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Characteristics and in-hospital mortality of patients with COVID-19 from the first to fifth waves of the pandemic in 2020 and 2021 in the Japanese Medical Data Vision database

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ABSTRACT

Objectives: We aimed to describe patient characteristics, healthcare utilization, and in-hospital mortality among patients with COVID-19 in Japan across waves.
Methods: Using a large-scale hospital-based database, we identified patients hospitalized for COVID-19 in the first (January–June 2020), second (June–October 2020), third (October 2020–February 2021), fourth (March–June 2021), and fifth (June–December 2021) waves. We summarized patient characteristics, healthcare utilization, and in-hospital mortality during each wave and performed multivariable logistic regression analyses for in-hospital mortality.
Results: From the first to fifth waves, the number of patients (mean age ± standard deviation, years) was 2958 (61.2 ± 22.8), 7981 (55.6 ± 25.3), 18,788 (63.6 ± 22.9), 17,729 (60.6 ± 22.6), and 23,656 (51.2 ± 22.3), respectively. There were 190 (6.4%), 363 (4.5%), 1261 (6.7%), 1081 (6.1%), and 762 (3.2%) in-hospital deaths, respectively. The adjusted odds ratios for in-hospital deaths (95% confidence interval) were 0.78 (0.65–0.95), 0.94 (0.79–1.12), 0.99 (0.84–1.18), 0.77 (0.65–0.92), in the second to fifth waves, respectively, compared with the first wave.
Conclusions: In-hospital COVID-19 mortality improved from the first to the second wave; however, during the third and fourth waves, mortality was as serious as in the first wave. Although in-

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hospital mortality during the fifth wave improved, careful monitoring is needed for upcoming waves, considering changing patient and viral characteristics.

1. Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global pandemic. There are periodic increases in the number of infected people and the number of severe cases in countries worldwide, which is called the "n-th wave" (e.g., the first wave and the second wave). To date, many countries have experienced multiple waves of the COVID-19 pandemic [1].

Because of the changing strategy in caring for patients with COVID-19, such as screening for COVID-19 in both the general and high-risk populations with symptoms, the characteristics of patients with COVID-19 differed between the waves. In addition, the prognosis of patients infected with COVID-19 may also change over time due to the characteristics of the virus and advances in medical care. Indeed, a meta-analysis showed that the crude case fatality rates were lower in the second wave than in the first wave in 43 of 53 countries, including the US, Europe, and Asia [2]. This trend was also observed in Japan, where the case fatality rate of patients admitted to facilities contributing to a hospital-based registry decreased from 7.3% in the first wave to 1.2% in the second wave of 2020 [3].

However, some studies have suggested that this improving trend does not continue from the third wave onwards. For example, a nationwide Korean study showed a higher case fatality rate during the third wave than during the second wave [4]. In Japan, using the same registry as above [3], the case fatality rate increased again in the third wave to 5.8% [5]. However, another Japanese single-center study reported no significant difference in mortality during the fourth wave (5.5%) compared to the first and third waves (5.4%) [6]. These data suggest that the later waves may not always be less fatal.

Therefore, continuous monitoring and reporting are warranted to understand the changing characteristics of COVID-19, wave by wave. Using the most recent data from a large-scale hospital-based database until the end of 2021, we aimed to describe patient characteristics, healthcare utilization, and in-hospital mortality during Japan's first five waves of the COVID-19 pandemic.

2. Methods

2.1. Data source

We used a commercially available database of Japanese Diagnosis Procedure Combination (DPC) data built by Medical Data Vision (MDV) Co., Ltd. (Tokyo, Japan) [7]. The DPC system is a case-mix patient classification and lump-sum payment system for inpatients in acute care hospitals in Japan [8]. The MDV database comprises more than 350 DPC participating hospitals that agreed to provide data to MVD Co., Ltd., accounting for approximately 20% of the DPC hospitals in Japan. The age distribution of inpatients in the MDV database is similar, whereas the hospital volume (i.e., the number of beds) tends to be larger than that of all DPC hospitals in Japan [9].

