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LETTER TO THE EDITOR

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Arrhythmia may contribute to neuropsychiatric symptoms in COVID-19 patients

Dear Editor,

Forero-Peña et al.[1] described immediate and long-term neuropsychiatric complications following the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and discussed the possible roles of (hydroxy)chloroquine and dexamethasone on these neuropsychiatric symptoms. The patients demonstrated multiple psychiatric symptoms, including bipolar I disorder, major depressive episodes, and brief psychotic disorder.[1] This is consistent with a previous report that depression and anxiety were the most common psychological distresses across patients infected by SARS-CoV-2.[2]

For (hydroxy)chloroquine administration, in four of the five patients presented, the rapid onset of symptoms after initiation of the drug and remission shortly after discontinuation, supporting (hydroxy)chloroquine as a potential trigger for their neuropsychiatric symptoms.[1] And the overall psychiatric impacts of corticosteroids in coronavirus disease 2019 (COVID-19) patients were minimal.[1] They presumed that the onset of neuropsychiatric symptoms may be because of direct central nervous system infection by SARS-CoV-2, indirect neuro-inflammation in the setting of SARS-CoV-2 infection, chloroquine, and/or corticosteroid neurotoxicity, or a combination of the aforementioned.

However, arrhythmia may also contribute to neuropsychiatric symptoms in COVID-19 patients and should not be neglected. Through a literature search, we summarized abnormal electrocardiographic findings in COVID-19 patients. Sinus tachycardia was the most common arrhythmia found in the patients, with frequencies of 16.9%–70.4% (Table 1). Atrial fibrillation (AF) may be the secondary common arrhythmia. However, its occurrence rates vary greatly between different reports, ranging from 1.9% to 62.5% (Table 1). Premature beat, ST-T segment and T wave changes, non-sustained ventricular tachycardia, QT-interval (QTc) prolongation, paroxysmal supraventricular tachycardia, atrioventricular block, bifascicular block, and left anterior hemi-block may also occur in the patients with frequencies higher than 10% (Table 1).

In many cases of sinus tachycardia, cognitive and behavioral factors, somatic hypervigilance associated with anxiety, depression, and behavioral amplification contributes to symptom chronicity.[3] And a previous study indicated that, for the patients with inappropriate sinus tachycardia, the most common comorbid conditions were depression (25.6%) and anxiety (24.6%).[4] Although no evidence of an association between symptoms of anxiety or severe depression and AF risk, a significant association of symptoms of mild to moderate depression with increased AF risk has been identified.[5] Moreover, anxiety and depression may be associated with worsened AF.[6]

Thus, antiarrhythmic drugs, such as amiodarone and metoprolol may be used for COVID-19 patients with ventricular arrhythmia.[7] We should pay attention to the COVID-19 patients with psychiatric disorders before COVID-19, as the infection may exacerbate pre-existing mental symptoms.[8] The antiarrhythmic drugs should be applied to these patients, if they showed arrhythmia after the infection, since that arrhythmia may worsen the neuropsychiatric symptoms.[3–6]

Chloroquine and hydroxychloroquine have been widely used in COVID-19 treatments. However, there is compelling evidence that chloroquine and hydroxychloroquine induce significant QTc prolongation and potentially increase the risk of arrhythmia (such as Torsade de pointes) (Table 2).[9] Actually, among COVID-19 patients, approximately 10% developed QTc prolongation to a degree that generally leads to withdrawal of the drug.[9] Although clinicians did not find evidence that occurrence of either depressive or anxiety disorder is associated with abnormalities in QTc,[10] increased anxiety scores were associated with prolonged QTc intervals.[11] Therefore, (hydroxy)chloroquine should not be used for COVID-19 patients with anxiety disorders to avoid severe QTc prolongation.

Neither psychiatric symptoms nor arrhythmia in COVID-19 patients undergoing steroid treatments has been well described in the literature. Corticosteroid-induced psychosis is a rare but well-documented disorder when corticosteroid was applied at a high dose.[12] And a rare case study in lupus previously reported that high dose corticosteroid was associated with increased AF.[13] However, no such side effects have been reported at lower doses. Indeed, low-dose corticosteroids have been shown in septic shock and prophylactic use for AF postcardiac surgery or ventilator-induced.[14,15] Although there is no direct evidence that corticosteroids can prevent arrhythmia, they are likely safe in low or moderate dosages and may have a role in preventing AF development in COVID-19.[15] Corticosteroids might be applied to the COVID-19 patients with psychiatric disorders, if they showed AF after the infection, as AF may worsen neuropsychiatric symptoms.[5,6]

