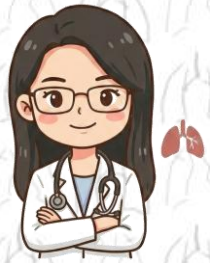
流感重症

中國附醫
胸腔暨重症系
郭育筑



Severe influenza

- **流感病毒造成的嚴重疾病**
  - 敗血症、敗血性休克
  - 嚴重肺炎、急性呼吸窘迫症候群
  - 多重器官衰竭
  - 慢性疾病急性發作
- 以至於需要住院或加護醫療

- 成人流感住院病患的死亡率約4-8%，在流行期間或免疫低下患者約10-15%。
- 5-10%的流感病人會需要住加護病房，死亡率約20%

Clinical practice guideline for influenza, WHO, 2024
Gao Y, Guyatt G, Uyeki TM, et al. *Lancet*. 2024; 404: 753–63

流感併發重症

- **臨床條件**
  - 出現類流感症狀**後兩週內**因併發症（如肺部併發症、神經系統併發症、侵襲性細菌感染、心肌炎或心包膜炎等）而**需加護病房治療**或死亡者。
- **檢驗條件**（具有下列任一個條件）：
  - 呼吸道臨床檢體（咽喉擦拭液等）分離並鑑定出流感病毒。
  - 臨床檢體分子生物學核酸檢測陽性。
  - 臨床檢體抗原檢測陽性。
  - 臨床檢體血清學抗體檢測陽性：急性期與恢復期流感病毒血清抗體效價≧4 倍上升。
- **流行病學條件**
  - 曾經與經實驗室證實之確定病例具有密切接觸，即照護、同住、或與其呼吸道分泌物、體液之直接接觸。

TW CDC

WHO is at RISK?

- At risk
  - **Age 65 years** or more
  - **Immunocompromising conditions**
  - Cardiovascular disease
  - Neurological disease
  - Chronic respiratory disease
- High risk
  - **Age 85 years** or more
  - Any age + **multiple major risk factors**

Table 4. Persons Who Are at High Risk of Complications From Influenza

Persons at High Risk of Complications
Children aged <5 years, and especially aged <2 years
Adults aged ≥65 years
Persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematologic (including sickle cell disease), or metabolic disorders (including diabetes mellitus) or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury)
Persons with immunosuppression, including that caused by medications or by HIV infection[a]
Women who are pregnant or postpartum (within 2 weeks after delivery)
Children and adolescents through 18 years who are receiving aspirin- or salicylate-containing medications and who might be at risk for experiencing Reye syndrome after influenza virus infection
American Indian/Alaska Native people[b]
Persons with extreme obesity (ie, body mass index ≥40 kg/m^2)
Residents of nursing homes and other chronic care facilities

Clinical practice guideline for influenza, WHO, 2024
IDSA, 2018

Diagnosis

- **流感快速診斷測試 (Rapid Influenza Diagnostic Test, RIDT)**：特異性很高，但如果重症風險高的病人驗出陰性，必須警惕 RIDT 的低敏感度，此時應考慮補做核酸檢測。
- **核酸擴增檢測(Nucleic Acid Amplification Test, NAAT)/PCR**：高敏感度、高特異性，但需要的檢驗時間較久。
  - 若超過24小時報告才會出來，需合併嚴重度考慮是否要在報告出來前就治療。
- 若為**免疫抑制病患**則建議做**大病原菌套組**，不要只單做流感檢驗。
- 症狀小於四天常在上呼吸道可驗出，但若症狀大於四天且有下呼吸道症狀，可能要在下呼吸道才驗得出來。

Clinical practice guideline for influenza, WHO, 2024
IDSA, 2018

Management

- Antiviral treatment.
- Supportive and symptomatic care.

Clinical practice guideline for influenza, WHO, 2024
IDSA, 2018

Antiviral treatment

- 在重症患者，即使發病超過48小時，給予抗病毒藥物仍然有臨床效益。

- **免疫抑制**或**重症患者**可考慮延長抗病毒藥物時間。
  - 流感病毒的複製和排除時間常常會延長。
  - 尤其是肺炎或急性呼吸窘迫症患者。
  - 可用再次檢驗來評估停藥時機。