The database includes administrative claims and discharges abstract data for all inpatients discharged from over 350 acute care hospitals, including the following information: sex, age, height, weight, smoking status, primary diagnosis, and comorbidities on admission, coded according to the *International Classification of Diseases,* 10th *Revision (ICD-10)*, procedures and prescriptions during admission; and in-hospital outcomes (dead or alive). In addition, outpatient data before hospital admission were available if the patient visited the same hospital where he or she was admitted.

In this study, we used data from patients admitted for COVID-19 (defined as ICD-10 code U071, recorded as the primary reason for hospital admission) and discharged from hospitals that continuously contributed their data to the MDV database during the study period between January 1, 2020, and December 31, 2021. Patients who were discharged on January 1, 2022, and later were not included because the data were not yet available when we extracted the data in March 2022.

The Ethics Committee of the University of Tsukuba (#1624-1) approved the present study. The need for informed consent was waived because of the anonymity of the data.

2.2. Definition of waves

To the best of our knowledge, there are no universally accepted definitions of COVID-19 pandemic waves. In this study, we defined the start and end of each wave according to the definition in a large prefecture (Osaka) of Japan: the first wave (from January to June 13, 2020), the second wave (from June 14 to October 9 in 2020), the third wave (from October 10, 2020, to February 28, 2021), the fourth wave (from March 1 to June 20, 2021), and the fifth wave (from June 21, 2021 and onwards) [10].

2.3. Patient characteristics, health care utilization, and in-hospital mortality

From the MDV database, we obtained individual patient information on sex, age, body mass index (BMI), smoking status, and comorbidities before or at admission, including cancer (ICD-10 codes: C00–C43, C45–C97), chronic lung disease (J40–J47), ischemic heart disease (I20–I25), heart failure (I50, I110), arrhythmia (I44, I45, I47–I49), hypertension (I10–I13, I15, I674), diabetes mellitus (E10–E14), cerebrovascular disease (I60–I69), peripheral artery disease (I702, I739), chronic kidney disease (N18), end-stage renal disease (N185, N19), dementia (F00–F03, F051, G30), cirrhosis (K703, K717, K743, K744, K745, K746), dyslipidemia (E78), and iron-deficiency anemia (D50).

We also acquired information on healthcare utilization during hospitalization, including ambulance transport, intensive care unit (ICU) admission, oxygen therapy, nasal high-flow, mechanical ventilation, extracorporeal membrane oxygenation, continuous renal replacement therapy, and the use of dexamethasone, remdesivir, and baricitinib.

As the primary in-hospital outcome, we identified whether patients were deceased or alive at discharge.

2.4. Statistical analysis

First, we summarized the patient characteristics, healthcare utilization, and in-hospital mortality of patients admitted for COVID-19 in each wave. We also described and compared patient characteristics and healthcare utilization between those discharged alive and those who died in the hospital, respectively, using the *t*-test for continuous variables and the chi-square test for categorical variables. Age was described by the mean and standard deviation, as well as the number and proportion (percentage) as age category (<20, 20–39, 40–64, 65–74, 75–84, and ≥85 years). All other variables were binary and expressed as numbers and proportions. Next, we calculated the in-hospital mortality (the number of deaths at discharge divided by the number of admissions) in each wave.

We then performed logistic regression analyses to estimate each wave's odds ratio for in-hospital mortality. We first conducted a univariable logistic regression analysis (model 1), followed by multivariable logistic regression analyses (i) adjusted for sex and age (model 2), (ii) adjusted for all patient characteristics, including sex, age, BMI, smoking status, and comorbidities (model 3), and (iii) further adjusted for treatments (oxygen use and dexamethasone use) on the day of admission (model 4). There were some missing values for BMI and smoking status, which are known risk factors for COVID-19 progression and death [11,12]. Assuming that these missing values were missing at random, we performed multiple imputations. In this study, we replaced each missing value with a set of substituted plausible values by creating 20 filled-in complete datasets using multiple imputations by the chained equation method. To create 20 complete datasets, we used all patient characteristics and in-hospital deaths [13].

All statistical analyses were performed using STATA version 15.0 (StataCorp, College Station, TX, USA).