TABLE 1 Arrhythmia in COVID-19 patients

Reference	Arrhythmia in COVID-19 patients	Frequency
Cho et al., *PLoS One* 2020, 15: e0244533	Sinus tachycardia	39.9% (57/143)
	Premature ventricular complexes	28.7% (41/143)
	Non-sustained ventricular tachycardia	15.4% (22/143)
	Sustained ventricular tachycardia	1.4% (2/143)
	Ventricular fibrillation	0.7% (1/143)
Song et al., *Front Cardiovasc Med* 2020; 7: 150	ST-T segment and T wave changes	33.3% (7/21)
	Sinus tachycardia	19.0% (4/21)
Kunal et al., *Indian Heart J* 2020; 72: 593-598	QT-interval (QTc) prolongation	17.6% (19/108)
	Sinus tachycardia	16.9% (18/108)
	First degree atrioventricular (AV) block	4.6% (5/108)
	Ventricular tachycardia/ventricular fibrillation (VT/VF) in two	1.8% (2/108)
	Sinus bradycardia	0.9% (1/108)
Chen et al., *Clin Cardiol* 2020; 43: 796-802	Sinus tachycardia	70.4% (38/54)
	Premature beat	18.5% (10/54)
	Ventricular tachycardia (VT)	5.6% (3/54)
	Sinus bradycardia	5.6% (3/54)
	Atrioventricular (AV) block	3.7% (2/54)
	Atrial fibrillation (AF)	1.9% (1/54)
Hsieh et al., *SAGE Open Med* 2021; 9: 20503121211054973	Sinus tachycardia	41.1% (97/236)
Mesquita et al., *Rev Port Cardiol (Engl Ed)* 2021; 40: 573-580	Atrial fibrillation (AF) or flutter	62.5% (40/64)
	Paroxysmal supraventricular tachycardia	26.6% (17/64)
	Increased QTc interval	10.9% (7/64)
	Sinus bradycardia	7.8% (5/64)
	Ventricular tachycardia	3.1% (2/64)
Antwi-Amoabeng et al., *Ann Noninvasive Electrocardiol* 2021; 26: e12833	T-wave abnormalities	38.7% (72/186)
	Sinus tachycardia	30.1% (56/186)
	Atrial fibrillation (AF) or flutter	12.9% (24/186)
	Atrioventricular (AV) block	11.8% (22/186)
	ST depression	8.6% (16/186)
	ST elevation	8.1% (15/186)
	Sinus bradycardia	7.5% (14/186)
	Right bundle branch block	7.5% (14/186)
	Premature atrial contraction	5.9% (11/186)
	Premature ventricular contraction	5.4% (10/186)
	Supraventricular tachycardia	1.6% (3/186)
	Left bundle branch block	1.6% (3/186)

TABLE 1 (Continued)

Reference	Arrhythmia in COVID-19 patients	Frequency
Aghajani et al., *Arch Acad Emerg Med* 2021; 9: e45	Sinus tachycardia	35.5% (317/893)
	Abnormal T wave	24.7% (221/893)
	ST depression	19.1% (171/893)
	Prolonged QT interval	18.2% (162/893)
	Bifascicular block	17.2% (154/893)
	Left anterior hemi-block	13.2% (118/893)
	Supraventricular arrhythmia	9.9% (88/893)
	Sinus bradycardia	6.2% (55/893)
	Q wave in inferior leads	5.6% (50/893)
	Abnormal R wave progression	4.8% (43/893)
	Right bundle branch block	4.6% (41/893)
	ST elevation	4.0% (36/893)
	Ventricular arrhythmia	3.1% (28/893)
	Interventricular conduction delay	3.0% (27/893)
	Q wave in precordial leads	3.0% (27/893)
	Left bundle branch block	2.9% (26/893)
	Incomplete right bundle branch block	2.8% (25/893)
	Incomplete left bundle branch block	1.2% (11/893)
	Q wave in lateral leads	0.3% (3/893)
	Left posterior hemi-block	0.2% (2/893)

TABLE 2 Arrhythmia in COVID-19 patients treated with (hydroxy)chloroquine

Reference	Arrhythmia in COVID-19 patients treated with (hydroxy)chloroquine	Frequency
Chang et al., *J Am Coll Cardiol* 2020; 75: 2992-2993	Atrial fibrillation with a rapid ventricular response	53.6% (15/28)
	QT-interval (QTc) > 500 ms	17.9% (5/28)
	First-degree atrioventricular block	14.3% (4/28)
	Nonsustained ventricular tachycardia	7.1% (2/28)
	Ventricular bigeminy	3.6% (1/28)
	Supraventricular tachycardia	3.6% (1/28)
Becker et al., *Cardiovasc Toxicol* 2021; 21: 314-321	QTc > 500 ms or the change in QTc > 60 ms	27.1% (19/70)
Jiménez-Jáimez et al., *Sci Rep* 2020; 10: 21417	QTc > 460 ms	14.2% (31/219)
Gopinathannair et al., *J Interv Card Electrophysiol* 2020; 59: 329-336	QTc > 500 ms	16.8% (80/477)
	Torsade de pointes	4.1% (20/489)
Saleh et al., *Circ Arrhythm Electrophysiol* 2020; 13: e008662	QTc > 500 ms	9.0% (18/201)
	The change in QTc > 60 ms	12.9% (26/201)
	New-onset atrial fibrillation	8.5% (17/201)
	Nonsustained, monomorphic ventricular tachycardia	3.5% (7/201)
	Sustained, monomorphic ventricular tachycardia	0.5% (1/201)

(Continues)

TABLE 2 (Continued)

Reference	Arrhythmia in COVID-19 patients treated with (hydroxy)chloroquine	Frequency
O'Connell et al., *JACC Clin Electrophysiol* 2021; 7: 16-25	QTc > 500 ms	21.0% (87/415)
Chorin et al., *Heart Rhythm* 2020; 17: 1425-1433	QTc > 500 ms	23.1% (58/251)
	Torsade de pointes	0.4% (1/251)
Fteiha et al., *Int J Clin Pract* 2020; 75: e13767	QTc prolongation	15.6% (14/90)
Mercuro et al., *JAMA Cardiol* 2020; 5: 1036-1041	QTc > 500 ms	20.0% (18/90)
	The change in QTc > 60 ms	11.1% (10/90)
	Torsade de pointes	1.1% (1/90)
Chorin et al., *Nat Med* 2020; 26: 808-809	QTc > 500 ms	10.7% (9/84)
Borba et al., *JAMA Netw Open* 2020; 3: e208857	QTc > 500 ms	18.9% (7/37)

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Shu Yuan conceptualized the analysis. All authors contributed to literature search, writing, and revision of the manuscript. All authors approved the final version.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author on a reasonable request.

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