Comparison of Blood Test Data Between Patients With COVID-19 and Influenza: a Retrospective Cross-sectional Survey in a Japanese University Hospital

Sayato Fukui (✉ sfukui@juntendo.ac.jp)

Juntendo University Faculty of Medicine

Akihiro Inui

Juntendo University Faculty of Medicine

Mizue Saita

Juntendo University Faculty of Medicine

Daiki Kobayashi

St. Luke's International Hospital

Toshio Naito

Juntendo University Faculty of Medicine

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Abstract

Background: Characteristics features, including blood test data, of COVID-19 compared to those of influenza have not been defined.

Purpose: We aimed to compare clinical parameters, including blood test data, between COVID-19 and influenza.

Methods: This retrospective cross-sectional survey was conducted at Juntendo University Nerima Hospital, Tokyo, Japan. We recruited patients diagnosed with COVID-19 between January 1 and December 31, 2020, and all patients underwent blood tests. For comparison, we recruited patients diagnosed with influenza. The number of patients with influenza and those with COVID-19 was the same. All patients with influenza underwent blood tests and the period was dated back from December 31, 2020 until the period that was the same number of COVID-19.

Results: During the study period, 228 patients (male:female, 123 [54.0%]:105 [46.0%], age [mean±standard deviation], 54.68±18.98 years) were diagnosed with COVID-19. We recruited the same number of influenza patients (228 patients; male:female, 129 [56.6%]:99 [43.4%], age [mean±standard deviation], 69.6±21.25). Age 15–70 years (vs. 71 years), difficulty in breathing, malaise, and percentage of lymphocytes >20% were significantly more frequent in COVID-19. However, nausea, body temperature >38.1°C, and white blood cell count >9000/μL were more frequent in influenza.

Conclusion: Our results are useful for differentiating COVID-19 from influenza.

Introduction

In December 2019, a series of pneumonia cases of unknown cause were reported, involving clinical presentations that greatly resembled those of viral pneumonia [1–3]. The coronavirus disease (COVID-19) pandemic has been a great threat to human life. Many case reports on the similarity between COVID-19 and influenza have been published [4–7], but the disease presentation continues to vary among individuals. Symptoms that are different from those seen in past viral infections have also been reported. For example, there are reports of patients presenting with major loss of smell and taste [8, 9]. The wide range of features reported is thought to reflect effects on non-respiratory systems and indicate that signs may be observed in patients who are infected, but lack apparent respiratory symptoms [10].

Before 2019, influenza was one of the common infectious diseases considered a cause of fever, especially in seasonal epidemic. However, it is difficult to discriminate influenza from COVID-19 because more emphasis is being placed on COVID-19 diagnosis. As described above, in COVID-19, characteristic symptoms such as loss of smell and taste are reported [8, 9]. Some studies have directly compared the burden of COVID-19 and influenza individually [11–14]. In a previous study, anosmia (53% vs. 17%, $p < 0.001$), dysgeusia (49% vs. 20%, $p = 0.001$), diarrhea (40% vs. 20%, $p = 0.021$), frontal headache (26% vs. 9%, $p = 0.021$), and bilateral crackling sounds (24% vs. 9%, $p = 0.034$) were significantly more frequent in

COVID-19 than in influenza. However, sputum production (52% vs. 29%, $p = 0.010$), dyspnea (59% vs. 34%, $p = 0.007$), sore throat (44% vs. 20%, $p = 0.006$), conjunctival hyperemia (30% vs. 4%, $p < 0.001$), tearing (24% vs 6%, $p = 0.004$), vomiting (22% vs 3%, $p = 0.001$), and rhonchi sounds (17% vs. 1%, $p = 0.002$) were more frequent in influenza than in COVID-19 [13]. However, studies comparing COVID-19 and influenza, using blood test data have not been conducted thus far. In a previous study, elevated red blood cell distribution width (RDW) at the time of hospital admission and an increase in RDW during hospitalization were associated with an increased risk of mortality in patients with COVID-19 [15]. In another study, the fibrinogen-to-albumin ratio and platelet count were independent risk factors for severe illness [16]. Thus, COVID-19 may be diagnosed based on not only clinical symptoms but also blood test data, and a comparison between COVID-19 and influenza using blood test data is thought have clinical significance. In influenza, physical examination is performed to examine characteristic features such as influenza follicles [17, 18], but the physical examination is often omitted after the COVID-19 outbreak. The results of this study will be useful for phylaxis purposes. Therefore, this cross-sectional study aimed to identify the characteristics of COVID-19 from blood test data and compare them with those of influenza.

