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Electrocardiographic findings and mortality in covid-19 patients hospitalized in different clinical settings

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ABSTRACT

Background: Twelve-lead electrocardiogram (ECG) represents the first-line approach for cardiovascular assessment in patients with Covid-19.
Objectives: We sought to describe and compare admission ECG findings in 3 different hospital settings: intensive-care unit (ICU) (invasive ventilatory support), respiratory care unit (RCU) (non-invasive ventilatory support) and Covid-19 dedicated internal-medicine unit (IMU) (oxygen supplement with or without high flow). We also aimed to assess the prognostic impact of admission ECG variables in Covid-19 patients.
Methods: We retrospectively analyzed the admission 12-lead ECGs of 1124 consecutive patients hospitalized for respiratory distress and Covid-19 in a single III-level hospital. Age, gender, main clinical data and in-hospital survival were recorded.
Results: 548 patients were hospitalized in IMU, 361 in RCU, 215 in ICU. Arrhythmias in general were less frequently found in RCU (16% vs 26%, $p<0.001$). Deaths occurred more frequently in ICU patients (43% vs 20–21%, $p<0.001$).
After pooling predictors of mortality (age, intensity of care setting, heart rate, ST-elevation, QTc prolongation, Q-waves, right bundle branch block, and atrial fibrillation), the risk of in-hospital death can be estimated by using a derived score. Three zones of mortality risk can be identified: <5%, score <5 points; 5–50%, score 5–10, and >50%, score >10 points. The accuracy of the score assessed at ROC curve analysis was 0.791.
Conclusions: ECG differences at admission can be found in Covid-19 patients according to different clinical settings and intensity of care. A simplified score derived from few clinical and ECG variables may be helpful in stratifying the risk of in-hospital mortality.

Introduction

Coronavirus-19 disease (Covid-19) is the definition issued by World Health Organization (WHO) to describe clinical manifestations caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection.[1,2] Covid-19 typically involves low respiratory tract infection causing interstitial pneumonia; multi-organ involvement however is not rare. In particular, cardiac involvement and acute myocardial injury have been shown to be associated with a worse prognosis.[3,4]

Traditional 12-lead electrocardiogram (ECG) approach may play an important role for the screening of cardiac involvement because it is fast, widely accessible, low cost and remotely interpretable. Moreover, ECG at admission has been demonstrated to predict 30-day mortality in patients affected by Covid-19.[5]

Several ECG abnormalities have been described in patients hospitalized for Covid-19. The incidence of arrhythmias in Covid-19 population reaches up to 16.7% and to 11.5% considering only malignant arrhythmias.[4,6] Moreover, ST-T tract abnormalities, atrio-ventricular and intra-ventricular conduction disorders have been described and referred to myocarditis, hypoxia or inflammatory myocardial damage and right ventricle overload.[7,8]

Interestingly, the incidence of arrhythmias was found to be significantly higher in critically ill patients undergoing invasive ventilatory support compared to non-Intensive Care Unit patients.[6] However, Covid-19 patients not requiring invasive ventilatory support represent a heterogeneous population including both patients requiring non-invasive ventilation and just oxygen supplement.

Therefore, we sought to describe and compare ECG findings in 3 different hospital settings: intensive care unit (ICU) (invasive

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ventilatory support), respiratory care unit (RCU) (non-invasive ventilatory support) and Covid-19 dedicated internal medicine unit (IMU) (oxygen supplement with or without high flow). We also aimed to assess the prognostic impact of admission ECG variables in Covid-19 patients.

Methods

We retrospectively analyzed the 12-lead ECG of 1124 consecutive patients hospitalized for respiratory distress in the Policlinico Riuniti University Hospital from the 1st of October 2020 to the 28th of February 2021. All patients were diagnosed with Covid-19 after naso-pharyngeal swab and hospitalized at Policlinico Riuniti Hospital in 3 different units according to the severity of respiratory distress. Critically ill patients needing an invasive ventilatory support were hospitalized in intensive care unit (ICU), those manageable with non-invasive ventilatory support in respiratory care unit (RCU), while those not needing ventilatory support (or just oxygen supplement) in a dedicated Internal Medicine Unit (IMU).

Patients were therefore divided into 3 groups: ICU, RCU and IMU. Admission setting was considered for study analysis; admission ECG was considered for data analysis. In case of transfer between units we considered the patients only once in the unit with the highest intensity of care.

