



Severe Influenza Patients Who Received Ventilator Management During the 2024 to 2025 Major Influenza-Endemic Season in a Tertiary Hospital in Japan

Masafumi Seki ¹, Daishi Shimada ²

¹Division of Infectious Diseases and Infection Control, Saitama Medical University International Medical Center, Hidaka City, Japan; ²Division of Respiriology, Tohoku Medical and Pharmaceutical University, Sendai City, Japan

Correspondence: Masafumi Seki, Division of Infectious Diseases and Infection Control, Saitama Medical University International Medical Center, Yamane, 1397-1, Hidaka City, Saitama, 350-1298, Japan, Tel +81-42-984-4392, Fax +81-42-984-0280, Email sekimm@saitama-med.ac.jp

Abstract: Three cases of severe influenza that required ventilator management in the 2024–2025 season, which was a major influenza season in Japan, are presented. Case 1: A 54-year-old man with obesity developed lobar pneumonia as a result of severe community-acquired pneumonia (CAP) secondary to methicillin-susceptible *Staphylococcus aureus* (MSSA), as confirmed on sputum culture. The nasal swab was positive for influenza A antigen. Intravenous peramivir and piperacillin/tazobactam were administered for 2 days followed by lascufloxacin and linezolid for 2 weeks. Veno-venous extracorporeal membrane oxygenation (VV-ECMO) was also performed. Case 2: A 63-year-old man with multiple myeloma and chronic kidney disease developed severe pneumonia as a result of CAP. Although influenza A antigen was detected, no bacteria were isolated from his specimens. He showed severe hypoxia and massive ground-glass opacities (GGOs) in both lung fields, but he recovered after administration of peramivir and levofloxacin with prednisolone for 2 days and 2 weeks, respectively, with non-invasive positive pressure support. Case 3: A 43-year-old man without any related medical history developed severe heart failure with mild bronchopneumonia and was admitted to our hospital. Acute heart failure caused by myocarditis and CAP due to influenza A were suspected and treated effectively with peramivir and a percutaneous ventricular assist device (IMPELLA), which involved an auxiliary circulating pump with veno-arterial ECMO (VA-ECMO) for 1 day and 2 weeks, respectively. In three middle-aged patients, influenza virus may have accelerated pneumonia/heart failure. All three patients had not received influenza vaccines and were not elderly. Although the emphasis on most vaccines has decreased after the COVID-19 pandemic appears to have subsided, we should stress the importance of influenza vaccines and improvement of critical care protocols, because severe influenza can be a concern for young and middle-aged adults during the influenza season after the post COVID-19 pandemic period.

Keywords: influenza, peramivir, extracorporeal membrane oxygenation, ECMO, myocarditis, pneumonia, vaccine

Introduction

Influenza has had an enormous impact on societies worldwide. It causes an acute febrile illness with malaise and respiratory failure and is sometimes lethal in elderly patients and/or patients with underlying diseases if the bronchitis develops into pneumonia.¹

There are two types of influenza-related pneumonia:^{2,3} bacterial pneumonia and pure viral pneumonia. The former type is induced by co-infected or secondarily infected bacteria, including *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*.^{3–5} Affected patients show lobar and massive pneumonia and are treated not only using antiviral agents, but also antibiotics. The latter type is induced by virus alone and shows massive ground-glass opacities (GGOs); it is usually treated by antiviral agents plus corticosteroids.³ Pulmonary edema may be frequently

observed, combined with lung inflammation and cell damage.^{6,7} Both types of influenza-related pneumonia are difficult to manage when severe respiratory failure develops, and patients sometimes require ventilator management.