3. Results

The MDV database contained 71,112 patients admitted for COVID-19 and discharged between 2020 and 2021. The number of patients admitted due to COVID-19 in the MDV database was proportional to the number of confirmed cases of COVID-19 according to the World Health Organization COVID-19 Dashboard until the fourth wave, but it was disproportionally low in the fifth wave (Fig. 1) [1]. There were 2958 (mean age ± standard deviation; 61.2 ± 22.8 years, male; 57.9%) in the first wave, 7981 (55.6 ± 25.3 years,

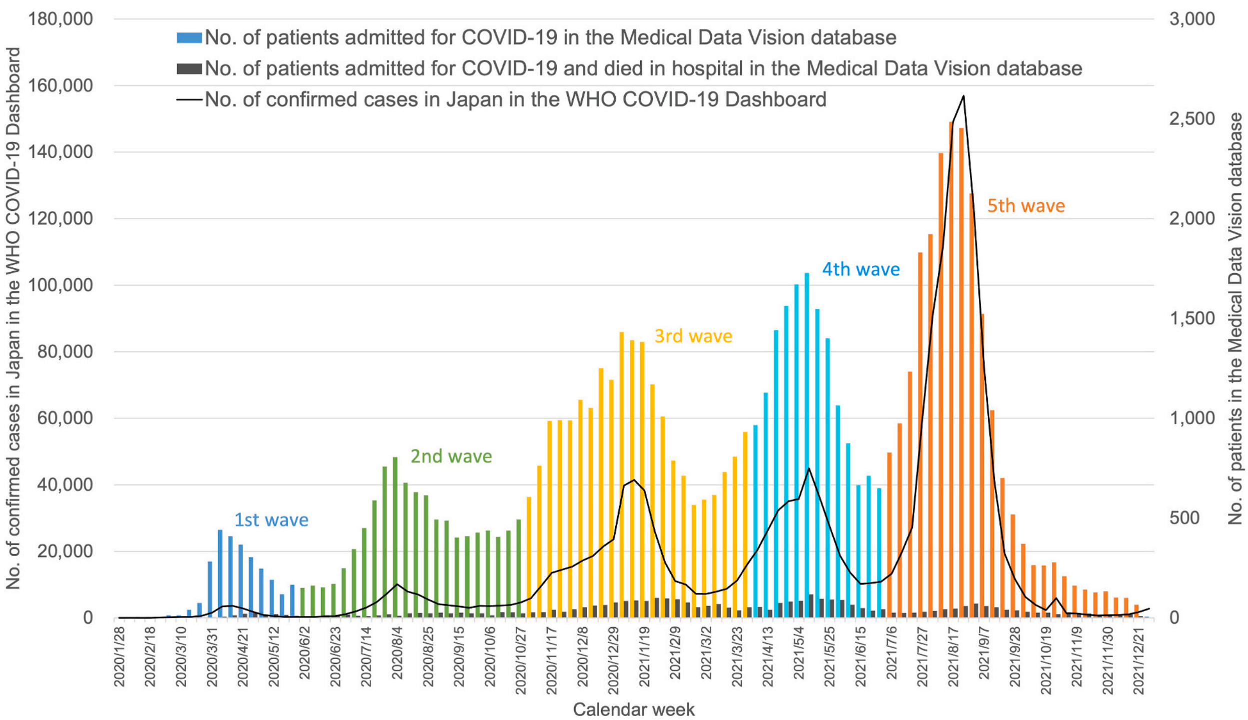

Fig. 1. The number of patients admitted for COVID-19 per week in the Medical Data Vision database and the number of confirmed cases in Japan in the World Health Organization COVID-19 Dashboard. Abbreviations: WHO = World Health Organization.

57.4%) in the second wave, 18,788 (63.6 ± 22.9 years, 55.9%) in the third wave, 17,729 (60.6 ± 22.6 years, 56.4%) in the fourth wave, and 23,656 (51.2 ± 22.3 years, 58.7%) in the fifth wave. Table 1 shows the baseline characteristics of the patients hospitalized during the first and fifth waves. In brief, patients in the second and fifth waves were younger and less likely to have comorbidities, whereas patient characteristics in the first, third, and fourth waves were similar. In every wave, compared to individuals discharged alive, those who died at hospital were older and more likely to have comorbidities (Supplementary Table 1).