Age, gender, main clinical data and in-hospital survival were recorded from all patients. Twelve-lead ECGs were recorded at admission with 25 mm/s and 1 mV/cm calibration, 0.05–150 Hz filter, using Schiller electrocardiograph (Cardiovit AT-102 G2, Schiller Inc., Baar, Switzerland). The ECGs were analyzed by accessing the hospital ECG storage server (Schiller SEMA, Schiller Inc., Baar, Switzerland). The following ECG parameters were recorded: heart rate (HR), PR interval, QRS duration (intra-ventricular block defined as QRS >0.12″), corrected QT (QTc) interval, ST tract -T wave abnormalities, Q waves, Cornell and Sokolow-Lyon voltage (mV), premature supraventricular and ventricular complexes, atrial fibrillation/flutter (AF), atrial tachycardia, ventricular tachycardia. ECG were analyzed after automated interpretation by at least 2 cardiologists (L.T, A.F., F. M., F.C., E.V., D.D.C.) with the supervision of at least one senior expert (M.M., N.D.B.). This is an observational non randomized study, conducted according to the declaration of Helsinki; the study was approved by the local ethics committee.

Statistical analysis

Data were reported as mean with standard deviation for continuous variables, proportions for discrete variables; Continuous variables were compared with Student's *t*-test, dichotomic with χ^2 test.

The association of individual clinical and ECG variables with death was assessed by multivariable forward stepwise regression analysis in a model which included all variables significant at univariable analysis. Variables statistically significant at multivariable stepwise forward analysis were used to derive a simplified score predictive for in-hospital mortality; the points for each predictor were derived from beta coefficients at multivariable regression analysis. The accuracy of the score was tested with ROC curve analysis. A $p<0.05$ was considered as statistically significant.

Results

Of the 1124 patients included in the study 548 patients were hospitalized in IMU, 361 in RCU, 215 in ICU; 265 died during hospitalization, 808 were discharge alive, 51 were missed at follow up.

ECG findings, age and gender were given and compared in Table 1. ICU and IMU patients were older (68±12/17 vs 64±16 years, $p<0.01$), with a higher proportion of male (57–74% vs 56%, $p<0.0001$). Sinus tachycardia (9–13% vs 7%), atrial fibrillation (AF) (13% vs 6%, $p<0.01$) were detected more frequently in IMU and ICU patients than RCU. Heart rates were lower in RCU (77±16 bpm vs 82/83±22 bpm, $p<0.001$). Arrhythmias in general were less frequently found in RCU (16% vs 26%, $p<0.001$), with no differences in ST-T abnormalities or Q-waves. Right bundle branch block (RBBB) was more common in ICU patients than RCU and IMU (10% vs 4–6%), as well as right frontal axis deviation and S1Q3T3 aspect (1% vs 0%). No statistically significant differences in the incidence of AV-blocks were found. QTc interval was significantly longer in ICU (452±38 msec) and IMU patients (441±34 msec) than in RCU (432±34 msec, $p<0.001$ in all cases); abnormal QTc duration occurred more often in ICU patients (35% vs 17–18%, $p<0.001$). Left ventricular hypertrophy was more frequent in IMU (7% vs 3%, $p<0.05$), QRS amplitude attenuation was less frequent in RCU (8% vs 10–14%).

Deaths occurred more frequently in ICU patients (43%, $p<0.001$), while no significant differences between IMU and RCU patients were detected (20% and 21% respectively).

After pooling predictors of mortality statistically significant at univariable analysis (Supplement Table 1) in a multivariable forward stepwise regression analysis model, 8 variables were found as independent predictors of mortality at admission: age, intensity of care setting (IMU<RCU<ICU), heart rate, ST-elevation, QTc prolongation, Q-waves, RBBB.

The risk of in hospital death can be estimated by using a derived score giving $^1/_2$ point for the age in years divided by 10, 2 points for the heart rate divided by 100, 2 points for the admission in RCU, 4 for ICU, and 1 point for the remaining factors. Three zone of mortality risk can be thus identified; a mortality risk <5% with a score <5 points, an intermediate risk (5–50%) with a score between 5 and 10 points, and a risk of death >50% with a score >10 points. The accuracy of the score assessed at ROC curve analysis was 0.791 (95% CI 0.792–0.860, $p<0.001$) (Table 2, Fig. 1).

