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Commentary

Clinical characteristics of COVID-19 patients who received ventilator management during the omicron variant period in a tertiary hospital in Japan

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Abstract: ***Background:*** Severe COVID-19 patients who received ventilator management were not very rare even when the omicron variant became dominant, but the clinical characteristics of these patients are still unclear. ***Methods:*** The clinical characteristics of severe COVID-19 patients requiring ventilator management were retrospectively investigated from January 2023 to December 2023. ***Results:*** Severe COVID-19 patients who received ventilator management accounted for 11 of 275 (4.2%) patients during the omicron variant period. Their mean age was 70.7 (51-85) years, and males were predominant. Ten of eleven (91.7%) patients were managed in the emergency department and had underlying diseases, including chronic lung/heart/kidney diseases and neurological diseases. However, only 4 of 11 (36.4%) had a clear history of vaccination. The patients showed a positive SARS-CoV-2 antigen titer of 3305.7 (12.9-20912). All 11 patients were treated with remdesivir and dexamethasone, and 5 (45.5%) also received sotrovimab. Pathogenic bacteria were isolated from 7 of 11 (63.6%) patients, and all 11 patients were treated with antibiotics. Only 3 of 11 (27.3%) patients were managed using extracorporeal membrane oxygenation (ECMO), but 9 of 11(81.8%) patients survived. ***Conclusions:*** These data suggest that severe COVID-19 patients who required ventilator management were less-vaccinated, elderly patients with underlying disease. These patients were treated successfully using antiviral agents, steroids, neutralizing antibodies, and antibiotics, with a few also treated using ECMO in the omicron era.

Keywords: SARS-CoV-2, Remdesivir, Dexamethasone, Sotrovimab, Extracorporeal membrane oxygenation Ventilator, Vaccine

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1. Commentary

COVID-19 has had an enormous impact on societies worldwide, and SARS-CoV-2 is currently well treated using antiviral agents, including remdesivir (RDV: Gilead, Foster City, CA, USA), which has been recommended as the first-choice treatment for moderate and hospitalized COVID-19 patients [1, 2]. In addition, COVID-19 vaccines have been developed and have shown extraordinary preventive effects on hospitalization and death [3, 4]. However, despite the use of antiviral agents and vaccines, some patients developed severe disease and required ventilator management in the era of the omicron variant, which was less pathogenic than the original strain of SARS-CoV-2 [5, 6].

In this study, the clinical characteristics of patients who received ventilator management in the dominant period of the omicron variant, which was from January 01, 2023 to December 31, 2023, were investigated retrospectively. This study and related analyses were approved by the Institutional Review Board of Saitama Medical University

International Medical Center on July 06 and December 27, 2022 as #2022-032 and #2022-146, and registered as UMIN000047691. The patients whose specimens were analyzed provided written, informed consent to have any accompanying images and their case details published. This study was performed in accordance with the Declaration of Helsinki.

In our hospital, a total of 257 COVID-19 patients were admitted, and 11 (4.2%) received ventilator management (Table 1). Their mean age was 70.7 (51-85) years, and 10 of 11 (91.7%) patients were male, managed in the emergency department and had underlying diseases, including chronic obstructive pulmonary disease, Parkinson's disease, amyotrophic lateral sclerosis, brain tumor, convulsions, chronic kidney disease with hemodialysis, and chronic heart disease, and were nursing home residents. Neurological diseases were the predominant underlying diseases. However, only 4 of 11 (36.4%) patients had a clear history of vaccination, and 3 of 11 patients (27.3%) did not receive any COVID-19 vaccines.

The patients had positive SARS-CoV-2 antigen titers (mean 3305.7, range 12.9-20912). All 11 patients were treated with remdesivir and dexamethasone, and 5 (45.5%) also received sotrovimab. Pathogenic bacteria, including *Haemophilus influenzae*, *Staphylococcus aureus*, and Enterobacteriaceae, were isolated from 7 of 11 (63.6%) patients, and all 11 patients were treated with antibiotics, such as meropenem, sulbactam/ampicillin, tazobactam/piperacillin, lascufloxacin, linezolid, and cefepime. Only 3 of 11 (27.3%) patients were managed using extracorporeal membrane oxygenation (ECMO), and all of these 3 patients were ≤64 years of age; the other 8 patients were ≥65 years of age. Ultimately, 9 of 11 (81.8%) patients survived, and the 2 non-surviving patients did not have a clear vaccination history.

In this study, only 11 COVID-19 patients (4.2%) received ventilator management. It has been reported that approximately 20% of hospitalized patients with COVID-19 had severe symptoms necessitating intensive care, such as ventilator management, in the original strain era [7]. Therefore, the present data suggest that the omicron variants were less pathogenic, compared with the original variants previously reported [6, 7]. Most patients requiring ventilator management were elderly men, and they were managed in the emergency department because they had severe underlying diseases, especially neurological diseases.