Methods

Study design and study population

We recruited patients diagnosed with COVID-19 from January 1, 2020 to December 31, 2020, and all patients underwent blood tests. For comparison, we recruited patients diagnosed with influenza; the number of patients with influenza and those with COVID-19 was the same. All patients with influenza also underwent blood tests and the period was dated back from December 31, 2020 until the period that was the same number of COVID-19. Furthermore, children (aged < 14 years) with COVID-19 and influenza were excluded. COVID-19 was diagnosed using a polymerase chain reaction text for the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid, and influenza was diagnosed using a rapid influenza diagnostic kit. Furthermore, more than two doctors were involved in each diagnosis. This retrospective, cross-sectional study was performed at Juntendo University Nerima Hospital, a 490-bed university-affiliated hospital in Tokyo, Japan.

Clinical information was extracted by chart review. Data on the following variables were collected: age, sex, history of malignant diseases, asthma, heart disease including hypertension, diabetes mellitus, hemodyscrasia, human immunodeficiency virus infection, use of immunosuppressive agents (including steroids), and general symptoms (chills, sore throat, cough, headache, diarrhea, nausea, joint pain, malaise, and difficulty in breathing). We also extracted data on axillary body temperature, systolic and diastolic blood pressure, pulse rate, respiratory rate, oxygen saturation (room air), white blood cell (WBC) count along with the percentage of neutrophils and lymphocytes, hemoglobin level, platelet count, RDW, serum parameters (levels of total protein, albumin, lactate dehydrogenase, blood urea nitrogen, creatinine, sodium, potassium, chloride, glucose, aspartate aminotransferase, alanine aminotransferase, total bilirubin, glucose, hemoglobin A1c, and C-reactive protein [CRP]).

Statistical analysis

Bivariate comparisons of each variable between COVID-19 and influenza were performed using independent samples *t*-tests for continuous data or chi-square tests for categorical data. Differences with *p* values of <0.05 were defined as statistically significant. Variables with a *p* value of <0.05 in bivariate analysis were entered into multivariable logistic regression models. The accuracy of the logistic regression models was assessed using the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. All statistical analyses were performed using EZR (Saitama Medical Center; Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). EZR is a modified version of R Commander designed to add statistical functions frequently used in biostatistics [19].

This study was conducted in accordance with relevant guidelines and regulations. This retrospective study was approved by the ethics committee of Juntendo University Nerima Hospital, Tokyo, Japan (approval number: 2020066).

Results

During the study period, 228 patients (male:female, 123 [54.0%]:105 [46.0%], age [mean $\pm$ standard deviation {SD}] 54.68 ± 18.98) were diagnosed with COVID-19. The number of patients with influenza (228 patients; male:female, 129 [56.6%]:99 [43.4%], age [mean $\pm$ SD] 69.6 ± 21.25) was the same as that of patients with COVID-19. Patients with influenza were recruited between January 11, 2015 and December 31, 2020. All influenza patients were classified as having type A disease. As shown in Table 1, a total of 456 patients (male:female, 252 [55.3%]:204 [44.7%]; mean $\pm$ SD age, 62.12 ± 21.47 years) were included in this study. Table 1 shows the characteristics of patients with COVID-19 and influenza and the results of the bivariable analysis. Age, cancer, asthma, heart diseases, difficulty in breathing, chills, nausea, malaise, body temperature, systolic blood pressure, heart rate, respiratory rate, saturation, WBC count, percentage of neutrophils, percentage of lymphocytes, hemoglobin level, RDW, platelet count, aspartate aminotransferase level, sodium level, chloride level, CRP level, creatine phosphokinase level, and creatine phosphokinase level were significantly different between the groups (Table 1). We conducted multivariable logistic regression analysis based on bivariable analysis (Table 2). The following variables were considered for multivariable regression analysis: age, chills, difficulty in breathing, nausea, malaise, body temperature, WBC count, percentage of lymphocytes, and creatine phosphokinase level. We incorporated these factors as they are thought to be clinically useful. For example, chloride, we excluded the factor which a significant difference was over in normal range even if significantly different. Based on the cutoff value, body temperature was categorized as hypothermia ($<35.9^{\circ}\text{C}$) and hyperthermia ($>38.1^{\circ}\text{C}$), and a body temperature of 36°C – 38°C was used as the reference range. Furthermore, the cutoff WBC count was $>9000/\mu\text{L}$, which was higher than the normal upper limit. For a similar reason, the cutoff value for the percentage of lymphocytes was $>20\%$, and that for the creatine phosphokinase level were $>300\text{ U/L}$. Because the percentage of neutrophils and lymphocytes was highly correlated with each other, the percentage of lymphocytes was used in multivariable analysis as a representative of these two