In addition, influenza can also cause a viral myocarditis, and the patients show secondary respiratory symptoms due to acute heart failure.^{8,9} Cardiovascular complications are the second most common cause of death due to influenza, and direct myocardial injury by the influenza virus and host cell immunity, such as increased expressions of trypsin, matrix metalloproteinases, and cytokines, such as tumor necrosis factor (TNF), are thought to be the cause of influenza myocarditis and its complications, but the pathogenesis is still largely unknown.⁹

However, the severe acute respiratory syndrome coronavirus 2/coronavirus disease 2019 (SARS-CoV-2/COVID-19) pandemic period from 2020 to 2023 led to significant reductions in influenza detection worldwide, fueling debates on whether influenza truly ceased circulating in communities.^{10,11} The number of influenza cases decreased significantly in Japan, raising concerns about the potential risk of decreased immunity to influenza in the population; an increase of not only the number of all influenza patients, but also of the number of severe to extremely severe influenza patients, including those hospitalized and who received intensive care after the post COVID-19 pandemic period, was also suggested.^{10–12}

In fact, in the 2023–2024 season, we saw a very large number of influenza patients (18,240,000 patients, of whom 19,389 were hospitalized), although there were only 4,850,000 patients and 3582 hospitalized patients in the 2022–2023 season in Japan.¹² Furthermore, there was a rapid increase in the number of influenza patients in the 2024–2025 season, and it was not possible to admit severe patients because of the insufficient number of hospital beds.¹⁰

In this study, three representative severe influenza patients who received ventilator management due to severe respiratory failure in the 2024–2025 season in Japan are presented. Of the many infected patients during the influenza season after the COVID-19 pandemic,¹⁰ they developed secondary bacterial pneumonia, pure viral pneumonia, and viral myocarditis, respectively.

This study and related analyses were approved by the Institutional Review Board of Saitama Medical University International Medical Center on July 6 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. Institutional approval was not required to publish the case details.

Case Series

Case 1

A 54-year-old man presented to the emergency department in December 2024 with dyspnea and high fever accompanied by extreme fatigue that had persisted for 2 days. He had no specific medical history, but had obesity (height: 169.0 cm, weight: 90.7 kg, body mass index: 31.76 kg/m²). On physical examination, his temperature was 38.3 °C, blood pressure was 86/50 mmHg, respiratory rate was 30 breaths/min, and his consciousness level was E3V3M4 on the Glasgow Coma Scale on admission (Day 0). There were crackles (rhonchi) over the right lung field, and the chest X-ray showed infiltrative shadows (Figure 1A and B). His initial white blood cell (WBC) count was 21,700/L, and C-reactive protein (CRP) was 11.58 mg/dL.

The rapid antigen test for influenza A was positive on Day 0. He had not received the influenza vaccine for the current season. *Staphylococcus aureus* was identified in his sputum and blood culture on Day 2, and it was found to be methicillin-susceptible *Staphylococcus aureus* (MSSA); the minimum inhibitory concentration (MIC) according to the Clinical and Laboratory Standards Institute criteria showed susceptibility to levofloxacin (LVFX), piperacillin (PIPC), ciprofloxacin (CPFX), and ampicillin/sulbactam (ABPC/SBT) on Day 3. Thus, influenza virus-related secondary bacterial pneumonia due to MSSA was diagnosed.

After tracheal intubation and the start of ventilator management on Day 0, he was treated with intravenous peramivir 300 mg daily and piperacillin/tazobactam (PIPC/TAZ) 4.5 g every 8 hours for 2 days, but the chest X-ray and inflammatory findings did not improve. Therefore, on Day 3, the antibiotic regimen was changed to lascefloxacin 300 mg once on the first day, followed by 150 mg once daily and linezolid 600 mg every 12 hours daily for 2 weeks.

