.
- Plus complexe qu'une interaction Ligand / récepteur

- Message clinique :
  - Activation RAS possible ?
  - **Surtout ne passer pas à cote de l'hypokaliemie**
  - **N'arrêter pas les traitements (Statement ESC / ESH / ACC / AHA)**

Research

JAMA Cardiology | Brief Report

Association of Renin-Angiotensin System Inhibitors With Severity or Risk of Death in Patients With Hypertension Hospitalized for Coronavirus Disease 2019 (COVID-19) Infection in Wuhan, China

Juyi Li, MD; Xiufang Wang, MS; Jian Chen, BS; Hongmei Zhang, MD; Aiping Deng, BS

Characteristic	Patients with hypertension						
	No. (%)				Survivor, No. (%)		
	Total (N = 362)	Severe (n = 173)	Nonsevere (n = 189)	*P* value	Yes (n = 285)	No (n = 77)	*P* value
Age, median (IQR), y	66.0 (59.0-73.0)	69.0 (62.0-76.0)	64.0 (57.0-70.5)	<.001	65.0 (57.5-71.0)	72.0 (64.5-82.0)	<.001
Distribution							
<40	9 (2.5)	3 (1.7)	6 (3.2)	.03	9 (3.2)	0 (0)	.004
40-60	94 (26.0)	35 (20.2)	59 (31.2)		82 (28.8)	12 (15.6)	
>60	259 (71.5)	135 (78.0)	124 (65.6)		194 (68.1)	65 (84.4)	
Sex							
Women	173 (47.8)	76 (43.9)	97 (51.3)	.16	146 (51.2)	27 (35.1)	.01
Men	189 (52.2)	97 (56.1)	92 (48.7)		139 (48.2)	50 (64.9)	
Chronic disease							
Cerebrovascular disease	68 (18.8)	50 (28.9)	18 (9.5)	<.001	31 (10.9)	37 (48.1)	<.001
Coronary heart disease	62 (17.1)	39 (22.5)	23 (12.2)	.01	41 (14.4)	21 (27.3)	.01
Heart failure	10 (2.8)	8 (4.6)	2 (1.1)	.08	5 (1.8)	5 (6.5)	.06
Diabetes	127 (35.1)	76 (43.9)	51 (27.0)	.001	89 (31.2)	38 (49.4)	.003
Digestive disorder	78 (21.5)	41 (23.7)	37 (19.6)	.34	66 (23.2)	12 (15.6)	.15
Respiratory disease	18 (5.0)	8 (4.6)	10 (5.3)	.77	12 (4.2)	6 (7.8)	.32
Neurological disease	38 (10.5)	25 (14.5)	13 (6.9)	.02	25 (8.8)	13 (16.9)	.04
Solid tumor	11 (3.0)	8 (4.6)	3 (1.6)	.09	6 (2.1)	5 (6.5)	.11
Chronic renal disease	35 (9.7)	30 (17.3)	5 (2.6)	<.001	15 (5.3)	20 (26.0)	<.001
Antihypertensive drugs							
Treatment scheme							
CCBs	168 (46.4)	79 (45.7)	89 (47.1)	.79	130 (45.6)	38 (49.4)	.56
CCBs+ARBs	59 (16.3)	32 (18.5)	27 (14.3)	.28	48 (16.8)	11 (14.3)	.59
CCBs+ACEIs	23 (6.4)	13 (7.5)	10 (5.3)	.39	17 (6.0)	6 (7.8)	.75
ACEIs	12 (3.3)	3 (1.7)	9 (4.8)	.11	11 (3.9)	1 (1.3)	.45
ARBs	24 (6.6)	11 (6.4)	13 (6.9)	.84	20 (7.0)	4 (5.2)	.57
β receptor blockers	14 (3.9)	8 (4.6)	6 (3.2)	.48	8 (2.8)	6 (7.8)	.09
No drug treatment	65 (18.0)	29 (16.8)	36 (19.0)	.57	53 (18.6)	12 (15.6)	.54
Classification							
ACEIs (contains ACEIs)	35 (9.7)	16 (9.2)	19 (10.1)	.80	28 (9.8)	7 (9.1)	.85
ARBs (contains ARBS)	83 (22.9)	43 (24.9)	40 (21.2)	.40	68 (23.9)	15 (19.5)	.42
ACEIs/ARBs (contains either)[a]	115 (31.8)	57 (32.9)	58 (30.7)	.65	94 (33.0)	21 (27.3)	.34
ACEIs/ARBs vs Non-ACEIs/ARBs							
ACEIs/ARBs	115 (31.8)	57 (32.9)	58 (30.7)	.65	94 (33.0)	21 (27.3)	.34
Non-ACEIs/ARBs	247 (68.2)	116 (67.1)	131 (69.3)		191 (67.0)	56 (72.7)	
Hospital stay, median (IQR), d	19.0 (12.0-27.0)	20.0 (12.0-32.0)	19.0 (11.0-24.0)	.002	19.0 (13.0-26.0)	15.0 (6.0-30.0)	.73
Nonsurvivor	77 (21.3)	77 (44.5)	0 (0)	<.001	NA	NA	NA

