

Evidencia Científica en Farmacología



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Mun. de Córdoba

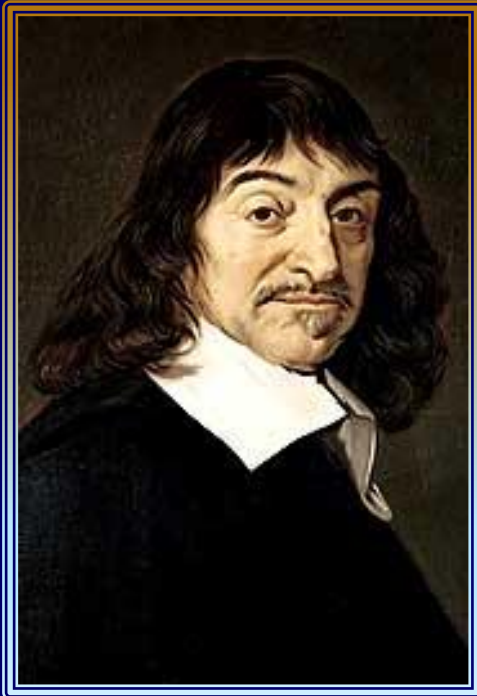


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*Hagan el inmenso esfuerzo de
NO DORMIRSE !*



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“...No admitir como verdadera cosa alguna, como no supiese con evidencia que lo es...”

El discurso del método. René Descartes. Leyda 1627



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El Conocimiento Médico se funda en una rama de la matemática...

“LA ESTADISTICA”

La Estadística Sólo informa PROBABILIDAD

ESTA PROHIBIDO GARANTIZAR RESULTADOS



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El conocimiento médico se funda sobre bases matemáticas

DIAGNÓSTICO: Sensibilidad, especificidad, VPP, VPN, etc.
Sesgos (*bias*), variación inter – intra ensayo, etc

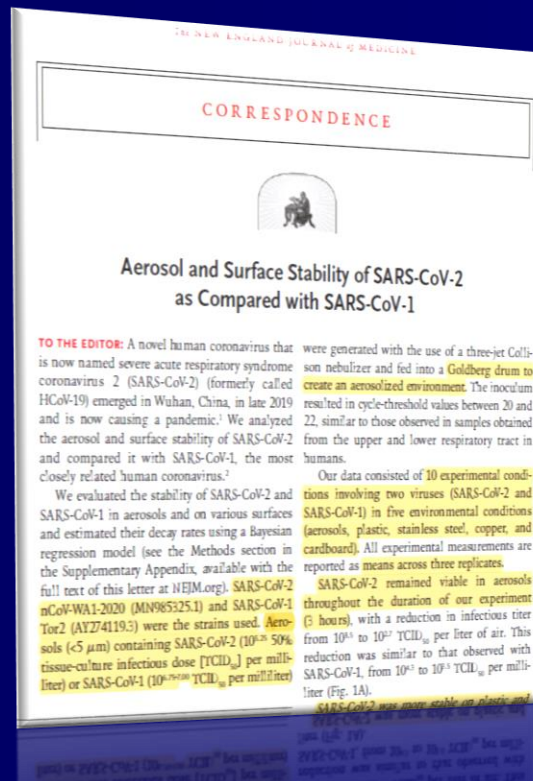
TRATAMIENTOS: IC, DE , RRR vs RRA, NNT, % sobrevida, etc
T_{1/2},

Poder estadístico y Significancia estadística: $P < 0,05$ y
significancia biológica.