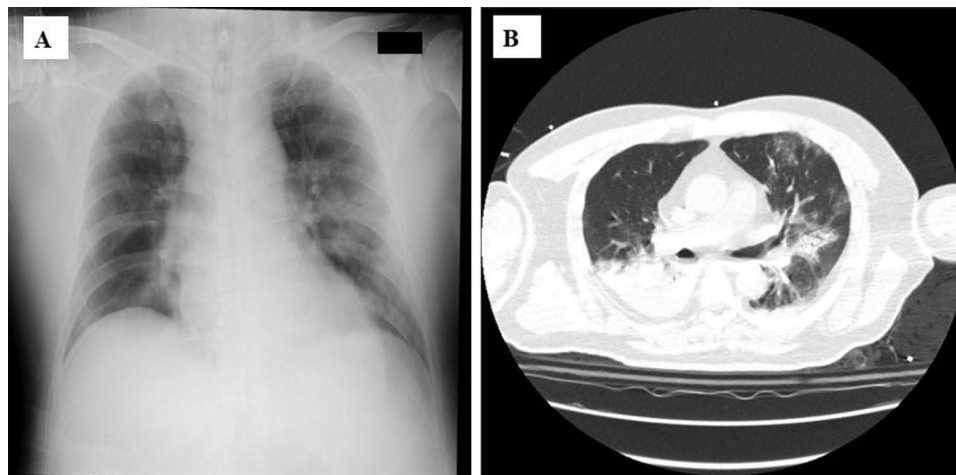


Figure 1 Chest X-ray (A) and computed tomography (B) on admission (Day 0) of Case 1.

Veno-venous extracorporeal membrane oxygenation (VV-ECMO) was also started. He eventually recovered on Day 14 and was moved to the general ward.

Case 2

A 63-year-old man with a history of multiple myeloma and suspected chronic kidney disease developed pneumonia and was admitted to our hospital 3 days after a nasal swab was positive for influenza A antigen in December 2024 (Day -3). He had not received the influenza vaccine for the current season. On physical examination on admission (Day 0), his temperature was 38.1 °C, blood pressure was 102/67 mmHg, respiratory rate was 32 breaths/min, he appeared dehydrated, and fine crackles were heard over both lung fields. Chest X-rays showed GGOs in both lung fields (Figure 2A and B). Oxygen saturation was 88% on O₂ at 15 L/min by face mask. His initial WBC count was 2,570 cells/L, and CRP was 5.992 mg/dL. No bacteria were isolated from blood cultures or respiratory specimens until Day 2.

He was diagnosed as having pure influenza-related viral pneumonia and placed on non-invasive positive pressure ventilation from Day 0, and his oxygenation improved. The administration of intravenous peramivir at a dosage of 300 mg once daily for 2 days from Day 0, followed by a regimen of LVFX 500 mg once daily combined with prednisolone 125 mg once daily for 14 days, resulted in significant improvement in both chest X-ray findings and pneumonia symptoms.

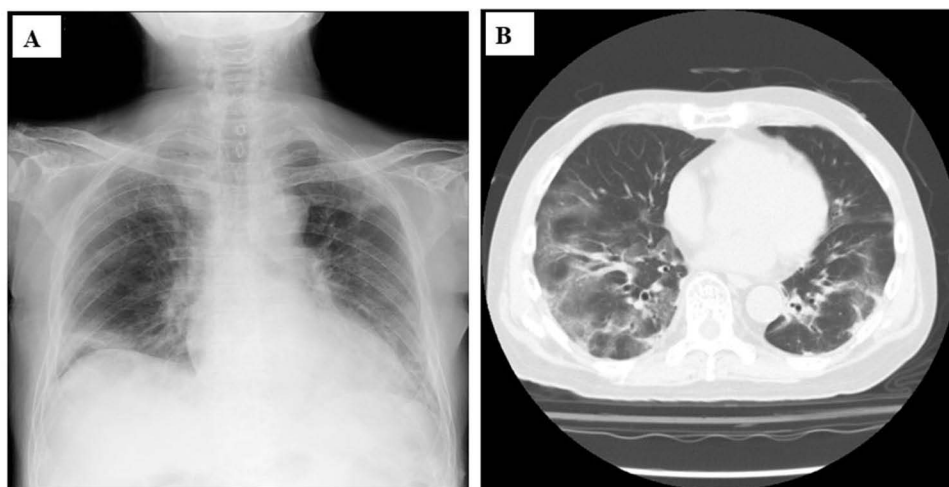


Figure 2 Chest X-ray (A) and computed tomography (B) on admission (Day 0) of Case 2.

