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Effects of COVID 19 on Electrocardiographic Parameters: Healthy ECGs vs COVID 19 ECGs

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Abstract: The coronavirus disease (COVID-19) started in 2019 and became a pandemic by infecting many people all over the world. It is known that COVID-19 affects the heart as well as the respiratory system, and the changes it causes on the electrical activity of the heart are among the common research topics of recent studies. The electrical activity of the heart is measured by Electrocardiography (ECG). While some ECG devices give the ECG signal directly as numeric vector format, others draw the signal on paper or give results as an image. ECG images drawn on paper are usually only visually examined by the doctor, and detailed analysis is mostly attempted with low-accuracy machine learning methods. In this study, a new approach that converts ECG images drawn on paper into signals is proposed. The proposed approach was used to convert the ECG images recorded from COVID-19 and healthy people in an open source ECG image database into signals, and the obtained ECG signals were analysed in detail with signal processing methods and compared statistically between COVID-19 and healthy group and with similar studies in the literature. Results showed that, ECG characteristics were significantly changed with the COVID-19.

Keywords: COVID-19; Electrocardiography (ECG); Feature Extraction; image-to-signal conversion

1 INTRODUCTION

Coronavirus Disease 2019, commonly known as COVID-19, is a disease that emerged in China at the end of December 2019, and spread all over the world [1]. COVID-19 is caused by Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) virus and The World Health Organization (WHO) had to declare a pandemic in 2020 due to the spread of the virus. Two years have passed since the emergence of the virus, and the total number of cases and deaths in worldwide have reached over 450 million and 6 million, respectively [2]. The clinical indications of the coronavirus are mostly manifested by respiratory system symptoms (cough, fever, shortness of breath, fatigue, etc.). With sudden changes in the respiratory system, pneumonia and acute respiratory diseases are observed in individuals. It is known that many patients have also persistent symptoms after COVID-19 [3]. According to studies, it has been observed that individuals with cardiovascular diseases face COVID-19-related problems more frequently and have higher mortality rates compared to the others [4].

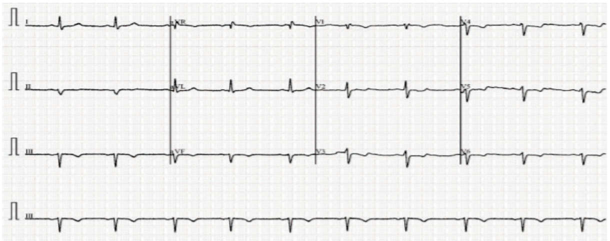
In general, the damages caused by SARS-CoV-2 infection in the respiratory tract, heart and lungs are observed with computed tomography (CT) and x-ray scans. Recent reports show that COVID-19 triggers diseases such as myocarditis and hypertension in the heart [5]. Recently, researchers focused on electrocardiographic (ECG) observations of individuals, since it is a more cost effective approach compared to CT and X-ray scans to obtain information from heart. In addition to that, it is possible to have more information of heart physiology using ECG. Therefore, studies using ECG have increased to observe the effects of COVID 19 on heart [6-7].

In a recent study with a shared COVID-19 ECG database, researchers observed the effects of COVID-19 on ECG [8]. This dataset contains 1937 ECG recordings obtained from distinct patients using 'EDAN SERIES-3' ECG device from different health care facilities across Pakistan. The team of senior medical professionals with experience of ECG interpretation reviewed the data using Telehealth ECG diagnostic system. The researchers distinguished the healthy and COVID-19 ECG images after the manual interpretation and 859 of the images belong to healthy people while 250 of the images belong to COVID-19 patients. Using the same database, different studies used convolutional neural network (CNN) models to classify ECG images [9-14]. Each of these studies exhibited a deep learning-based approach through imagery. However, since not having a signal dataset, it is impossible to make a precise ECG signal analysis over this important database. In this study, ECG paper images of this COVID-19 ECG database were converted into digital vector arrays using image-processing techniques. During this process, low quality or corrupted images were also eliminated and finally, a high quality Lead-II ECG signal dataset consisting of 118 COVID-19 patient and 156 healthy individual ECGs were obtained. Furthermore, converted signal dataset was analysed using signal processing techniques and their features were extracted. Results were statistically analysed and distinguishing features in ECGs between COVID-19 patients and healthy individuals were revealed. The results were compared with the studies using the images of the same dataset.

