Original Article

The inciting factor for bradycardia in COVID-19 patients: a potential harm of steroid treatment

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Background: The coronavirus disease 2019 (COVID-19) is a condition caused by the novel severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2). Although several papers have reported the presence bradycardia in patients with COVID-19, the pathophysiology behind this remains unclear. Therefore, we investigated the presence of bradycardia in patients with COVID-19.

Methods: We conducted a retrospective cohort study in a total of 153 patients with COVID-19 and 90 patients with influenza who were hospitalized in our hospital from January 1, 2020 to December 31, 2021 and from January 1, 2014 to December 31, 2021, respectively. Data were collected from patient medical records, which included sex, age, duration of hospitalization, pneumonia complications, supplemental oxygen therapy, antiviral treatment, past history, and vital signs.

Results: After adjustment, the incidence of bradycardia and steroid use in patients with COVID-19 were significantly higher than those in patients with influenza (P=0.007 and P<0.001, respectively). We then compared the detailed characteristics of patients with COVID-19 to evaluate risk factors for bradycardia. Multivariate logistic regression analysis revealed that steroid use was significantly related to bradycardia [P=0.031; odds ratio (OR): 3.67; 95% confidence interval (CI): 1.12–11.96]. Overall, results showed a higher incidence of bradycardia in patients with COVID-19 who received steroid treatment.

Conclusions: Our results showed that steroid treatment in patients with COVID-19 may be associated with the incidence of bradycardia.

Keywords: Steroid; coronavirus disease 2019 (COVID-19); bradycardia; influenza

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Introduction

The coronavirus disease 2019 (COVID-19) is a condition caused by the novel severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) presenting as a cluster of patients with pneumonia of unknown cause (1). SARS-CoV-2 is highly contagious, which has spread globally in a short period of time, and was declared a global pandemic by the World Health Organization on March 11, 2020. Although effective vaccines and various novel treatments have been developed, the COVID-19 pandemic remains

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an ongoing global threat that has infected over 700 million individuals and caused more than 6 million deaths as of July 2023. COVID-19 is associated with a cytokine storm that can further deteriorate the clinical condition; therefore, its effective detection and suppression are of paramount importance for a positive outcome (2). Therefore, in the absence of contraindications and/or side effects, steroid use should be considered for coronavirus infection including COVID-19 (3). In addition to respiratory involvement, cardiovascular complications, such as myocardial infarction, arrythmia, and myocarditis; and other respiratory conditions, such as pulmonary embolism, have received increasing attention as they contribute to the overall morbidity and mortality of patients with COVID-19 (4-6). COVID-19-induced bradyarrhythmia was reported (7,8), in addition to it, the many nonspecific bradycardia cases in patients without cardiovascular risk factors was also observed. Several reports have suggested that medications for COVID-19, such as remdesivir (9-14) or steroids (15), may be associated with the incidence of bradycardia; whereas bradycardia may also be linked to the SARS-CoV-2 infection itself, as previously reported in cases of influenza infection (16). To further understand the pathophysiology behind bradycardia in COVID-19, we evaluated whether the incidence rate of bradycardia in patients with COVID-19 was higher than that in patients with influenza and COVID-19. Furthermore, the true risk factors of bradycardia were assessed by multivariate analysis of the retrospective cohort study. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1382/rc).

Highlight box

Key findings

- Steroid treatment in patients with the coronavirus disease 2019 (COVID-19) may be associated with the incidence of bradycardia.

What is known and what is new?

- Various factors such as remdesivir, high levels of cytokines, and direct impairment caused by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) toxicity can influence the onset of bradycardia of COVID-19.
- The previous retrospective study showed that the incidence of bradycardia was suppressed by steroid use.

What is the implication, and what should change now?

- Although steroid use may be associated with the inciting factor of developing bradycardia, we believe that steroids are one of the most preferred treatment options due to their strong anti-inflammatory effects and evidence of good outcomes, even in patients developing bradycardia.

