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Letters

Prognostic Value of Electrocardiographic QRS Diminution in Patients With COVID-19
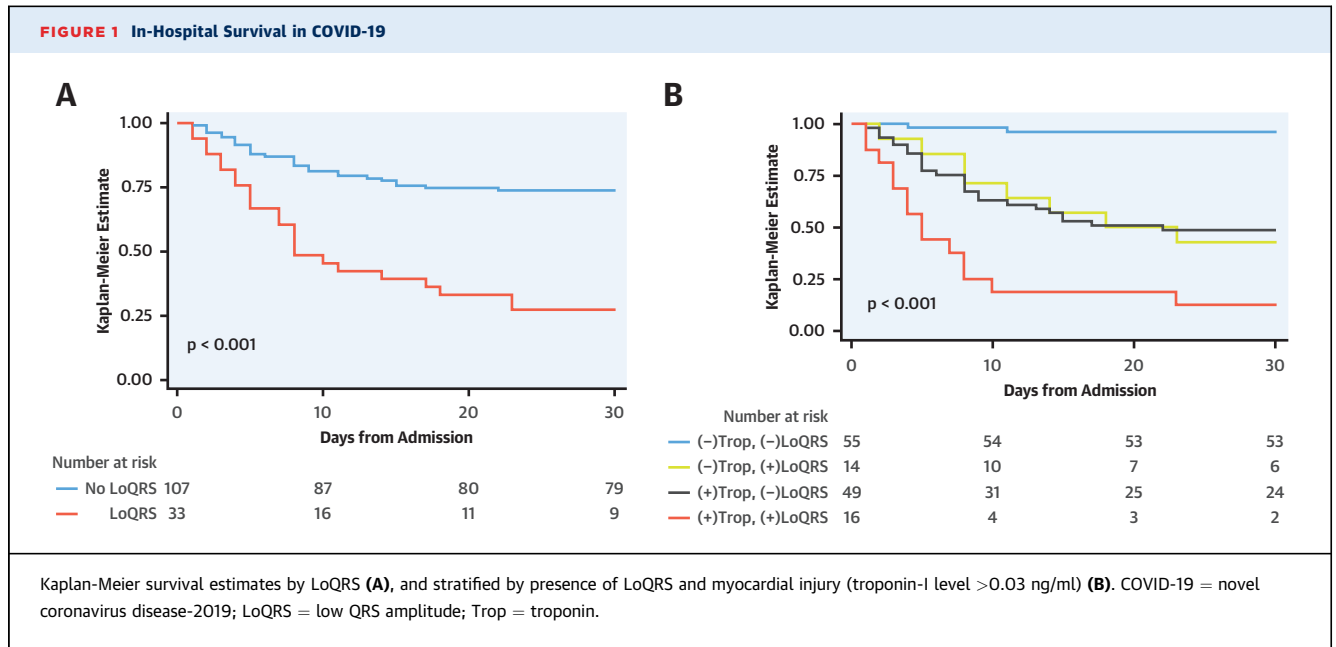
Myocardial injury has been observed in 33.7% of hospitalized patients with novel coronavirus disease-2019 (COVID-19), but there are limited data on abnormalities on the electrocardiogram (ECG) (1). The mechanism of injury remains poorly understood despite abnormal findings demonstrated by echocardiography and cardiac magnetic resonance imaging (2,3). Likewise, electrocardiographic voltage may be diminished by various cardiac and extra-cardiac etiologies (4,5). While caring for patients hospitalized with COVID-19, we noted significant reduction in QRS amplitude on the 12-lead ECG coincident with worsening clinical status and death. This observation prompted investigation into the prevalence and prognostic significance of QRS amplitude diminution in hospitalized COVID-19 patients.