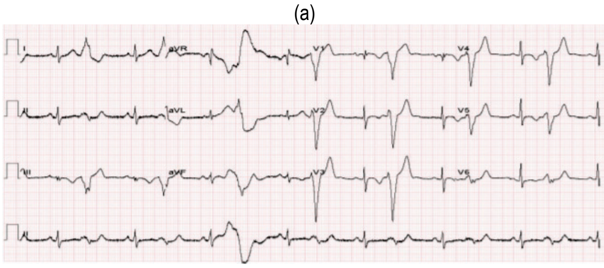
2 MATERIALS AND METHOD

2.1 Database

In this study, the COVID-19 ECG database consisting of COVID-19 patients' and healthy individuals' ECGs shared by Khan et al [5] were used. ECG recordings of that dataset were obtained using a 12-channel ECG device with a sampling frequency of 500 Hz and recorded on thermal paper using the built-in thermal array recorder. Shared 859 healthy individual ECGs were directly saved as jpeg image by the device while 250 COVID-19 patient ECGs were saved by scanning the paper output. Sample recordings of a COVID-19 patient and a healthy individual are given in Fig. 1.



(a)



(b)

Figure 1 a) Healthy ECG, b) COVID-19 ECG

2.2 Preprocessing

Since healthy and COVID-19 ECG images exhibit different image formations, different methodology were applied for each of them. Firstly, healthy individual ECG images were processed. These images were directly recorded by the device and all of them were in the same formation as given in Fig. 1a. In each image, the signal at fourth raw corresponds to Lead-II ECG data and a square wave at the beginning of this signals shows the zero line of the signal together with its amplitude and time information. Quick visual inspection showed us that the Lead-II data varies between ±3 mV and all of them have at least 9 seconds duration. Thanks to all Lead-II data were at the same location of the recorded images, an image mask was constructed by calculating the corresponding corner pixels to be extracted and applied to all healthy group dataset.

Similar procedure was applied for the extraction of Lead-II ECG images of COVID-19 patients. But, since the recorded images were obtained via scanning or photographing the ECG papers, Lead-II data in each of them have different locations as well as different aspect ratios. Therefore, each of the data were manually investigated and zero line of the signal was determined using the square wave indicator at the beginning of each Lead-II image. After detecting the corresponding corner pixels for ±3 mV range and 0-9s duration for each image, Lead-II images were extracted from the recordings and saved for further processing. Sample extracted images for a random ECG Lead-II data are given in Fig. 2.

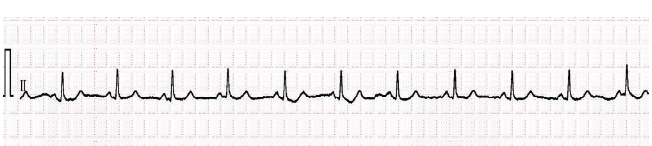


Figure 2 Extracted Lead II ECG

After extracting all Lead II derivation images from recordings, they were converted to vectoral signal format using image and signal processing techniques. Firstly, a binary mask was applied to image using a threshold to get rid of background paper and leave only ECG pattern on the image. Then, the amplitude and time value of each pixel on the extracted images was calculated and they converted into the ECG signal values.

The generalized formulation for the vectoral conversion used are as follows:

$$d = (a - b) / h / sqr/\mathrm{mV} \tag{1}$$

Here, d corresponds to the potential value of the converted ECG signal, while a is the pixel number of the extracted ECG pattern in vertical axis (amplitude of ECG – y axis), b is the pixel number corresponds to the baseline of square indicator in vertical axis, h is the total number of pixels of the extracted image in vertical axis, sqr is the number of squares the extracted image has along vertical axis, and mV is the millivolts value of each square in ECG paper, as seen in Fig. 3.

