



# HTA y Bloqueo del SRA en tiempos de la COVID-19

***“Donde dije digo, digo Diego”***

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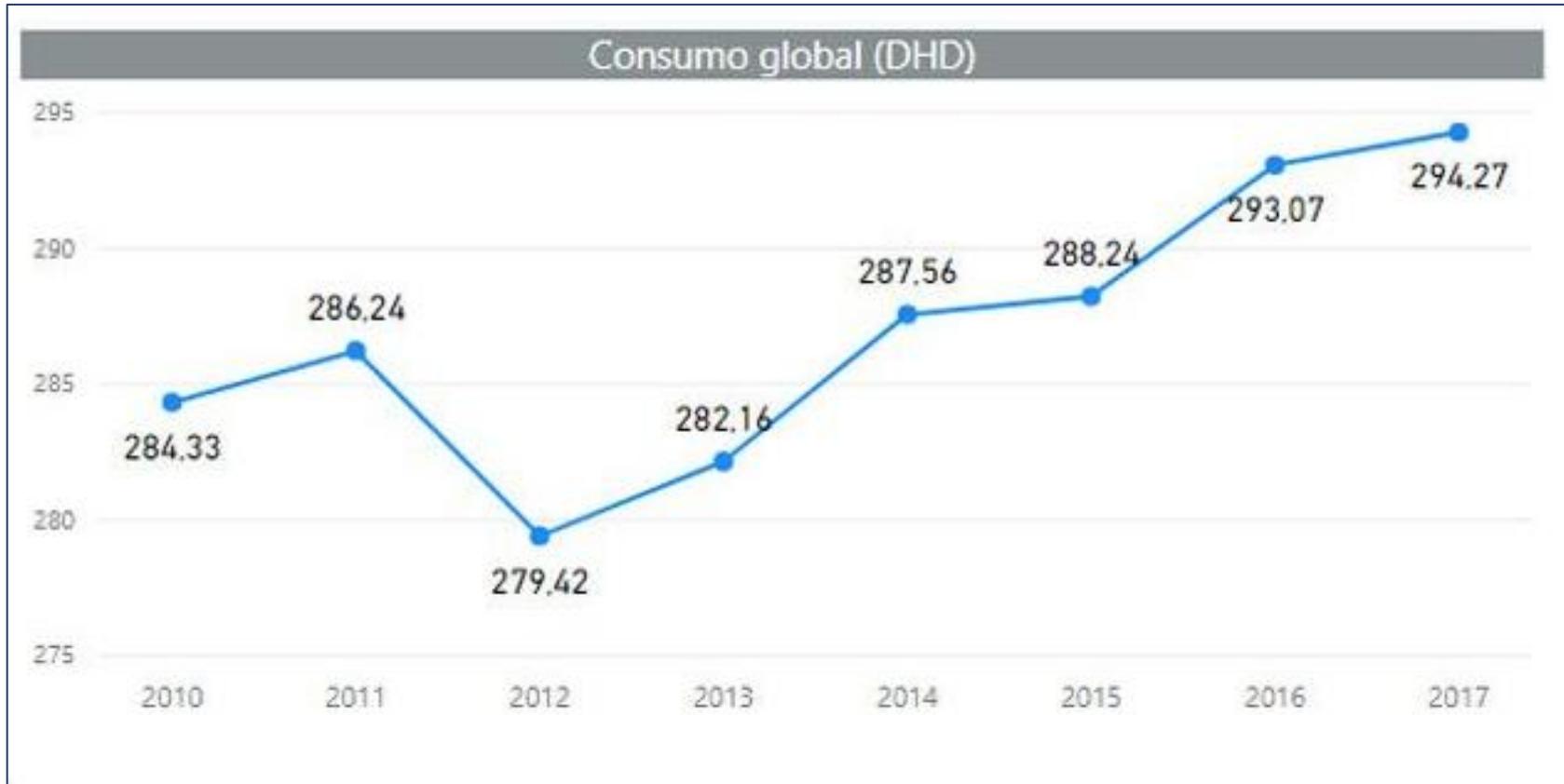


# HTA y Bloqueo del SRA en tiempos de la COVID-19

***“Donde dije digo, digo Diego”***

Vicente Pallarés  
Médico de Familia  
Castellón

# Consumo global de fármacos para la hipertensión en España (periodo 2010-2017)



BSRAA: 179,20 Rec/1000 hab/día  
CA: 38,72 Rec/1000 hab/día  
DIU: 43,33 Rec/1000 hab/día  
BB: 24,06 Rec/1000 hab/día

Fuente: AEMPS. Julio 2018



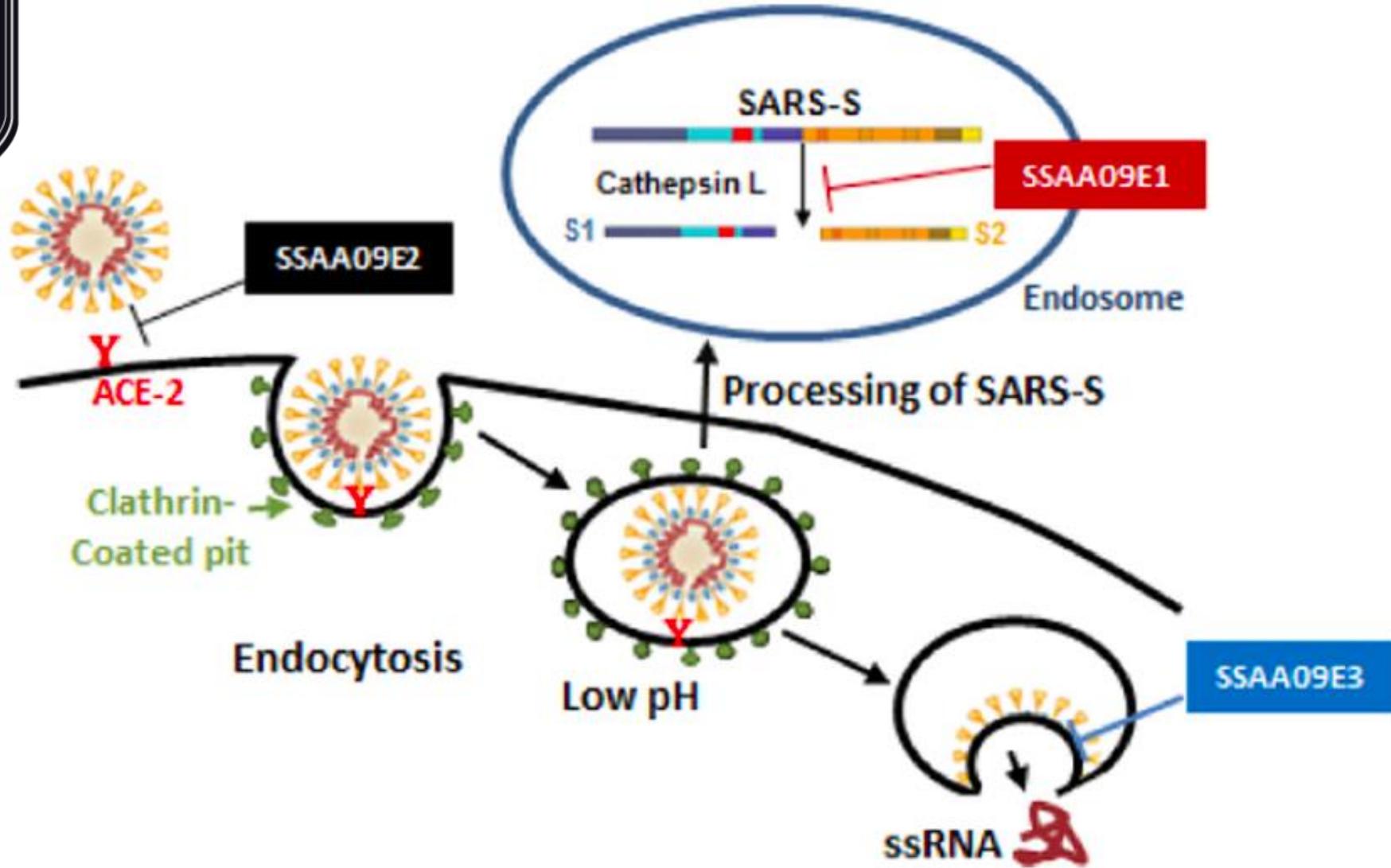
# Qué sabemos sobre los medicamentos para la hipertensión en pacientes con coronavirus