variables. The significant factors in multivariable analysis were age 15–70 years (vs. 71 years) (odds ratio [OR] = 5.53, 95% confidence interval [CI]: 2.86–10.70, $p < 0.001$), difficulty in breathing (OR = 3.20, 95% CI: 1.37–7.47, $p < 0.01$), nausea (OR = 0.10, 95% CI: 0.01–0.97, $p = 0.04$), malaise (OR = 2.43, 95% CI: 1.06–5.53, $p = 0.03$), body temperature $> 38.1^{\circ}\text{C}$ (OR = 0.07, 95% CI: 0.03–0.14, $p < 0.001$), WBC count $> 9000/\mu\text{L}$ (OR = 0.12, 95% CI: 0.03–0.43, $p < 0.001$), and percentage of lymphocytes $> 20\%$ (OR = 3.74, 95% CI: 1.91–7.31, $p < 0.001$). We evaluated the quality of this model using the discrimination of ROC–AUC; the ROC–AUC was 0.922 (95% CI: 0.89–0.95). Thus, the model used in this study had sufficient power.

Table 1
Patient variables and results of univariate analysis

	Total	COVID-19	Influenza		<i>p</i> value
Variables	n = 456	n = 228	n = 228	Test performed	
Demographic factors					
Age, years, mean $\pm$ SD	62.12 $\pm$ 21.47	54.68 $\pm$ 18.98	69.6 $\pm$ 21.25	t-test	< 0.001*
Female sex, n, %	204 (44.7%)	105 (46.0%)	99 (43.4%)	χ^2	0.64
Underlying condition					
Cancer, n, %	45 (9.8%)	13 (5.7%)	32 (14.0%)	χ^2	< 0.01*
Hemodyscrasia, n, %	11 (2.4%)	8 (3.5%)	3 (1.3%)	χ^2	0.22
Diabetes mellitus, n, %	55 (12.1%)	26 (11.4%)	29 (12.7%)	χ^2	0.77
Asthma, n, %	41 (8.9%)	29 (12.7%)	12 (5.2%)	χ^2	< 0.01*
Heart disease, n, %	152 (33.3%)	61 (26.7%)	91 (39.9%)	χ^2	< 0.01*
Human immunodeficiency syndrome, n, %	0	0	0	χ^2	NA
Use of immunosuppressive agents, n, %	25 (5.5%)	8 (3.5%)	17 (7.5%)	χ^2	0.10
Smoker, n, %	77 (16.9%)	46 (20.2%)	31 (13.6%)	χ^2	0.14
Symptoms					
Headache, n, %	58 (12.7%)	27 (11.8%)	31 (13.6%)	χ^2	0.67
Cough, n, %	177 (38.9%)	98 (43.0%)	79 (34.6%)	χ^2	0.08
Sore throat, n, %	64 (14.0%)	35 (15.4%)	29 (12.7%)	χ^2	0.50
Difficulty in breathing, n, %	74 (16.2%)	48 (21.6%)	26 (11.4%)	χ^2	< 0.01*
Chill, n, %	40 (8.8%)	8 (3.5%)	32 (14.0%)	χ^2	< 0.001*
Joint pain, n, %	36 (7.9%)	16 (7.0%)	20 (8.8%)	χ^2	0.60
COVID-19, coronavirus disease; SD, standard deviation					