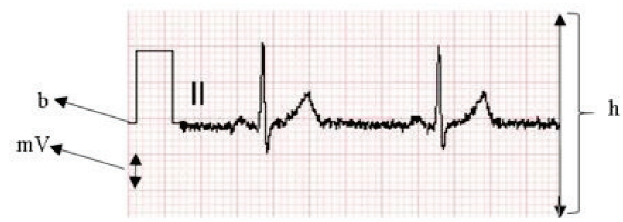


Figure 3 Demonstration of ECG graph conversion parameters

After obtaining all ECG Lead-II data as numeric signals, the analysis phase was started. The first part of the analysis was to filter the signals to remove unwanted noises that embarrass them during analysis. Wavelet transform-based filtering using Debuchies 6 wavelet was utilized as proposed in [15].

After filtering the signals, characteristic points of the signal, the onset, peak and offset points of P, QRS complex and T waves, were determined numerically using wavelet transform based algorithms proposed in [15] and [16].

Furthermore, the scalogram of each signal was calculated as explained in [15] and [16] and energy values of each wave was obtained for both groups.

By using the obtained characteristic points and scalogram data, following parameters given in Tab. 1 were calculated from each ECG signal and stored for statistical analysis.

As a descriptive statistical result, mean and standard deviations of the calculated parameters were obtained using a statistical package program. The normality of variables and the homogeneity of variances were evaluated with the Kolmogorov-Smirnov test. In data analysis, independent 2 group t-test (Student's t-test) was used for the comparison of two groups, while the relationship between two continuous variables was evaluated with the Pearson Correlation Coefficient. The significance level of the tests was accepted to be $p < 0.05$.

Table 1 Description of obtained ECG parameters [17]

ECG Parameter	Information
RR interval	The duration between two consecutive R peak points, in milliseconds
ST interval	The duration between end of T wave and end of the previous QRS complex, in milliseconds
ST segment	The duration between onset of T wave and end of the previous QRS complex, in milliseconds
QT interval	The duration between end of T wave and onset of the previous QRS complex, in milliseconds
PR (or PQ) interval	The duration between onset of QRS complex and onset of previous P wave, in milliseconds
QRS complex interval	The duration from beginning to end of an QRS complex, in milliseconds
QRS complex amplitude	Amplitude difference between R peak and S deflection downwards point of a QRS complex, in millivolts
T wave amplitude	Amplitude difference between peak and offset points of a T wave, in millivolts
P wave amplitude	Amplitude difference between peak and offset points of a P wave, in millivolts
QTc	$QTc = QT\_interval/(RR\_Interval)^{\frac{1}{3}}$
ECG Scalogram	Energy content of the signal obtained from Scalogram analysis [20]

3 RESULTS

Fig. 4 shows a sample signal converted from extracted image using Eq. (1) as described in section 2.2.

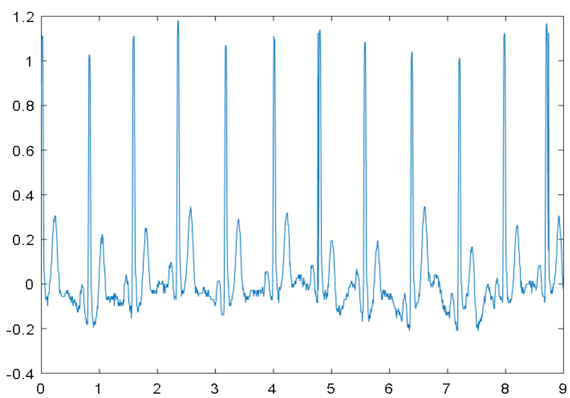


Figure 4 A sample of converted Lead II derivation vectoral signal from image (amplitude (voltage) vs time (seconds)).