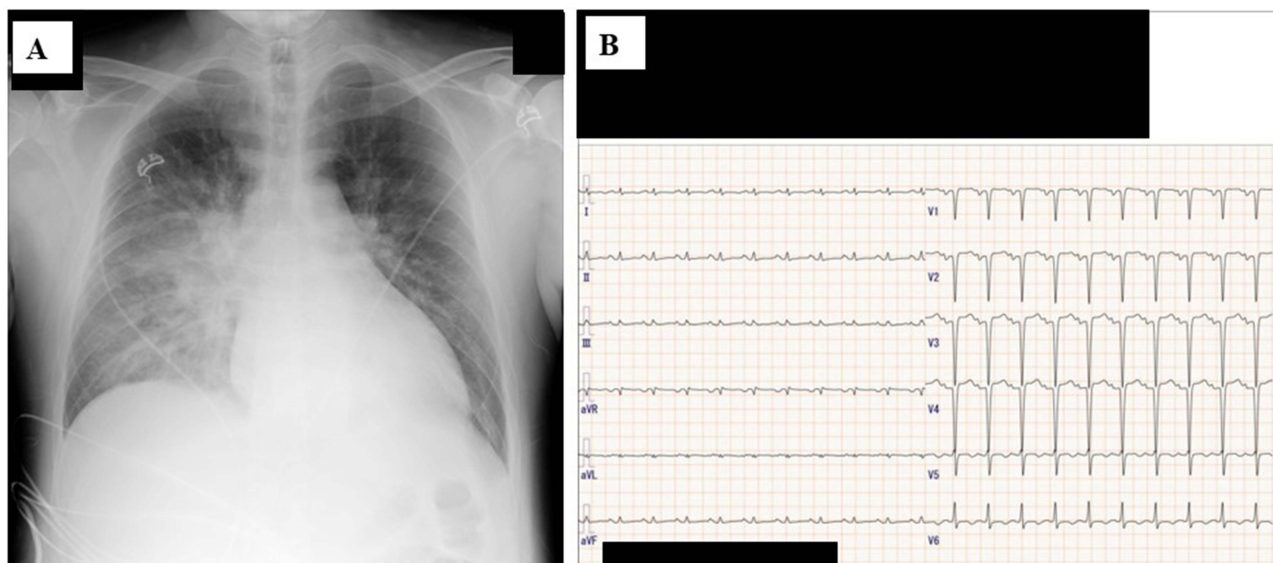


Figure 3 Chest X-ray (A) and electrocardiography (B) on admission (Day 0) of Case 3.

Case 3

A 43-year-old man with no prior history was admitted to the emergency department in December 2024 due to dyspnea and disturbed consciousness. On physical examination on admission (Day 0), his temperature was 39.1 °C, respiratory rate was 26 breaths/min, and blood pressure was 82/54 mmHg. There were coarse crackles over both lung fields, and oxygen saturation was 90% on O₂ at 5 L/min by mask. Chest X-rays showed bronchopneumonia, but the electrocardiogram showed low voltage (Figure 3A and B). Echocardiography showed poor cardiac movement. His initial WBC count was 6,700/L, and CRP was 8.441 mg/dL. Although no bacteria were isolated from blood cultures or respiratory specimens until Day 2, the nasal swab was positive for influenza A antigen on Day 0. He had not received the influenza vaccine for the current season.

Thus, influenza virus-related myocarditis was suspected, and from Day 0, he received intravenous peramivir 300 mg once daily for 1 day and a percutaneous ventricular assist device (IMPELLA), which was an assisted auxiliary circulating pump with veno-arterial ECMO (VA-ECMO) for 2 weeks (Day 14). He eventually recovered and was moved from the intensive care unit to the general ward one month (Day 28) after admission.

