Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/16607
DOI URL: http://dx.doi.org/10.21474/IJAR01/16607

*RESEARCH ARTICLE*

# COVID ET QT : ETAT DES LIEUX

**M. Ztati, S. El Karimi and M. Elhattaoui**
Service De Cardiologie, CHU Mohammed VI Marrakech.

## *Manuscript Info*

***Manuscript History***
Received: 31 January 2023
Final Accepted: 28 February 2023
Published: March 2023

***Key words:-***
Coronavirus (SARS-CoV-2), QT Interval, Torsades De Pointes

## *Abstract*

**Introduction** During the current COVID-19 pandemic, there has been increased interest in using off-label medications for treatment of the novel coronavirus (SARS-CoV-2), including drugs with a propensity for QT prolongation such as hydroxychloroquine and azithromycin.(1) to evaluate and manage the QT interval in patients undergoing therapy
**Materials and methods:** A prospective study of 156 Covid patients In all department of the Mohammed VI university hospital in Marrakech during the period from 1 April 2020 to 15 April 2020.
**Résultats:**
**Conclusion:** Les thérapies pour COVID-19 peuvent entraîner des effets indésirables cardio - vasculaires à la phase aigue¨ potentiellement graves et nécessitant une surveillance rapprochée surtout de l interval QT par l electrocardiogramme.



## Introduction:-

During the current COVID-19 pandemic, there has been increased interest in using off-label medications for treatment of the novel coronavirus (SARS-CoV-2), including drugs with a propensity for QT prolongation such as hydroxychloroquine and azithromycin.(1) to evaluate and manage the QT interval in patients undergoing therapy

The objective of our study is to analyze the effect of treatment in QT interval.

## Matériels et Method:-

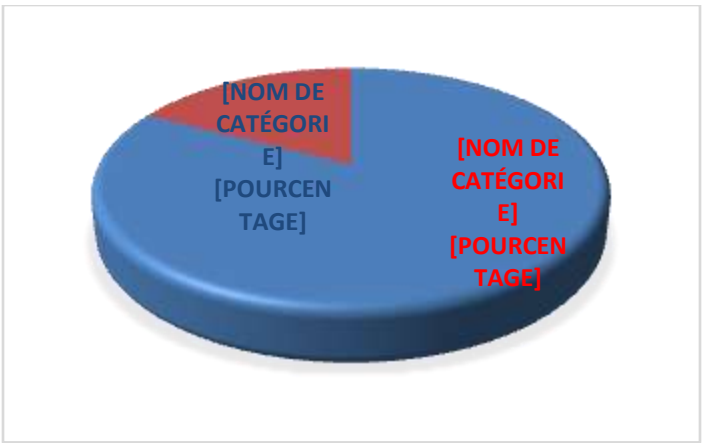
We undertook a prospective study in 156 patients in the all department of the Mohammed VI Hospital in Marrakech during the period from 1 April 2020 to 15 April 2020.

La plupart de nos patient ont bénéficier d un ECG avant traitement et un autre de controle avec des intervalles différents le calcul de QTc ( selon Bazt) si FC entre 60 – 85 bpm et frederichia si patient tachy ou bradycarde

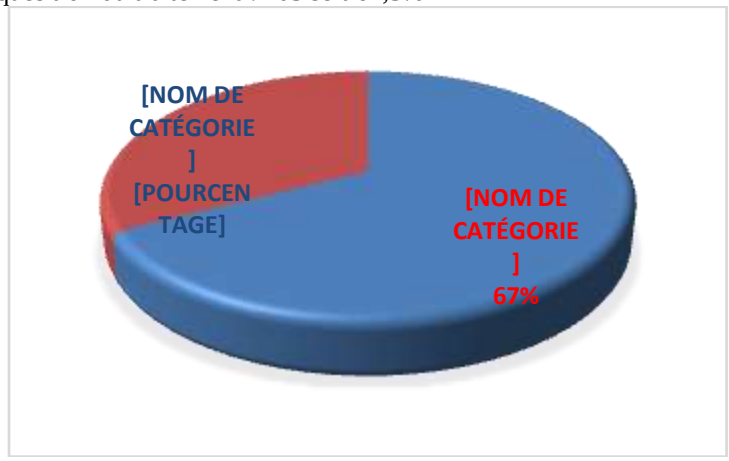
## Résultats:-

-Nombre total des patients hospitalisés : 156
-Nombre des ECG pratiqués à l'admission : 129 soit 82,69%

