

## How to manage QT prolongation in COVID-19 patients

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### Abstract

Indonesia has declared a COVID-19 outbreaks because of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in March 2020. COVID-19 has significantly increased morbidity and mortality worldwide. Some studies have shown good clinical outcomes with the use of combination of chloroquine or hydroxychloroquine and azithromycin. That drugs can prolong the QT interval and increase the risk of Torsade de Pointes (TdP). The risk is increasing in several conditions such as in critical patients, metabolic disorders, sepsis, multiorgan dysfunction and with drug-drug interactions. Cardiologists need to know how to manage this condition to reduce the risk of TdP.

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**Keyword:** COVID-19, hydroxychloroquine, azithromycin, QT prolongation, TdP

## Introduction

Indonesia is currently suffering through a pandemic outbreak of Coronavirus Disease 2019 (COVID-19) that caused by severe respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 is a newly recognized viral infectious disease that has spread rapidly throughout Wuhan, Hubei, China and several countries around the world.<sup>1</sup> The rapid spread of this disease has significantly increased

in morbidity and mortality worldwide. Studies have shown clinically improved outcome with the use of chloroquine or hydroxychloroquine in COVID-19 patients, even though still controversial.<sup>2,3</sup>

Combination of azithromycin and hydroxychloroquine or with chloroquine significantly reduced SARS-CoV-2 in swab samples.<sup>4</sup> Those combinations are known to prolong the QT interval and will increase the incident of Torsades de Pointes (TdP). The risk of TdP increases in critical patients,

metabolic problems, multiorgan dysfunction or failure, sepsis and with drug-drug interaction. This article emphasizes the role of cardiologist in managing the risk of QT prolongation.

**Assessment and Monitoring of QT Interval**

Time from the beginning of the QRS complex to the end of the T wave is known as QT interval.<sup>5</sup> QT interval below 400 to 440 ms is considered normal. Men have a relatively shorter QT interval than women. The corrected QT interval (QTc) is used due to the heart rate variation. Male has QT prolongation if greater than 450 ms and women if more than 470 ms.<sup>6</sup> Tisdale et al.<sup>7</sup> has been developed a risk score tool (table 1) to predict QT prolongation that uses age, gender, diuretic drug, potassium serum level, QTc, QT prolonging drugs, acute myocardial infarction, heart failure condition and sepsis.

Table 1. Risk score for QT prolongation. Score less than 7 was considered low and had 15% incidence for QTc prolongation. Score 7-10 was moderate risk score with 37% incidence of QTc prolongation and high (> 11) risk was 73%.<sup>7</sup>

Risk factors	Points
Age ≥ 68 years	1
Female sex	1
Loop diuretic	1
Serum K+ ≤ 3.5 mEq/L	2
Baseline QTc ≥ 450 ms	2
Acute myocardial infarction	2
≥ 2 QTc prolonging drugs	3
One QTc prolonging drugs	3
Heart failure	3
Sepsis	3
Maximum risk score	21

Drug-induced QT prolongation has known as a surrogate indicator for increased risk of drug-associated torsades de pointes (TdP), can be a lethal polymorphic ventricular tachycardia.<sup>8</sup> Theoretically, the risk of QT prolongation and TdP are very low if used alone or in combination with those drugs. The risk of QT prolongation and TdP are increasing in COVID-19 patients due to previous or concurrent treatments, older age (> 60 years old), sex, metabolic disorders (hypoxia,

multiorgan failure, electrolyte abnormalities or sepsis) and history of cardiovascular disease.<sup>9,10</sup>

COVID-19 patients with treatment of hydroxychloroquine, chloroquine with or without azithromycin, consider the following modifiable options:

- Calculating Tisdale risk score
- ECG for QT interval evaluation
- Stop and discontinuing of unuseful QT-prolonging drugs
- Checking electrolyte serum level (potassium and magnesium)

We must know the high-risk patient to develop QT prolongation such as, low level of potassium, existing QT prolongation, bradycardia, heart failure condition, myocardial ischemia, and antiarrhythmic medications.<sup>11</sup> The mechanism of most drugs that can prolong the QT interval and increase the risk of TdP are blocking the potassium channel.<sup>12</sup> Lidocaine can block the late sodium current (INA-L) channel and slightly shorten the QT interval.<sup>13</sup> Flowchart (figure 1) showed how to manage the drug induced QT prolongation in hospitalized COVID-19 patients.

**Conclusion**

COVID-19 treatment using chloroquine, hydroxychloroquine with or without addition of azithromycin can lead to QT prolongation and TdP. Cardiologists should know how to manage that conditions.