Clinical practice guideline for influenza, WHO, 2024
IDSA, 2018

	Oseltamivir	**Peramivir**	Zanamivir	Baloxavir
使用方式	PO	IV	INH	PO
劑量	75mg BID	300mg QD	重症不建議使用	40mg STAT
療程	5天	1-5天		單次
臨床益處	縮短住院天數	縮短住院天數		重症研究尚不多
注意事項	腎功能不佳需調整劑量	腎功能不佳需調整劑量		
缺點	吸收不佳 不適合	需自費		

台灣感染症醫學會 抗流感病毒藥物使用建議 2024

Lancet. 2024; 404: 753–63

Antivirals for treatment of severe influenza: a systematic review and network meta-analysis of randomised controlled trials

Ya Gao, Gordon Guyatt, Timothy M Uyeki, Ming Liu, Yamin Chen, Yunli Zhao, Yanjiao Shen, Jianguo Xu, Qingyong Zheng, Zhifan Li, Wanyu Zhao, Shuyue Luo, Xiaoyan Chen, Jinhui Tian, Qiukui Hao

	Study results and measurements	Absolute effect estimates, mean duration in days	Mean difference (95% CI)	Certainty in effect estimates	Summary
Oseltamivir *vs* standard care or placebo	The lower the duration of hospitalisation, the better the result; based on data from 104 participants in two studies	3·37 *vs* 5·00	−1·63 (−2·81 to −0·45)	Low*†	Oseltamivir might reduce duration of hospitalisation
Peramivir *vs* standard care or placebo	The lower the duration of hospitalisation, the better the result; based on indirect evidence	3·27 *vs* 5·00	−1·73 (−3·33 to −0·13)	Low*†	Peramivir might reduce duration of hospitalisation
Oseltamivir *vs* peramivir	The lower the duration of hospitalisation, the better the result; based on data from 122 participants in one study	3·37 *vs* 3·27	0·10 (−0·98 to 1·18)	Low*†	There might be little or no difference between oseltamivir and peramivir for duration of hospitalisation

GRADE=Grading of Recommendations Assessment, Development and Evaluation. *Rating decreased by one level for risk of bias. †Rating decreased by one level for imprecision.

Table 3: GRADE summary of findings for duration of hospitalisation for different comparisons

Lancet. 2024; 404: 753–63

ORIGINAL

Corticosteroid treatment in critically ill patients with severe influenza pneumonia: a propensity score matching study