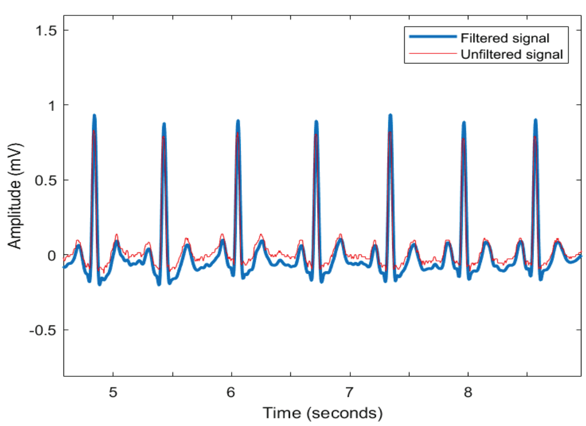


Figure 5 Unfiltered and Filtered signal

Extracted ECG signal was filtered using a 30 Hz low pass filter and the signal was removed from recording and conversion noises. Unfiltered and filtered signals are given in Fig. 5 and signal became ready for further analysis.

Detection of ECG characteristic points was performed using the technique proposed in [15] to calculate analysis parameters. Fig. 6 shows detected characteristic points on a digitized and filtered Lead-II signal.

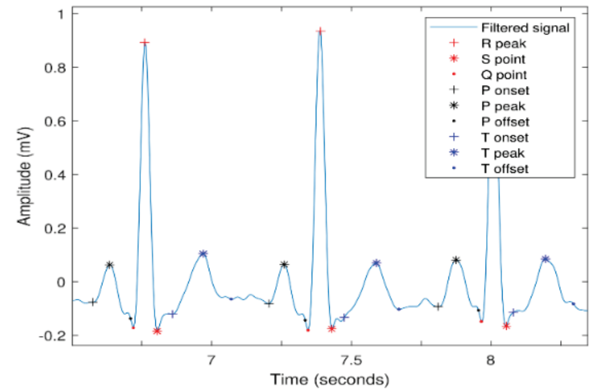


Figure 6 Detection of characteristic points

After detecting the characteristic points of ECG, all analysis parameters together with PED values were obtained from all ECGs and stored.

Calculated analysis parameters were first statistically analyzed for significant differences. In the statistical analysis, the repolarization and depolarization phase components in a cardiac cycle between healthy and COVID-19 groups were compared. Statistical analysis results for the parameters described in Table 1 are given in Table 2. Only, the parameters with the significant results were included to the table due to space considerations.

Table 2 Calculated parameters and statistical results ($p<0.05$)

Parameters	Groups	Mean ± Std
QRS Interval	Healthy	,08244489 ± ,008749325
	COVID-19	,07640352 ± ,009865149
RR Interval	Healthy	,77713988 ± ,123476589
	COVID-19	,73862431 ± ,136015762
ST Interval	Healthy	,25398596 ± ,020334934
	COVID-19	,26051331 ± ,021274567
QRS Amplitude	Healthy	,67467538 ± ,221686010
	COVID-19	,95626246 ± ,329996678
T Amplitude	Healthy	,13402635 ± ,058020148
	COVID-19	,17376008 ± ,065838637
ST Segment	Healthy	,08552178 ± ,026174769
	COVID-19	,09562169 ± ,026431562
P Amplitude	Healthy	,05607699 ± ,021190891
	COVID-19	,07527458 ± ,032294691
PR Interval	Healthy	,14473479 ± ,014319553
	COVID-19	,13424571 ± ,013382206
QTC	Healthy	,70238590 ± ,042035582
	COVID-19	,72015280 ± ,051170380
ECG Scalogram	Healthy	,00369673 ± ,000235811
	COVID-19	,00379381 ± ,000281916

According to the statistical analysis results, COVID-19 patients had significantly lower QRS and PR intervals; higher P and T amplitudes; ST segment; compared to healthy group.

A significant difference on RR interval was also observed between two groups. The QTc interval, which carries information about QT syndrome, is higher compared to healthy group and indicates long QT syndrome in COVID group. Evaluation of these results are given in the discussion section in a detailed manner.

3.1 Comparison with Related Studies and Major Contributions of this Study

In Tab. 3, a comparison of different methods is given.

Tab. 3 summarizes the experimental results of relevant studies using the same ECG dataset and showing the comparisons in between those. In these studies, it's clear that all authors applied CNN architectures using 12-lead ECG paper images for comparison of the normal and COVID-19 while some of them were added the other ECG papers containing MI and other diseases.

