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The impact of COVID-19 on cardiovascular disorders in patients who admitted to cardiology outpatient unit

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Abstract

The coronavirus outbreak is an important challenge and has affected the world since December 2019. Little is known, however, regarding the impact of the coronavirus disease 2019 (COVID-19) pandemic on cardiovascular disorders in the cardiology outpatient unit. This trial aimed to examine the nature of patients who were admitted the cardiology outpatient unit before and after the COVID-19 pandemic. Totally, 6254 patients who were admitted to the cardiology outpatient unit from January 1, 2020 to December 31, 2020 and January 1, 2022 to December 31, 2022 were included. The patients who admitted from January 1, 2020 to December 31, 2020 were defined as pre-pandemic group. The patients who were admitted from January 1, 2022 to December 31, 2022 were defined as post-pandemic group. There were 2575 (mean age 57.9±16.9 years, male 47%) patients in pre-pandemic group, while 3679 (mean age 59.1±17.0 years, male 47%) patients in post-pandemic group. The patients in post-pandemic group were significantly older than those in pre-pandemic group (60.0 (46.0-71.0) vs. 62.0 (47.0-73.0) years, p = 0.005). The number of patients who were admitted for hypertension (HT) significantly higher in post-pandemic group compared to pre-pandemic group (930 (36%) vs. 1646 (45%), p<0.001). The new-onset HT was significantly higher in post-pandemic group than in pre-pandemic group (407 (11%) vs. 186 (7%), p<0.001). Admission for atrial fibrillation (AF) was significantly increased after coronavirus pandemic when compared to before (324 (13%) vs. 670 (18%), p<0.001). New-onset AF was also significantly higher in post-pandemic group than in pre-pandemic group (35 (1%) vs. 95 (3%), p=0.001). Not all cardiovascular disorders but admission for HT and AF were significantly increased in the post-pandemic period. With the end of pandemic, physicians should be more careful in the risk prediction of patients who potentially have HT and AF in cardiology outpatient unit.

Keywords: Cardiovascular disorders, COVID-19, atrial fibrillation, hypertension

Introduction

The coronavirus outbreak is an important challenge and has affected the world since December 2019. The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is responsible for the coronavirus disease 2019 (COVID-19) [1]. Almost 7 million patients died due to COVID-19 so far [2]. The number of new cases decreased with the discovery of the vaccine. The most common complaints are cough, fever, malaise, and myalgia in COVID-19 [3]. Additionaly, studies have shown that thrombus formation and thrombotic events can be a serious complication of COVID-19 [4,5].

There are few studies showing the impact of COVID-19 on cardiovascular disorders. Recently published data showed that COVID-19 causes hypertension (HT) in the short term period after infection [6]. Myocardial injury and acute coronary syndrome due to COVID-19 infection is also reported in case series [7-9]. Little is known, however, the impact of COVID-19 pandemic on cardiovascular disorders in cardiology outpatient unit. The aim of the present trial was to examine the nature of patients who admitted the cardiology outpatient unit before and after the COVID-19 pandemic.

Material and Methods

The present retrospective study was consisted of 6254 consecutive patients who admitted to cardiology outpatient unit from January 1, 2020 to December 31, 2020 and January 1, 2022 to December 31, 2022. The patients who admitted from January 1, 2020 to

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December 31, 2020 were defined as pre-pandemic group. The patients who admitted from January 1, 2022 to December 31, 2022 were defined as post-pandemic group. Patients those under 18 years old were excluded. The patient characteristics, physical examination findings, signs, symptoms, laboratory results and achieved diagnosis were recorded to medical software and National data registry (e-Nabız®). For the classification of the diagnosis of the patients who admitted to cardiology outpatient unit, international classification of diseases 10 (ICD-10) coding system was used. The ICD-10 codes examined are as follows; I48 Atrial fibrillation (AF) and flutter, R00.2 Palpitation, R07.4 Chest pain, I10 Primary essential HT, I50 Heart failure, I24 Acute ischemic heart disease, I25 Chronic ischemic heart disease, Valvular heart disease (I34, I08.9, I35, I39, I05, I07, Q25).