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**Abbreviations:**

Bpm : beats per minute

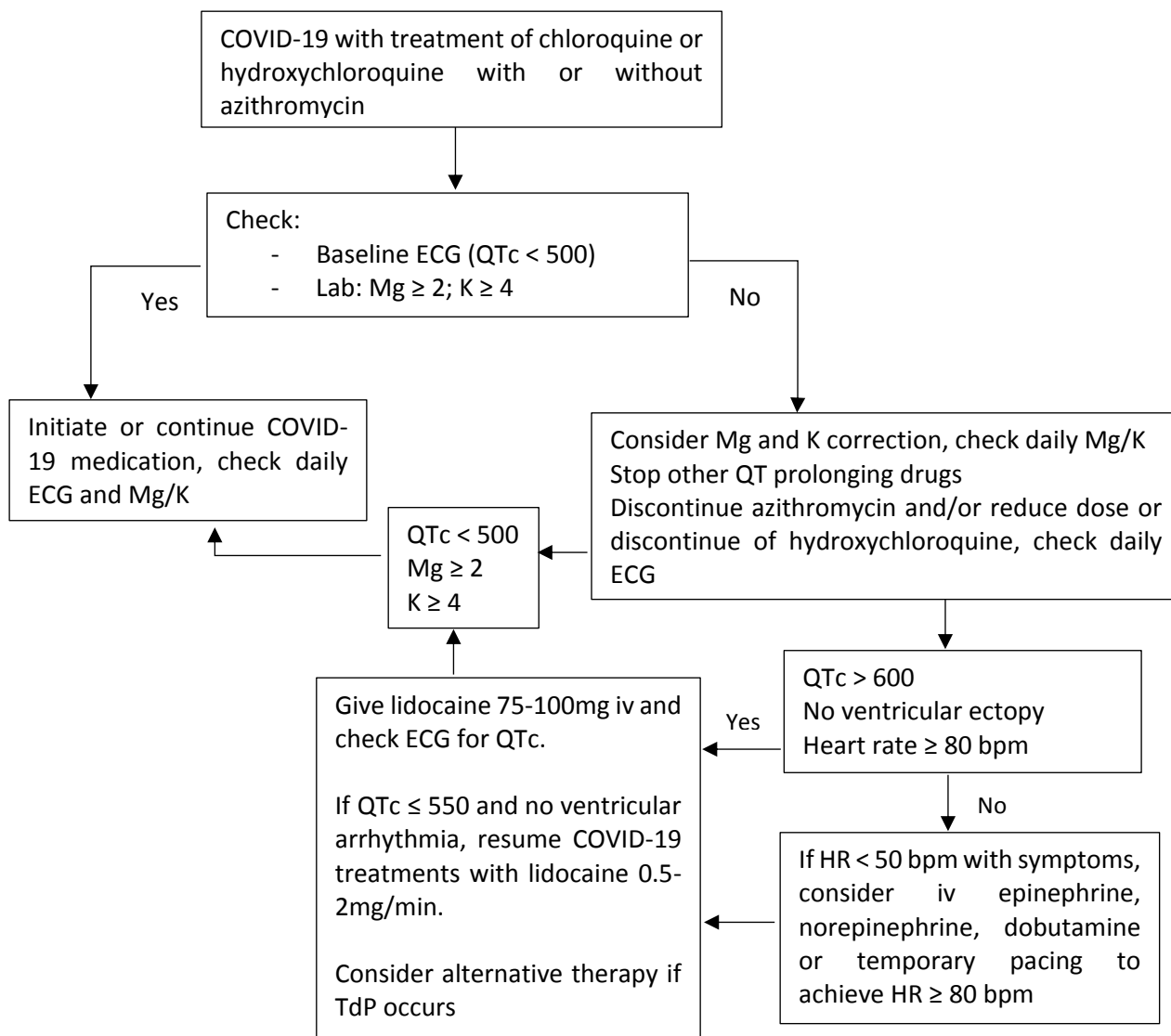


Figure 1. Flow chart to manage QT prolongation due to chloroquine or hydroxychloroquine with or without azithromycin. This flow chart may not be appropriate for all patients. Clinical judgements are needed by cardiologist or electrophysiologist. Abbreviation: bpm: beats per minute; HR: heart rate; iv: intravenous; Mg: magnesium; ms: milliseconds; K: potassium; TdP: Torsades de Pointes.

- COVID-19 : Coronavirus Disease 2019
- HR : heart rate
- Iv : intravenous
- K : serum potassium
- Mg : serum magnesium
- ms : milliseconds
- QTc : corrected QT interval
- SARS-CoV-2 : Severe Acute Respiratory Syndrome CoronaVirus 2
- TdP : Torsade de Pointes

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