Diversos textos virales sugieren que quienes toman los antihipertensivos IECA o ARA II pueden ver agravada su situación si han enfermado por COVID-19. Los mensajes también mencionan ciertos antiinflamatorios. Esto es lo que dicen las autoridades sanitarias





# Stages of SARS-CoV entry inhibited by novel SARS-CoV small-molecule inhibitors





# ¿Algunos antihipertensivos pueden agravar la infección por SARS-CoV2?

 Rapid response to:

Preventing a covid-19 pandemic

28/febrero/2020

*BMJ* 2020 ; 368 doi: <https://doi.org/10.1136/bmj.m810> (Published 28 February 2020)

Cite this as: *BMJ* 2020;368:m810

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Article

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03/marzo/2020

Rapid Response:

Re: Preventing a covid-19 pandemic: ACE inhibitors as a potential risk factor for fatal Covid-19

Dear Editor,

03 March 2020

Rami Sommerstein

Infectious Diseases Physician and Hospital Epidemiologist

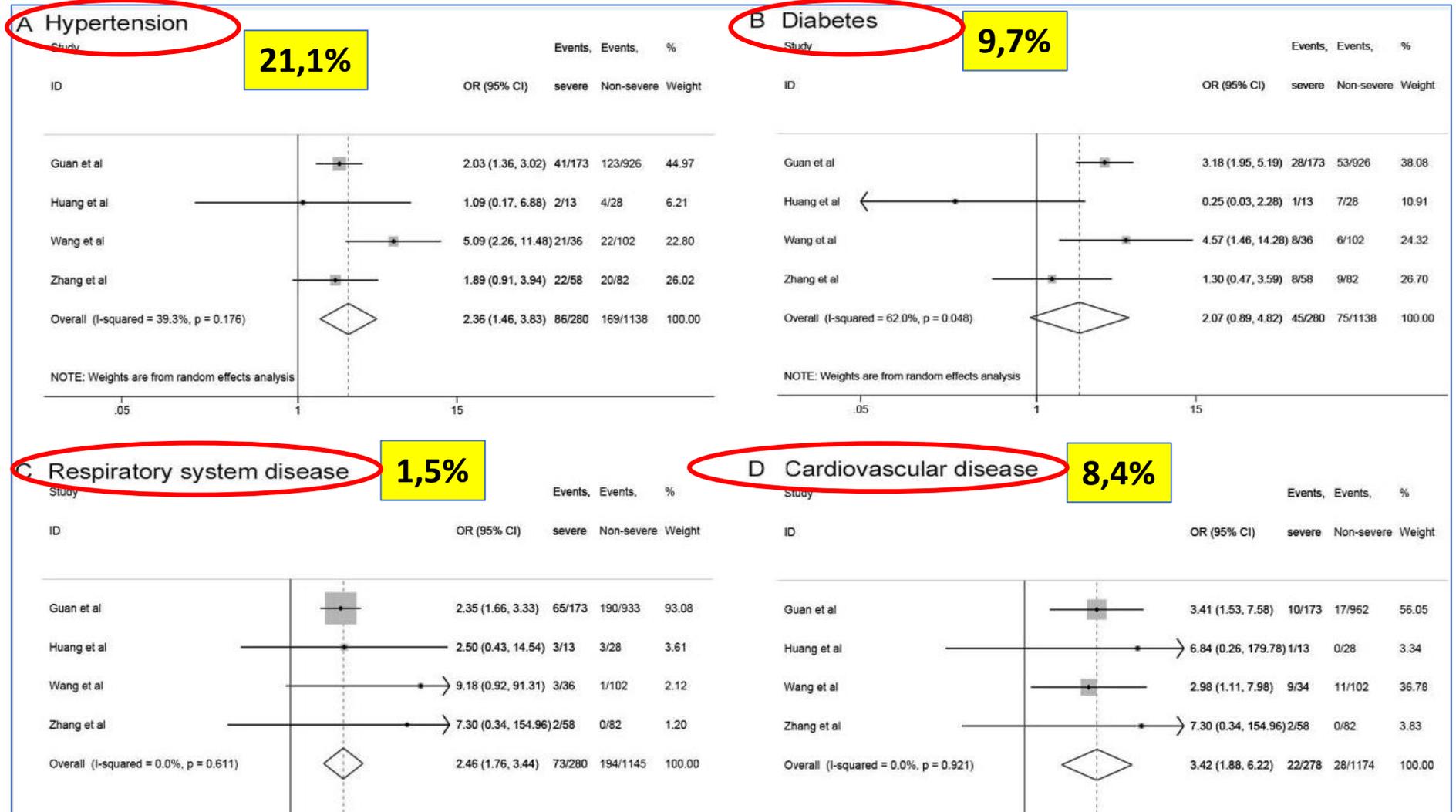
Christoph Gräni, Department of Cardiology, Bern University

Hospital, Switzerland



# Prevalencia de comorbilidades y sus efectos en pacientes infectados con SARS-CoV-2: una revisión sistemática y un meta-análisis

**N=1.576**





# ¿Algunos antihipertensivos pueden agravar la infección por SARS-CoV2?

THE LANCET  
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## Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?