Discussion

Despite major efforts for prevention and treatment, influenza A virus infection accounts for significant morbidity and mortality,^{13,14} which have been attributed to the development of respiratory and cardiac complications, including pneumonia and myocarditis.

In this report, three cases of severe influenza-related complications, including one case of secondary bacterial pneumonia, one case of pure viral pneumonia, and one case of myocarditis that received ventilator management due to hypoxia, were described and compared (Table 1). All three patients had not received influenza vaccines and were not elderly, but middle-aged men. These cases were all found in one season and hospitalized during the same period, although each case occurred sporadically.

Influenza has become a major issue again after the COVID-19 pandemic period because it re-appeared from the 2023–2024 season, although it seemed to have disappeared from 2020 to 2023 during the COVID-19 pandemic period in Japan.¹⁵ In addition, in the 2024–2025 season, an influenza-endemic period was also identified, and many patients were hospitalized in Japan.^{10,16} Influenza is usually known to result in severe disease due to complications, including pneumonia and heart failure, and the patients are hospitalized. Such hospitalized patients have usually been elderly

Table 1 Comparison of the Three Cases of Severe Influenza-Related Pneumonia and Myocarditis That Received Ventilator Management

	Case 1	Case 2	Case 3
Category	Secondary bacterial pneumonia	Pure viral pneumonia	Myocarditis
Age/Sex	54/Male	63/Male	43/Male
Comorbidity	Obesity	MM, CKD	None
Chest X-ray	Lobar/Nodules	GGO	Bronchopneumonia
Shock	Yes	No	Yes
Respirator	Intubated/VV-ECMO	NIPPV	Intubated/IMPELLA/VA-ECMO
WBC (cells/L)	21,700	2,570	6700
CRP (mg/dL)	11.58	5.992	8.441
Influenza type	A	A	A
Bacteria	MSSA	None	None
Influenza vaccine	None	None	None
30-day Survival	Survived	Survived	Survived

Notes: Bold font indicates particular findings.

persons, more than 65 years old, but severe cases, such as fatal cases, might not be elderly but relatively young adults.^{17,18}

The recent prospective, multicenter, cohort study in Japan via internet surveillance also showed that patients who did not survive had an age ranging from the thirties to the sixties with comorbidities, including pregnancy, chronic renal failure with hemodialysis, and collagen diseases.¹⁷ Surprisingly, patients without underlying diseases were also included among patients who did not survive.^{17,18} Obesity was also found to be one of the risk factors on multivariate analysis. These data suggested that complications of influenza infection remain a heavy burden, especially for elderly patients, but severe complications of influenza that require hospitalization may occur in a certain proportion of patients with no risk factors. Efforts are needed to diagnose and treat influenza appropriately, even in previously healthy younger patients.

In the post COVID-19 pandemic period, there was increased concern because there were larger numbers of influenza cases and hospitalized patients in the 2023–2024 season and the 2024–2025 season than in 2020 to 2023 because of the suggested decreased immunity to influenza in the population. In this situation, there would be some severe and extremely severe influenza cases.^{10–12} Pure viral pneumonia and myocarditis patients, similar to Cases 2 and 3, are usually very rare, but decreased immunity and the related huge and rapid increase of influenza cases might have led to the appearance of the pure viral pneumonia and myocarditis patients in the 2024–2025 season. Broader and more appropriate surveillance is needed for young adult patients in the influenza season of the post COVID-19 period.

In addition, all three patients in the present report had not received influenza vaccination for the current strains. Vaccinations are obviously effective for preventing hospitalization and death by influenza infection.^{19,20} Not only immunosuppressed patients and elderly persons, but relatively young adults can develop severe influenza.²¹ In Japan, the influenza vaccination rate changed during the COVID-19 pandemic because of negative factors, such as “allergy and pain”, “COVID-19 vaccine hesitancy”, and “rumors from social media, including infection from the vaccines”.^{22,23} We should increase vaccination rates by providing appropriate information about influenza vaccines to young persons.