**Corresponding Author:- M. Ztati**
Address:- Service De Cardiologie, CHU Mohammed VI Marrakech.

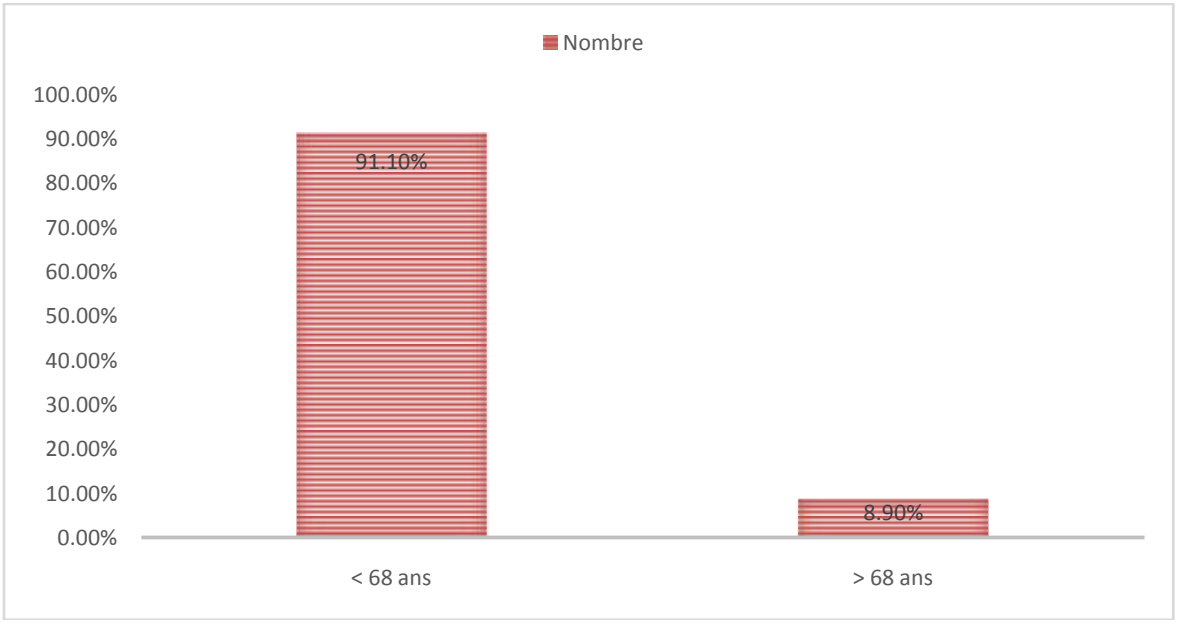



-Nombre des ECG pratiqués à J1 du traitement : 105 soit 67,3%