A previous history of acute coronary syndrome, angina pectoris, coronary intervention, and/or coronary artery bypass graft was defined as coronary artery disease. New coronary artery disease was defined as follows: detection new coronary lesion (narrowing more that 50%) in coronary angiography that performed due to typical chest pain, and/or a positive troponin-I level, and/or evidence of ischemic 12-lead electrocardiogram in the post-pandemic period. As defined in the Eighth Joint National Committee (JNC 8) and European Society of Cardiology guidelines, a measurement of systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg in cardiology outpatient unit was defined as HT. A measurement of systolic ≥135 mmHg and/or diastolic ≥85 mmHg blood pressure at home or in ambulatory blood pressure monitoring was defined as HT, as well [10,11].

AF and flutter were diagnosed according to electrocardiogram and/or at least 30 seconds documented atrial fibrillation or flutter in the 24-hour ambulatory holter monitoring. Heart failure was defined as clinical syndrome that consisted of cardinal signs and symptoms in the light of the 2016 European Society of Cardiology Guidelines [12]. Worsening of already existing heart failure and/or hospitalization for heart failure were also defined as new heart failure. Valvular heart disease was defined as clinically significant (moderate or severe) valvular stenosis or regurgitation detected on transthoracic echocardiography. The Kütahya Health Sciences University, Non-invasive Clinical Research Ethics Committee was approved the present study (Protocol no: E-41997688-050.99-8877).

Kolmogorov–Smirnov test was performed to evaluate the distribution of continuous variables. The variables were expressed as median (interquartile range) or mean±standard deviation. Mann-Whitney U test was performed to compare the not-normally distributed continuous variables between groups. Categorical variables were compared with Chi-square test. A p value <0.05 was considered as significant. The SPSS statistical package for Windows version 15.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses.

Results

Totally 6254 (mean age 58.6±17.0, years) patients who admitted to cardiology outpatient unit in pre-pandemic and post pandemic period were included in to the study. The 2929 patients (47%) were male. Age, sex and admission diagnoses were shown in Table 1. Study population divided into two groups according to pre-pandemic and post-pandemic admission. There were 2575 (mean age 57.9±16.9 years, male 47%) patients in pre-pandemic group, while 3679 (mean age 59.1±17.0 years, male 47%) patients in post-pandemic group. The post-pandemic group was significantly older than pre-pandemic group (60.0 (46.0-71.0) vs. 62.0 (47.0-73.0) years, p=0.005). Gender distribution was not significantly differ between the two groups (1209 (47%) vs. 1734 (47%) male, p=0.888). A total of 743 patients had a history of COVID-19 illness (20%). The number of patient who received at least one vaccine dose was 3354 (91%). With respect to diagnosis of patients, the number of patients who admitted for HT significantly higher in post-pandemic group compared to pre-pandemic group (930 (36%) vs. 1646 (45%), p<0.001). New-onset HT was also significantly higher in post-pandemic group than in pre-pandemic group (407 (11%) vs. 186 (7%), p<0.001) (Figure 1). The diagnosis of coronary artery disease was not differ between groups (838 (23%) vs. 604 (24%), p=0.531). New coronary artery disease cases were also not differ between groups (66 (3%) vs. 97 (3%)). Admission for AF was significantly increased after coronavirus pandemic when compared to before (324 (13%) vs. 670 (18%), p<0.001). New-onset AF was also significantly higher in post-pandemic group than in pre-pandemic group (35 (1%) vs. 95 (3%), p=0.001). There were no difference regarding admission for chest pain (754 (29%) vs. 998 (27%)) and palpitation (359 (14%) vs. 568 (16%)) between in pre-pandemic and post-pandemic period (p=0.062 and p=0.101, respectively). The number of patients who admitted with heart failure (195 (8%) vs. 312 (9%) and valvular heart disease (97 (4%) vs. 150 (4%)) were not significantly differ between groups (p=0.196 and p=0.535, respectively).