Furthermore, VV or VA-ECMO was used for two of the three present patients. The respiratory status and oxygenation of these two patients deteriorated even though they were intubated and received ventilator management. No specific biomarker for the implementation of VV/VA-ECMO was identified from these two cases, but both patients started VV/VA-ECMO on Days 0 and 3 and finally survived. These data suggest that early implementation of VV/VA-ECMO and intensive care unit (ICU) management might be associated with a better prognosis, as previously reported from other countries.^{24,25}

In conclusion, severe influenza cases that required ventilator management in one season and were hospitalized during the same period, although they occurred sporadically, were presented. Each patient showed different types of severe

influenza complications, including secondary bacterial pneumonia, pure viral pneumonia, and myocarditis. All three patients were not elderly, but they had not received the latest influenza vaccination, which suggested vaccine hesitancy, though post-COVID-19 immunity might have been decreased. Two of three patients did not have any underlying diseases, but they developed severe diseases. Appropriate care and more detailed surveillance will be required not only for elderly persons with comorbidities, but also for young healthy adults during the influenza-endemic season.

Author 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.

Disclosure

The authors report no conflicts of interest in this work.

References

- Mauad T, Hajjar LA, Callegari GD, et al. Lung pathology in fatal novel human influenza A (H1N1) infection. *Am J Respir Crit Care Med*. 2010;181(1):72–79. doi:10.1164/rccm.200909-1420OC
- Louria DB, Blumenfeld HD, Ellis JT, Ilbourn ED, Rogers DE. Studies on influenza in the pandemic of 1957-1958. II. Pulmonary complications of influenza. *J Clin Invest*. 1959;21(1–2):213–265. doi:10.1172/JCI1103791
- Almond MH, McAuley DF, Wise MP, Griffiths MJ. Influenza-related pneumonia. *Clin Med Lond*. 2012;12(1):67–70. doi:10.7861/clinmedicine.12-1-67
- Seki M, Yanagihara K, Higashiyama Y, et al. Immunokinetics in severe pneumonia due to influenza virus and bacteria coinfection in mice. *Eur Respir J*. 2004;24(1):143–149. doi:10.1183/09031936.04.00126103
- Seki M, Fuke R, Oikawa N, Hariu M, Watanabe Y. Association of influenza with severe pneumonia/empyema in the community, hospital, and healthcare-associated setting. *Respir Med Case Rep*. 2016;24:1.
- Seki M, Kohno S, Newstead MW, et al. Critical role of IL-1 receptor-associated kinase-M in regulating chemokine-dependent deleterious inflammation in murine influenza pneumonia. *J Immunol*. 2010;184(3):1410–1418. doi:10.4049/jimmunol.0901709
- Fujita J, Ohtsuki Y, Higa H, et al. Clinicopathological findings of four cases of pure influenza virus A pneumonia. *Intern Med*. 2014;53(12):1333–1342. doi:10.2169/internalmedicine.53.1174
- Ammirati E, Moslehi JJ. Diagnosis and Treatment of Acute Myocarditis: a Review. *JAMA*. 2023;329(13):1098–1113. doi:10.1001/jama.2023.3371
- Baral N, Adhikari P, Adhikari G, Karki S. Influenza Myocarditis: a Literature Review. *Cureus*. 2020;12(12):e12007. doi:10.7759/cureus.12007
- WHO. *FluNet*. 2025. Available from: <https://www.who.int/tools/flunet>.
- Takahashi H, Nagamatsu H, Yamada Y, et al. Surveillance of seasonal influenza viruses during the COVID-19 pandemic in Tokyo, Japan, 2018–2023, a single-center study. *Influenza Other Respir Viruses*. 2024;18(1):e13248. doi:10.1111/irv.13248