Methods

Study design and study population

This was a retrospective cohort study of hospitalized patients in Koto Hospital (Tokyo, Japan). We included consecutive patients aged ≥15 years who were diagnosed with influenza and COVID-19 from January 1, 2014 to December 31, 2021, and from January 1, 2020 to December 31, 2021, respectively. Study participants were followed-up until discharge. Influenza was diagnosed using the rapid antigen test, and COVID-19 was diagnosed using the rapid antigen test or the polymerase chain reaction (PCR) test. All patients received available approved treatment, as well as regular clinical and laboratory monitoring.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board at Koto Hospital (Approval No. 2022-6-1, approved on 13 June 2022), and approval for an opt-out consent method was given.

Outcome measures

Data were collected from patient medical records, which included sex, age, duration of hospitalization, pneumonia complications, supplemental oxygen therapy, antiviral treatment, past history, and vital signs. There was no missing data in the medical records. From there, the number of patients with in-hospital bradycardia was evaluated, in which bradycardia was defined as a heart rate ≤50 bpm. The presence of pneumonia complications, supplemental oxygen therapy, and antiviral treatment was evaluated on the first hospital day.

Statistical analysis

Continuous variables were compared using the Student's *t*-test, whereas categorical variables were compared using the chi-square test or Fisher's exact test. Logistic regression analyses were performed to measure outcomes between the bradycardia and non-bradycardia groups. All statistical tests were two-tailed, and a $P<0.05$ was considered statistically significant.

To avoid confounding differences due to baseline variables between the influenza and COVID-19 groups, we performed propensity score matching for the baseline characteristics. A multivariate logistic regression analysis was then performed to estimate the propensity scores with the following five variables: sex, age, duration of hospitalization, pneumonia complications, and supplemental oxygen therapy. Subsequently, a one-to-one match between the two groups was performed using the nearest available matching with a caliper of 0.2 × SD, wherein SD is the SD of logit values of all patients in both groups. All statistical analyses were performed using the JMP software (version 14, SAS Institute, Tokyo, Japan).

Results

A total of 153 patients with COVID-19 and 90 patients with influenza who were admitted in Koto hospital from January 1, 2014 to December 31, 2021 and from January 1, 2020 to December 31, 2021, respectively, were enrolled in this study. Medical records of study participants were checked until discharge. Patient characteristics are described in *Table 1*. The median age of patients with COVID-19 and influenza was 51 (range: 16–94) and 79.5 (range: 23–95) years, respectively. There were 96 (62.8%) males in the COVID-19 group and 42 (46.7%) males in the influenza group. The median hospitalization days in patients with COVID-19 and influenza were 10 (range: 1–66) and 9 (range: 1–45), respectively. Regarding steroid treatment, 100 patients (65.4%) in the COVID-19 group and 21 patients (23.6%) in the influenza group were treated with steroids. Of the 100 steroid-treated patients with COVID-19, 84 were treated with 6 or 6.6 mg of dexamethasone, 14 underwent steroid pulse or semi-pulse therapy, two underwent other treatments, and no patients received routine oral steroids. Meanwhile, of the 21 steroid-treated patients with influenza, 8 were routinely treated with steroids. Regarding fatality, both the COVID-19 and influenza groups had 3 fatal cases each (2.0% and 3.3%, respectively). Various characteristics of study participants were also found to be imbalanced between the COVID-19 and influenza groups. Following adjustment for confounding factors, the incidence of bradycardia and steroid use in patients with COVID-19 were found to be significantly higher than those in patients with influenza (37.8% *vs.* 10.8%, P=0.007 and 56.8% *vs.* 16.2%, P<0.001, respectively).