Lei Fang • George Karakiulakis • Michael Roth 

Published: March 11, 2020 • DOI: [https://doi.org/10.1016/S2213-2600\(20\)30116-8](https://doi.org/10.1016/S2213-2600(20)30116-8)

 PlumX Metrics

- ✓ Sugerimos que los pacientes con enfermedades cardíacas, hipertensión o diabetes, que son tratados con medicamentos que aumentan la ECA2, tienen un mayor riesgo de infección grave por COVID-19 y, por lo tanto, deben controlarse para detectar medicamentos moduladores de la ECA2, como inhibidores de la iECA o ARA2.
- ✓ Según una búsqueda en PubMed el 28 de febrero de 2020, no encontramos ninguna evidencia que sugiera que los bloqueadores de los canales de calcio aumentan la expresión o actividad de ACE2, por lo tanto, estos podrían ser un tratamiento alternativo adecuado en estos pacientes.



**Table. Recommendations on the Use of Angiotensin-Converting Enzyme Inhibitors (ACEIs) and Angiotensin Receptor Blockers (ARBs) in Patients With Coronavirus Disease 2019 (COVID-19)**

Professional society; source	Date of release	Key statements
HFSA, ACC, and AHA; <a href="https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19">https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19</a>	March 17, 2020	"The HFSA, ACC, and AHA recommend continuation of RAAS antagonists for those patients who are currently prescribed such agents for indications for which these agents are known to be beneficial, such as heart failure, hypertension, or ischemic heart disease. In the event patients with cardiovascular disease are diagnosed with COVID-19, individualized treatment decisions should be made according to each patient's hemodynamic status and clinical presentation. Therefore, be advised not to add or remove any RAAS-related treatments, beyond actions based on standard clinical practice."
ESC Council on Hypertension; <a href="https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-council-on-hypertension-on-ace-inhibitors-and-ang">https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-council-on-hypertension-on-ace-inhibitors-and-ang</a>	March 13, 2020	"The Council on Hypertension strongly recommend that physicians and patients should continue treatment with their usual anti-hypertensive therapy because there is no clinical or scientific evidence to suggest that treatment with ACEi or ARBs should be discontinued because of the Covid-19 infection."
ESH; <a href="https://www.eshonline.org/spotlights/esh-statement-on-covid-19/">https://www.eshonline.org/spotlights/esh-statement-on-covid-19/</a>	March 12, 2020	<ul style="list-style-type: none"> <li>• "In stable patients with COVID-19 infections or at risk for COVID-19 infections, treatment with ACEIs and ARBs should be executed according to the recommendations in the 2018 ESC/ESH guidelines."</li> <li>• "The currently available data on COVID-19 infections do not support a differential use of RAS blockers (ACEi or ARBs) in COVID-19 patients."</li> </ul>
Hypertension Canada; <a href="https://hypertension.ca/wp-content/uploads/2020/03/2020-30-15-Hypertension-Canada-Statement-on-COVID-19-ACEi-ARB.pdf">https://hypertension.ca/wp-content/uploads/2020/03/2020-30-15-Hypertension-Canada-Statement-on-COVID-19-ACEi-ARB.pdf</a>	March 13, 2020	<ul style="list-style-type: none"> <li>• "However, there is no evidence that patients with hypertension or those treated with ARB or ACE inhibitor antihypertensive therapy are at higher risk of adverse outcomes from COVID-19 infection."</li> <li>• "We endorse patients with hypertension to continue with their current blood pressure treatment."</li> </ul>
The Canadian Cardiovascular Society and the Canadian Heart Failure Society; <a href="https://www.ccs.ca/images/Images_2020/CCS_CHFS_statement_regarding_COVID_EN.pdf">https://www.ccs.ca/images/Images_2020/CCS_CHFS_statement_regarding_COVID_EN.pdf</a>	March 15, 2020	"The Canadian Cardiovascular Society and the Canadian Heart Failure Society strongly discourage the discontinuation of guideline directed medical therapy (GDMT) involving Angiotensin Converting Enzyme Inhibitors (ACEi), Angiotensin Receptor Blockers (ARB) or Angiotensin Receptor Neprilysin Inhibitors (ARNi) in hypertensive or heart failure patients as a result of the COVID-19 pandemic."
International Society of Hypertension; <a href="https://ish-world.com/news/a/A-statement-from-the-International-Society-of-Hypertension-on-COVID-19/">https://ish-world.com/news/a/A-statement-from-the-International-Society-of-Hypertension-on-COVID-19/</a>	March 16, 2020	"[T]here is no good evidence to change the use of ACE-inhibitors or ARBs for the management of raised blood pressure in the context of avoiding or treating COVID-19 infection."
BCS and BSH; <a href="https://www.britishcardiosvascularsociety.org/news/ACEi-or-ARB-and-COVID-19">https://www.britishcardiosvascularsociety.org/news/ACEi-or-ARB-and-COVID-19</a>	March 19, 2020	"[T]he BCS and the BSH...share the view of the European Society of Hypertension and the Renal Association that patients should continue treatment with ACEi and ARB unless specifically advised to stop by their medical team."

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; BCS, British Cardiovascular Society; BSH, British Society for Heart Failure; ESC, European Society of Cardiology; ESH, European Society of Hypertension; HFSA, Heart Failure Society of America; RAAS, renin angiotensin aldosterone system.



16 de Marzo de 2020

## **"No se dispone de evidencia suficiente para suspender/modificar el tratamiento establecido con IECA o ARA II debido a la probable infección por COVID-19"**

### ***Grupo de Trabajo de HTA y ECV***

Desde el Grupo de trabajo de HTA y ECV de SEMERGEN, ante la gran difusión de noticias alarmantes relacionadas con el posible efecto perjudicial de los bloqueadores del sistema renina angiotensina (IECA/ARA II) muy utilizados en el tratamiento de la HTA, y otras patologías como la ICC, que pueden aumentar el riesgo de infección por COVID-19 y la severidad de ésta. En línea con los recientes comunicados publicados tanto por la ESH como por la ESC (1,2), queremos enviar un mensaje de calma tanto a nuestros compañeros de Atención Primaria como, a sus pacientes, y expresar lo siguiente:

1. En el momento actual no existe suficiente evidencia científica de que la hipertensión per se, esté asociada con un mayor riesgo de infección por COVID-19.
2. Los pacientes con hipertensión deben seguir las mismas recomendaciones y precauciones que el resto de la población.
3. En pacientes estables con infecciones por COVID-19 o en riesgo de infección, el tratamiento con IECA y ARA II, debe mantenerse de acuerdo con las recomendaciones de las guías de práctica clínica más recientes (Guías ESC/ESH 2018) (3,4).
4. Los datos disponibles actualmente sobre las infecciones por COVID-19 no respaldan la suspensión o modificación del tratamiento con IECA o ARA II en los pacientes hipertensos o con insuficiencia cardíaca con infección por COVID-19.