In this study, we extracted only lead-II ECG images from the paper and converted these extracted images into 1-D signals. Our purpose was to investigate ECG signal differences between COVID-19 and healthy in statistical manner. Purpose of vectoral conversion was to prevent the low quality of the paper images. In addition to that, another problem of the image dataset was very clear. Healthy ECG images were clearly distinguished from COVID-19 ECGs since COVID-19 ECGs are basically have a lot of abnormalities in paper. Our main contribution was to present abnormalities in ECG characteristics and what could be the underlying reasons of these abnormalities related to COVID-19. We published the results based on which part of the heart was most effected with COVID-19. Therefore, in our study we focused on lead-II ECGs which are the most common derivation for ECG interpretation. In discussion section, we interpreted all the differences and underlying reasons behind these differences using the relevant literature.

Table 3 A comparison between image based studies

Study	Method	Accuracy %	Sensitivity %	Precision %	Specificity %
[11]	Densenet201	99.1±0.44	99.1±0.44	99.11±0.43	96.9±0.8
[35]	CNN with RC model	99.0±1.05	99.6±1.26	-	98.4±2.06
[13]	CNN	98.57±1.14	99.23±0.59	97.73±1.91	98.0±1.29
[36]	CNN	98.81	98.81	98.81	-
[12]	Efficient Net B3	81.80	-	80.8	-
[37]	Efficient-ECGNet	98.66	-	98.74	-
[38]	SEResNet18	97.72	97.35	-	98.14
[10]	MobileNet v2	98.33	-	-	-
[14]	CNN	98.11	98.60	-	96.40
[9]	Hexaxial feature mapping with CNN	96.20	-	94.33	94.00
[39]	ECG-BiCoNet	98.80	98.80	98.80	98.80

4 DISCUSSION

In this study, all the ECG graphs are converted into vector format with its exact time and amplitude values via proposed image to vector standardization methodology. Unlike machine learning studies using this dataset, characteristics of ECGs are revealed numerically from the data, not from the pattern. Therefore, evaluation metrics are composed of numerical values obtained from quantitative analysis of healthy and COVID-19 ECGs.

When the electrocardiographic findings presented in the study are examined, it is observed that the QTc is significantly longer on COVID-19 patients ($p < 0.05$). Fig. 7a and Fig. 7b shows the significant differences on QT interval parameters as a box plot containing outliers.

In clinical trials, physicians use QT interval assessments as a syndrome marker based on prolongation of the interval [22, 23]. During the current pandemic, the presence of hospitalized patients with prolonged QTc has been reported [24]. Prolonged Qt syndrome, characterized by arrhythmias, has a high tendency to heart attack. In addition, long QTc may indicate a risk factor for long QT syndrome, which is characterized by severe arrhythmias and carries a greater risk of comorbidities [26, 27]. Therefore, prolonged QTc in COVID-19 patients of this study can be interpreted as a risk factor for heart problems in their future lives.

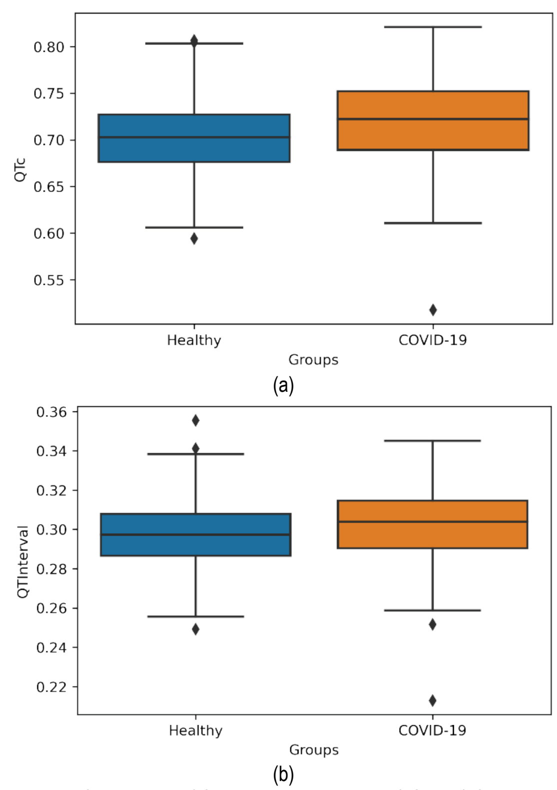


Figure 7 Comparison of QT Interval parameters: a) QTc, b) QT interval

As it can be seen from Tab. 2, COVID-19 patients had significantly lower RR intervals, which indicate higher heart rate compared to healthy individuals ($p < 0.05$).