We also compared the detailed characteristics of patients with COVID-19 presenting with and without bradycardia to evaluate risk factors for bradycardia. The distribution of the ratio of patients by age group and the number of patients by hospitalization days are demonstrated in *Figures 1*,*2*, respectively. Comparisons of age and hospitalization days revealed no significant differences between the bradycardia and no bradycardia groups (P=0.47 and P=0.93, respectively). Two fatalities were observed in the study population, and seven patients underwent respirator or high-flow oxygen therapy (HFOT). Among the 66 bradycardia cases, 3 were caused by atrial fibrillation, whereas the others were sinus bradycardia. Moreover, univariate analysis revealed significant differences in various parameters, including pneumonia comorbidity, remdesivir use, steroid use, and baricitinib use (*Table 2*). Multivariate logistic regression analysis of the incidence of bradycardia was performed, and analysis revealed that only steroid use was significantly related [P=0.031, odds ratio (OR): 3.67, 95% confidence interval (CI): 1.12–11.96]. Additionally, multivariate logistic regression analysis of steroid use was also performed, the incidence of bradycardia and remdesivir treatment were significantly related (P=0.02, OR: 4.69, 95% CI: 1.31–16.79; P<0.001, OR: 43.21, 95% CI: 8.36–223.30, respectively) (*Table 3*). Subsequently, the association between bradycardia and steroid use in patients with COVID-19 not using remdesivir was evaluated as the remdesivir therapy may be a risk factor for bradycardia. Furthermore, patients utilizing steroids demonstrated a significantly high incidence of bradycardia (P=0.01, OR: 4.09, 95% CI: 1.28–13.09) (Table S1). Based on this result, we hypothesized that a relatively high-dose steroid might induce bradycardia. Additionally, we evaluated the association between bradycardia and physical examination data in patients with COVID-19 who were treated with 6 or 6.6 mg of dexamethasone. However, significant differences were not observed for each physical examination data (*Table 4*).

Discussion

This study distinctly demonstrated a higher incidence of bradycardia in patients with COVID-19 than the incidence in patients with influenza. Furthermore, the analysis revealed a correlation between steroid treatment and the occurrence of bradycardia. However, remdesivir treatment was not analyzed in our study population.

Steroid-induced bradycardia is a rare but known side effect, probably due to the suppression of cytokine

Table 1 The characteristics of hospitalized patients with COVID-19 and influenza

Variables	Before matched			Propensity score-matched		
	COVID-19 (n=153[†])	Influenza (n=90[‡])	P	COVID-19 (n=37)	Influenza (n=37)	P
Bradycardia	66 (43.1)	7 (7.8)	<0.0001	14 (37.8)	4 (10.8)	0.007
Age (years)*	51 [16–94]	79.5 [23–95]	<0.0001	70 [24–94]	67 [23–94]	0.91
Hospitalization days*	10 [1–66]	9 [1–45]	0.02	9 [2–47]	8 [1–45]	0.85
Sex, male*	96 (62.8)	42 (46.7)	0.02	23 (62.2)	23 (62.2)	>0.99
Pneumonia*	118 (77.1)	44 (48.9)	<0.0001	27 (73.0)	24 (68.3)	0.45
Oxygen supplement*	45 (29.4)	42 (46.7)	0.007	20 (54.1)	17 (45.9)	0.49
Comorbidity						
AF	8 (5.2)	6 (6.7)	0.64	2 (5.4)	4 (10.8)	0.67
CD other than AF	6 (3.9)	16 (17.8)	0.0003	2 (5.4)	5 (13.5)	0.43
Malignancy	11 (7.2)	23 (25.6)	<0.0001	7 (18.9)	8 (21.6)	0.77
CKD	8 (5.2)	9 (10.0)	0.16	3 (8.1)	1 (2.7)	0.61
COPD	2 (1.3)	8 (8.9)	0.006	1 (2.7)	2 (5.4)	>0.99
BA	17 (11.1)	10 (11.1)	>0.99	3 (8.1)	3 (8.1)	>0.99
DM	22 (14.4)	21 (23.3)	0.077	9 (24.3)	8 (21.6)	0.78
HT	50 (32.7)	38 (42.2)	0.14	18 (48.6)	10 (27.0)	0.055
Smoking history	70 (45.8)	35 (38.9)	0.30	29 (87.4)	16 (43.2)	0.48
Medications						
Remdesivir	85 (55.6)	–	–	16 (39.0)	–	–
Steroid	100[#] (65.4)	21[§] (23.6)	<0.0001	21 (56.8)	6 (16.2)	<0.001
Baricitinib	17 (11.1)	–	–	3 (7.3)	–	–
Casirivimab/imdevimab	10 (6.5)	–	–	7 (17.1)	–	–
Oseltamivir	–	10 (11.1)	–	–	3 (8.1)	–
Zanamivir	–	1 (1.1)	–	–	1 (2.7)	–
Peramivir	–	70 (77.8)	–	–	27 (73.0)	–
Laninamivir	–	11 (12.2)	–	–	7 (18.9)	–
Baloxavir	–	2 (2.2)	–	–	2 (5.4)	–

