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## Letter to the Editor

### Letter regarding “The clinical efficacy of low-dose whole-lung irradiation in moderate-to-severe COVID-19 pneumonia: RTMX-20 trial”



#### To the Editor

Low-dose whole-lung irradiation (LDWLI), a novel potential therapy of coronavirus disease 2019 (COVID-19) pneumonia, is a readily available modern medical resource worldwide [1]. Many clinical trials have been conducted to investigate the efficacy of LDWLI in reducing the COVID-19-related mortality risk [1–7]. As per our knowledge, the study published in the Green Journal by Ortiz et al. [2] has the largest sample size among similar studies published to date [1–7]. The authors conducted a prospective comparative cohort study to evaluate the clinical efficacy of LDWLI in moderate-to-severe COVID-19 pneumonia. We congratulate Ortiz et al. for their inspiring conclusions and for having the largest sample size in this research [1–7]. However, some potential pitfalls should be addressed before we proceed with this evidence for clinical practice and research.

First, there are some substantial discrepancies between the registered protocol (NCT04534790, [clinicaltrials.gov](https://clinicaltrials.gov)) and the eventually reported article [2,8]. The study design and primary outcome measures (endpoints) in this article deviate substantially from those in the initially registered protocol (randomized trial with improvement in oxygen saturation as the primary outcome measure) [2,8]. Moreover, the authors wrote “with high suspicion of COVID-19 pneumonia without laboratory confirmation” in the Inclusion Criteria subsection of this paper [2]. However, the corresponding item for this subsection is “Laboratory confirmation of SARS-CoV-2 infection” in the online registered protocol [8].

Second, the authors have reported in the first paragraph of the Results section that 59 patients were analyzed finally [2]. However, 58 cases are shown in Table 1 [2].

Third, although the authors wrote “matched” and “In both groups, there was an equal distribution among the patients.” in the Study design subsection, there were significant differences between the radiotherapy group and control group with respect to the baseline data of obesity and image classification by COVID-19 Reporting and Data System (Table 1) [2]. However, there was no corresponding analysis or appropriate remediation for the undeniable selection bias of the participants reflected in Table 1 [2].

Fourth, the survival curves in Figure 1 differed substantially from the descriptive report of mortality and survival in the second paragraph of the Results section [1,2].

Fifth, it would be difficult for the readers to understand the contrastive groups in the sentence, “When comorbidities were analysed, we did not find any difference in survival between patients treated with radiotherapy and patients with hypertension ( $P$  0.8), diabetes ( $P$  1.09) or obesity ( $P$  0.6)” in the third paragraph of the Results section [2]. Furthermore, it is not clear which is the radiotherapy group in the sentence, “none of the moderate cases in the control group required OTI, while 45% of the control group required OTI.” in the fourth paragraph of the Results section [2]. The authors should improve the accuracy of the results interpretation and reporting.

This study by Ortiz et al. has contributed greatly to this controversial subject [2,9]. However, addressing the aforementioned flaws is necessary to further enhance the value of this cohort study and promote wide citations of the article.

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#### Conflict of Interest

The authors declare no conflicts of interest.

#### Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.radonc.2022.11.009>.

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