Between March 6 and April 12, 2020, 1,354 patients with laboratory-confirmed COVID-19 were admitted to the Mount Sinai Health System in New York City and included in a COVID-19 registry approved by the Institutional Review Board (Cardiac Arrhythmias In Patients With Coronavirus Disease [COVID-19]; NCT04358029). Consecutive patients (n = 140) both observed on telemetry and having a final disposition—death or discharge—were analyzed. Low QRS amplitude (LoQRS) was defined by a composite of: 1) QRS amplitude <5 mm in the limb leads AND <10 mm in the precordial leads; 2) QRS amplitude <5 mm in the limb leads OR <10 mm in the precordial leads; or 3) QRS amplitude diminution by ≥50% compared with the baseline or admission ECG in the limb leads or precordial leads (a composite of leads V_1 to V_3 and V_4 to V_6). Continuous and categorical variables were compared using the Wilcoxon rank sum or chi-square tests, respectively. Cox proportional hazards models were performed to evaluate the association between LoQRS and in-hospital mortality.

LoQRS occurred in 24.3% of COVID-19 patients and was more frequent in patients who died compared with those who survived to discharge (48.1% vs. 10.2%; p < 0.001). A 50% or greater decrease in QRS amplitude occurred in 17.1% of patients (36.5% vs. 5.7% in the mortality and discharged groups, respectively; p < 0.001). QRS amplitude met the threshold <5 mm in the limb leads or <10 mm in the precordial leads in 15.7% of patients, and was more prevalent in those who died (28.9% vs. 8.0%; p = 0.001).

Overall mortality occurred in 37.1% of the COVID-19 cohort, but was 73.5% in patients with LoQRS compared with 25.5% in patients without LoQRS (p < 0.001) (Figure 1A). The median time to the first ECG with LoQRS was 5.3 days (interquartile range: 2.1 to 11.1 days). The median time to death from the first ECG with LoQRS was 52 h (interquartile range: 18 to 130 h). Patients with LoQRS had higher median levels of D-dimer (2.1 vs. 1.2 μg/ml; p = 0.01), C-reactive protein (130 vs. 102 mg/l; p = 0.05), and pro-calcitonin (0.3 vs. 0.1 ng/ml; p = 0.04). There were no significant differences in median admission (60.45 vs. 36.0; p = 0.31) or peak (131.9 vs. 63.0; p = 0.18) B-type natriuretic peptide (BNP) levels between LoQRS and stable-QRS groups, respectively.

When adjusted for baseline clinical variables including age, body mass index, chronic kidney disease, smoking, liver disease, and hypertension, LoQRS was independently associated with mortality (hazard ratio [HR]: 4.18; 95% confidence interval [CI]: 2.33 to 7.51; p < 0.001). This strong association persisted after adjustment for presenting troponin, peak troponin, peak D-dimer, C-reactive protein, and last available albumin in addition to baseline clinical covariates (HR: 2.83; 95% CI: 1.28 to 6.23; p = 0.01), and when intubation and inotrope or vasopressor requirement were added to the model (HR: 2.31; 95% CI: 1.03 to 5.20; p = 0.042). A significant interaction between myocardial injury (troponin level >0.03 ng/ml) and LoQRS was demonstrated by Cox proportional hazards models (p-interaction = 0.037). Patients with LoQRS and concomitant myocardial injury had higher mortality than expected for exhibiting both findings (Figure 1B).

FIGURE 1 In-Hospital Survival in COVID-19

Kaplan-Meier survival estimates by LoQRS **(A)**, and stratified by presence of LoQRS and myocardial injury (troponin-I level >0.03 ng/ml) **(B)**. COVID-19 = novel coronavirus disease-2019; LoQRS = low QRS amplitude; Trop = troponin.

This analysis is limited by a lack of corroborating imaging and autopsy data and inclusion of only patients receiving telemetric monitoring, which may overestimate the magnitude of association and limit generalizability. On the other hand, data were manually extracted at a patient level, buttressing data quality.

This study demonstrates that LoQRS is an independent predictor of mortality in hospitalized patients with COVID-19, captures a dynamic process during the course of illness, and underscores the prognostic utility of both an absolute and relative reduction in QRS amplitude. A median time of 52 h from the first ECG with LoQRS until death in COVID-19 may provide an opportunity to focus clinical reassessment. Further studies should address whether intensification of therapy in individuals manifesting LoQRS would improve clinical outcomes.

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