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Association of Inpatient Use of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Mortality Among Patients With Hypertension Hospitalized With COVID-19

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Parameters	Unmatched			Matched (1:2)		
	ACEI/ARB[†] (n = 188)	Non-ACEI/ARB[‡] (n = 940)	SD[§]	ACEI/ARB[†] (n = 174)	Non-ACEI/ARB[‡] (n = 348)	SD[§]
Clinical characteristics on admission						
Age, median(IQR)	64 (55-68)	64 (57-69)	-0.035	64(56-68)	64(56-69)	-0.046
Male gender, n (%)	100(53.2)	503(53.5)	-0.006	94(54.0)	197(56.6)	-0.052
Female gender, n (%)	88(46.8)	437(46.5)	0.006	80(46.0)	151(43.4)	0.052
Heart rate, median(IQR)	82.0(76.0-95.3)	84.0(78.0-96.0)	-0.062	82(76-94)	82(77-94)	-0.004
Respiratory rate, median(IQR)	20.0(19.0-21.0)	20.0(19.0-22.0)	-0.049	20(19-21)	20(18-21)	0.013
SBP, median(IQR)	132.5(123.0-145.8)	132.0(120.0-144.0)	0.064	134(124-148)	132(121-145)	0.027
DBP, median(IQR)	80.0(72.0-87.8)	80.0(72.0-88.0)	-0.020	80(74-88)	80(73-87)	0.072
Symptom onset to admission, median(IQR), day	10.0(7.0-15.0)	10.0(7.0-15.0)	-0.055	10(7-15)	10(7-15)	-0.111
Fever, n(%)	126(67.0)	700(74.5)	-0.164	120(69.0)	235(67.5)	0.031
Cough, n(%)	122(64.9)	653(69.5)	-0.098	111(63.8)	223(64.1)	-0.006
Fatigue, n(%)	65(34.6)	363(38.6)	-0.084	60(34.5)	131(37.6)	-0.066
Dyspnea, n(%)	38(20.2)	260(27.7)	-0.175	34(19.5)	66(19.0)	0.015
Comorbidities on admission						
Diabetes, n(%)	44(23.4)	196(20.9)	-0.062	40(23.0)	86(24.7)	-0.040
Coronary heart disease, n(%)	29(15.4)	102(10.9)	0.136	24(13.8)	46(13.2)	0.017
Chronic renal diseases, n(%)	7(3.7)	28(3.0)	0.041	7(4.0)	11(3.2)	0.046
Cerebrovascular diseases, n(%)	5(2.7)	36(3.8)	-0.066	4(2.3)	8(2.3)	0.000
Chronic liver disease, n(%)	4(2.1)	17(1.8)	0.023	4(2.3)	5(1.4)	0.064
Chronic obstructive pulmonary disease, n(%)	1(0.5)	5(0.5)	0.000	1(0.6)	1(0.3)	0.044
Chest CT on admission						
Unilateral lesion, n/N(%)	16/173(9.3)	42/895(4.7)	0.180	13/159(8.2)	18/329(5.5)	0.107
Bilateral lesions, n/N (%)	146/173(84.4)	795/895(88.8)	-0.130	137/159(86.2)	284/329(86.3)	-0.005
Laboratory examination on admission						
Leukocyte count > 9.5, 10^9/L, n/N (%)	22/183(12.0)	101/883(11.4)	0.018	20/170(11.8)	32/325(9.9)	0.062

Table 3 Hazard ratios and incidence rate ratios for outcomes in ACEI/ARB group versus non-ACEI/ARB group under mixed-effect Cox model and propensity score-matching model

	Unmatched					Matched (1:2) †		
		Crude		Mixed-effect Model*		Mixed-effect Model		
ACEI/ARB vs non-ACEI/ARB	IRD (100 Person-Day) (95%CI)	HR(95%CI)	*P* value§	HR(95%CI)	*P* value‖	IRD (100 Person-Day) (95%CI)	HR(95%CI)	*P* value‖
All-cause mortality	-0.24(-0.43,-0.05)	0.37(0.17,0.79)	0.01	0.42(0.19,0.92)	0.03	-0.27(-0.48,-0.07)	0.37(0.15-0.89)	0.03
Septic shock	-0.19(-0.36,-0.01)	0.38(0.17,0.87)	0.02	0.36(0.16,0.84)	0.02	-0.20(-0.39,-0.01)	0.32(0.13-0.80)	0.01
ARDS	-0.23(-0.52,0.07)	0.70(0.47,1.02)	0.06	0.69(0.47,1.02)	0.06	-0.32(-0.65,0.01)	0.65(0.41-1.04)	0.07
DIC	-0.09(-0.19,0.00)	0.04(0.0, 4.50)	0.18	-‡	-‡	-0.10(-0.19,0.00)	-‡	-‡
Acute kidney injury	0.05(-0.10,0.20)	1.17(0.60,2.25)	0.65	1.03(0.51,2.07)	0.94	-0.04(-0.23,0.16)	0.78(0.37-1.65)	0.52
Acute heart injury	-0.10(-0.29,0.08)	0.91(0.57,1.45)	0.70	0.89(0.55,1.44)	0.64	0.00(-0.27,0.27)	0.76(0.44-1.32)	0.33