Data are presented as median [range] or n (%). *, variables using propensity score matching; [†], including 3 fatal cases; [‡], including 3 fatal cases; [#], including 84 cases of 6 mg or 6.6 mg dexamethasone, 14 cases of steroid pulse or semi-pulse therapy, and 2 cases of the other treatment; [§], including 8 cases of routine oral steroid use. COVID-19, coronavirus disease 2019; AF, atrial fibrillation; CD, cardiac disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; BA, bronchial asthma; DM, diabetes mellitus; HT, hypertension.

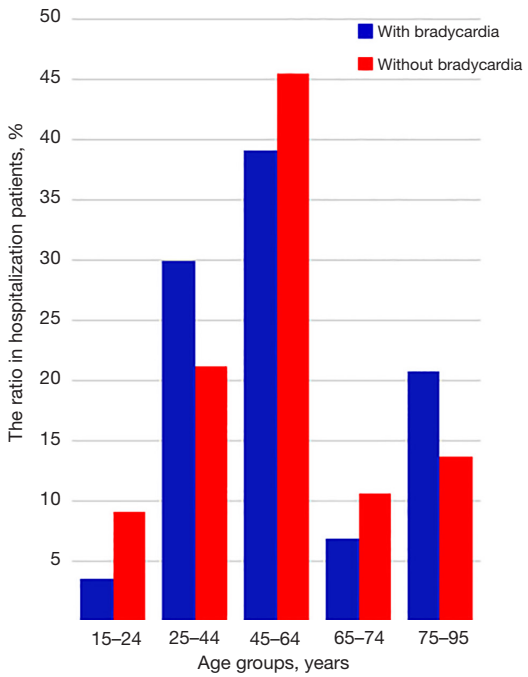

Figure 1 The ratio of bradycardia or non-bradycardia to the total patients by age groups.

production and sympathetic nervous system function (15). In the field of pediatrics, several retrospective studies have revealed the relation of steroid administration and heart rate. In one study, the pulse rates of 61 steroid-treated children (1–5 mg/kg/d of prednisone) were decreased by 31 bpm (95% CI: 23–39) after 72 hours of treatment, and 63.9% of children developed a pulse rate below the 2.5 percentile for age during the first 88 hours of treatment; however, none of the children developed symptoms of reduced cardiac output (17). Another study reported that five children with rheumatic diseases who were treated with intravenous pulse methylprednisolone and subsequent steroid treatments showed reductions in resting heart rate ranging from 35–50% as compared to baseline levels, although all cases were asymptomatic and recovered spontaneously after pulse therapy cessation (18). Given this observation in the pediatric population, steroid treatment may also induce bradycardia in the adult population. Stroeder *et al.* reviewed studies on steroid-induced bradycardia and speculated that high-dose steroid use was involved in its incidence (19). In contrast, there has been no association between the