- Japan Institute for Health Security. Influenza 2023–2024 season in Japan. *IASR*. 2024;45(11):179–181.
- Glezen WP, Greenberg SB, Atmar RL, Piedra PA, Couch RB. Impact of respiratory virus infections on persons with chronic underlying conditions. *JAMA*. 2000;283(4):499–505. doi:10.1001/jama.283.4.499
- Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza. *Clin Infect Dis*. 2019;68(6):895–902. doi:10.1093/cid/ciy874
- Lee SS, Viboud C, Petersen E. Understanding the rebound of influenza in the post COVID-19 pandemic period holds important clues for epidemiology and control. *Int J Infect Dis*. 2022;122:1002–1004. doi:10.1016/j.ijid.2022.08.002
- Fukuda Y, Ogashi A, Hirakawa S, et al. Resurgence of human metapneumovirus infection and influenza after three seasons of inactivity in the post-COVID-19 era in Hokkaido, Japan, 2022-2023. *J Med Virol*. 2023;95(12):e29299. doi:10.1002/jmv.29299
- Ishida T, Seki M, Oishi K, et al. Clinical manifestations of adult patients requiring influenza-associated hospitalization: a prospective multicenter cohort study in Japan via internet surveillance. *J Infect Chemother*. 2021;27(3):480–485. doi:10.1016/j.jiac.2020.10.021
- Ishida T, Seki M, Oishi K, et al. Clinical manifestations of hospitalized influenza patients without risk factors: a prospective multicenter cohort study in Japan via internet surveillance. *J Infect Chemother*. 2022;28(7):853–858. doi:10.1016/j.jiac.2022.02.001
- Seki M. Strategies for Geriatric Pneumonia in Healthcare Facilities -How Effective is Combined Influenza and Pneumococcal Vaccination? *Int J Gene Med*. 2020;13:663–666. doi:10.2147/IJGM.S264835
- Bosaed M, Kumar D. Seasonal influenza vaccine in immunocompromised persons. *Hum Vaccin Immunother*. 2018;14(6):1311–1322. doi:10.1080/21645515.2018.1445446
- Frutos AM, Price AM, Harker E, et al. CDC Influenza Vaccine Effectiveness Collaborators. Interim Estimates of 2023–24 Seasonal Influenza Vaccine Effectiveness - United States. *MMWR Morb Mortal Wkly Rep*. 2024;73(8):168–174. doi:10.15585/mmwr.mm7308a3
- Shojima K, Kobayashi T, Tabuchi T. Impact of COVID-19 Pandemic on the Influenza Vaccination and Predictors of Influenza Vaccination in Japan: a Cross-sectional Study. *J Public Health Manag Pract*. 2023;29(5):701–707. doi:10.1097/PHH.0000000000001755
- Goodwin R, Ben-Ezra M, Takahashi M, et al. Psychological factors underpinning vaccine willingness in Israel, Japan and Hungary. *Sci Rep*. 2022;12(1):439. doi:10.1038/s41598-021-03986-2

24. Buchner J, Mazzeffi M, Kon Z, et al. Single-Center Experience With Venovenous ECMO for Influenza-Related ARDS. *J Cardiothorac Vasc Anesth.* 2018;32(3):1154–1159. doi:10.1053/j.jvca.2017.09.031
25. Steimer DA, Hernandez O, Mason DP, Schwartz GS. Timing of ECMO Initiation Impacts Survival in Influenza-Associated ARDS. *Thorac Cardiovasc Surg.* 2019;67(3):212–215. doi:10.1055/s-0038-1642066

International Medical Case Reports Journal

Dovepress
Taylor & Francis Group

Publish your work in this journal

The International Medical Case Reports Journal is an international, peer-reviewed open-access journal publishing original case reports from all medical specialties. Previously unpublished medical posters are also accepted relating to any area of clinical or preclinical science. Submissions should not normally exceed 2,000 words or 4 published pages including figures, diagrams and references. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-medical-case-reports-journal-journal>