COMMENT & RESPONSE

In Reply We appreciate Song’s interest in our article\(^1\) and would like to address the concerns about potential study limitations as detailed in Song’s Letter to the Editor. First, we emphasize that all patients in our study met the US Centers for Disease Control and Prevention (CDC) case definition for multisystem inflammatory syndrome in children (MIS-C),\(^2\) described in our Methods; as such, all had at least 2 organ systems involved. While lymphopenia, neutrophilia, and interleukin 6 elevation are markers of inflammation in the CDC case definition, those are not required for diagnosis, as other laboratory parameters can be sufficient to satisfy this criterion. As per eTable 3 in the Supplement to our article,\(^1\) the median lymphocyte and neutrophil count values did not significantly differ between groups. Notably, lymphopenia is not universal in MIS-C, being reported in only 30% of cases.\(^3\) In addition, levels of interleukin 6 were not routinely obtained, as the long turnaround times limit their use in our practice. For these reasons, we favored the inclusion of other relevant and widely used laboratory markers of inflammation in our multivariate model.

Similarly, though MIS-C has been associated with a wide array of manifestations, including articular involvement as referenced by Song, visceral, hematologic, and dermatologic manifestations are more common, usually more severe, and listed in the CDC case definition.\(^2\) Therefore, we focused on these features to enhance the potential significance and generalizability of our findings.

To address Song’s point about vaccination status, we highlight that most of the patients were ineligible for SARS-CoV-2 immunization based on their age (median [IQR], 8.5-12 years), as vaccines became available in the US for children aged 12 to 15 years in May 2021, after our study completion.\(^4\) While vaccination for individuals 16 years and older was authorized in the US in December 2020, among the patients in our cohort diagnosed after this date, only 14 (6.5%) were 16 years and older. None of these vaccine-eligible patients had documented SARS-CoV-2 immunization prior to their MIS-C diagnosis. This renders vaccination status irrelevant to our study. Similarly, only 7 patients within our cohort (3.2%) received remdesivir. Furthermore, antivirals are not routinely used in the management of MIS-C, a postinfectious phenomenon. Hence, antiviral use is not pertinent to our findings.

Lastly, as pointed out by Song, the patients in the intravenous immunoglobulin therapy plus corticosteroids group in our study had higher frequencies of several markers indicative of severe disease in univariate analysis compared with those in the corticosteroids group. Through the application of inverse probability of treatment-weighting methodology, we balanced these characteristics between the groups, as demonstrated in Table 1 in the article.\(^1\) As a result, we report similar rates of treatment failure after adjustment for disease severity markers. Our article also calls for caution at interpreting the increased likelihood of cardiac parameters as the reason for initial treatment failure in the corticosteroid group, as this relied on clinician assessment, while other objective echocardiographic outcomes did not differ between groups. Although prospective international cohorts are still needed to further define optimal therapies for MIS-C, we reiterate our conclusion that corticosteroid monotherapy could be considered as a therapeutic alternative in a subset of those patients.

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