	Total	COVID-19	Influenza		<i>p</i> value
Variables	n = 456	n = 228	n = 228	Test performed	
Nausea, n, %	24 (5.3%)	3 (1.3%)	21 (9.2%)	χ^2	< 0.001*
Diarrhea, n, %	24 (5.3%)	14 (6.1%)	10 (4.3%)	χ^2	0.53
Malaise, n, %	105 (23.0%)	71 (31.1%)	34 (14.9%)	χ^2	< 0.001*
Vital signs					
Body temperature, °C, $\pm$ SD	37.57 $\pm$ 1.10	36.93 $\pm$ 0.76	38.22 $\pm$ 1.00	t-test	< 0.001*
Systolic blood pressure, mmHg, $\pm$ SD	134.44 $\pm$ 24.05	128.21 $\pm$ 19.82	141.01 $\pm$ 26.31	t-test	< 0.001*
Diastolic blood pressure, mmHg, $\pm$ SD	79.47 $\pm$ 14.97	79.36 $\pm$ 14.34	79.59 $\pm$ 15.65	t-test	0.88
Heart rate, bpm, $\pm$ SD	90.85 $\pm$ 18.00	85.00 $\pm$ 15.82	96.94 $\pm$ 18.14	t-test	< 0.001*
Respiratory rate, n, $\pm$ SD	18.08 $\pm$ 3.92	17.25 $\pm$ 3.24	18.96 $\pm$ 4.37	t-test	< 0.001*
Saturation, %, $\pm$ SD	95.39 $\pm$ 3.82	95.85 $\pm$ 3.59	94.90 $\pm$ 4.00	t-test	< 0.01*
Laboratory data					
White blood cell counts, / μ L, $\pm$ SD	6249.34 $\pm$ 3003.32	5249.12 $\pm$ 2269.90	7249.56 $\pm$ 3304.15	t-test	< 0.001*
Neutrophils, %, $\pm$ SD	68.81 $\pm$ 15.14	63.81 $\pm$ 14.32	75.32 $\pm$ 13.67	t-test	< 0.001*
Lymphocytes, %, $\pm$ SD	21.33 $\pm$ 12.47	26.49 $\pm$ 11.78	14.60 $\pm$ 9.89	t-test	< 0.001*
Hemoglobin, g/dL, $\pm$ SD	13.79 $\pm$ 1.72	13.96 $\pm$ 1.93	13.62 $\pm$ 1.48	t-test	0.04*
Red blood cell distribution width, %, $\pm$ SD	15.18 $\pm$ 4.65	12.84 $\pm$ 1.47	17.52 $\pm$ 5.49	t-test	< 0.001*
Platelet, 10 ⁴ / μ L, $\pm$ SD	17.46 $\pm$ 7.70	21.51 $\pm$ 9.07	13.42 $\pm$ 1.95	t-test	< 0.001*
Blood urea nitrogen, mg/dL, $\pm$ SD	16.86 $\pm$ 13.38	15.88 $\pm$ 13.79	17.84 $\pm$ 12.92	t-test	0.12

COVID-19, coronavirus disease; SD, standard deviation

	Total	COVID-19	Influenza		<i>p</i> value
Variables	n = 456	n = 228	n = 228	Test performed	
Creatinine, mg/dL, $\pm$ SD	1.02 $\pm$ 1.07	0.95 $\pm$ 0.79	1.09 $\pm$ 1.29	t-test	0.16
Total protein, g/dL, $\pm$ SD	7.08 $\pm$ 0.68	7.08 $\pm$ 0.69	7.08 $\pm$ 0.67	t-test	0.92
Albumin, g/dL, $\pm$ SD	3.92 $\pm$ 0.59	3.97 $\pm$ 0.60	3.86 $\pm$ 0.57	t-test	0.07
Total bilirubin, g/dL, $\pm$ SD	0.60 $\pm$ 0.45	0.57 $\pm$ 0.52	0.64 $\pm$ 0.34	t-test	0.09
Lactate dehydrogenase, IU/L, $\pm$ SD	252.56 $\pm$ 103.54	246.76 $\pm$ 101.40	258.76 $\pm$ 105.67	t-test	0.23
Aspartate aminotransferase, IU/L, $\pm$ SD	35.30 $\pm$ 31.46	32.26 $\pm$ 22.57	38.36 $\pm$ 38.15	t-test	0.04*
Alanine aminotransferase, IU/L, $\pm$ SD	30.04 $\pm$ 32.72	32.76 $\pm$ 38.48	27.32 $\pm$ 25.85	t-test	0.08
Sodium, mEq/L, $\pm$ SD	137.39 $\pm$ 3.90	138.39 $\pm$ 3.51	136.38 $\pm$ 4.01	t-test	< 0.001*
Potassium, mEq/L, $\pm$ SD	4.06 $\pm$ 0.52	4.07 $\pm$ 0.46	4.05 $\pm$ 0.61	t-test	0.79
Chloride, mEq/L, $\pm$ SD	102.30 $\pm$ 4.06	103.36 $\pm$ 3.85	101.24 $\pm$ 3.99	t-test	< 0.001*
C reactive protein, mg/dL, $\pm$ SD	3.88 $\pm$ 5.54	3.19 $\pm$ 4.66	4.56 $\pm$ 6.23	t-test	< 0.01*
Creatine phosphokinase, U/L, $\pm$ SD	305.56 $\pm$ 1391.28	121.44 $\pm$ 198.79	500.25 $\pm$ 1968.86	t-test	< 0.01*
Glucose, mg/dL, $\pm$ SD	120.08 $\pm$ 38.22	113.76 $\pm$ 36.53	128.13 $\pm$ 38.90	t-test	< 0.001*
Hemoglobin A1c, %, $\pm$ SD	6.10 $\pm$ 0.92	6.04 $\pm$ 0.87	6.30 $\pm$ 1.04	t-test	0.06
* <i>p</i> < 0.05					
COVID-19, coronavirus disease; SD, standard deviation					