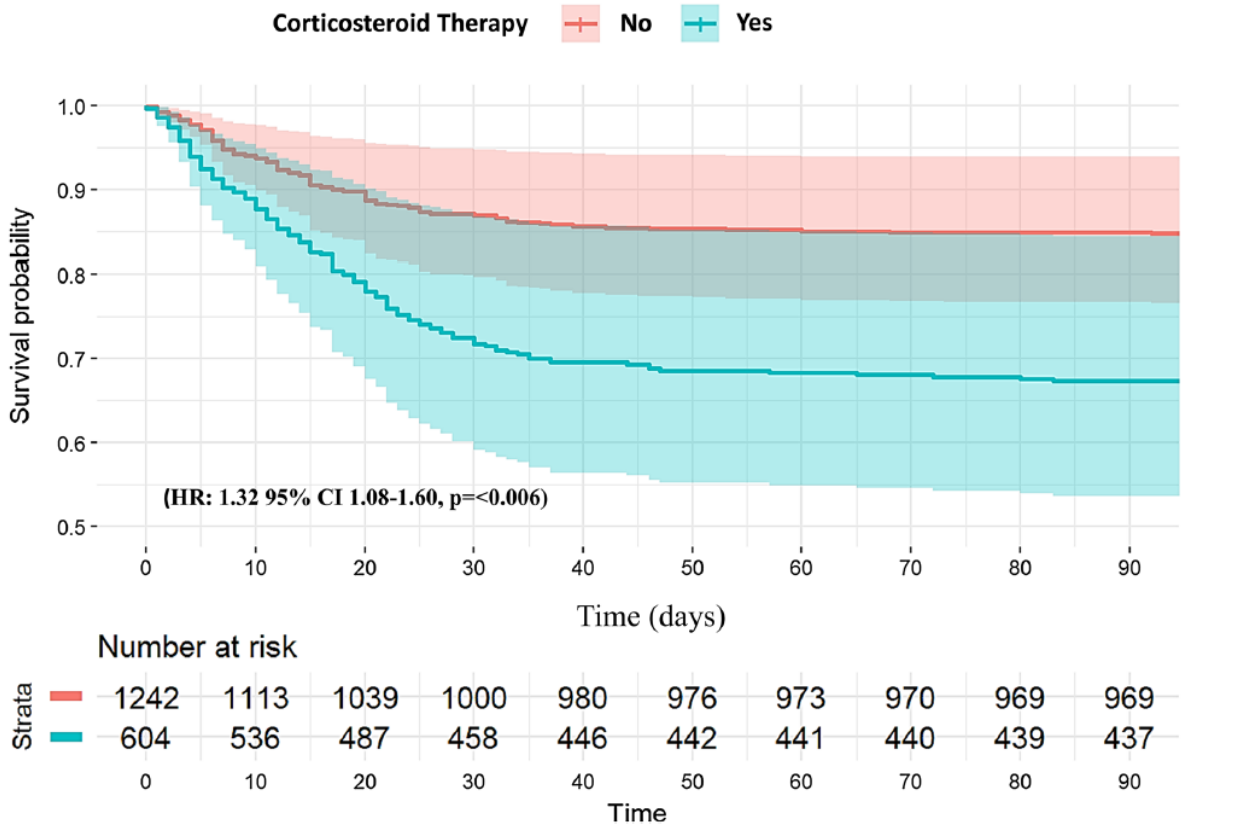


Fig. 3 Cox regression survival plot during ICU admission according to corticosteroid therapy

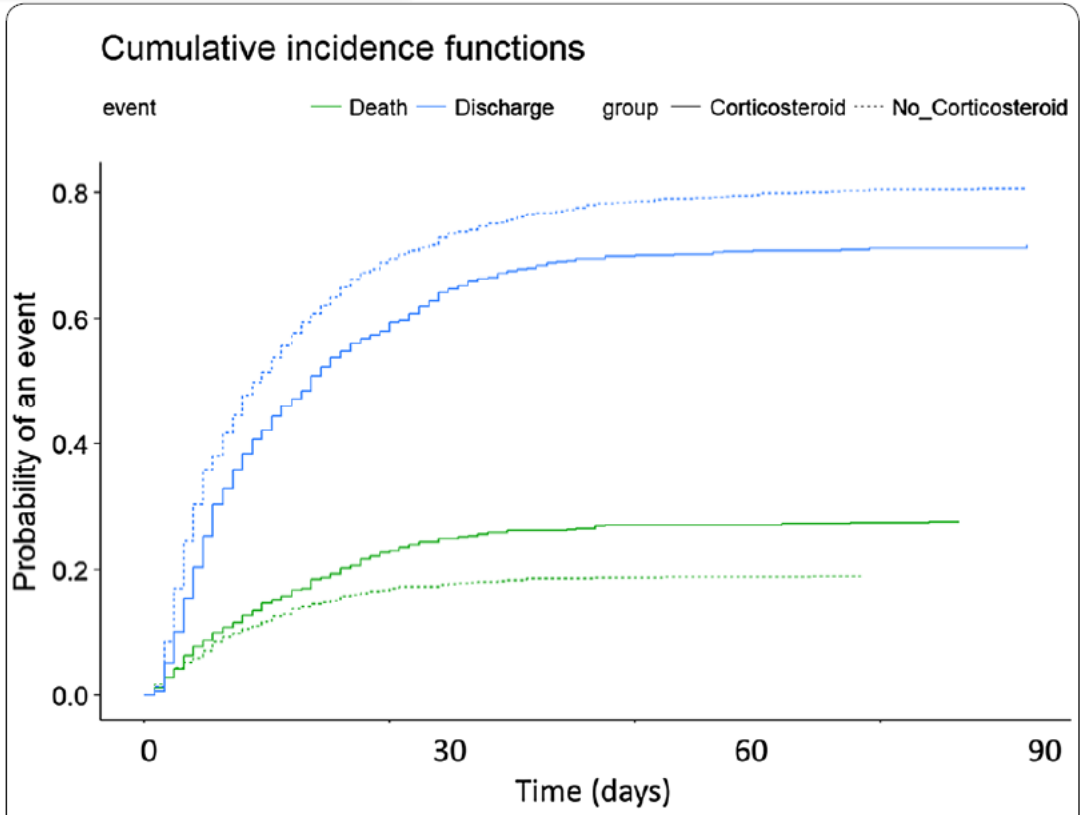


Fig. 4 Cumulative incidence function of ICU death and being discharged alive according to corticosteroid therapy