Regarding healthcare utilization, there was no clear trend in ambulance transport or ICU admission (Table 2). The proportion of patients receiving oxygen therapy was lower in the second wave than in the other waves. The nasal high flow was used more frequently in the later waves. The proportion of patients requiring mechanical ventilation was the highest during the first wave (5.9%), whereas the proportions were 2.6%, 4.3%, 4.8%, and 3.7% in the second, third, fourth, and fifth waves, respectively. The proportion of patients receiving dexamethasone increased constantly from 1.2% in the first wave to 39.7% in the fourth wave, followed by a small decrease in the fifth wave. Other drugs indicated for COVID-19, such as remdesivir and baricitinib, were used more frequently in the later waves. In all waves, compared with participants who were discharged alive, those who died at the hospital were more likely to receive all kinds of treatments and have a longer length of stay (Supplementary Table 2).

The crude in-hospital mortality was 6.4% (190/2958), 4.5% (363/7981), 6.7% (1261/18,788), 6.1% (1081/17,729), 3.2% (762/23,656) in the first-to-fifth waves, respectively. Fig. 2 shows the unadjusted and adjusted odds ratios of in-hospital mortality. Compared with the first wave, the odds ratio for in-hospital death in the second wave was significantly lower, with or without adjustment for patient characteristics and oxygen use on the day of admission. The odds ratios in the third and fourth waves were approximately 1 (i.e., no statistical significance compared with the first wave), although the adjustment for patient characteristics and treatments changed the odds ratios to some extent. The crude odds ratio in the fifth wave was notably low, at 0.48 (95% confidence interval [CI], 0.41–0.57), but it became closer to 1 after adjusting for patient characteristics, especially age and sex. In the model adjusting for all patient characteristics and treatments on the day of admission, compared with the first wave, the adjusted odds ratios for in-hospital death (95% CI) were 0.78 (0.65–0.95), 0.94 (0.79–1.12), 0.99 (0.84–1.18), 0.77 (0.65–0.92), in the second, third,

Table 1
Baseline characteristics of patients admitted for COVID-19 in the Medical Data Vision database.

Variables	1st wave ($N = 2958$) n (%)	2nd wave ($N = 7981$) n (%)	3rd wave ($N = 18,788$) n (%)	4th wave ($N = 17,729$) n (%)	5th wave ($N = 23,656$) n (%)
Sex (male)	1713 (57.9)	4584 (57.4)	10,493 (55.9)	9996 (56.4)	13,880 (58.7)
Age (years), mean ± SD	61.2 ± 22.8	55.6 ± 25.3	63.6 ± 22.9	60.6 ± 22.6	51.2 ± 22.3
Age (years), category					
<20	114 (3.9)	573 (7.2)	937 (5.0)	914 (5.2)	1811 (7.7)
20–39	466 (15.8)	1865 (23.4)	2188 (11.7)	2375 (13.4)	5118 (21.6)
40–64	872 (29.5)	2119 (26.6)	4913 (26.2)	5615 (31.7)	10,346 (43.7)
65–74	484 (16.4)	1005 (12.6)	3414 (18.2)	3148 (17.8)	2184 (9.2)
75–84	535 (18.1)	1251 (15.7)	3813 (20.3)	3106 (17.5)	2246 (9.5)
≥85	487 (16.5)	1168 (14.6)	3523 (18.8)	2571 (14.5)	1951 (8.3)
Body mass index (kg/m^2)					
<18.5	376 (12.7)	1167 (14.6)	2386 (12.7)	1912 (10.8)	2836 (12.0)
18.5–25	1399 (47.3)	3848 (48.2)	8828 (47.0)	8408 (47.4)	11,162 (47.2)
25–30	446 (15.1)	1311 (16.4)	3553 (18.9)	3728 (21.0)	5354 (22.6)
≥30	151 (5.1)	484 (6.1)	1227 (6.5)	1526 (8.6)	2485 (10.5)
missing	586 (19.8)	1171 (14.7)	2794 (14.9)	2155 (12.2)	1819 (7.7)
Smoking status					
Current or ex-smoker	836 (28.3)	2201 (27.6)	4856 (25.9)	4611 (26.0)	6970 (29.5)
Non-smoker	1591 (53.8)	4452 (55.8)	10,826 (57.6)	10,290 (58.0)	13,583 (57.4)
missing	531 (18.0)	1328 (16.6)	3106 (16.5)	2828 (16.0)	3103 (13.1)
Recorded diagnosis					
Cancer	383 (13.0)	947 (11.9)	1954 (10.4)	1559 (8.8)	1716 (7.3)
Chronic lung disease	593 (20.1)	1444 (18.1)	3778 (20.1)	3252 (18.3)	3996 (16.9)
Ischemic heart disease	287 (9.7)	619 (7.8)	1463 (7.8)	1463 (8.3)	2446 (10.3)
Heart failure	456 (15.4)	1097 (13.8)	2850 (15.2)	2353 (13.3)	2514 (10.6)
Arrhythmia	296 (10.0)	724 (9.1)	1913 (10.2)	1644 (9.3)	1762 (7.5)
Hypertension	963 (32.6)	2248 (28.2)	6946 (37.0)	6109 (34.5)	5853 (24.7)
Diabetes mellitus	698 (23.6)	1585 (19.9)	5264 (28.0)	5319 (30.0)	6359 (26.9)
Cerebrovascular disease	315 (10.7)	731 (9.2)	2032 (10.8)	1635 (9.2)	1449 (6.1)
Peripheral artery disease	41 (1.4)	98 (1.2)	268 (1.4)	199 (1.1)	205 (0.9)
Chronic kidney disease	204 (6.9)	485 (6.1)	1153 (6.1)	958 (5.4)	896 (3.8)
End-stage renal disease	132 (4.5)	347 (4.4)	677 (3.6)	558 (3.2)	548 (2.3)
Dementia	263 (8.9)	652 (8.2)	1962 (10.4)	1428 (8.1)	1077 (4.6)
Cirrhosis	34 (1.2)	109 (1.4)	234 (1.3)	145 (0.8)	178 (0.8)
Dyslipidemia	505 (17.1)	1248 (15.6)	3627 (19.3)	3621 (20.4)	3390 (14.3)
Iron-deficiency anemia	311 (10.5)	712 (8.9)	1938 (10.3)	1740 (9.8)	2327 (9.8)

