Journal of Electrocardiology 66 (2021) 48

Contents lists available at ScienceDirect

Journal of Electrocardiology

journal homepage: www.jecgonline.com

A statistical perspective to the QTc interval in the treatment of COVID-19

We read with interest the article by Echarte-Morales et al. which evaluated Effect of hydroxychloroquine, azithromycin and lopinavir/ritonavir on the QT corrected interval (QTc) in patients with COVID-19 infection. [1] Although its original concept, we want to address some methodological and statistical points that merit more attention.

In the methodology section high risk QTc pattern determined as a peak QTc ≥ 500 ms and those with an increase in the QTc ≥ 60 ms from baseline values. [1] However, according to literature it should be defined "as a peak QTc ≥ 500 ms and/or those with an increase in the QTc ≥ 60 ms from baseline values". It may be only a typing error but it must be corrected because it alters the results and precision of the study. Furthermore, the statistically significant threshold of p value was not mentioned in the methodology. It was demonstrated in the table 1 that other QTc prolonging therapy (levofloxacin, amiodarone, olanzepine, haloperidol etc.) significantly higher in double therapy group (33.3% vs 17.3%; $p = 0.021$). [1] Baseline characteristics of the groups, namely medications, were different and this needs to be discussed more detailed in the manuscript.

The authors compared change in QTc between treatment groups and found no difference by an unpaired t-test (31.2 ± 30.6 ms vs 29.8 ± 36.5 ms; $p = 0.813$). However, standard deviations of ΔQTc values higher than mean values which indicates the skewed distribution. As a rule of thumb, it is customary to use the median instead of the mean if the data is not normally distributed. [2] ΔQTc values should be depicted as medians and interquartile range and non-parametric tests should be performed rather than a t-test. [3] Therefore, we wonder whether there were any differences in ΔQTc value with any statistical mixed effects model. Moreover, the results are certainly subject to statistical power and Type I error rates due to unequal sizes and variances ($n = 54$ vs $n = 114$). [4,5]

Finally, the authors also were not present any detail about intra- and interobserver variability in QTc measurement in their study. Regarding to the subjective evaluation of very sensitive surrogate marker such as QTc interval, we think that these values should be presented in the results section.

References

[1] Echarte-Morales J, et al. Effect of hydroxychloroquine, azithromycin and lopinavir/ritonavir on the QT corrected interval in patients with COVID-19. J Electrocardiol. 2020;64:30–5.
[2] Mert KU, Dural M, Mert GO. Is electrical cardioversion doable in atrial fibrillation without transesophageal echocardiography? Int J Cardiol. 2017;247:20.
[3] Vickers AJ, Altman DG. Statistics notes: analysing controlled trials with baseline and follow up measurements. Bmj. 2001;323(7321):1123–4.
[4] Rusticus S, Lovato C. Impact of sample size and variability on the power and type I error rates of equivalence tests: a simulation study. Pract Assess Res Eval. 2014;19:11.
[5] Mert G, Dural M, Mert KU. Comparison of acute management of atrial fibrillation in heart failure with unequal sized groups. Am J Emerg Med. 2018;36(9):1693.

Kadir Ugur Mert MD
aEskisehir Osmangazi University, Faculty of Medicine, Department of Cardiology, Eskisehir, Turkey
*Corresponding author at.: Eskişehir Osmangazi University, Department of Cardiology, Büyükdere Mah. Meşelik Kampüsü Odunpazarı/Eskişehir, Turkey.
E-mail address: kugurmert@gmail.com

Ugur Onsel Turk MD
bIzmir Economy University, Faculty of Medicine, Department of Cardiology, Izmir, Turkey

Bulent Gorenek MD
aEskisehir Osmangazi University, Faculty of Medicine, Department of Cardiology, Eskisehir, Turkey

https://doi.org/10.1016/j.jelectrocard.2021.03.002