

# Role for digoxin in patients hospitalized with COVID-19 and atrial arrhythmias

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We thank Dr. Siniorakis et al. for their interest in our study on the prevalence of atrial arrhythmias among patients hospitalized with coronavirus disease 2019 (COVID-19).<sup>1</sup> In their letter, Siniorakis et al.<sup>2</sup> postulate several mechanisms by which digoxin may confer benefits for patients with COVID-19 and atrial arrhythmias. The authors cite several in vitro and in vivo studies linking cardiac glycosides with antiviral and anti-inflammatory properties via inhibition of coronavirus entry into cells and suppression of cytokine storm.<sup>3,4</sup> Cho et al. demonstrated significant inhibition of severe acute respiratory syndrome coronavirus 2 replication with administration of digoxin and ouabain when compared to controls and chloroquine.<sup>5</sup> Therefore, Siniorakis et al. conclude that digoxin and other cardiac glycosides should be prioritized for use in the management of patients with COVID-19 and atrial arrhythmias.

We agree with Siniorakis et al. that given that a significant proportion of patients in our study were on vasopressor support, digoxin may be particularly useful in patients with COVID-19 and atrial arrhythmias whose hypotension may preclude the use of beta blockers and calcium channel blockers. However, in the absence of prospective, randomized clinical trial data demonstrating benefits of digoxin use over other rate controlling agents in the treatment of patients with COVID-19 and atrial arrhythmias, we believe that further study is required before digoxin can be considered as a first-line agent. In our study, a significant proportion of the patients hospitalized with

COVID-19 who developed atrial arrhythmias were critically ill and had respiratory and renal failure.<sup>1</sup> Additionally, the mean age of patients who developed atrial arrhythmias was  $74.5 \pm 13.0$  years. Patients with multiorgan dysfunction, electrolyte abnormalities, and advanced age are at particularly high risk of digoxin toxicity. These considerations, combined with results from meta-analyses and large observational studies that have shown an association between digoxin use and increased all-cause mortality, should temper the routine use of digoxin in patients with COVID-19 and atrial arrhythmias.<sup>6,7</sup> However, we acknowledge that if a beneficial role for digoxin use in patients with COVID-19 can be demonstrated in prospective clinical trials with an acceptable safety profile, then a reappraisal of digoxin use in patients with COVID-19 and atrial arrhythmias is warranted.

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