Abbreviations: SD, standard deviation.

Table 2
Healthcare utilization during hospitalization of patients admitted for COVID-19 by wave.

Variables	1st wave ($N = 2958$) n (%)	2nd wave ($N = 7981$) n (%)	3rd wave ($N = 18,788$) n (%)	4th wave ($N = 17,729$) n (%)	5th wave ($N = 23,656$) n (%)
Ambulance transport	878 (29.7)	2120 (26.6)	5206 (27.7)	5159 (29.1)	6664 (28.2)
ICU admission	203 (6.9)	473 (5.9)	1304 (6.9)	1303 (7.4)	1550 (6.6)
Oxygen therapy	1174 (39.7)	2297 (28.8)	7820 (41.6)	8414 (47.5)	9918 (41.9)
Nasal high flow	32 (1.1)	73 (0.9)	557 (3.0)	973 (5.5)	1159 (4.9)
Mechanical ventilation	175 (5.9)	209 (2.6)	809 (4.3)	848 (4.8)	874 (3.7)
ECMO	19 (0.6)	16 (0.2)	36 (0.2)	51 (0.3)	70 (0.3)
CRRT	24 (0.8)	25 (0.3)	89 (0.5)	73 (0.4)	71 (0.3)
Dexamethasone	35 (1.2)	770 (9.7)	5274 (28.1)	7039 (39.7)	8236 (34.8)
Remdesivir	0	0	0	0	162 (0.7)
Baricitinib	0	1 (0.01)	6 (0.03)	902 (5.1)	2158 (9.1)

Abbreviations: ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation; CRRT, continuous renal replacement therapy.

