CORRESPONDENCE

Reply to De Nunzio, Franco, and Lombardo

Prostate Cancer and Prostatic Diseases (2022) 25:129; https://doi.org/10.1038/s41391-021-00476-4

To the Editor:

This letter is in response to the letter by De Nunzio et al. [1], which discussed several points regarding our systematic review on the possible role of SARS-CoV-2 in the progression of benign prostatic hyperplasia (BPH) and its related lower urinary tract symptoms (LUTS) [2]. We appreciate their comments on our manuscript, and we wish to address our response and the updated data regarding this issue.

The authors mentioned that the lack of evidence on the relation between SARS-CoV-2 and BPH/LUTS does not offer a rationale for further investigations and hypotheses. We believe that the absence of studies cannot invalidate the possible scientific pathways leading to exacerbation of BPH/LUTS secondary to SARS-CoV-2 infection. As a matter of fact, sometimes digging through novel hypotheses by studying the potential mechanisms of a condition can motivate further studies to unravel the unknown aspects of a disease. It is noteworthy that the involvement of different organs such as kidneys, pancreas, gastrointestinal tract, and worsening comorbidities, including diabetes and cardiovascular diseases due to SARS-CoV-2 seemed very unlikely at the beginning of the pandemic [3]. However, with further studies based on primary hypotheses stated in various papers, such possibilities became bolder and finally were confirmed.

As stated by De Nunzio et al., the possible connection between the androgen pathway and SARS-CoV-2 infection still needs further investigation. Similarly, in our review, we noted the studies were contradictory regarding the androgen-related hypothesis, and we summed up both the studies supporting and opposing the hypothesis that COVID-19 may be androgen related.

Recent accumulating evidence on this topic can now better emphasize the probable correlation between SARS-CoV-2 infection and BPH/LUTS progression in older patients with a higher risk of hospitalization due to COVID-19. In a recent study by Can et al., they prospectively gathered IPSS of 94 confirmed patients with COVID-19 before and during the disease, and they found that in patients older than 50 years of age ($n = 62$), IPSS was both statistically and clinically increased during their hospitalization period (before $= 5.1 \pm 4.1$, during$=9 \pm 6.4$) [4]. As we know, older populations are at higher risk of contracting BPH/LUTS, and the authors assumed that high distributions of ACE2 receptors in urothelium should be one of the predisposing factors of higher scores of IPSS secondary to SARS-CoV-2 infection. In another study by Cinislioglu et al., serum PSA was measured before, during, and after the course of COVID-19 in 91 patients diagnosed with BPH/LUTS. Their results confirmed that serum PSA levels increased by about 3 levels during their hospitalization compared to before the infection [5]. Taken together, it can be concluded that contemporary data are in accordance with our systematic review. We believe that any hypothetical theory is worth presenting and investigating during this mysterious pandemic, especially in some fields such as prostatic diseases which research data are scarce. It can encourage researchers to help clarify the unknown aspects of this infection, which still puzzle scientists.

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AUTHOR CONTRIBUTIONS

A Ha, and FM made substantial contributions to discussions of content, FM and A Ho wrote the article, and AD reviewed and edited the manuscript before submission.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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Received: 23 October 2021 Revised: 28 October 2021 Accepted: 8 November 2021
Published online: 22 November 2021