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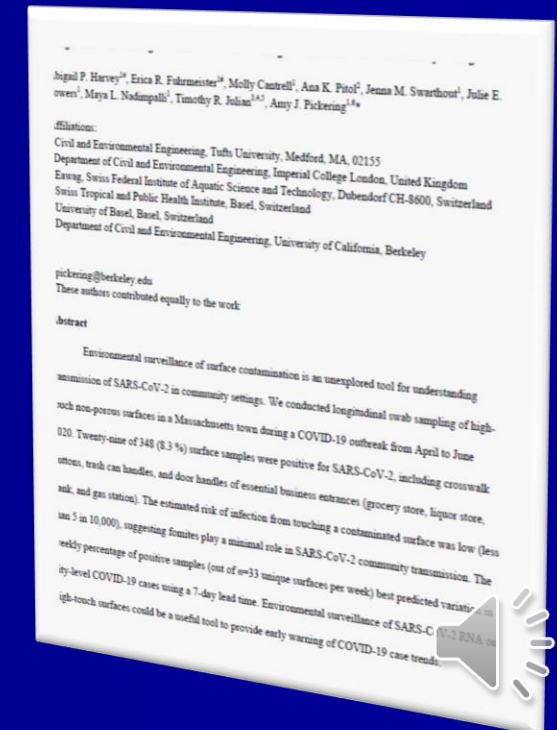
JAMÁS se puede extrapolar de una investigación básica (tejidos, animales, simulaciones computacionales, testeos en laboratorios) a un resultado en humanos.



Aerosol and surface stability of SARS CoV2 as compared with SARS CoV2
NEJM 16 abril 2020

Longitudinal monitoring of SARS CoV2 RNA on high touch surfaces in a community setting.

27 oct 2020



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Aún el mejor criterio o razonamiento clínico son INVÁLIDOS ante la EVIDENCIA CIENTÍFICA

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

The most distinctive comorbidities of 32 non-survivors from a group of 52 intensive care unit patients with novel coronavirus disease 2019 (COVID-19) in the study by Klasebo Yang and colleagues¹ were cerebrovascular diseases (22%) and diabetes (22%). Another study² included 1059 patients with confirmed COVID-19, of whom 373 had severe disease with comorbidities of hypertension (23.7%), diabetes mellitus (16.2%), coronary heart diseases (5.8%), and cerebrovascular disease (2.3%). In a third study³ of 340 patients who were admitted to hospital with COVID-19, 30% had hypertension and 12% had diabetes. Notably, the most frequent comorbidities reported in these three studies of patients with COVID-19 are often treated with angiotensin-converting enzyme (ACE) inhibitors; however, treatment was not assessed in either study.

Human pathogenic coronaviruses (severe acute respiratory syndrome coronavirus [SARS-CoV] and SARS-CoV-2) bind to their target cells through angiotensin-converting enzyme 2 (ACE2), which is expressed by epithelial cells of the lung, intestine, kidney, and blood vessels.⁴ The expression of ACE2 is substantially increased in patients with type 1 or type 2 diabetes, who are treated with ACE inhibitors and angiotensin II type-1 receptor blockers (ARBs).⁵ Hypertension is also treated with ACE inhibitors and ARBs, which results in an upregulation of ACE2. ACE2 can also be increased by thiazolidinediones and ibuprofen. These data suggest that ACE2 expression is increased in diabetes and treatment with ACE inhibitors and ARBs increases ACE2 expression. Consequently, the increased expression of ACE2 would facilitate infection with COVID-19. We therefore hypothesize that diabetes and hypertension treatment with ACE-stimulating drugs increases the risk of developing severe and fatal COVID-19.

If this hypothesis were to be confirmed, it could lead to a conflict regarding treatment because ACE2 reduces inflammation and has been suggested as a potential new therapy for inflammatory lung diseases, cancer, diabetes, and hypertension. A further aspect that should be investigated is the genetic predisposition for an increased risk of SARS-CoV-2 infection, which might be due to ACE2 polymorphisms that have been linked to diabetes mellitus, cerebral stroke, and hypertension, specifically in Asian populations. Summarizing this information, the sensitivity of an individual might result from a combination of both therapy and ACE2 polymorphism.

We suggest that patients with cardiac diseases, hypertension, or diabetes, who are treated with ACE-increasing drugs, are at higher risk for severe COVID-19 infection and, therefore, should be monitored for ACE2-modulating medications such as ACE inhibitors or ARBs. Based on a PubMed search on Feb 28, 2020, we did not find any evidence to suggest that antihypertensive calcium channel blockers increased ACE2 expression or activity, therefore these could be a

available alternative treatment in these patients.