COVID-19 and neurological damage are well known because neurons and glial cells express angiotensin-converting enzyme 2 (ACE2) receptors, which are the receptors for the virus, and recent studies suggest that activated glial cells contribute to neuroinflammation and the devastating effects of SARS-CoV-2 infection on the CNS [8]. These mechanisms might also be responsible for the severe status of COVID-19 patients requiring ventilator management. In addition, a clear vaccine history was found in only 4 (36.4%) patients, which was extremely low, because more than 80-90% of people had already been vaccinated in Japan [9], and this suggested the importance of the vaccine to prevent severe and symptomatic COVID-19 [4, 10].

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Table 1. Clinical characteristics of 11 adult COVID-19 received with ventilator management

	Age	M/F	Ward	Underlying diseases	Vaccine	Ag titer	Bacteria	Antivirals	Antibiotics	Steroid	NAb	ECMO	Survive/Death
1	72	M	ER	COPD,	Unknown	190	Hi	RDV	MEPM	Dex	STV	None	S
2	76	M	ER	COPD,	Unknown	42.7	Hi, Ef	RDV	LSFX	Dex	None	None	S
3	79	M	SCU	Parkinson Dis	Unknown	670	None	RDV	SBT/ABPC	Dex	None	None	Death
4	81	M	ER	Nursing home	5	3457	None	RDV	SBT/ABPC	Dex	STV	None	S
5	76	M	ER	CKD	6	2916	MSSA, Kp	RDV	MEPM	Dex	STV	None	S
6	72	M	ER	ALS	6	20912	E coli	RDV	MEPM	Dex	STV	None	S
7	55	M	ER	Brain tumor	3	15,4	MSSA	RDV	TAZ/PIP	Dex	None	Positive	S
8	85	M	ER	CHD	None	4809	None	RDV	SBT/ABPC	Dex	None	None	Death
9	51	F	ER	Conversion	Unknown	19.2	MRSA	RDV	LZD	Dex	STV	Positive	S
10	54	M	ER	None	None	28.3	None	RDV	TAZ/PIPC	Dex	None	Positive	S
	Age	M/F	Ward	Underlying diseases	Vaccine	Ag titer	Bacteria	Antivirals	Antibiotics	Steroid	NAb	ECMO	Survive/Death

Abbreviations: M/F: male/female, ER: emergency department, SCU: stroke intensive care unit, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, ALS: amyotrophic lateral sclerosis, CHD: chronic heart disease, HD: hemodyalysis, Hi: Haemophilus influenzae, Ef: enterococcus faecalis, MSSA: methicillin susceptible Staphylococcus aureus, Kp: Klebsiella pneumoniae, MRSA: methicillin resistance Staphylococcus aureus, RDV: remdesivir, MEPM: meropenem, LVFX: levofloxacin, SBT/ABPC: sulbactam/ampicillin, TAZ/PIPC: tazobactam/piperacillin, LZD: linezolid, CFPM: cefepime, Dex: dexamethasone, N ab: neutralizing antibody, STV: sotrovimab, ECMO: extracorporeal membrane oxygenation, S: survive

The patients showed high viral titers and positive results on pathogenic bacteria isolation from the sputum. COVID-19 patients did not usually develop secondary bacterial pneumonia, and only 3 to 5% were reported with the original strain, although 33 to 99% of influenza cases developed bacterial pneumonia [11-13]. These data were also characteristic of the omicron variants in COVID-19 patients. Omicron variant were less pathogenic, but aspiration pneumonia might become common in elderly patients, and most patients received not only antiviral agents, but also antibiotics according to the isolated bacteria, which were similar to those of community-acquired and hospital-acquired pneumonia [14-16]. Patients treated with ventilator management received RDV and steroid treatment. This regimen might be suitable according to the guidelines for severe COVID-19 patients [1, 17]. Furthermore, the patients also received sotrovimab, neutralizing antibody, and recently its poor effectiveness was reported [1, 17]; however, this agent was used adjunctively because sotrovimab has been reported to have additional effects to activate immunological systems, such as lymphocytes and the complement cascade [18]. Three (27.3%) patients were ≤64 years of age, and they were all managed using ECMO and survived; these data suggest the effectiveness of ECMO in severe COVID-19, as previously suggested [17].

Finally, 9 (81.8%) patients survived. The 2 (19.2%) non-surviving patients were very old and had severe underlying diseases, but did not have a clear vaccine history. This mortality rate was very high compared with the 0.1% reported for common COVID-19 patients in the omicron variant era, and 8-9% for all hospitalized patients that we previously reported [9]. These data also suggest the importance of vaccination for elderly people with underlying diseases.

In conclusion, the characteristics of severe COVID-19 patients treated with ventilator management were identified and analyzed. There was a predominance of male, less-vaccinated elderly patients with underlying disease. These patients were treated successfully using antiviral agents, steroid, neutralizing antibody, and antibiotics. ECMO was also successfully used for younger patients. Vaccine status might be a very important factor for survival although the patients were infected with the omicron variant.

Contributions:

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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