<https://www.semergen.es/?seccion=noticias&subSeccion=detalleNoticia&idN=618>



**ALERTA COVID-19**

# ...y además



25/03/2020 22:13

SOCIEDAD - CORONABULOS

## No está demostrado que los antihipertensivos agraven la infección por COVID-19

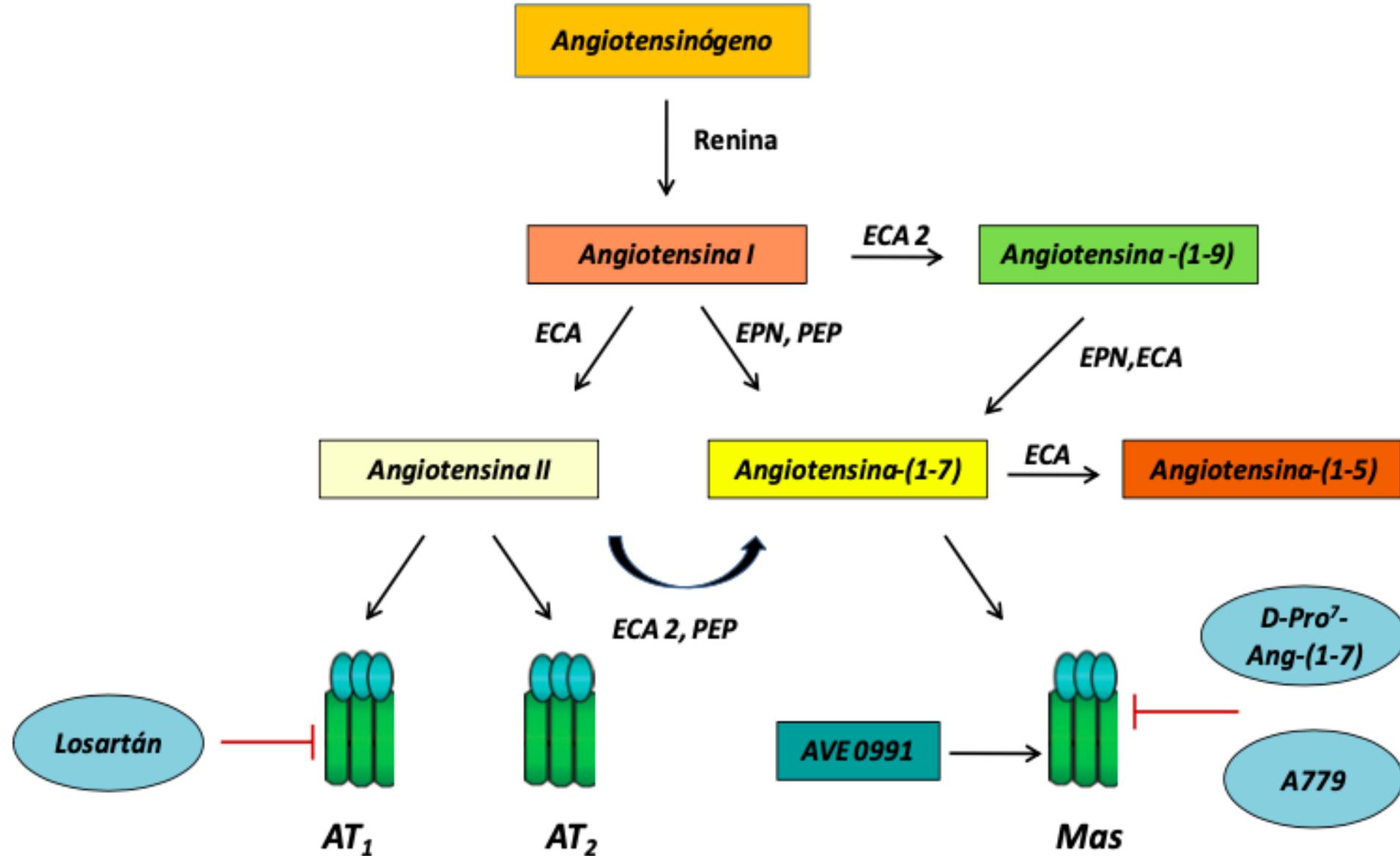
EITB

Un mensaje de WhatsApp alerta sobre el supuesto peligro que supone la utilización de medicamentos contra la hipertensión ante el coronavirus.