We declare no competing interests.

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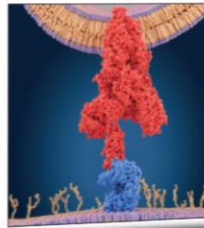
1. Klasebo Yang J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centre, retrospective, observational study. *Lancet Respir Med* 2020; published online Feb 28. [https://doi.org/10.1016/S2213-2600\(20\)30184-5](https://doi.org/10.1016/S2213-2600(20)30184-5)

2. Guan WJ, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; published online Feb 28. <https://doi.org/10.1056/NEJMoa2002032>

3. Zhang Q, Jiang J, Cao F, et al. Clinical characteristics of 140 patients infected by SARS-CoV-2 in Wuhan, China. *Emerg Infect Dis* 2020; published online Feb 19. <https://doi.org/10.1093/eid/26.3>

4. Wang Y, Shang H, Graham R, Baric RS, Li F. Receptor recognition by novel coronavirus from Wuhan: a comparison between ACE2 and other candidates based on docking and structural studies of SARS. *Virology* 2020; published online Jan 19. <https://doi.org/10.1016/j.virol.2020.01.012>

5. Li XC, Zhang J, Zhou J. The upregulation of ACE2 in the renin-angiotensin system: physiological relevance and therapeutic implications in cardiovascular hypertension.



Are patients with HT and Diabetes at high risk for Covid 19 infection?
Lancet Resp Med 11 marzo 2020

Covid 19 and ACEI and ARB. What is the evidence?
JAMA 24 marzo 2020

VIEWPOINT COVID-19 AND ANGIOTENSIN-CONVERTING ENZYME INHIBITORS AND ANGIOTENSIN RECEPTOR BLOCKERS
What Is the Evidence?

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Coronavirus disease 2019 (COVID-19) is a current pandemic infection caused by a positive-sense RNA virus named the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The particularly infectious capacity of the virus, along with mortality rates ranging from 1% to above 5%, has raised concerns across the globe.¹ Older patients with comorbid conditions including pulmonary disease, cardiac disease, kidney disease, diabetes, and hypertension have been associated with even higher mortality rates, suggesting particularly susceptible populations.

The increased mortality and morbidity of COVID-19 in patients with hypertension is an association that has been observed in a number of initial epidemiological studies outlining the characteristics of the COVID-19 epidemic in China. Wu et al² found hypertension to have a hazard ratio of 1.70 for death and 1.82 for acute respiratory distress syndrome in 201 patients with COVID-19. Zhou et al³ found hypertension to have a hazard ratio of 3.05 for in-hospital mortality in 191 patients with COVID-19.

Neither of these studies^{2,3} adjusted for confounding variables and thus it remains unclear if this association is related to the pathogenesis of hypertension or another associated comorbidity or treatment. There has been a growing concern that this association with hypertension is confounded by treatment with antihypertensive medications with specific anzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs).

The link with ACEIs and ARBs is because of the known association between angiotensin-converting enzyme 2 (ACE2) and SARS-CoV-2. ACE2 has been

ARBs; however, there is limited evidence showing changes in serum or pulmonary ACE2 levels. More relevant, the significance of ACE2 expression on COVID-19 pathogenesis and mortality is not specifically known.

ACE2 primarily acts to counterbalance the effect of ACE. As ACE generates angiotensin II from angiotensin I, ACE2 generates angiotensin (1-7) from angiotensin II which, after binding to the Mas receptor broadly shifts the balance from vasoconstriction with angiotensin II to vasodilation with Mas receptor activation in the affected vascular bed. The role this vasodilatory effect has in the pathogenesis of COVID-19 is unclear but some animal data suggest a link. ACE2 and angiotensin (1-7) have been found to be protective in a number of different lung injury models.