Intensive Care Med (2018) 44:1470–1482

Corticosteroid

- **Avoid**
- **除非有其他臨床需求**
  - 氣喘急性發作
  - COPD
  - Adrenal insufficiency
  - Refractory septic shock
- 對於hospital day、呼吸器需求、mortality未見到好處
- 可能會延長influenza viral shedding、增加次發性感染

Clinical practice guideline for influenza, WHO, 2024
IDSA, 2018

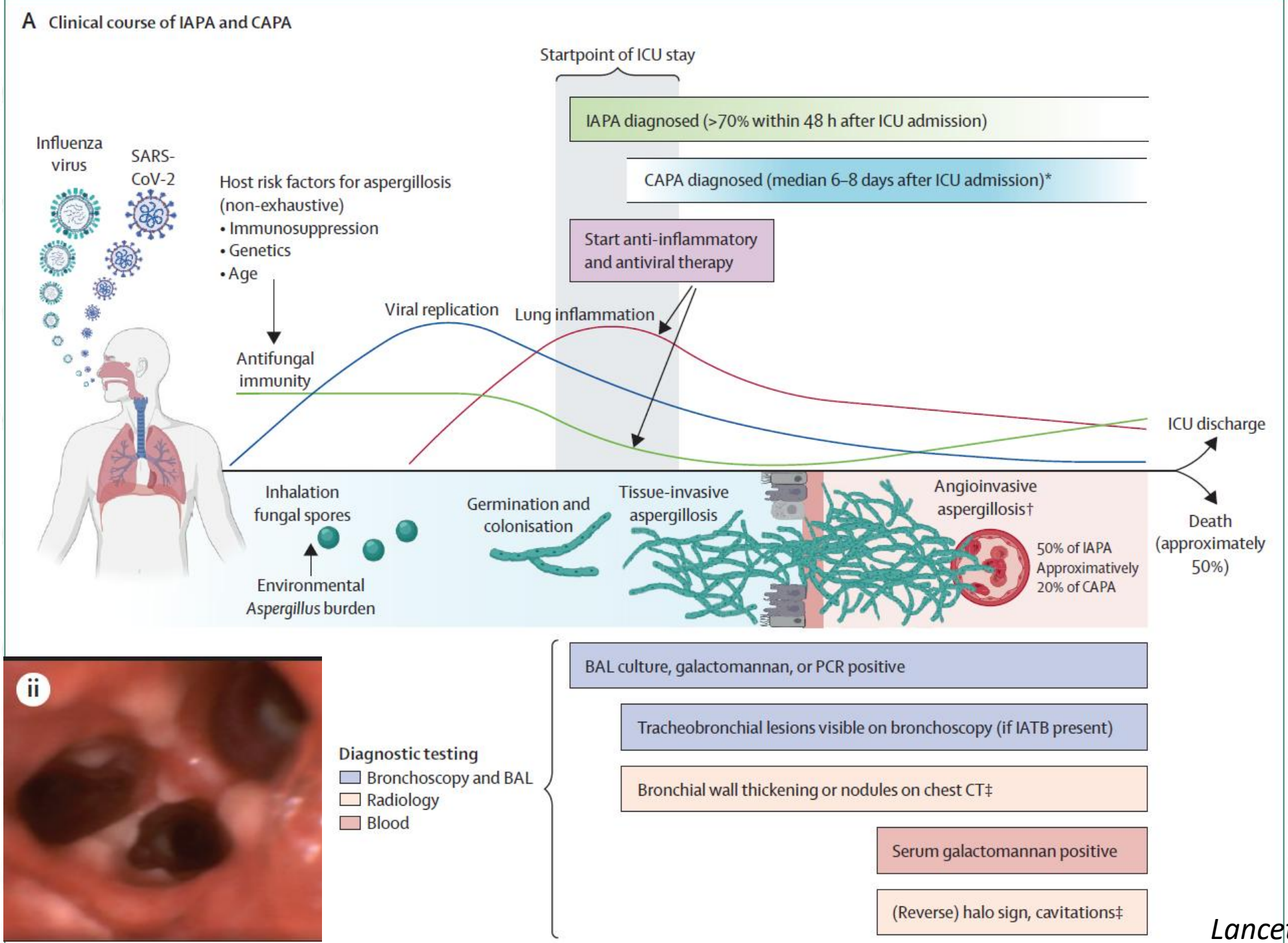
Bacteria co-infection?