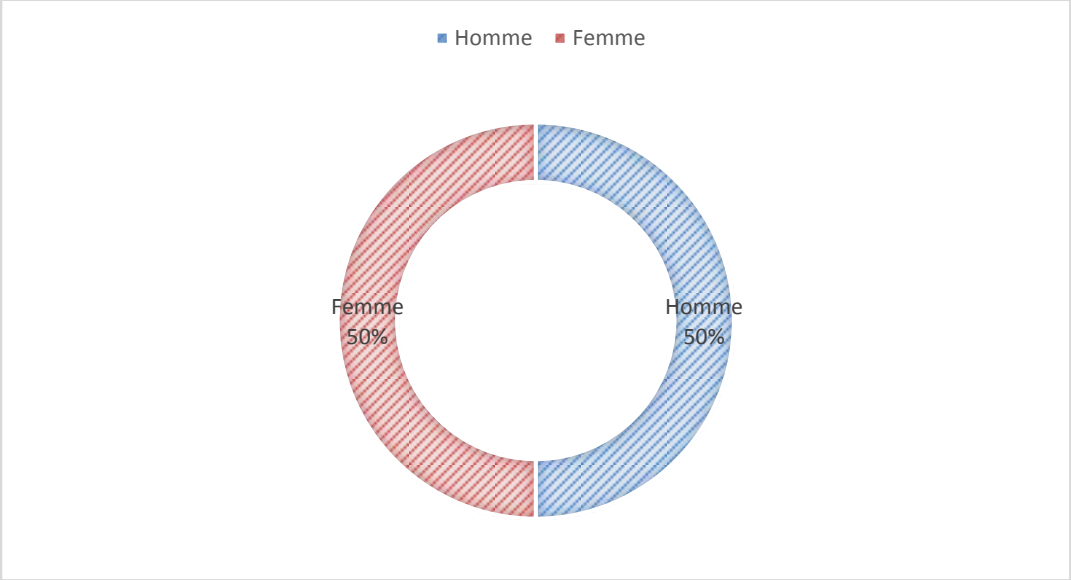



-Age moyen des patients : 45,95 ans avec extrêmes entre 10 et 82 ans

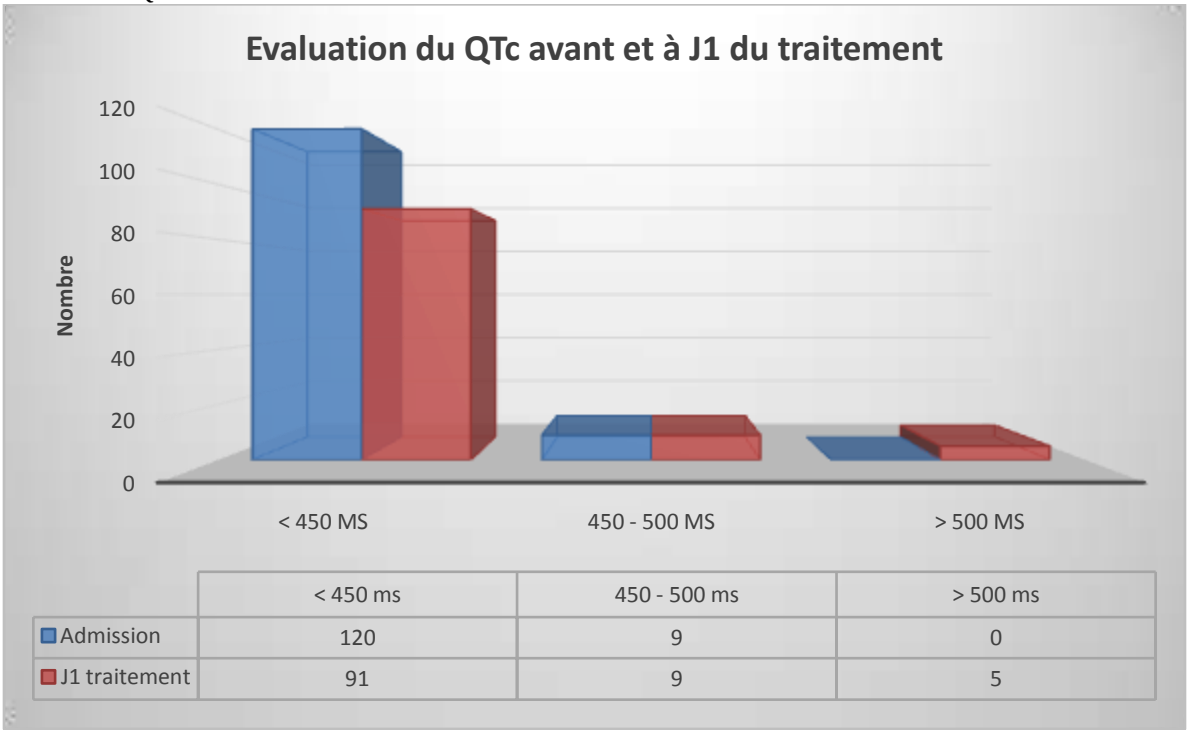
-Répartition des patients selon leur tranche d'âge :



