Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Comments on "Whole lung irradiation as a novel treatment for COVID-19: Final results of the prospective randomized trial (WINCOVID trial)"

Dear Editor,

We read the article titled "Whole lung irradiation as a novel treatment for COVID-19: Final results of the prospective randomized trial (WINCOVID trial)" with great interest [1]. The authors designed prospective, randomized trial with 51 patients to detect benefit of low dose radiotherapy (LDRT) on moderate to severe COVID-19 pneumonia. COVID-19 pandemic has been global catastrophe especially for health-care system. There are many challenges like shortage of beds and intensive care units, pharmacological therapies cost, and high workload. Treatment of COVİD-19 pneumonia is trending topic, and the amount of promising data on this subject is increasing gradually. LDRT is a potential lifesaving treatment for COVID-19-induced acute respiratory distress syndrome (ARDS). However, there are limited data about its effectiveness in moderate to severe COVID-19 pneumonia. Therefore, we appreciate the authors for their contribution to this problem. However, we believe that there are some issues that need to be clarified for further understanding of the study.

Firstly, COVID-19 vaccines reduce hospitalization rate and disease progression to death or invasive mechanical ventilation [2]. In addition, smoking is related with progression of COVID-19 [3]. However, vaccination and smoking status were not mentioned in the article. Difference in vaccination and smoking rate between two groups could interfere with effect of LDRT on the results of trial. We thought that vaccination and smoking status should have been specified in the study to interpret results more accurately.

Secondly, Radiotherapy (RT) has been used as safe and successful treatment option for many inflammatory diseases like tendonitis, bursitis, and arthritis [4]. X-ray therapy was also used in the treatment of pneumonia in the 20th century [5]. LDRT exerts its anti-inflammatory effect by various mechanisms such as shifting from pro-inflammatory macrophages (M1 phenotype) to anti-inflammatory macrophages (M2 phenotype) [6,7], increasing secretion of transforming growth factor (TGF) -β [8,9], and interleukin (IL) −10 [10], decreasing secretion of IL −1 [9]. Although there was no statistically significant difference with inflammatory biomarkers between two groups, LDRT arm showed early clinical recovery, early hospital discharge, and better reduction of CT severity score in the current study. We wonder authors' opinion how LDRT arm could have these improvements without changing inflammatory factors.

Finally, randomization is basic cornerstone of scientific research methodology. The effects of the treatment would be indistinguishable from the effect of covariates if randomization were inadequate. Stratified or covariate adaptive randomization must be used if sample size below 200 and covariates need to be controlled [11]. Diabetes and hypertension are independent risk factor for COVID-19 related mortality [12]. Therefore, comorbidity rates must be similar between two groups. However, there was significant difference with comorbidity rates between LDRT arm (85%) and control arm (59%). Interpreting the results of the study has become more difficult because of this difference.

In conclusion, this is an important study with impressive findings considering the effectiveness of LDRT in the treatment of moderate to severe COVID-19 pneumonia. Yet three issues, as mentioned previously, require further clarification for the better understanding of this important study.

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