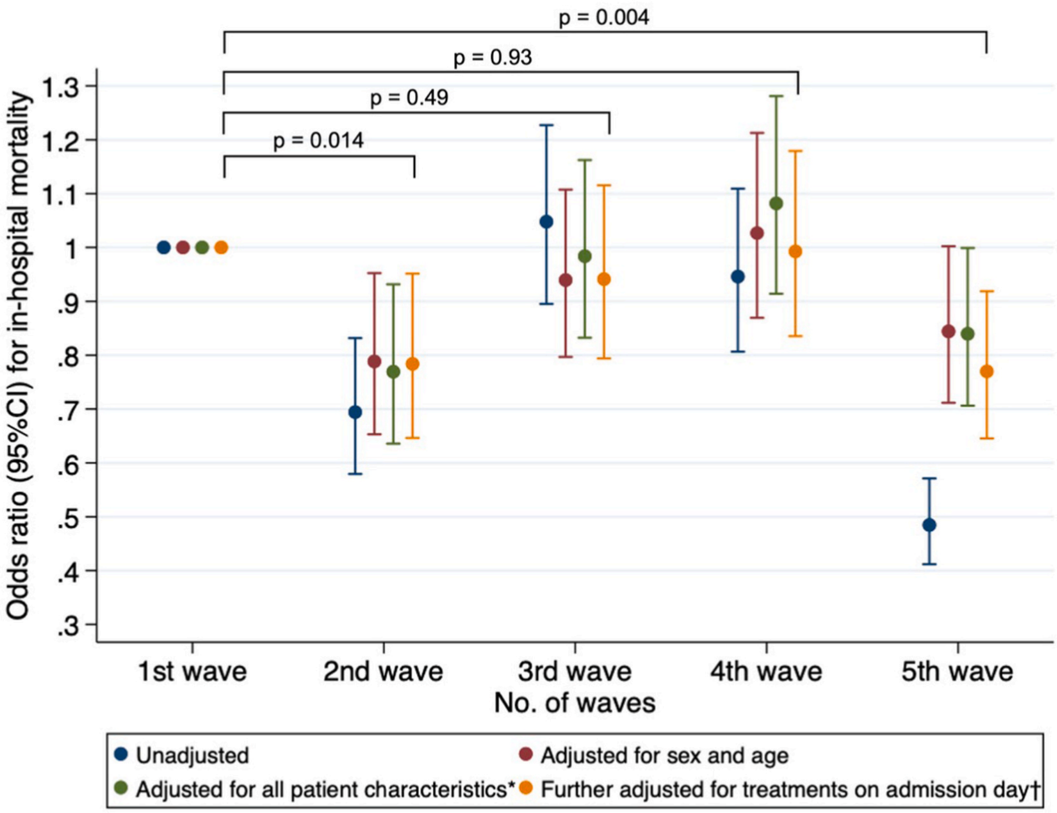

Fig. 2. Univariable and multivariable logistic regression analyses for in-hospital death in patients admitted for COVID-19. Abbreviations: CI = confidence interval. Note: Circles indicate the point estimates of odds ratios and bars refer to the 95% confidence intervals. P values for the final model are shown. *Sex, age, body mass index, smoking status, recorded diagnosis of cancer, chronic lung disease, ischemic heart disease, heart failure, arrhythmia, hypertension, diabetes mellitus, cerebrovascular disease, peripheral artery disease, chronic kidney disease, end-stage renal disease, dementia, cirrhosis, dyslipidemia, and iron deficiency anemia using multiple imputations for body mass index and smoking status. † Oxygen use and dexamethasone use.

fourth, and fifth waves, respectively. Supplementary Table 3 shows the odds ratios of all the covariates in the fully adjusted model (model 4).

4. Discussion

The present observational study, using a large-scale Japanese hospital-based database, suggested that the in-hospital mortality of COVID-19 patients improved significantly from the first to the second wave in 2020. However, the third and fourth waves in 2021 were as serious as the first wave, with or without considering (i.e., statistically adjusting for) the differences in patient characteristics between the waves. In addition, the in-hospital mortality of patients in the fifth wave tended to be better again, but this was largely explained by the younger age structure in the fifth wave.