Age and sex distributions according to diagnosis of patients who admitted to cardiology outpatient unit were shown in Table 2. In patients who admitted with HT, age (65.0 (55.0-74.0) vs. 66.0 (53.0-75.0), years, p=0.108) and sex distribution (374 (40%) vs. 652 (40%) male, p=0.764) were not different in post-pandemic period when compared to pre-pandemic period. Patients who admitted with the diagnosis of AF were also not differ regarding age (74.0 (68.0-80.0) vs. 74.0 (68.0-79.0) years, p=0.544) and sex distribution (114 (35%) vs. 224 (33%) male, p=0.585) between groups. When patients who diagnosed as coronary artery disease were examined, the age (69.0 (61.0-76.0) vs. 68.0 (58.0-75.0) years) and sex distribution (336 (56%) vs. (501 (60%) male) were not differ between groups (p=0.196, p=0.115, respectively). With respect to patients who admitted for heart failure, the age (71.0 (65.0-78.0) vs. 72.0 (66.0-79.0) years) and sex distribution (120 (62%) vs. 171 (55%) male) also were not differ between groups (p=0.146 and p=0.136, respectively).

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Table 1. Baseline characteristics and distribution of cardiovascular disorders between groups

Variable	Pre-pandemic n=2575	Post-pandemic n=3679	p value
Age (year)	60.0 (46.0-71.0)	62.0 (47.0-73.0)	0.005
Men (n)	1209 (47%)	1734 (47%)	0.888
History of COVID-19 (n)	-	743 (20%)	-
Vaccination (n)	-	3354 (91%)	-
Diagnoses			
Hypertension (n)	930 (36%)	1646 (45%)	<0.001
Coronary artery disease (n)	604 (24%)	838 (23%)	0.531
Atrial fibrillation (n)	324 (13%)	670 (18%)	<0.001
Chest pain (n)	754 (29%)	998 (27%)	0.062
Palpitation (n)	359 (14%)	568 (16%)	0.101
Heart failure (n)	195 (8%)	312 (9%)	0.196
Valvular heart disease (n)	97 (4%)	150 (4%)	0.535

Data are expressed as median (Interquartile range) for continuous variables and count (percentage) for categorical variables. COVID-19; Coronavirus disease 2019

Table 2. Age and sex distribution of cardiovascular disorders

Variable	Pre-pandemic n=2595	Post-pandemic n=3679	p value
Coronary artery disease	n=604	n=838	
Age (year)	69.0 (61.0-76.0)	68.0 (58.0-75.0)	0.196
Men (n)	336 (56%)	501 (60%)	0.115
Hypertension	n=930	n=1646	
Age (year)	65.0 (55.0-74.0)	66.0 (53.0-75.0)	0.108
Men (n)	374 (40%)	652 (40%)	0.764
Atrial fibrillation	n=324	n=670	
Age (year)	74.0 (68.0-80.0)	74.0 (68.0-79.0)	0.544
Men (n)	114 (35%)	224 (33%)	0.585
Heart failure	n=195	n=312	
Age (year)	71.0 (65.0-78.0)	72.0 (66.0-79.0)	0.146
Men (n)	120 (62%)	171 (55%)	0.136

Data are expressed as median (Interquartile range) for continuous variables and count (percentage) for categorical variables

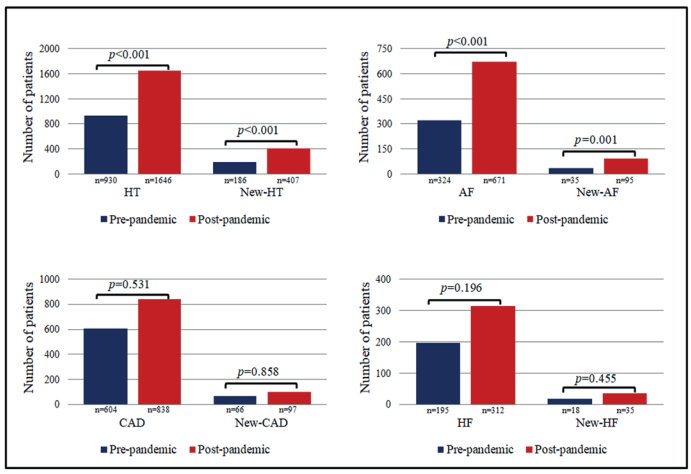

Figure 1. The newly diagnosed and already following up patients. HT: hypertension, AF: atrial fibrillation, CAD: coronary artery disease, HF: heart failure