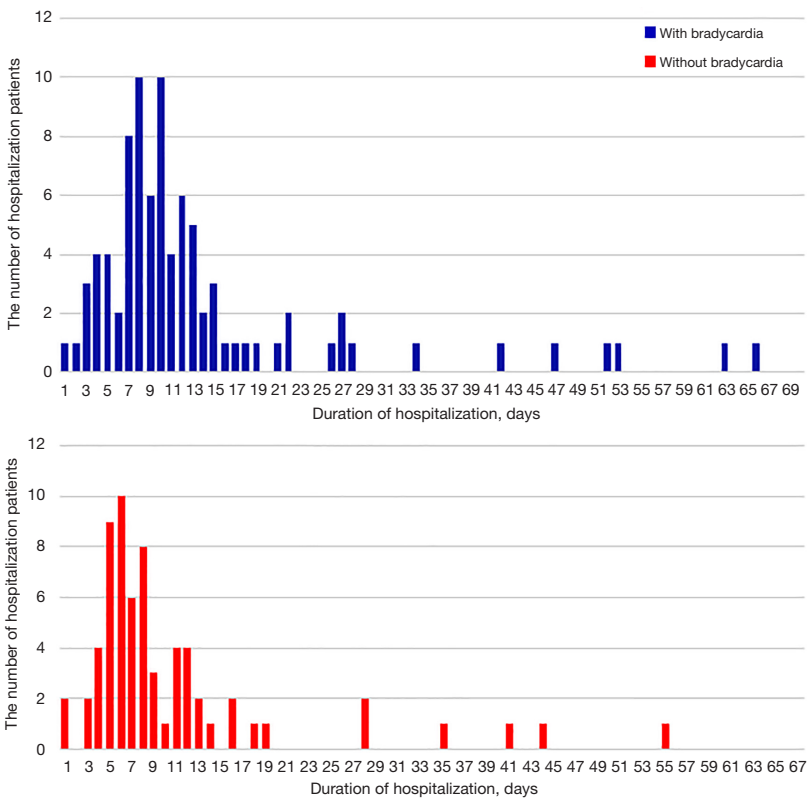

Figure 2 The number of bradycardia or non-bradycardia patients by hospitalization days.

Table 2 Analyses evaluating the risk factors for bradycardia in COVID-19 patients

Variables	With bradycardia (n=66)	Without bradycardia (n=87)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	P	OR (95% CI)	P
Age ≥65 years	16 (24.2)	24 (27.6)	0.84 (0.40–1.75)	0.64	0.96 (0.42–2.21)	0.93
Hospitalization days ≥11	33 (50.0)	38 (43.7)	1.29 (0.68–2.45)	0.44	1.42 (0.69–2.95)	0.34
Sex, male	40 (60.6)	56 (64.4)	0.85 (0.44–1.65)	0.64	–	–
Pneumonia	58 (87.8)	62 (71.3)	2.25 (1.00–5.11)	0.048	0.71 (0.22–2.32)	0.57
Oxygen supplement	23 (34.9)	22 (25.3)	1.58 (0.78–3.18)	0.20	–	–
Mortality event	2 (2.3)	–	–	0.18		
Respirator/HFOT	4 (6.1)	3 (3.4)	1.81 (0.39–8.36)	0.47	–	–
Comorbidity						
AF	3 (4.6)	5 (5.8)	0.78 (0.18–3.39)	>0.99	–	–
CD other than AF	1 (1.5)	5 (5.8)	0.25 (0.029–2.21)	0.24	–	–
Malignancy	2 (3.0)	9 (10.3)	0.27 (0.056–1.30)	0.12	–	–
CKD	3 (4.6)	5 (5.8)	0.78 (0.18–3.39)	>0.99	–	–
COPD	1 (1.5)	1 (1.2)	1.32 (0.081–21.55)	>0.99	–	–
BA	7 (10.6)	10 (11.4)	0.91 (0.33–2.54)	0.86	–	–
DM	7 (10.6)	15 (17.2)	0.57 (0.22–1.49)	0.25	–	–
HT	23 (34.9)	27 (31.0)	1.19 (0.60–2.35)	0.62	–	–
Smoking history	32 (48.5)	38 (43.7)	1.21 (0.64–2.31)	0.55	–	–
Medications						
Remdesivir	46 (69.7)	39 (44.8)	2.83 (1.44–5.55)	0.0022	1.24 (0.42–3.68)	0.69
Steroid	54 (81.8)	46 (52.9)	4.01 (1.89–8.52)	0.0002	3.67 (1.12–11.96)	0.03
Baricitinib	12 (18.2)	5 (5.8)	3.64 (1.22–10.93)	0.02	2.25 (0.70–7.21)	0.17
Casirivimab/imdevimab	4 (6.1)	6 (6.9)	0.87 (0.24–3.22)	>0.99	–	–

Data are presented as n (%) unless otherwise stated. COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; HFOT, high-flow oxygen therapy; AF, atrial fibrillation; CD, cardiac disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; BA, bronchial asthma; DM, diabetes mellitus; HT, hypertension.

incidence of bradycardia and physical examination data among steroid-treated patients with COVID-19, indicating that steroid-induced bradycardia may not have been dose dependent. The exact cause behind this remains unclear, but some mechanisms have been proposed. In animal studies, high-dose methylprednisolone has significant effects on cardiovascular physiology, which may be mediated by direct action on myocardial cell membranes and by alterations in cardiovascular sensitivity to catecholamines (20,21). Moreover, sudden electrolyte shifts due to steroids may be also involved in causing bradycardia (22).

