

# Editorial to "Atrial fibrillation and the risk of 30-day incident thromboembolic events and mortality in adults $\geq 50$ years with COVID-19"

Atrial fibrillation (AF) is associated with a 2- and 1.5-fold increased risk of all-cause mortality in women and men, respectively. AF was also associated with 5- to 8-folds increased risk of stroke and systemic embolization. These associations were observed in patients without respiratory infectious diseases. As the World Health Organization announced coronavirus disease 2019 (COVID-19) as a public health emergency on January 30th 2020, such viral respiratory illness has caused over one million deaths worldwide since then. During this pandemic emergency, cardiac arrhythmia including AF has been a common cardiovascular manifestation described in patients with COVID-19 infection. In patients with COVID-19, whether AF is also a risk factor for increased all-cause mortality remains unclear. Since the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) might cause excessive inflammation, platelet activation, endothelial dysfunction, and stasis, patients with COVID-19 caused by this virus might have high risk of thrombosis both in the venous and arterial circulations.<sup>1</sup> The thromboembolism risk caused by COVID-19 in patients with AF comparing to AF patients without COVID-19 remains to be explored.

By using a global research network and propensity score matched over 13,000 adults with COVID-19, Harrison et al in this issue reported that the survival probability was significantly lower in adults with COVID-19 and AF compared to matched adults without AF (risk ratio 1.61), and risk of thromboembolic events was also higher in patients with AF (risk ratio 1.41).<sup>2</sup> These findings indicated that AF remains a risk marker for increased all-cause mortality and thromboembolic events. Furthermore, the survival probability was significantly lower for adults with AF and COVID-19 compared to adults with AF while without COVID-19. Interestingly, there was no significant difference in risk of thromboembolic events between AF patients with and without COVID-19. The authors recommended that AF might be an important risk factor for inclusion in risk modeling and subsequent stratification of adults with COVID-19, and a target for intervention strategies.

This study firstly elucidated the association of AF on mortality and thromboembolic events in patients with COVID-19. However, several limitations of this study remain to be investigated. Firstly, the 30-day mortality rates were extremely high (82.7% in non-AF cohort and 88.3% in AF cohort) comparing to those reported by Wang et al (4.3%)<sup>3</sup>, Shi et al (13.7%)<sup>4</sup>, and Inciardi et al (26%)<sup>5</sup>. This

finding indicated that the current cohort might be representative of COVID-19 disease patients with severe illness. Whether such association also applied to COVID-19 patients of less severity remain to be explored. Secondly, the mechanisms of increased mortality and thromboembolism events with AF in patients with COVID-19 in this cohort remain unclear. AF is associated with in-hospital mortality in patients with acute myocarditis. In patients with COVID-19, evidence of myocardial injury was associated with higher mortality rate (51.2%) compared with those without myocardial injury (4.5%).<sup>4</sup> Therefore, it is speculated that elevated serum levels of Inflammatory cytokines including C-reactive protein, interleukin-6, and tumor necrosis factor- $\alpha$  caused by SARS-CoV-2 might mutually contribute to myocardial injury, AF genesis, thromboembolic events, and mortality.

With the findings from this study, optimal management of AF in patients with COVID-19 might be necessary to improve outcomes of patients with COVID-19 and AF. A major concern in this scenario is that all antiarrhythmic drugs (AADs) for rate/rhythm control may have significant side effects due to drug-drug interactions with emerging COVID-19 pharmacotherapy, leading to increased risk for bradycardia or tachyarrhythmias. Furthermore, drug-drug interaction between anti-coagulants and COVID-19 pharmacotherapy might lead to inadequate coagulation or bleeding events. Guideline for the management of AF in patients with COVID-19 has been published, which includes considerations of important potential drug-drug interactions of anticoagulants and AADs with emerging COVID-19 pharmacotherapies.<sup>6</sup> Clinicians should be aware of the indications/contraindications and major drug-drug interactions among AADs, anticoagulants, and emerging COVID-19 treatments in AF patients with COVID-19 to improve their clinical outcomes.

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**CONFLICTS OF INTEREST**

None.

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