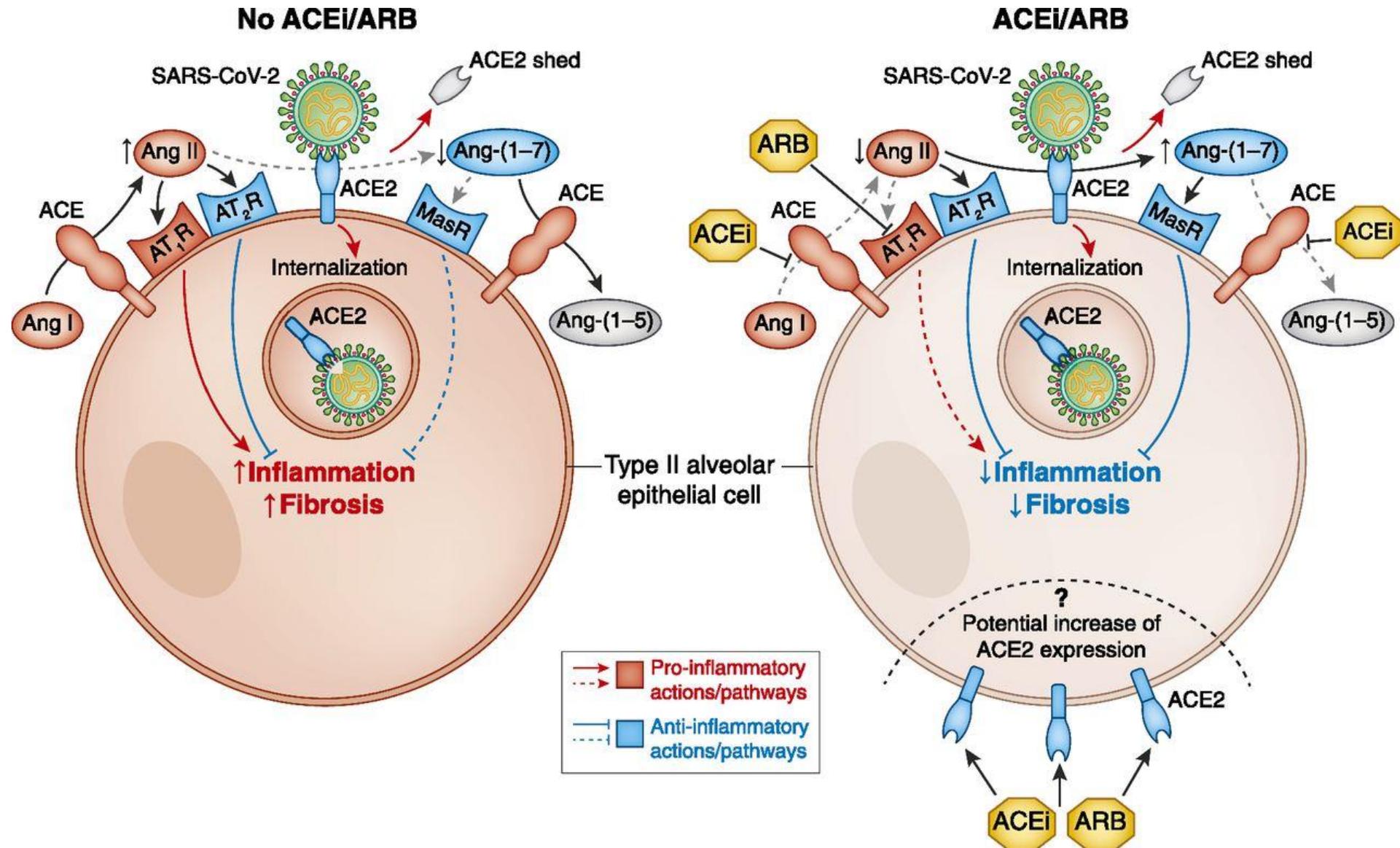
través del receptor ECAll. Cuando se une a él lo sobreexpresa y mata la célula alveolar. De ahí todo lo que produce. Los hombres tienen más receptores que las mujeres, los asiáticos más que los caucásicos y la gente que toma antihipertensivos del tipo antiECAs y sobre todo Anti-ECAll tiene una sobreexpresión brutal del receptor y por