Discussion

In the present study ECG differences in Covid-19 patients according to different clinical settings and intensity of care are provided. We also found that simple clinical and ECG variables, mixed in a simple clinical score, may stratify prognosis and mortality since hospital admission in Covid-19 patients.

On the basis of our results, in Covid-19 patients hospitalized in IMU and ICU both AF and all arrhythmias occur more frequently than RCU patients. This higher prevalence in IMU patients may be explained by their older age. On the other hand, the higher prevalence of AF and any arrhythmia in ICU patients may be related to clinical setting and, ultimately, to the (need for) invasive respiratory support. However, in spite of the higher prevalence of arrhythmias, there is no difference in term of mortality in IMU patients in comparison with RCU patients. It is possible that the higher age and prevalence of arrhythmias in IMU patients are balanced by the severity of respiratory distress in RCU patients.

The intensity of care reflects respiratory distress in Covid-19 patients and our multivariable analysis shows that is independently associated with in-hospital mortality; these data are in line with prior studies from other authors.[9]

In addition to respiratory distress, cardiac involvement is associated with a worse outcome in Covid-19 patients.[5] Acute myocardial injury and myocarditis in SarsCov-2 infection may be the result of different pathological mechanisms. Respiratory distress and the consequent myocardial oxygen supply/demand mismatch may lead to a type 2 myocardial infarction.[10] A direct interaction virus-myocardiocytes and cytokine hyper-response leading to apoptosis may represent other possible mechanisms.[11-12] Moreover, it was demonstrated that the prognosis of patients with respiratory distress affected by SarsCov-2 infection is worse in the presence of underlying heart disease.[13] In other words, not only cardiac involvement in SarsCov-2

Table 1
Clinical and electrocardiogram characteristics according to intensity of care.

	IMU 548 Mean	Std. Dev.	RCU 361 Mean	Std. Dev.	ICU 215 Mean	Std. Dev.	IMU vs RCU p	IMU vs ICU p	RCU vs ICU p
age (years)	68	17	64	16	68	12	0.0016	0.8766	0.0021
male	56%		57%		74%		0.7355	<0.0001	<0.0001
mortality rate	20%		21%		43%		0.8490	<0.0001	<0.0001
sinus rhythm	67%		74%		66%		0.0195	0.7148	0.0268
sinus bradycardia	11%		12%		7%		0.5662	0.1460	0.0715
sinus tachycardia	9%		7%		13%		0.3841	0.0752	0.0185
atrial fibrillation	13%		6%		13%		0.0005	0.8449	0.0015
PM/AICD	2%		1%		1%		0.0706	0.3004	0.5997
heart rate (bpm)	82	22	77	16	83	22	0.0004	0.3767	0.0001
SVPB	8%		8%		7%		0.7311	0.5167	0.7312
SVPB repetitive	2%		4%		2%		0.1911	0.6670	0.1789
VPB	7%		4%		7%		0.0993	0.9118	0.1409
VT	0%		0%		0%				
any arrhythmia	26%		16%		26%		0.0008	0.9664	0.0071
PR interval (msec)	155	27	154	24	150	25	0.8589	0.0224	0.0283
I degree AV block	4%		3%		2%		0.5925	0.2305	0.4587
II degree AV block type I	0%		0%		0%				
II degree block type II	0%		0%		0%				
III degree AV block	0%		0%		0%				
any AV block	4%		3%		2%		0.5038	0.2166	0.4943
RBBB	6%		4%		10%		0.1022	0.0680	0.0022
LBBB	3%		2%		3%		0.3678	0.5906	0.2103
LAFB	13%		11%		12%		0.2661	0.6284	0.6686
LPFB	0%		0%		0%				
QRS duration	93		92		93		0.4549	0.9454	0.5884
Frontal left axis deviation	20%		14%		19%		0.0361	0.8998	0.1153
Frontal right axis deviation	0%		0%		1%		0.4169	0.0366	0.0241
S1Q3T3	0%		0%		1%			0.0236	0.0660
QTc (msec)	441	34	432	34	452	38	0.0001	<0.0001	<0.0001
QTc prolongation	17%		18%		35%		0.7050	<0.0001	<0.0001
LVH	7%		3%		3%		0.0113	0.0374	0.9726
Cornell index	1.4	0.8	1.4	0.7	1.3	0.7	0.1595	0.1226	0.7277
Sokolow index	1.8	0.8	1.7	0.8	1.5	0.7	0.1762	<0.0001	0.0001
RVH	0%		0%		0%			0.1099	0.1949
ST elevation	0%		1%		1%		0.3525	0.1120	0.5181
negative T-waves	22%		21%		18%		0.6943	0.2578	0.4544
R amplitude attenuation	10%		8%		14%		0.4540	0.0713	0.0229
Q-waves	3%		2%		2%		0.1758	0.5661	0.5722