In an acid lung injury model in mice, ACE2 downregulation by SARS-CoV, the SARS virus responsible for the SARS outbreak in 2003, worsened lung injury that was improved by treatment with ARB. This suggested that ACE2 exacerbates lung injury by decreasing ACE2 that is reversed by ARB treatment.⁴ Although these preclinical data suggest that increasing ACE2 expression can attenuate SARS-CoV-2-induced lung injury, there is no direct clinical evidence that has proven ACE2 to be an effective treatment for viral-induced lung injury. Of note, a preliminary trial of ACE2 infusion in 10 patients with acute respiratory distress syndrome was completed in humans but was not powered to show efficacy on pulmonary function.⁵ There is even less evidence to demonstrate that treatment with ACEIs or ARBs can decrease severity of pulmonary injury by SARS-CoV-2, though preclinical data suggest a potential mechanism

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para obtener: EVIDENCIA CIENTÍFICA

METODOLOGÍA RIGUROSA

Investigación Clínica

Seres humanos



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METODOLOGÍA RIGUROSA

Investigación: Seres humanos

Prospectivos

Controlados

Compados

Aleatorizados

A Doble Ciego

en Grandes Poblaciones



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METODOLOGÍA RIGUROSA

Prospectivos

Registrarse en organismos competentes

De ahora en adelante.

Los estudios Retrospectivos NO permiten el CONTROL / registro apropiado de las variables a estudiar.



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METODOLOGÍA RIGUROSA

Controlados

Criterios de inclusión y exclusión pre establecidos

Variables de estudio parametrizadas, estandarizadas y validadas. Eficacia o seguridad

Metodología estadística apropiada



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METODOLOGÍA RIGUROSA

Comparativos

No existe evidencia clínica sin comparador.

No hay forma de saber si la evolución fue por el tratamiento o la patología.

Si la patología tiene otros tratamientos se debe comparar contra ellos.

Sería antiético no hacerlo.



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METODOLOGÍA RIGUROSA

Aleatorizados

Evita los SESGOS de selección.

Balancea las características de los sujetos de investigación.



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METODOLOGÍA RIGUROSA

Doble ciego

Ni el paciente ni el médico tratante conocen el tto.
Evita la subjetividad de ambos.

Triple ciego: También está cegado quien analiza los datos.



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METODOLOGÍA RIGUROSA

Grandes poblaciones

Si es posible. Excepto para “patologías raras”.

Le ofrecen potencia estadística.

Permiten conocer RAM poco frecuentes

Evaluar eficacia en distintas etnias



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METODOLOGÍA RIGUROSA

Meta-análisis

Son estudios que resumen varios trabajos científicos con el mismo objetivo.

Para ser **VÁLIDOS** deben:

Incluir poblaciones muy similares

Tener intervenciones casi idénticas

Tener todas cantidades parecidas de pacientes



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¿La Evidencia Científica se puede clasificar?

Niveles: **A** — **B** — **C** — **D**

Clasificación simplificada que usaremos en la cátedra



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Clasificación de la Evidencia Científica. SAC

■ Nivel de evidencia A

Múltiples ensayos clínicos, aleatorios, controlados, comparados o meta-análisis.

■ Nivel de evidencia B

Único ensayo clínico con distribución aleatoria o de grandes estudios sin distribución aleatoria

■ Nivel de evidencia C

Pequeños estudios, retrospectivos o práctica habitual.

■ Nivel de evidencia D

Opinión de expertos.



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“El mundo del hombre contemporáneo se funda sobre los resultados de la ciencia: la teoría reemplaza a la fantasía, el dato al mito, la predicción a la profecía.”

Mario Bunge

(Físico y Filósofo Argentino. 1919 - 2020)



Evidencia Científica en Farmacología



“El mundo del hombre contemporáneos se funda sobre los resultados de la ciencia: la farmacología reemplaza a la pócima, la evidencia a la experiencia, la probabilidad a la profecía.”

Mario Bunge

(Físico y Filósofo Argentino. 1919 - 2020)



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**!!! ESTUDIEN y
Analicen la información !!!**