Bulo sobre los medicamentos antihipertensivos y el COVID-19. Foto: EITB

# Esquema del Sistema Renina Angiotensina

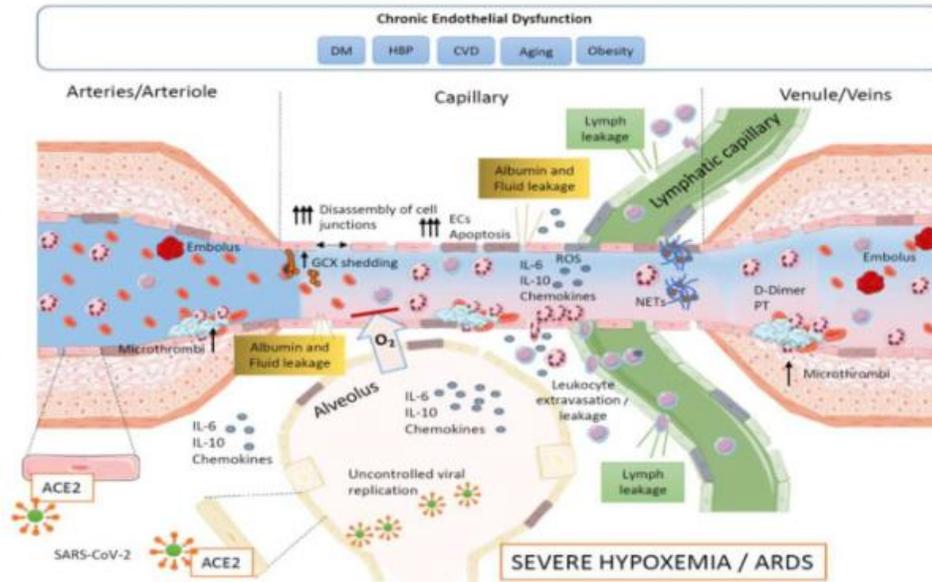


# Efecto potencial de los BSRA sobre el síndrome respiratorio agudo severo coronavirus 2 (SARS-CoV-2)

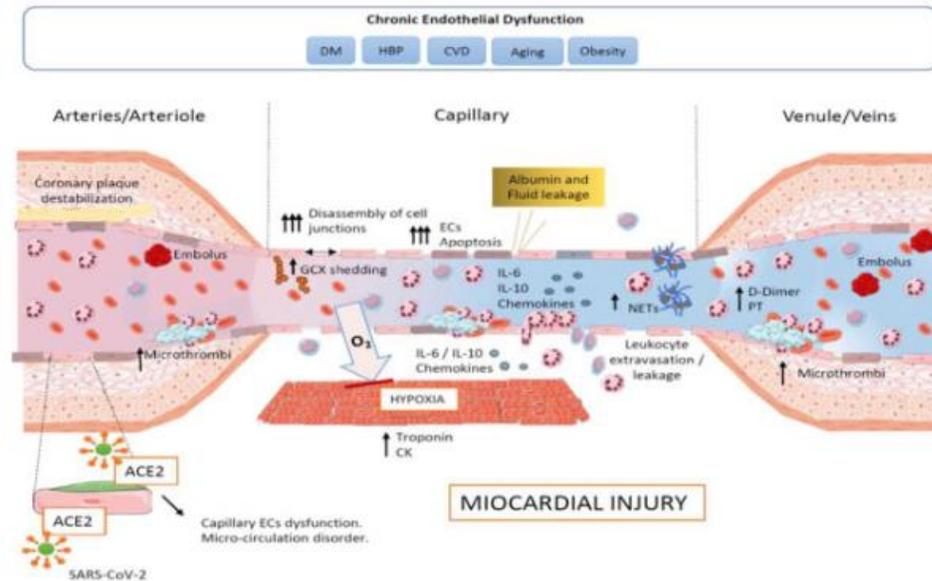


# Disfunción endotelial en COVID-19

ENDOTHELIAL DYSFUNCTION IN THE LUNGS IN COVID-19

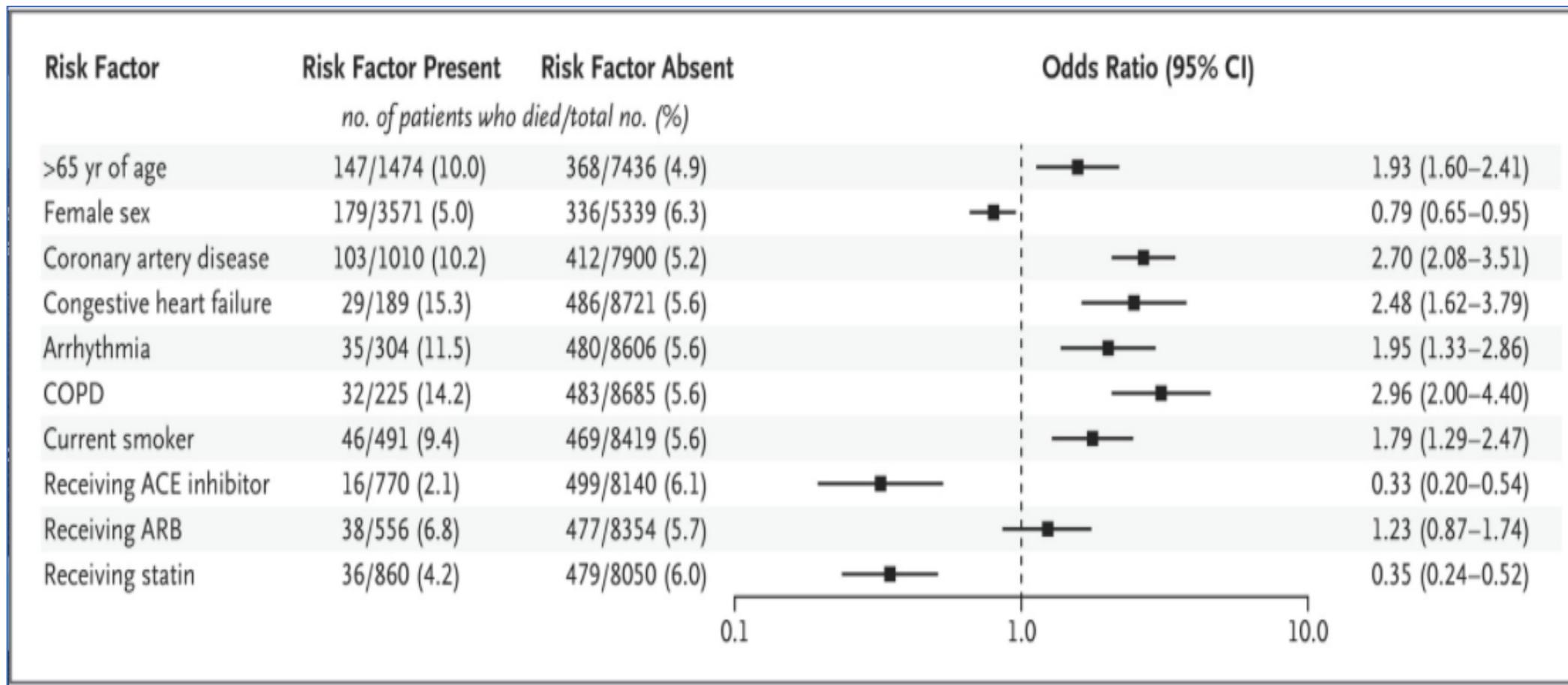


ENDOTHELIAL DYSFUNCTION IN THE HEART IN COVID-19



En un paciente incapaz de controlar el virus, la infección viral podría inducir daño directo a las células endoteliales.

Junto con factores virales, la existencia de disfunción endotelial previa debido al envejecimiento y enfermedades crónicas podría favorecer el desarrollo de una respuesta disfuncional a la infección, con la producción de citoquinas por las propias células endoteliales del paciente, neumocitos o neutrófilos, especies reactivas de oxígeno y trampas extracelulares de neutrófilos.

Cardiovascular Disease, Drug Therapy,  
and Mortality in Covid-19Mandeep 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.Enfermedad cardiovascular, fármacos,  
y mortalidad en Covid-19 (N= 8.910)

## Renin–Angiotensin–Aldosterone System Blockers and the Risk of Covid-19

Giuseppe Mancía, M.D., Federico Rea, Ph.D., Monica Ludergnani, M.Sc., Giovanni Apolone, M.D., and Giovanni Corrao, Ph.D.

# Bloqueantes del Sistema Renina-Angiotensina y riesgo de la Covid-19

*Estudio casos (6.272) y controles (30.759) en Lombardia (Italia)*

**Table 4. Adjusted Odds Ratios for Covid-19 Associated with Use of RAAS Blockers and Other Antihypertensive Drugs.**

Variable	Odds Ratio for Covid-19 (95% CI)*				
	ACE Inhibitors	ARBs	Calcium-Channel Blockers	Diuretics	Beta-Blockers
Severity of clinical manifestations†					
Mild to moderate	0.97 (0.88–1.07)	0.96 (0.87–1.07)	1.01 (0.92–1.10)	1.07 (0.97–1.19)	0.98 (0.89–1.07)
Critical or fatal	0.91 (0.69–1.21)	0.83 (0.63–1.10)	1.15 (0.91–1.44)	0.96 (0.74–1.26)	1.07 (0.84–1.37)
Sex‡					
Female	0.95 (0.81–1.12)	0.89 (0.76–1.05)	1.06 (0.92–1.23)	1.12 (0.94–1.34)	1.04 (0.91–1.20)
Male	0.98 (0.87–1.11)	0.98 (0.86–1.11)	1.00 (0.90–1.11)	1.02 (0.91–1.15)	0.97 (0.87–1.08)
Age at diagnosis§					
<60 Yr	0.94 (0.71–1.25)	0.89 (0.67–1.18)	1.13 (0.88–1.46)	0.99 (0.75–1.31)	1.00 (0.78–1.29)
≥60 Yr	0.97 (0.87–1.08)	0.95 (0.85–1.06)	1.01 (0.93–1.11)	1.07 (0.97–1.19)	0.99 (0.90–1.08)

# Probabilidad de Covid-19 grave en hipertensos tratados con cinco clases de antihipertensivos

(*n*=12.594; 4.357 hipertensos)

## Renin–Angiotensin–Aldosterone System Inhibitors and Risk of Covid-19

Harmony R. Reynolds, M.D., Samrachana Adhikari, Ph.D.,  
Claudia Pulgarin, M.A., M.S., Andrea B. Troxel, Sc.D.,