-Répartition des patients selon le sexe :




-Evaluation du QTc avant et à J1 du traitement :




-Facteurs de risque d'allongement du QTc étudiés :

| Facteurs de risque | Nombre de patients | Pourcentage |
|---|---|---|
| Age > 68 ans | 15 | 9,6% |
| Sexe féminin | 78 | 50% |
| Diurétique | 5 | 3,2% |
| QTc l'admission> 450 ms | 9 | 5,76% |
| IDM aigu | 1 | 0,64% |
| IC | 5 | 3,2% |
| Sepsis | 5 | 3,2% |
| K+ < 3,5 Meq | 23 | 14,74% |

## Discussion:-

hydroxychloroquine and azithromycin have been touted for potential prophylaxis or treatment for COVID-19 (coronavirus disease 2019) infection. Both drugs are listed as definite causes of torsade de pointes

Raoult et al. presented the results of their non-randomized study which analyzed 24 patients with coronavirus, 3/4 were cured in 6 days after receiving chloroquine and especially in combination with azithromycin [38]

There are occasional case reports of hydroxychloroquine 1-4 prolonging the QT interval and provoking torsade de pointes erythematosus. Antimalarial prophylactic drugs, such as hydroxychloroquine, are believed to act on the entry and post-entry stages of SARS-CoV (severe acute respiratory syndrome–associated coronavirus) and SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection, likely via effects on endosomal pH and the resulting under-glycosylation of angiotensin-5 converting enzyme 2 receptors that are required for viral entry.

Closer monitoring is recommended, in particular in the case of co-prescription with azithromycin, an ECG must be performed before the start of treatment with the measurement of QTc and then 3 to 4 hours following the first administration (at the assumed maximum concentration hydroxychloroquine ± azithromycin), then twice a week for the duration of treatment and in the event of a symptom which may suggest a disturbance of the heart rhythm (sudden and brief palpitations, syncope, comitia crisis..).

If the QTc is ≥ 500 ms, the treatment should be reduced or stopped depending on the clinician's decision, and a continuous cardiac monitor put in place until the ECG is normalized [44].

The widely used antibiotic azithromycin is increasingly recognized as a rare cause of QT 11,12 non-pause–dependent polymorphic ventricular tachycardia. the observations that azithromycin administration leaves the patient vulnerable to QTc interval 13 prolongation and torsade de pointes.

Basic electrophysiologic studies suggest that both drugs can provoke proarrhythmia via 14,15 6,7 8,9 10 serious arrhythmias, and increased risk for sudden death prolongation, the combination of these agents on QT or arrhythmia risk has not been studied. There are very limited data evaluating the safety of combination therapy.

Multiple randomized trials are currently being initiated.

The risk of arrhythmia is increased in case of frequent hypokalaemia in sepsis. Any sign of rhythmic instability should prompt an ECG.

Indeed the risk of torsades de pointes is real beyond a measurement of the QTc, greater than 500ms, a monitoring of serum potassium and magnesemia in these rare cases is necessary, and the healthcare team should be ready to mount a temporary stimulation probe if necessary.

These extrinsic factors must always be corrected to allow prescription under the best conditions.

Seriously ill patients often have comorbidities that can increase risk of serious
16 17 arrhythmias.