As reported in a meta-analysis comparing the first and second waves in 53 countries and previous Japanese studies [2,3,5], the current study confirmed that the characteristics (e.g., median age and frequency of comorbidities) and prognosis of COVID-19 patients were generally better in the second wave. From the first to the second wave, the number of reverse-transcription polymerase chain reaction tests for COVID-19 and the number of hospital beds accepting COVID-19 patients rapidly increased [14,15]. Thus, COVID-19 patients with mild symptoms were more likely to be captured and admitted during the second wave. However, even after adjusting for patient characteristics, the in-hospital mortality of COVID-19 patients was still better in the second wave than in the first wave. Possible explanations for this phenomenon could include "harvesting" (meaning that patients susceptible to COVID-19 died during the first wave) [2], standardization and improvement of inpatient care (particularly the increased use of dexamethasone for patients requiring oxygen therapy, as discussed below) in the second wave, and residual confounding in the statistical analysis (meaning that statistical adjustment for measured factors cannot fully remove the confounding effect between the wave and mortality of COVID-19). The original Wuhan strain caused both waves in Japan in 2020; therefore, the viral virulence could be regarded as the same.

However, this improving trend from the first to the second wave in 2020 did not continue until 2021, although not many studies have been published to date [4–6,16,17]. A nationwide Korean study showed a higher case fatality rate during the third wave (1.26%) than during the second wave (0.91%) among laboratory-confirmed cases [4]. In Thailand and South Africa (except for the fourth wave in 2022 with the Omicron variant) [16,17], subsequent waves resulted in higher case fatalities. In a hospital-based COVID-19 registry in Japan, the in-hospital mortality of patients with COVID-19 was 7.3%, 2.8%, and 5.8% in the first, second, and third waves, respectively [5]. The trends in patient characteristics and in-hospital mortality in our study's first to third waves were roughly similar to those in the registry study [5].

Additionally, we showed that the characteristics and prognoses of patients in the fourth wave were similar to those in the first and third waves, whereas those in the fifth wave were younger and had fewer comorbidities than those in the second wave. Alpha variants appeared in early January 2021 in Japan and almost completely replaced other variants in the fourth wave [18]. The Delta variant appeared in June 2021 and was the main variant of the fifth wave. The virulence of the alpha variant was reported to be higher than that of the original Wuhan strain, and that of the delta variant was even higher [19,20]. Our data also support the higher virulence of the Delta variants; in the fifth wave, the proportion of patients who required oxygen was similar to that in the preceding waves, despite the average age of the hospitalized patients being younger by approximately 10 years.

There was a clear increasing trend in the proportion of patients receiving dexamethasone in the current study, from 1.2% in the first wave to 39.7% in the fourth wave. Dexamethasone use was approved for COVID-19 by the Ministry of Health, Labour, and Welfare in July 2020, which was during the first half of the second wave. The effect of dexamethasone was confirmed in a randomized controlled trial by the RECOVERY Collaborative Group in early 2021 [21], which may have spurred the prescription of dexamethasone in hospitals. In addition, other drugs for COVID-19, including remdesivir (approved in August 2021) and baricitinib (approved in April 2021), became available during subsequent waves. As such, we identified a signal for improving management of COVID-19 in subsequent waves. However, such an improvement may not necessarily result in an apparent improvement in in-hospital mortality during the third and fourth waves, probably because in-hospital mortality reflects several factors, such as patient characteristics and virulence of SARS-CoV-2 variants, as discussed above.

In-hospital mortality in the fifth wave was generally better than in the previous waves (except for the second), with or without adjustment for patient characteristics and treatments on the day of admission. Despite the higher virulence of the Delta variants in the fifth wave, this result may be associated with the trend in vaccine uptake rate for COVID-19. In Japan, COVID-19 mRNA vaccines were approved in February 2021, but vaccinations were mainly administered to healthcare workers during the first 3 months. Thus, the vaccine uptake rate remained low until June (i.e., the end of the fourth wave), at approximately 10% throughout Japan [22]. However, it dramatically increased thereafter, exceeding 70% by November 2021 [22]. This trend could partly explain the changing characteristics of patients admitted with COVID-19 and their in-hospital mortality.

To discuss the burden of COVID-19 in inpatient healthcare settings, the current study's findings should be interpreted with respect to both the absolute number and relative risk of in-hospital deaths. For example, although the relative risk for in-hospital mortality was lower in the second wave than in the first wave, the absolute number of in-hospital deaths in the current study was larger in the second wave because the denominator (i.e., the number of patients admitted for COVID-19) was much larger in the second wave than in the first wave. In the third and fourth waves, the relative risk for in-hospital mortality was as high as that in the first wave, whereas the denominator was over five times larger; therefore, the participating hospitals experienced a much larger volume of deaths due to COVID-19 than that in the first wave. The relative risk of in-hospital mortality improved in the fifth wave, but the number of patients admitted for COVID-19 was the largest in the current study; thus, the number of deaths remained large.