Discussion

This study evaluated the changes in cardiology outpatient unit after the COVID-19 pandemic. There are three major findings of the present study. It has been showed that patients who admitted for HT and AF were significantly increased in post-pandemic group. In particular, new cases in both HT and atrial fibrillation were significantly higher in post-pandemic population. After the pandemic, patients who admitted to cardiology outpatient unit were older than in pre-pandemic period. With respect to admission due to coronary artery disease and the complaints of chest pain and palpitation were not different between groups.

With the initiation of pandemic, investigators gave their effort to determine the better treatment protocols, define the parameters for disease severity and reduce the morbidity and mortality rates of COVID-19 [13]. After the pandemic, studies focused on better understanding the cardiovascular manifestations of COVID-19.

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Commonly reported data demonstrated micro-vascular ischemia and non-ischemic myocardial damage, dysrhythmias, and dysautonomia both during and early after COVID-19 illness [14]. However, long-term cardiovascular sequelae in particular new-onset cardiovascular diseases are less understood. The public speculates that the COVID-19 pandemic increases heart disease. Hence, this trial was conducted to explore the impact of COVID-19 on cardiovascular disorders in the post-pandemic period.

The presence of HT is a well established risk factor of severe COVID-19 disease and linked with the increased intensive care unit admission, intubation requirement and adverse outcomes in COVID-19 patients [15,16]. In a previous study, it has been demonstrated that both systolic and diastolic blood pressure increases after one month of COVID-19 illness. Additionally, new onset of HT incidence was increased in the early-after COVID-19, as well [6]. The long term impact of COVID-19 on HT has not been elucidated yet. The present study explored that admission due to HT in cardiology outpatient unit was significantly increased after pandemic of COVID-19. In particular, newly diagnosed hypertensive patients were also significantly higher in 12 months after pandemic when compared to pre-pandemic period. The direct pathophysiologic link is unclear. One possible explanation for this issue is the imbalance of the renin angiotensin aldosterone system (RAAS) that is the cornerstone in the physiopathology of HT [17]. Angiotensin converting enzyme 2 (ACE-2) is commonly expressed in the cardiovascular system and the cellular receptor of the SARS-CoV-2 [6]. Taking into consideration that ACE-2 has a negative impact on RAAS, an imbalance of ACE-2/Angiotensin 2 ratio may be related with the increase in blood pressure. It has been showed that circulating levels of angiotensin 2 (ANG-2) were significantly higher in patients with COVID-19 [18]. Hence, the down regulation of ACE-2 and RAAS imbalance were associated and may cause to higher levels of ANG-2 and blood pressure.