In addition to our study, two reports have evaluated the relationship between bradycardia and different variables in patients with COVID-19 by using multivariate analysis. Bistrovic *et al.* conducted a retrospective cohort study to evaluate the incidence of bradycardia and mortality in patients with COVID-19, who received concurrent treatment with corticosteroids and remdesivir (14). The rate of bradycardia steadily increased until the 5th day of remdesivir treatment and subsequently diminished at the end of treatment. Further, the incidence of bradycardia on 5th day of remdesivir treatment was significantly associated with low odds for death during hospitalization (P=0.01, OR: 0.33, 95% CI: 0.14–0.79), HFOT use (P=0.004, OR: 0.33,

Table 3 The association between steroid use and various variables in COVID-19 patients

Variables	With steroid (n=100)	Without steroid (n=53)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	P	OR (95% CI)	P
Age ≥65 years	23 (23.0)	17 (32.1)	0.63 (0.30–1.33)	0.22		
Hospitalization days ≥11	45 (45.0)	26 (49.1)	0.85 (0.44–1.66)	0.23		
Sex, male	67 (67.0)	29 (54.7)	1.68 (0.85–3.33)	0.13		
Bradycardia	54 (54.0)	12 (22.6)	4.02 (1.89–8.52)	0.0002	4.69 (1.31–16.79)	0.02
Pneumonia	96 (96.0)	22 (41.5)	33.82 (10.82–105.71)	<0.0001	3.92 (0.91–16.88)	0.07
Oxygen supplement	40 (40.0)	5 (9.4)	6.40 (2.34–17.47)	<0.0001	2.28 (0.49–10.55)	0.29
Mortality event	2 (2.0)	–	–	0.54		
Respirator/HFOT	5 (5.0)	–	–	0.16		
Comorbidity						
AF	5 (5.0)	3 (5.7)	0.87 (0.20–3.82)	>0.99		
CD other than AF	3 (3.0)	3 (5.7)	0.52 (0.10–2.65)			
Malignancy	3 (3.0)	8 (15.1)	0.17 (0.044–0.69)	0.02	0.46 (0.053–3.96)	0.48
CKD	3 (3.0)	5 (9.4)	0.30 (0.068–1.29)	0.13		
COPD	1 (1.0)	1 (1.9)	0.53 (0.032–8.57)	>0.99		
BA	12 (12.0)	5 (9.4)	1.31 (0.44–3.94)	0.79		
DM	12 (12.0)	10 (18.9)	0.59 (0.23–1.46)	0.25		
HT	32 (32.0)	18 (34.0)	0.92 (0.45–1.86)	0.81		
Smoking history	48 (48.0)	22 (41.5)	1.30 (0.66–2.55)	0.59		
Medications						
Remdesivir	83 (83.0)	2 (3.8)	124.50 (27.61–561.38)	<0.0001	43.21 (8.36–223.30)	<0.001
Baricitinib	17 (17.0)	–	–	<0.001	–	0.99
Casirivimab/imdevimab	–	10 (18.9)	–	<0.0001	–	0.99

Data are presented as n (%). COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; HFOT, high-flow oxygen therapy; AF, atrial fibrillation; CD, cardiac disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; BA, bronchial asthma; DM, diabetes mellitus; HT, hypertension.

Table 4 The comparison of physical examination data in COVID-19 patents with 6 mg or 6.6 mg of dexamethasone treatment

Variables	With bradycardia (n=39)	Without bradycardia (n=29)	P
Height (cm)	168.6 (9.97)	165.3 (11.2)	0.21
Body weight (kg)	67.9 (13.4)	69.7 (15.3)	0.61
BMI (kg/m^2)	23.8 (3.93)	25.3 (4.57)	0.14
BSA (m^2)	1.77 (0.20)	1.76 (0.23)	0.91

Data are presented as mean (SD). COVID-19, coronavirus disease 2019; SD, standard deviation; BMI, body mass index; BSA, body surface area.

