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: Interim results of an ongoing phase 2 trial in India"

To the Editor,

We have read with much interest the clinical trial study of Govindaraj et al. who recently published a paper entitled "Whole lung irradiation as a novel treatment for COVID-19: Interim results of an ongoing phase 2 trial in India" [1]. They performed low-dose radiation therapy (LDRT) to treat COVID-19 patients. In their study, the whole lungs of 25 patients with the mean age of 57 (±13) were irradiated by a single dose of 0.5 Gy. After two weeks follow up, they found out that clinical recovery for patients was 88%, and the patients were discharged from the hospital within 10 days after LDRT. Although the utilization of LDRT to treat COVID-19 pneumonia is a promising strategy, this study has several shortcomings. Firstly, patients in the study conducted by Govindaraj et al. received drugs such as corticosteroids (methyl prednisolone/dexamethasone), anti-coagulants (enoxaparin sodium), Vitamin C, Zinc supplementation and the antiviral remdesivir. It is known that dexamethasone limits the protective function of T cells, hinders antibody production of B cells, and prevents the macrophage clearance mechanism, possibly resulting in a higher plasma viral load and a greater risk of secondary infections [2]. Therefore, it may only be useful for a group of patients, such as those with severe COVID-19 who need respiratory support, either with invasive mechanical ventilation or oxygen alone [3]. It is worth noting that, patients who did not require oxygen not only showed no benefit but also had a possibility of harm with corticosteroid therapy [3].

Thus, generalizing this treatment protocol for all COVID-19 patients may need further evidence [4]. In Govindaraj et al. study, patients with moderate to severe COVID-19 infection, with moderate to severe dyspnea, respiratory frequency $\geq$ 24/min, oxygen saturation on room air SpO2 < 94 % and SpO2/FiO2 ratio > 89 and < 357 were included. Based on these criteria, it is probable that all patients were on respiratory support (at least nasal oxygen therapy), but indeed, the patients requiring oxygen were not clearly described/identified in this study. Moreover, while in some countries, dexamethasone and methylprednisolone are a part of treatment protocol for COVID-19 infection (particularly in moderate to severe cases) [5], due to the immunosuppressive effects of glucocorticoids, patients might become more vulnerable to secondary infections. Given this consideration, it has been reported that concurrent glucocorticoid therapy may increase the risk of mucormycosis in COVID patients [6,7].

Regarding remdesivir, a very large-scale study funded by the World Health Organizaton (WHO) that was conducted at 405 hospitals in 30 countries, showed that "*remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay*"[8]. On the other hand, other studies shows that treating patients with COVID-19 with high-dose zinc gluconate, ascorbic acid or a combination of the two supplements cannot significantly reduce the duration of symptoms compared to the standard care [9]. Thus, while these interventions may interfere with the outcome of LDRT, they have no known COVID-19 therapeutic effects.

Additionally, follow up of patients were conducted 14 days after LDRT. In the study performed by Papachristofilou et al. [10], while 72.7% of patients survived 15 days after LDRT, the survival rate reduced to 63.6% 28 days after LDRT (the same as the control group). Therefore, for evaluating the efficacy of LDRT for COVID-19, it is necessary to increase the follow-up at least to 4 weeks after radiation therapy.

Readers are cautioned to carefully interpret the results of LDRT treatments when accompanied by various chemical agents. These chemical interventions may interfere with the outcome of LDRT, and their associated COVID-19 therapeutic effects must be carefully evaluated. In addition, evaluating the efficacy of LDRT for COVID-19 requires an appropriate evaluation period. As noted above, it may be necessary to increase the follow-up at least to 4 weeks after radiation therapy.

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