IMU: internal medicine unit; RCU: respiratory care unit; ICU: intensive care unit; PM: pacemaker; AICD: automated implantable cardioverter defibrillator; SVPB: supra-ventricular premature beat; VPB: ventricular premature beat; VT: ventricular tachycardia; AV: atrio-ventricular; RBBB: right bundle branch block; LBBB: left bundle branch block; LAFB: left anterior fascicular block; LPFB: left posterior fascicular block; LVH: left ventricular hypertrophy; RVH: right ventricular hypertrophy.

infection but also underlying cardiac conditions may play a key prognostic role in Covid-19 patients. For all such reasons cardiovascular conditions may significantly mirror and summarize the entity of respiratory distress, the presence of an underlying heart disease and the degree of myocardial damage due to SarsCov2.

ECG remained the first and most promptly available tool for first cardiac assessment even in the context of Covid-19 pandemic. ECGs can be easily transmitted by telemedicine support and remotely interpreted by specialists, minimizing the risk of contagion and infection.

We found that 2 simple clinical variables and 6 ECG variables were independently associated with in-hospital death on multivariable analysis (*Table 2*). Age, which obviously reflects general comorbidities, and intensity of care, which reflects the severity of respiratory distress, are clinical variables associated with risk of in-hospital death. The 6 ECG variables independently associated with

Table 2
Multivariable stepwise forward analysis model for in-hospital mortality. A simplified score is derived to predict the risk of mortality.

	beta	st err	p	Derived score	Risk
age	0.35	0.03	<0.001	1/2 point for age/10	<5 points low
intensity of care setting	0.16	0.03	<0.001	2 points RCU, 4 ICU	Mortality <5%
heart rate	0.14	0.03	<0.001	2 points for HR/100	5–10 points intermediate
ST elevation	0.09	0.03	0.0010	1 point	Mortality 5–50%
QTc prolongation	0.07	0.03	0.0072	1 point	
Q-waves	0.06	0.03	0.0168	1 point	>10 points high
RBBB	0.06	0.03	0.0275	1 point	Mortality >50%
atrial fibrillation	0.06	0.03	0.0474	1 point	

RBBB: right bundle branch block; RCU: intermediate respiratory care unit; ICU: intensive care unit; HR: heart rate.