95% CI: 0.16–0.7), and intensive care unit stay (P=0.03, OR: 0.43, 95% CI: 0.2–0.91). Umeh *et al.* showed that the incidence of bradycardia was associated with length of hospital stay (OR: 1.071, 95% CI: 1.049–1.094), mortality (OR: 1.600, 95% CI: 1.070–2.394), respirator use (OR: 0.470, 95% CI: 0.298–0.742), and steroid use (OR: 0.559, 95% CI: 0.402–0.776), whereas remdesivir treatment did not reveal any significant difference (23). Interestingly, the results of our study, Bistrovic *et al.*'s study, and Umeh *et al.*'s study all reached completely different conclusions despite a similar retrospective cohort study of COVID-19. These conclusions indicate that the incidence of bradycardia was associated with steroid use in our study, linked to the remdesivir treatment in the study by Bistrovic *et al.*, and suppressed by steroid use in the study by Umeh *et al.*

Considering these discrepancies, medications for COVID-19, such as steroids and remdesivir, might have an ambivalent effect on the incidence of bradycardia, possibly due to the association between inflammation-related bradycardia and the anti-inflammation effect. It was proposed that the mechanism of inflammation-related bradycardia was due to the cross-talk between the autonomic nervous system and immune responses that are affected by circulating immune cells and various inflammatory cytokines (24). Among these cytokines, interleukin-6 (IL-6) exhibited the strongest correlation with decrease in heart rate in a variety of clinical conditions, including sepsis (25,26). IL-6 is also one of the most important inflammatory mediators associated with cytokine storm in COVID-19, and it has been reported that patients with COVID-19 and bradycardia were found to have high IL-6 levels (27,28). Judging from these reports, medications for COVID-19 could also prevent the incidence of bradycardia in patients with high inflammation due to the strong protective effect of cytokines such as IL-6. High IL-6 levels are associated with the incidence of bradycardia, whereas a decrease in IL-6 levels is associated with the suppression of sympathetic adrenergic stimulation as a result of inflammation. Bradycardia in COVID-19 may be a predictor of favorable prognosis, similar to the results of Bistrovic *et al.* (14). Possible mechanisms assumed to be the cause of bradycardia in COVID-19 include (I) inflammation-related bradycardia, (II) direct impairment of normal sinus node activity or the automatic nervous system caused by SARS-CoV-2 toxicity, and (III) side effects of various agents for COVID-19 (29,30). Considering the high incidence of bradycardia in patients with COVID-19 in our study, COVID-19 infections may cause higher levels of inflammatory markers or more severe cardiotoxicity and neurotoxicity than influenza infection. The treatment strategies of COVID-19 with bradycardia are difficult. The treatment of COVID-19 was strongly suspected to be the cause of significant or symptomatic bradycardia, discontinuing treatment was considered; whereas, it also has high risks of disease progression. Further, based on the study by Bistrovic *et al.* (14), the incidence of bradycardia may be associated with a good prognosis. We thought that discontinuing treatment due to bradycardia should be minimized.

Our study has two major limitations. First, this was a single-center retrospective study with a small number of patients. Second, our study population consisted mainly of patients with relatively mild COVID-19 infection, with only two fatal cases, and critically ill patients were not evaluated. Therefore, large-scale analyses are needed to confirm our hypotheses.

Conclusions

Our results showed that steroid treatment in patients with COVID-19 may be associated with the incidence of bradycardia. Considering the insights from previous studies, it is assumed that various factors such as steroids, remdesivir, high levels of cytokines, and direct impairment caused by SARS-CoV-2 toxicity can influence the onset of bradycardia. Although steroid use may be associated with the inciting factor of developing bradycardia, we believe that steroids are one of the most preferred treatment options due to their strong anti-inflammatory effects and evidence of good outcomes, even in patients developing bradycardia.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1382/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board at Koto Hospital (Approval No. 2022-6-1, approved on 13 June 2022), and approval for an opt-out consent method was given.

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