Rodríguez *et al. Crit Care* (2021) 25:297
https://doi.org/10.1186/s13054-021-03721-3

Critical Care

LETTER

Open Access

Corticosteroids and RCTs against the supposed undervaluation of real data evidence

Alejandro Rodríguez[1], Gerard Moreno[1], Maria Bodi[1], Josep Gomez[2] and Ignacio Martín-Loeches[3,4*]

Dear Editor

The alleged supremacy of the Randomized control trials (RCTs) is based on the possibility of causal inference. But, is this true?

In order to define what we mean by a causal effect, for each subject we assume the existence of the potential outcomes $Y^{\alpha=0}$ and $Y^{\alpha=1}$ corresponding to what value the outcome would take if we do not apply the intervention ($\alpha=0$) or we apply the intervention ($\alpha=1$), respectively. For an individual, it is assumed that the intervention has a causal effect whenever $Y^{\alpha=0}$ different to $Y^{\alpha=1}$, that is, the outcome would take a different value depending on whether the individual is given the intervention or not. To calculate the causal effect of the intervention we would need to somehow obtain or discover the values $Y^{\alpha=0}$ and $Y^{\alpha=1}$. Consider that "A" denote a random variable indicating whether an individual receives the intervention ($A=1$) or not ($A=0$), and Y a random variable for the observed outcome. If a particular individual received the intervention, the observed value is $Y=Y^{\alpha=1}$, but for the potential outcome value $Y^{\alpha=0}$ is unknown. The unobserved outcome is called the "counterfactual" outcome and a causal inference is not possible to obtain [1].

According to the RECOVERY trial results, an adaptive RCT [2], during the second pandemic wave, corticosteroid use was generalized in all critical COVID-19 patients. However, the role of corticosteroids in the treatment of COVID-19 remains controversial. A recent study [3] comparing first versus second wave reported that, despite of the systematic and early administration of glucocorticoids in the second wave, the ICU mortality (50% vs. 52%, $p=0.96$) and of ICU length of stay did not differ between the two waves.

Late complications, as well as medium-term evolution, were not evaluated in the RECOVERY study [2]. A recent research letter [4] found that corticosteroid use, and tocilizumab treatment were associated with ventilator-associated pneumonia (VAP).

Should physicians continue to ignore the results of well-adjusted observational studies in favor of the results of an adaptive RCT with many inconsistencies? We are convinced that steroid treatment can be effective but there are different patients' phenotypes and their use should be re-evaluated [5].

Possibly, the future of research and clinical practice is not conceived as a confrontation between RCT and observational studies, but rather as the sum of knowledge between RCTs and its clinical application.

Acknowledgements
Not applicable.

*Correspondence: drmartinloeches@gmail.com
[3] Hospital Clinic, IDIBAPS, Universidad de Barcelona, CIBERes, Barcelona, Spain
Full list of author information is available at the end of the article

Authors' contributions
IML and AR wrote the first draft and the rest of the authors provide critical review of the manuscript.

Funding
Not applicable.

Availability of data and materials
Not applicable.

Declarations

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
No COI from any of the authors of the manuscript.

Author details
[1]ICU Hospital Universitario Joan XXIII/IISPV/URV, CIBERes, Tarragona, Spain. [2]Tarragona Health Data Research Working Group (THeDaR), ICU Hospital Universitario Joan XXIII, Tarragona, Spain. [3]Hospital Clinic, IDIBAPS, Universidad de Barcelona, CIBERes, Barcelona, Spain. [4]Multidisciplinary Intensive Care Research Organization (MICRO), Department of Intensive Care Medicine, St. James's Hospital, Dublin 8, Dublin, Ireland.

Received: 27 July 2021 Accepted: 28 July 2021
Published online: 18 August 2021

References

1. Morgan SL, Winship C. Counterfactuals and the potential outcome model. Massachusetts: Harvard University; 2014. p. 37–76. https://doi.org/10.1017/CBO9781107587991.003.
2. RECOVERY collaborative Group. Dexamethasone in hospitalized patients with Covid-19—preliminary report. N Engl J Med. 2020:1–11. https://doi.org/10.1056/nejmoa2021436.
3. Contou D, Fraissé M, Pajot O, Tirolien JA, Mentec H, Plantefève G. Comparison between first and second wave among critically ill COVID-19 patients admitted to a French ICU: no prognostic improvement during the second wave? Crit Care. 2021;25:3. https://doi.org/10.1186/s13054-020-03449-6.
4. Martínez-Martínez M, Plata-Menchaca EP, Nuvials FX, Roca O, Ferrer R. Risk factors and outcomes of ventilator-associated pneumonia in COVID-19 patients: a propensity score matched analysis. Crit Care. 2021;25:235. https://doi.org/10.1186/s13054-021-03654-x.
5. Rodríguez A, Ruiz-Botella M, Martín-Loeches I, Jimenez Herrera M, Solé-Violan J, Gómez J, et al. Deploying unsupervised clustering analysis to derive clinical phenotypes and risk factors associated with mortality risk in 2022 critically ill patients with COVID-19 in Spain. Crit Care. 2021;25:63. https://doi.org/10.1186/s13054-021-03487-8.

Publisher's Note