Alors
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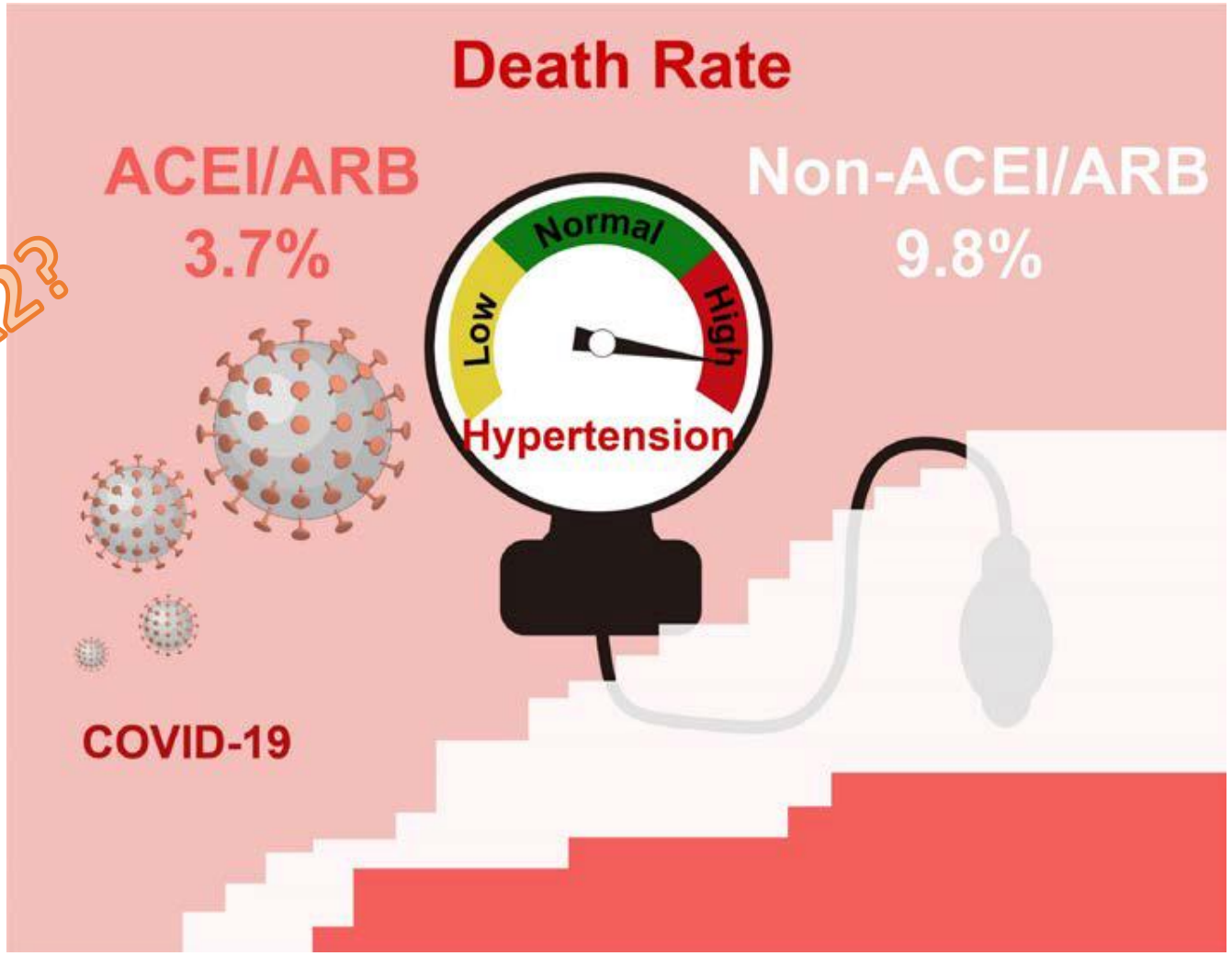

Conclusion

Les malades du cardiologues constituent les patients les plus souvent infectés par le COVID19

Toute présentation CV peut être imputable au COVID19

La lésion cardiaque aigue est la complication la plus délétère

Le SRAA est implique dans la physiopathologie de l'infection COVID19

Ne pas arrêter les médicaments CV

TROD, Serodiagnostic , PCR changeront la donne