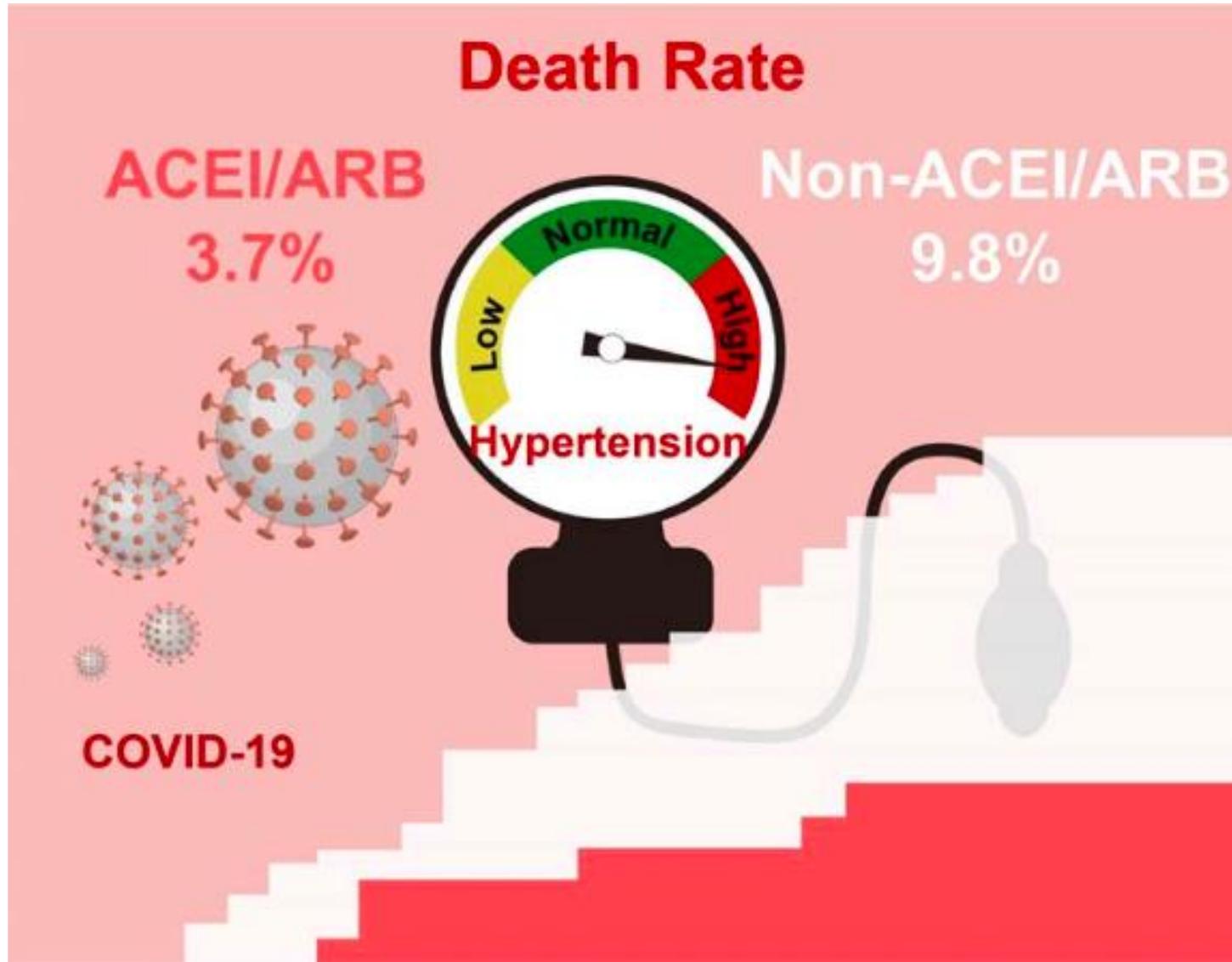
Sin diferencias en las 5 clases independiente del riesgo del paciente

**Table 3.** Likelihood of Severe Covid-19, According to Treatment with Various Antihypertensive Agents, in Propensity-Score–Matched Patients with a Positive Test for Covid-19, with Hypertension and Overall.\*

Medication	Matched Patients with Hypertension			All Matched Patients		
	Severe Covid-19 in Patients Treated with Medication	Severe Covid-19 in Patients Not Treated with Medication	Median Difference (95% CI)	Severe Covid-19 in Patients Treated with Medication	Severe Covid-19 in Patients Not Treated with Medication	Median Difference (95% CI)
	<i>no./total no. (%)</i>	<i>no./total no. (%)</i>	<i>percentage points</i>	<i>no./total no. (%)</i>	<i>no./total no. (%)</i>	<i>percentage points</i>
ACE inhibitor	139/584 (23.8)	158/583 (27.1)	-3.3 (-8.2 to 1.7)	150/627 (23.9)	169/653 (25.9)	-1.9 (-6.6 to 2.8)
ARB	161/629 (25.6)	156/612 (25.5)	0.1 (-4.8 to 4.9)	162/664 (24.4)	165/639 (25.8)	-1.4 (-6.1 to 3.3)
ACE inhibitor or ARB	252/1019 (24.7)	249/986 (25.3)	-0.5 (-4.3 to 3.2)	275/1110 (24.8)	274/1101 (24.9)	-0.1 (-3.7 to 3.5)
Beta-blocker	210/792 (26.5)	231/829 (27.9)	-1.4 (-5.7 to 3.0)	230/912 (25.2)	250/976 (25.6)	-0.4 (-4.3 to 3.6)
Calcium-channel blocker	253/950 (26.6)	207/930 (22.3)	4.4 (0.5 to 8.2)	263/992 (26.5)	235/976 (24.1)	2.4 (-1.4 to 6.2)
Thiazide diuretic	116/515 (22.5)	114/520 (21.9)	0.6 (-4.5 to 5.7)	120/549 (21.9)	149/590 (25.3)	-3.4 (-8.3 to 1.6)

\* Severe Covid-19 was defined as admission to the intensive care unit, the use of noninvasive or invasive mechanical ventilation, or death.

# IECA/ARA2 y COVID-19 en pacientes hospitalizados con HTA



Entre los pacientes hospitalizados con COVID-19 con hipertensión, el uso hospitalario de IECA / ARAII se asoció con un menor riesgo de mortalidad por todas las causas en comparación con los no usuarios de IECA / ARAII.

## COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options

**Table 7 Summary of current key considerations in COVID-19 diagnosis and treatment**

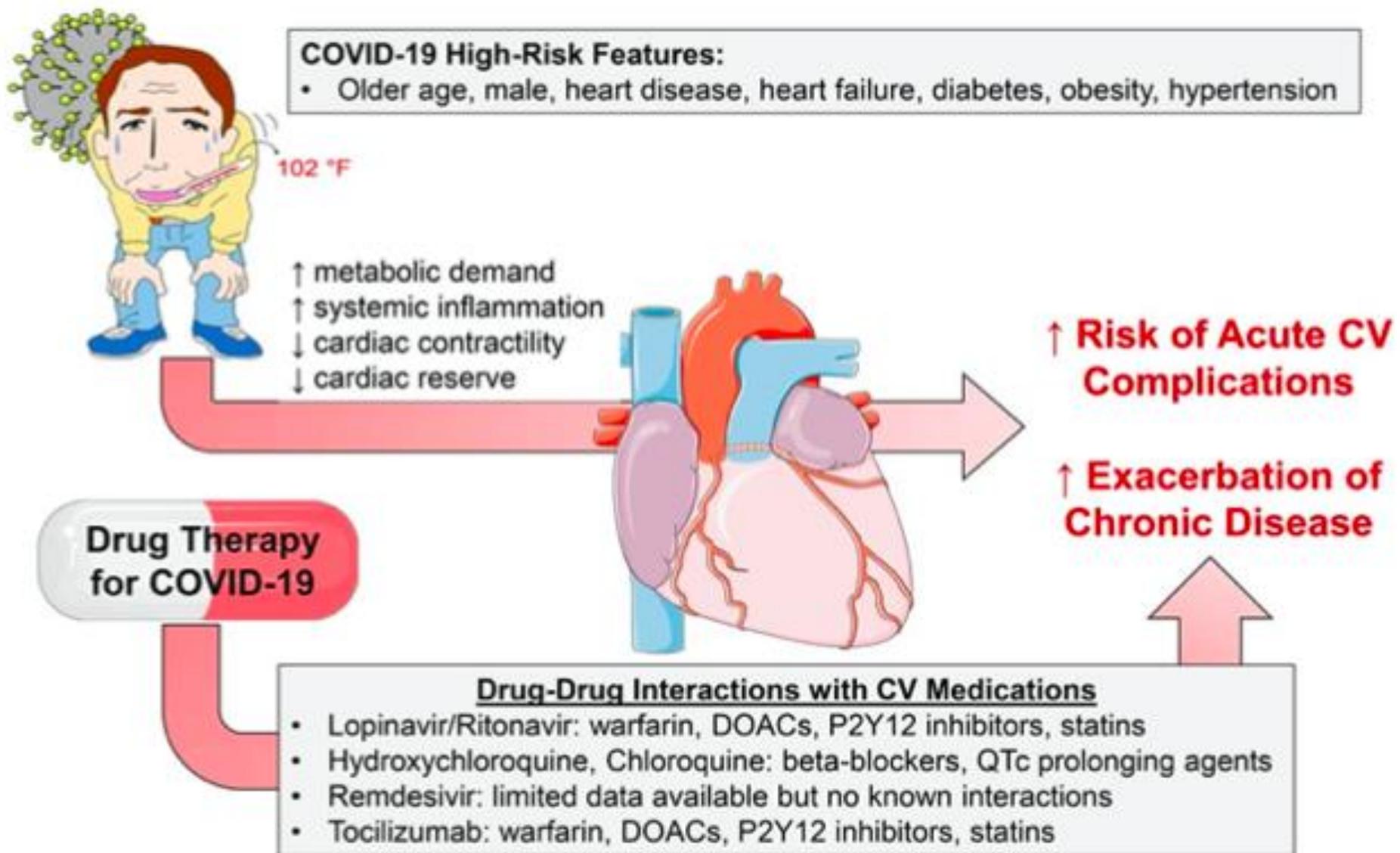
**Key take-home messages:**

- Cardiovascular patients are at increased risk of severe COVID-19 and its complications. Intensive preventive measures should be followed in this group in accordance with WHO and CDC guidelines. This should include wider use of telemedicine tools in day to day monitoring of the patients during the outbreak to limit their exposure.
- The heterogeneity of responses between individual patients indicates that it is unlikely that it can be considered as a single disease phenotype. Host characteristics promote more or less severe progression of the disease.
- The most common cardiac complications include arrhythmia (AF, ventricular tachyarrhythmia, and ventricular fibrillation), cardiac injury (elevated hs-cTnI and CK), fulminant myocarditis, and heart failure.
- Cardiac complications often appear >15 days after initiation of the fever (symptoms)
- Evaluation of cardiac damage (particularly cTnI levels) immediately after hospitalization for COVID-19, as well as monitoring during the hospital stay, may help in identifying a subset of patients with possible cardiac injury and thereby predict the progression of COVID-19 complications.
- Some of the medications used in COVID-19 treatment may contribute to cardiac toxicity, while their effectiveness in treating COVID-19 is unconfirmed.

**Cardiovascular comorbidities**

- Hypertension is one of the most common risk-associated comorbidities, but this association is confounded by age. It is not clear if hypertension is an age-independent risk factor of COVID-19-associated outcomes. As a precaution, it is essential that hypertension remains well controlled.
- There is no evidence that ACEIs or ARBs are associated with worse prognosis, and patients should not discontinue use of these medications.
- Based on experimental evidence in other conditions, particularly ARBs and possibly also ACEIs might exert a potentially protective influence in the setting of COVID-19.
- COVID-19 may lead to plaque instability and MI, which has a common cause of death in SARS/COVID-19 patients. However, the evidence of effectiveness of primary PCI for type 2 MI during acute viral disease is limited.
- ACE2 can be considered as a Cinderella of cardiovascular medicine. A molecule which has been underappreciated in cardiovascular pathology is taking centre stage in understanding and potentially combating COVID-19.

# Cardiovascular considerations in patients with COVID-19



# Conclusiones

- ❑ En algunos estudios se ha observado un menor riesgo de mortalidad asociado con el tratamiento con IECA. Es importante ser cautos ya que dicho efecto deberá comprobarse en ensayos clínicos futuros que permitan demostrar causalidad <sup>(1)</sup>.
- ❑ No se ha podido determinar que los tratamientos con BSRA tengan un impacto negativo en la evolución de la infección.
- ❑ Es importante señalar que los pacientes que toman estos fármacos padecen de HTA u otras dolencias cardiovasculares, que incrementan de manera independiente el riesgo de complicaciones por COVID-19, y que podrían estar más relacionadas con el propio perfil de los pacientes que con los tratamientos en sí mismos.
- ❑ **Como conclusión final podemos afirmar que suspender el tratamiento con IECA/ARA no está justificado en pacientes que padecen COVID-19.**

(1) Es necesario realizar ensayos controlados aleatorios tanto del inicio como del reemplazo de los BSRAA para responder de manera definitiva a la pregunta de si estos agentes son perjudiciales, beneficiosos o neutros en pacientes con COVID-19.

***Clinical Trials: 31 Studies Angiotensin Converting Enzyme Inhibitors, ACE Inhibitors, and SARS-CoV-2.***