COVID-19 has been shown to promote arrhythmias including sinus tachycardia, atrial fibrillation and ventricular premature complex in hospitalized COVID-19 patients [19]. According to literature, COVID-19 increases the risk for the onset of AF in hospitalized patients and presence of AF might be a risk factor of higher mortality rates in hospitalized COVID-19 patients [20,21]. However, data is limited regarding the impact of COVID-19 on late onset AF. According to present study, in post-pandemic follow-up to 1 year admission of patients with the diagnosis of AF significantly increased when compared to pre-pandemic. In addition, new onset AF rate was also increased in post-pandemic period. Possible underlying mechanism between increased AF cases and COVID-19 are as follows. Recently published data demonstrates that via the promotion of the prothrombotic state COVID-19 increases the vulnerability to dysrhythmic events during the COVID-19 illness and probably post-recovery period. However, the impact of COVID-19 on the AF does not seem to be explained solely by the increased prothrombotic state in long-term follow-up period. The other molecular factor involved in COVID-19-related new AF cases is the ACE-2 availability and its well established link with HT [22]. Atrial fibrillation and HT are commonly coexisting. A main reason for this issue, first, presence of HT is best established predisposing factor for the new onset AF [23]. Second, similar conditions and risk factors are related with the higher incidence of both AF and HT [24,25]. In a previous study 34.221 healthy women prospectively followed up to 12.4 years detect the relation of blood pressure and new onset AF. A strong association between the incidence of AF and increased blood pressure was demonstrated [26]. Taking into consideration that AF and HT share common risk factors and conditions, the higher incidence of HT may leads to higher incidence of AF in post COVID-19 period. In order to better recognize the relation of COVID-19 and AF larger studies should be designed. In the present study, the diagnosis of AF was significantly increased after COVID-19 pandemic, while complaint of palpitation was not different between groups. The palpitation is only a symptom of patients and has a subjective fashion. After the examination of palpitation with electrocardiogram or further investigation, if necessary, the exact diagnosis is determined. As such, the atrial fibrillation is a result of examination and significantly higher in post-pandemic group.

Approximately 25% of patients have chest pain as a post COVID-19 symptom. Although post-COVID-19 chest pain might be due to non cardiac issues including musculoskeletal system, anxiety or pulmonary factors or angina pectoris might be present, as well. Acute myocardial infarction has been observed in the acute phase of COVID-19 illness. In a published study, patients who have simultaneously acute coronary syndrome and COVID-19 exhibit three-fold increased mortality rate when compared patients suffering from acute coronary syndrome without COVID-19 [27]. However, data about coronary artery disease rates in post pandemic phase is limited [28]. The published trials revealed that prothrombotic state due to inflammation and endothelial dysfunction in the COVID-19 were responsible for the ischemic heart disease in the early-after phase of illness [29-31]. According to present study, admission due to coronary artery disease did not increase in the post-pandemic period of COVID-19. Possible explanation of this result is ending the pro-coagulant state and its negative effects on endothelial dysfunction with the end of disease activity. Therefore, it can be speculated that the effect of COVID-19 on coronary artery disease reduces over time.

The limitations of the present study are the retrospective fashion and being a single-center experience. However, the large number of homogenous unselected COVID-19 patients enrolled in the study should be considered as an advantage and could be mirroring the real world population. The study population consists of unselected patients who admitted to cardiology outpatient unit. Almost all of the patients who admitted in post-pandemic period were vaccinated and/or had COVID-19 disease. Therefore, it is not known whether the results of this study depend

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on conditions associated with COVID-19 or vaccine-related complications. The study results reflect the nature of cardiology outpatient unit after the pandemic. For this reason, further studies that examine the impact of both COVID-19 and various vaccines for COVID-19 on long-term cardiovascular outcomes are needed to elucidate this association.

Conclusion

In conclusion, this trial draws an attention of potential cardiovascular disorders that seen in cardiology outpatient units after one year follow-up period of COVID-19. Patients admitted to cardiology outpatient unit became older. Not all cardiovascular disorders but new-onset HT and AF were significantly increased in the post-pandemic period. However, the incidence of heart failure, valvular heart disease and in particular coronary artery disease were not changed. The massages of the present study are as follows. After the COVID-19 pandemic, older patients may have been more affected by the COVID-19 pandemic. With the end of the pandemic physicians should be more carefully in the risk prediction of patients who potentially have HT and AF in cardiology outpatient unit. Hopefully, the present study will encourage physicians to be aware of potential cardiovascular risks and can serve as a starting point for the more detailed and large scale studies including imaging modalities and molecular data in order to increase our pathophysiological understanding between cardiovascular disorders and COVID-19 in long-term follow-up period.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
This trial was approved by Kütahya Health Sciences University, Non-invasive Clinical Research Ethics Committee. (protocol number: E-41997688-050.99-8877 2022/82).

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