Table 2
Multivariable logistic regression model

Variables	Multivariable OR	Multivariable 95% CI	Multivariable <i>p</i> -value
Age 15–70 (vs. 71) years	5.53	2.86–10.70	< 0.001*
Chills	0.77	0.20–2.97	0.71
Difficulty in breathing	3.20	1.37–7.47	< 0.01*
Nausea	0.10	0.01–0.97	0.04*
Malaise	2.43	1.06–5.53	0.03*
Body temperature <35.9 °C	1.91	0.20–18.13	0.57
36.0–38.0 °C	□	Reference	□
>38.1 °C	0.07	0.03–0.14	< 0.001*
White blood cell count > 9000/μL	0.12	0.03–0.43	< 0.01*
Lymphocyte > 20%	3.74	1.91–7.31	< 0.001*
Creatine phosphokinase > 300 U/L	0.69	0.24–1.94	0.48
* <i>p</i> < 0.05			
OR, odds ratio; CI, confidence interval			

Discussion

To the best of our knowledge, this is the first study to directly compare patients with COVID-19 and influenza using laboratory test data in a university hospital. Age 15–70 years (vs. 71 years), difficulty in breathing, malaise, and percentage of lymphocyte > 20% were significantly more frequent in patients with COVID-19 than in those with influenza. However, nausea, body temperature > 38.1°C, and WBC count > 9000/μL were more frequent in patients with influenza than in those with COVID-19.

Other studies have reported that age at the onset of COVID-19 is lower than that at the onset of influenza [14, 20]. The results of these studies support the results of the present study.

SARS-CoV-2 mainly invades respiratory epithelial cells by adhesion to angiotensin-converting enzyme 2; thus, infected patients may develop mild-to-severe inflammatory responses and acute lung injury [21]. Another study has reported that COVID-19 causes acute respiratory failure in the predominance of influenza [14]. These studies support the results of our study, revealing a higher number of cases of dyspnea cases than those of influenza.

Similarly, malaise is a symptom that has been reported in many patients with COVID-19 [14]. According to a previous study, 63% patients with COVID-19 have malaise [22]. These studies support the results of our study, revealing a higher number of cases of malaise than those of influenza cases. Malaise may be related to an increase in viral load and immune response to the infection [23]. In addition, insufficient energy production to meet the required metabolic demands is related to malaise [24].