Statistical analysis also showed that COVID-19 patients had significantly longer ST segment compared to healthy group. Fig. 8 shows the ST segment differences as a box plot.

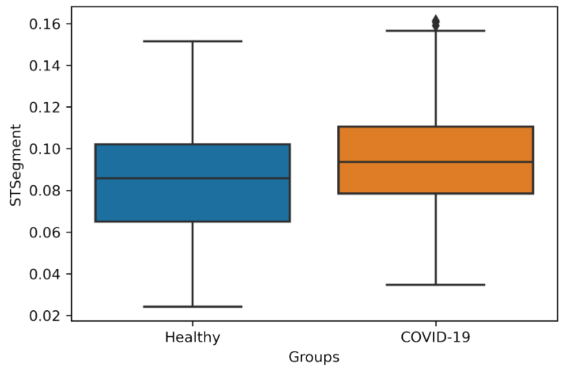
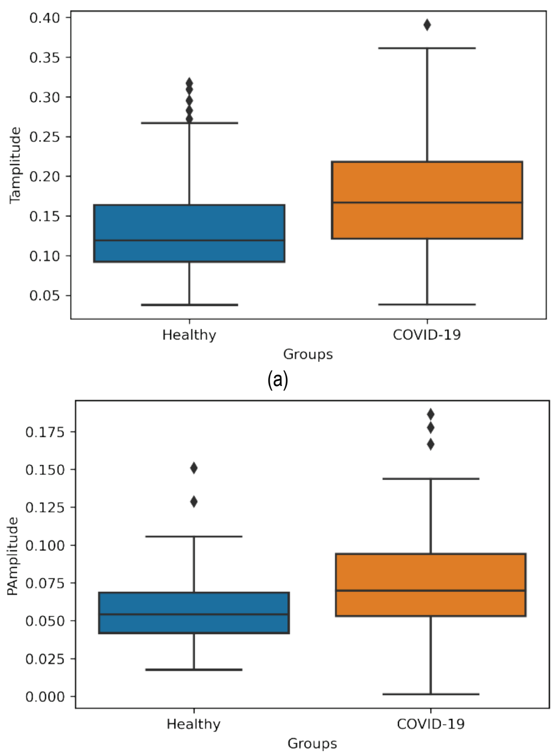


Figure 8 ST Segment differences



(a)

(b)

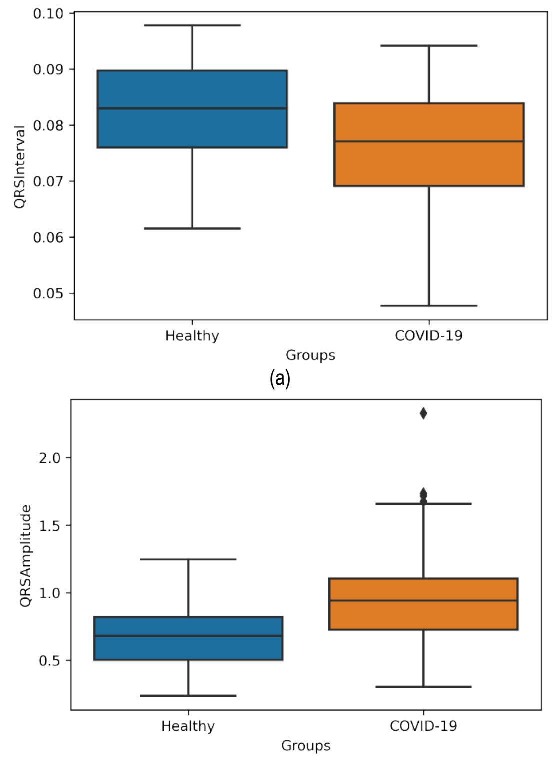
Figure 9 Comparison of P and T wave amplitudes between groups: a) P wave. b) T wave