Mechanisms to minimize arrhythmia risk include:
The effect of

- . Electrocardiographic/QT interval monitoring:

o Withhold the drugs in patients with baseline QT prolongation (eg, QTc ≥500 msec) or with known congenital long QT syndrome.
o Monitor cardiac rhythm and QT interval; withdrawal of the drugs if QTc exceeds a preset threshold of 500 msec.
o In patients critically ill with COVID-19 infection, frequent caregiver contact may need to be minimized, so optimal electrocardiographic interval and rhythm monitoring may not be possible.

1. Correction of hypokalemia to levels of >4 mEq/L and hypomagnesemia to levels of >2 mg/dL.
2. Avoid other QTc prolonging agents[5] whenever feasible.

Safety considerations for use of hydroxychloroquine and azithromycin in clinical practice 18 have been described.

Some of the current COVID-19 repurposed drugs are listed in the Table.

**Table. Torsade de pointes potential and post-marketing adverse events associated with possible COVID-19 repurposed pharmacotherapies.**

| Possible COVID-19 Treatment | CredibleMeds Classification | VT/VF/TdP/LQTS in FAERS | Cardiac Arrest in FAERS |
|---|---|---|---|
| **Repurposed antimalarial agents** | | | |
| Chloroquine | Known risk | 72 | 54 |
| Hydroxychloroquine | Known risk | 222 | 105 |
| **Repurposed antiviral agents** | | | |
| Lopinavir/ritonavir | Possible risk | 27 | 48 |
| **Adjunct agents** | | | |
| Azithromycin | Known risk | 396 | 251 |

COVID-19 indicates coronavirus disease 2019; FAERS, US Food and Drug Administration Adverse Event Reporting System; LQTS, long QT syndrome; and TdP, torsade de pointes.

## Conclusion:-

Les thérapies pour COVID -19 peuvent entraîner des effets indésirables cardio - vasculaires à la phase aigue ¨ potentiellement graves et nécessitant une surveillance rapprochée surtout de l interval QT par l electrocardiogramme

Les personnes déjà atteintes de maladies cardiovasculaires infectées par le virus ont un risque plus élevé d'effets indésirables , et sont considérées de mauvais pronostic . D ou l ineteret d un suivi interdisciplinaire , prolongé et rapproché.

## References:-


1. Chen CY, Wang FL, Lin CC. Chronic hydroxychloroquine use associated with QT prolongation and refractory ventricular arrhythmia. Clin Toxicol (Phila). 2006;44:173-175.
2. Morgan ND, Patel SV, Dvorkina O. Suspected hydroxychloroquine-associated QT-interval prolongation in a patient with systemic lupus erythematosus. J Clin Rheumatol. 2013;19:286-288.
3. O'Laughlin JP, Mehta PH, Wong BC. Life threatening severe QTc prolongation in patient with systemic lupus erythematosus due to hydroxychloroquine. Case Reports in Cardiology. 2016:4626279.
4. de Olano J, Howland MA, Su MK, Hoffman RS, Biary R. Toxicokinetics of hydroxychloroquine following a massive overdose. Am J Emerg Med. 2019;37:2264.e5-2264.e8.
5. Giudicessi JR, Noseworthy P A, Friedman P A, Ackerman MJ. Urgent guidance for navigating and circumventing the QTc prolonging and torsadogenic potential of possible pharmacotherapies for COVID-19 [published online ahead of print March 25, 2020]. Mayo Clin Proc. doi: 10.1016/j.mayocp.2020.03.024. https://www.elsevier.com/__data/assets/pdf_file/0004/996745/MCP_Possible-COVID-19-Pharmacotherapies.pdf. Accessed April 2, 2020.
6. Choi Y, Lim H-S, Chung D, Choi J-G, Yoon D. Risk evaluation of azithromycin-induced QT prolongation in real-world practice. BioMed Research International. 2018:1574806.