Many studies have reported low lymphocyte counts in patients with COVID-19 [25, 26]. The host immune responses strongly try to involve all potential cells and cytokines. In chronic COVID-19 cases, natural killer cells and T cells become exhausted, and a decrease in their count leads to lymphopenia. The inability to eradicate the infection in the affected organ causes hyper-initiation of the immune system, which releases excessive amounts of inflammatory cytokines to compensate for the exhausted ones and the low lymphocyte count [25]. Similarly, a low lymphocyte count has been reported in influenza [27, 28]. However, our study shows that the lymphocyte counts are lower in patients with COVID-19 than in patients with influenza. Furthermore, regarding WBC count, a study has shown that low leukocyte counts are markers of COVID-19 [29]. In our study, WBC counts $> 9000/\mu\text{L}$ were more frequently associated with influenza than with COVID-19. This finding suggests the likelihood of it being useful for the differentiation of COVID-19 from influenza. In addition, our study showed that CRP levels are not useful for the differentiation of COVID-19 from influenza. Similarly, a previous study showed that CRP levels were not an effective discriminator of COVID-19 and non-COVID-19 cases [29]. However, a significantly higher level of CRP was observed in the severe COVID-19 group than in the non-COVID-19 group, which confirms the findings of previous studies regarding the clinical utility of CRP levels as an indicator of severe disease and progressive inflammation [30, 31]. In our study, a significant difference in CRP levels was possibly not observed because none of the patients with COVID-19 had severe disease. In contrast to a previous meta-analysis [32], a recent meta-analysis revealed that procalcitonin levels were not significantly different between the severe and non-severe groups. The procalcitonin level was only assessed in a few cases in this study; therefore, we did not add this in the extraction item; however, we think that it is the contents that procalcitonin level may be argued comparison between COVID-19 and influenza in the future.

Body temperature $> 38.1^{\circ}\text{C}$ was more frequent in patients with influenza than in those with COVID-19. Many cases not involving fever have been reported in COVID-19 [33, 34]. We believe that these findings support our results. However, the result may be effects that patients receiving antipyretics could not be excluded. Furthermore, many patients with COVID-19 had to be hospitalized for isolation owing to the high infectious control, and they underwent laboratory tests even if they were asymptomatic.

Nausea is more frequently associated with influenza than with COVID-19. In a study, nausea occurred in approximately 3.9% patients with COVID-19 [33]. Similarly, the ratio of nausea is unknown, but it can cause digestive symptoms including nausea in influenza. The mechanism to cause nausea is unclear and requires further investigation. Inflammatory reactions may occur when a virus infects gastrointestinal mucosal bleeding cells, and digestive symptoms such as nausea are thought to occur during these reactions. In this study, significantly fewer symptoms of nausea in patients with COVID-19 may reflect the

greater strength of the respiratory tract infection than the gastrointestinal cells of COVID-19. Difficulty in breathing was significantly more frequent in patients with COVID-19 than in those with influenza, which may support our hypothesis.

There are some limitations to this study. First, there is a greater possibility that patients with COVID-19 are hospitalized as per law in Japan. Many patients with COVID-19 are hospitalized for isolation, which can help in controlling the spread of the highly infectious disease, even if present in young and asymptomatic patients. Furthermore, an influenza extraction period of several years passed (from December 31, 2020 to January 11, 2015). Annually, the seasonal flu may vary in symptoms, and this effect may have influenced the results of our study. However, the type of influenza did not influence the results, as there were no patients with influenza type B who underwent blood tests. In addition, we did not extract the data of three symptoms (taste disturbance, dysosmia, and conjunctival hyperemia) as they were inaccurate; therefore, these symptoms were not included in the chart review of patients with influenza. Finally, the patient population enrolled in this study was limited to that from a single hospital. Additionally, this was a retrospective study. Hence, a multicenter prospective study should be conducted with a larger number of patients to verify our results.

In conclusion, our results are useful for differentiating patients with COVID-19 from those with influenza. Age 15–70 years (vs. 71 years) years, difficulty in breathing, malaise, and percentage of lymphocytes > 20% were significantly more frequent in COVID-19 than in influenza. However, nausea, body temperature > 38.1°C, and WBC counts > 9000/ μ L were more frequent in influenza than in COVID-19.

Declarations

Ethics approval and consent to participate

The Ethics Committee of Juntendo University Nerima Hospital approved this study (Approval Number 2020066). This study was an observational study and written informed consent was waived due to a public health outbreak investigation by the Ethics Commission (Juntendo University Nerima Hospital).

Consent for publication

All authors agreed to publish this study.

Availability of data and materials

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Competing interests

Nothing to disclose for all authors

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Authors' contributions

SF, AI, MS and TN contributed to study concept and design. SF and AI were involved in acquisition of participants and data. SF and DK were involved in analysis and interpretation of data. SF, AI, MS, DK and TN were involved in preparation of the manuscript.

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Figures

Figure 1

The area under the receiver operating characteristic curve of the model was 0.922 (95% confidence interval: 0.89–0.95).