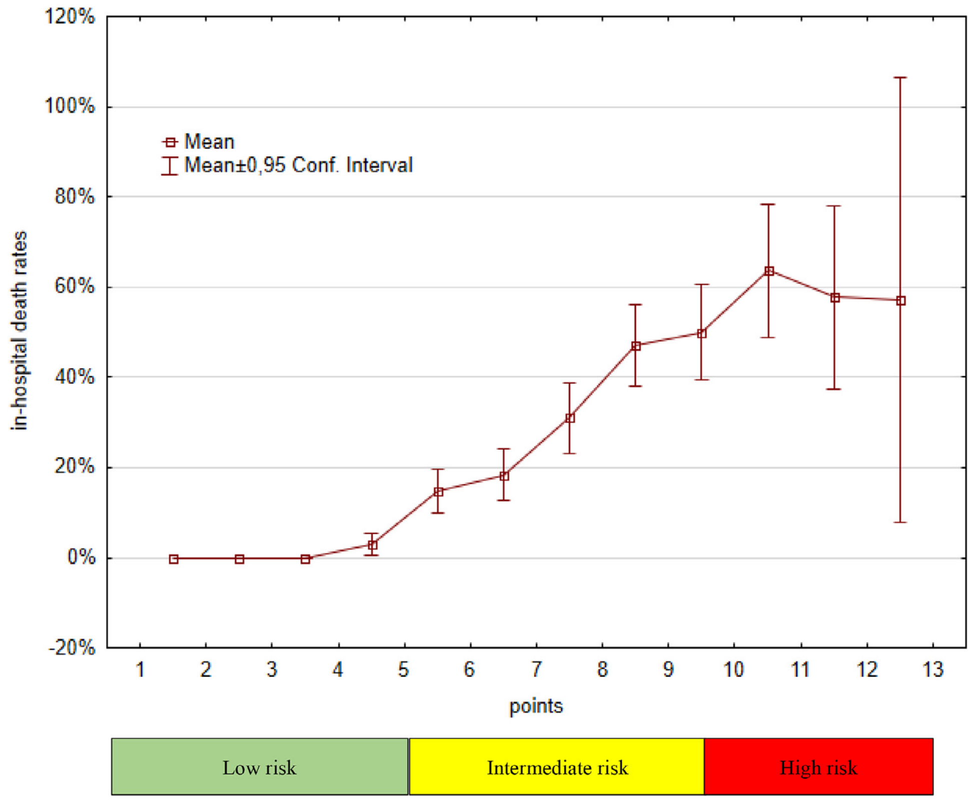

Fig. 1. Mortality rates according to derived score.

the risk of in-hospital death, instead, may reflect the entity of cardiac involvement.[7,8] Heart rate is related to sympathetic system activation due to systemic inflammatory activation, RBBB may probably reflects alterations of load conditions of right ventricle as a consequence to interstitial pneumonia, Q waves are related to an underlying heart disease, AF may reflect cardiac involvement in terms of abnormal load conditions, myocardial injury or increase of plasma catecholamines.[14] QTc prolongation may be due to changes in serum electrolytes or drug therapy and may carry an increased risk of ventricular arrhythmias. ST tract elevation may herald myocardial transmural ischemia or several types of myocardial injury; heightened coagulation state may be partly reflected by ST tract changes and D-dimer levels are an independent marker of mortality linked to inflammation as well as coagulation state in Covid-19.[15]

A simplified score was therefore derived from these simple clinical and electrocardiographic variables; this score can identify the risk of in-hospital death on the basis of 2 clinical variables (age and intensity of care) and 6 simple electrocardiographic variables (*Table 2*). The score has a good accuracy and seems particularly useful in identifying low risk patients, maybe requiring less intense monitoring or earlier discharge.

Previously, other scores assessing mortality and/or the risk of invasive ventilation have been assessed.[16-17] However, such tools do not take into account cardiac involvement and cardiovascular conditions[16] or utilize echocardiogram and left ventricle ejection fraction for cardiac evaluation.[17] Echocardiography, even if more accurate in comparison with ECG, remains less available, more expensive, and difficult to interpret remotely, even in Covid-19 patients.

ECG, however, may add prognostic value when added to age and intensity of clinical setting but does account for other variables which are also known to have prognostic valve in Covid-19 patients (i.e. diabetes, CKD, LVEF, COPD, troponin level) but have not been considered in this study.

According to our data, admission ECG findings, different in different levels of care for Covid-19 patients hospitalized with respiratory distress, may however contribute, beyond different clinical settings, contribute to risk stratification at admission. Further validation in larger cohort of patients, however, are required to confirm such preliminary data.

Conclusions

ECG differences at admission can be found in Covid-19 patients according to different clinical settings and intensity of care.

A simplified score derived from few clinical and ECG variables may be helpful in predicting in-hospital mortality with a good accuracy. If validated, this score could be a useful, inexpensive, widely available tool to stratify the risk of in-hospital death in Covid-19 patients.

Limitations

Despite the large number of patients included in the study and admitted for Covid-19 at Policlinico Riuniti in Foggia, this is a single medical center study.

Few clinical variables were collected and no echocardiographic data were recorded and reported. No data are available on oxygen levels, pre-admission ECG, pre-existing atrial fibrillation, baseline QT levels, drug therapy, sedation, antibiotic therapy, diabetes, previous cardiovascular disease, thyroid disease, underlying heart disease, heart failure, atrial fibrillation, COPD, all conditions that could have influenced the results. However, the study was mainly focused on ECG findings at admission in Covid-19 patients and ECG comparison in different clinical settings. The derived score needs to be further validated in larger populations of patients.

Conflict of interest

None to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hrtlng.2022.02.007.

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