Our results may be helpful in understanding the different characteristics of COVID-19 across waves. It would be important for public health researchers and policy makers to consider these differences when evaluating the impact of public health interventions or policies implemented during each wave in preparation for future pandemics.

This study has several limitations. First, although the MDV database contains a large amount of data from over 350 acute care hospitals, covering approximately 20% of DPC hospitals in Japan, it does not cover all medical facilities in the country. Therefore, our results do not represent all patients admitted for COVID-19 in Japan, although patient characteristics and in-hospital mortality trends in the first three waves of the current study were broadly similar to those reported in a hospital-based COVID-19 registry [5]. Second, during the study period in Japan, the admission criteria (i.e., indications for admission) changed over time and location, depending on the capacity of the local healthcare system [23]. Thus, to calculate in-hospital mortality, both the number and severity/characteristics of patients (i.e., denominators) were different. Although we statistically adjusted for various patient characteristics and required treatments (the main factors comprising the admission criteria) when comparing different waves, there may have been unmeasured confounders and selection bias. For example, vital signs and SpO_2 were not recorded in the MDV database, which might explain the difference in the prognosis of patients admitted for COVID-19 between waves. In addition, prescribed drugs, such as remdesivir and baricitinib, were only recorded in the database when they were reimbursed according to government approval. It is possible that these drugs and other drugs with potential effects against COVID-19 (such as molnupiravir and casirivimab/imdevimab) were used off-label. Furthermore, information on vaccination status was also lacking, as mass vaccination was provided outside the health insurance system in Japan. Therefore, we could not statistically adjust for the effects of vaccination status or compare patient prognoses between waves among those who were not vaccinated. However, the majority of hospitalized patients in the fifth wave had not yet been fully vaccinated, and a survey at COVID-19 outpatient testing centers reported that 80.3% (498/636) of patients who tested positive in August 2021 in Japan were unvaccinated [24]. The hypothesis that vaccination may reduce the risk of in-hospital mortality among those admitted for COVID-19 should be examined in future studies that record the vaccination status. Finally, the current data comprised patients discharged by the end of 2021. In-hospital mortality during the fifth wave might have been underestimated if severe patients were still inpatients in 2022.

5. Conclusion

Using a large-scale hospital-based database in Japan between 2020 and 2021, we described and compared the characteristics, healthcare utilization, and in-hospital mortality of patients admitted for COVID-19 in the five waves. In-hospital mortality due to COVID-19 improved significantly from the first to the second waves in 2020, but the third and fourth waves in 2021 were as serious as the first wave in Japan. The fifth wave may have been less fatal; however, careful monitoring is needed for upcoming waves, given that patient and viral characteristics change across waves.

Ethical approval statement

This study was approved by the Ethics Committee of the University of Tsukuba (#1624-1) approved the present study. The need for informed consent was waived because of the anonymity of the data.

Author contribution statement

TS designed the study, processed, and analyzed the data, and wrote the initial draft. MI contributed to the conception and acquisition of data, study design, interpretation, and revision of the manuscript. TOK contributed to the conception, study design, interpretation, and revision of the manuscript. JK, YT, and MA accessed and verified the data and participated in the data processing, interpretation, and revision of the manuscript. TA, RI, AM, SI, MS, HO, SA, TAK, and NT contributed to study design, data interpretation, and manuscript revision. All authors approved the final version and are responsible for submitting the manuscript for publication

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Data availability statement

The data supporting the findings of this research were acquired from Medical Data Vision Co., Ltd. (MDV), and the authors were not allowed to share the data with others. Researchers can obtain data from the MDV (https://en.mdv.co.jp) upon reasonable request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

COVID-19 Coronavirus disease 19
SARS-CoV-2 severe acute respiratory syndrome coronavirus 2
MDV Medical Data Vision
DPC Diagnosis Procedure Combination
CI confidence interval

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e19490.

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