Multiple studies in the literature support the findings of this study. In a study, examining the ECG recordings of COVID-19 positive paediatric patients, ST segment elevation have been reported [28]. In another multicentre cohort study in which the ECG data obtained from COVID-19 patients during their hospitalization, prolongation of ST segment was observed in COVID-19 patients [29]. In a retrospective study carried out to investigate ST segment depletion-induced Myocardial infarction (MI). MI caused by ST-segment elevation has been one of the most common conditions during the pandemic [30], and therefore increased ST segment can be an indicator for COVID-19 diagnosis using ECG analysis.

According to the findings, there are also notable differences on P and T waves between two groups. Fig. 9 shows the P wave and T wave amplitude differences between groups.

Similar to our results, ECG of most patients with MI showed nonspecific features; including T-wave abnormalities has also been presented in literature. T wave abnormalities are often a precursor of ST elevation MI (STEMI). T wave amplitude alteration in COVID-19 positive ECG analyses during clinical evaluations were observed in a study [31]. Thus, T-waves and P-waves alterations may indicate electrical stimulation and conduction problems in case of COVID-19.

Another remarkable parameter among the ECG parameters, the PR interval, had also significances between two groups. As it can be seen from table 2, healthy group had longer PR interval compared to COVID-19 patients ($p < 0.05$). Similar to our results, it was shown that PR interval was shortened in COVID-19 patients. In addition, PR interval considered for atrial fibrillation has also been shown by some researchers to be different in COVID-19 patients [32, 33].



(a)

(b)

Figure 10 Comparison of QRS Complex Parameters: a) QRS Complex Interval, b) QRS Complex Amplitude

Other remarkable findings were observed on QRS interval and QRS complex amplitude. As seen in Tab. 2, the QRS interval, which represents the time between the onset of the QRS complex and the onset of the previous P wave, was significantly decreased in COVID-19 patients in addition to the decrease in PR interval ($p < 0.05$). Furthermore, the QRS complex amplitude was significantly greater in COVID-19 patients compared to healthy group. Fig. 10 shows the significance levels of QRS parameters between two groups.

In a hospital-based descriptive study, electrocardiographic changes in COVID-19 patients were presented and similar to our results, short QRS complex was seen in COVID-19 patients [34].

5 CONCLUSION

In the present study, ECG image recordings from 859 healthy individuals and 250 COVID-19 patients included in the open source dataset were analyzed with a comprehensive analysis, and different features of ECG were revealed by the further signal analysis. Our results showed that there are statistically significant effects on most of the ECG parameters in COVID-19 positive individuals compared to the healthy group. The remarkable point of the signal analysis was that achieving further analysis in a shorter time with a less noisy data compared to the original image dataset. Since the image data set contains twelve ECG leads per image, and recording of ECGs were applied with different papers and devices, a normalization was proposed to increase reliability. First, vectoral conversion to ECG images was applied using binarization and threshold, and each image was normalized using the pixel value of square indicator on the ECG paper. Therefore, only Lead-II images were extracted as a signal vector from the whole dataset. Then, the ECG signals were filtered and valuable characteristics were extracted from the noiseless signals. Finally, significant differences between groups were revealed using statistical analysis.

The proposed work presents a novel approach to analyze ECG image dataset obtained from COVID-19 and healthy individuals. Previous studies using this dataset focused on machine learning approaches to classify ECG papers as COVID-19 or healthy, using the properties of ECG image patterns. With the help of the approach proposed in this study, ECG signals instead of ECG images were evaluated to distinguish differences on characteristics of two groups. Even though it is important to distinguish COVID-19 ECGs from healthy ECGs, it is more important to determine ECG characteristics to understand the effects of COVID-19 on heart. The proposed methodology contributes on both classification and examination of ECGs. Our results are also supported by most of the studies in the literature investigating the effects of COVID-19 on ECG. It is thought that, our study can support the ECG image analysis since we have the properties of ECG paper. In future works, our algorithm can be adapted as a standardization method for the ECG image studies to extract characteristics of ECGs which is very helpful for physicians to interpret ECGs.

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