- 何時要考慮co-infection?
  - 一開始就以重症表現。
  - 曾經改善過，又再度惡化。
  - 即使治療仍持續惡化。

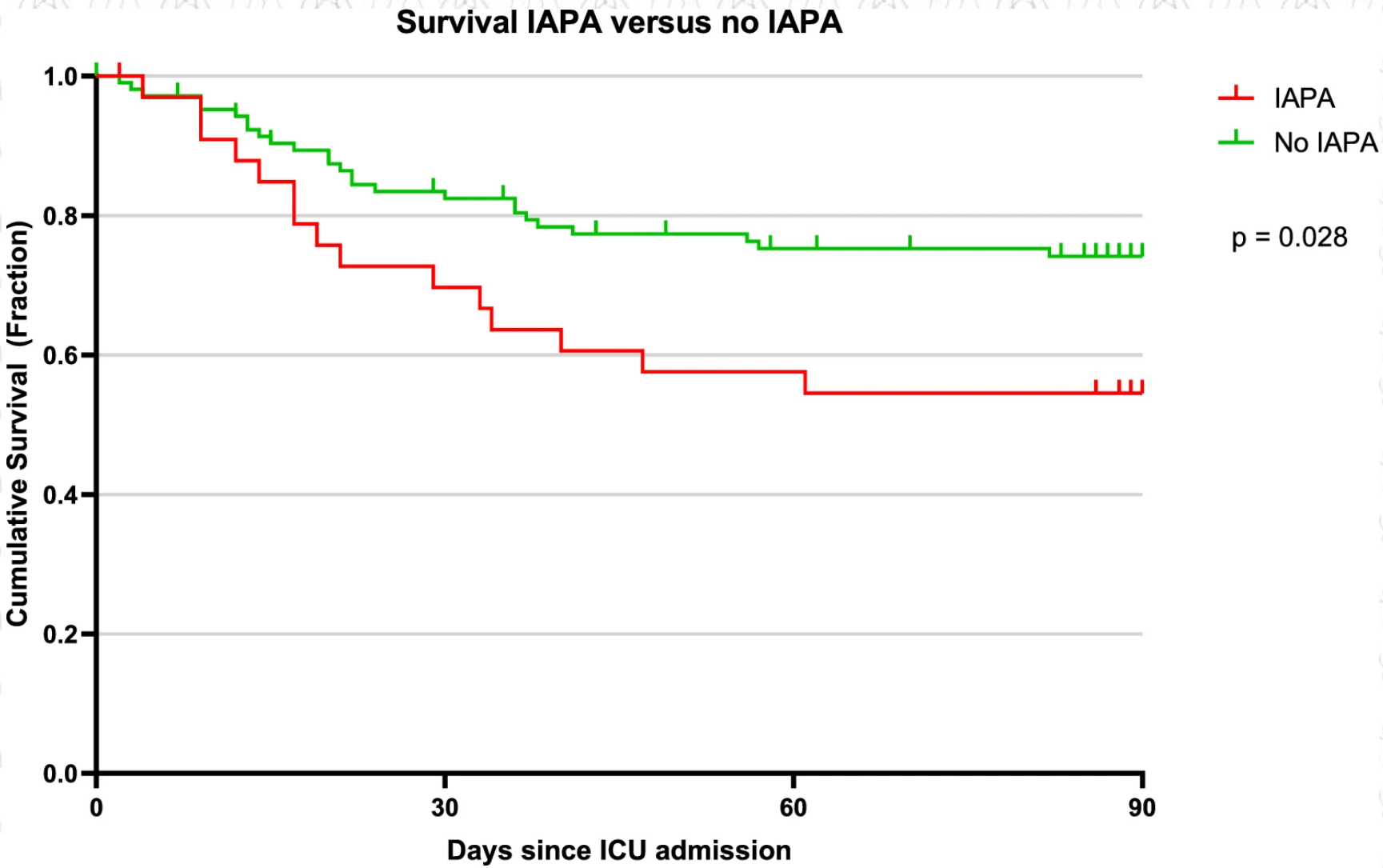
- 有肺炎患者均要懷疑是否同時有coinfection。

Clinical practice guideline for influenza, WHO, 2024
IDSA, 2018

Aspergillus



Lancet Respir Med 2024; 12: 728–42



Days since ICU admission	0	30	60	90
Number at risk – IAPA	34	24	20	12
Number at risk – No IAPA	106	83	72	57

Janssen *et al. Critical Care* (2026) 30:183

Thromboembolism

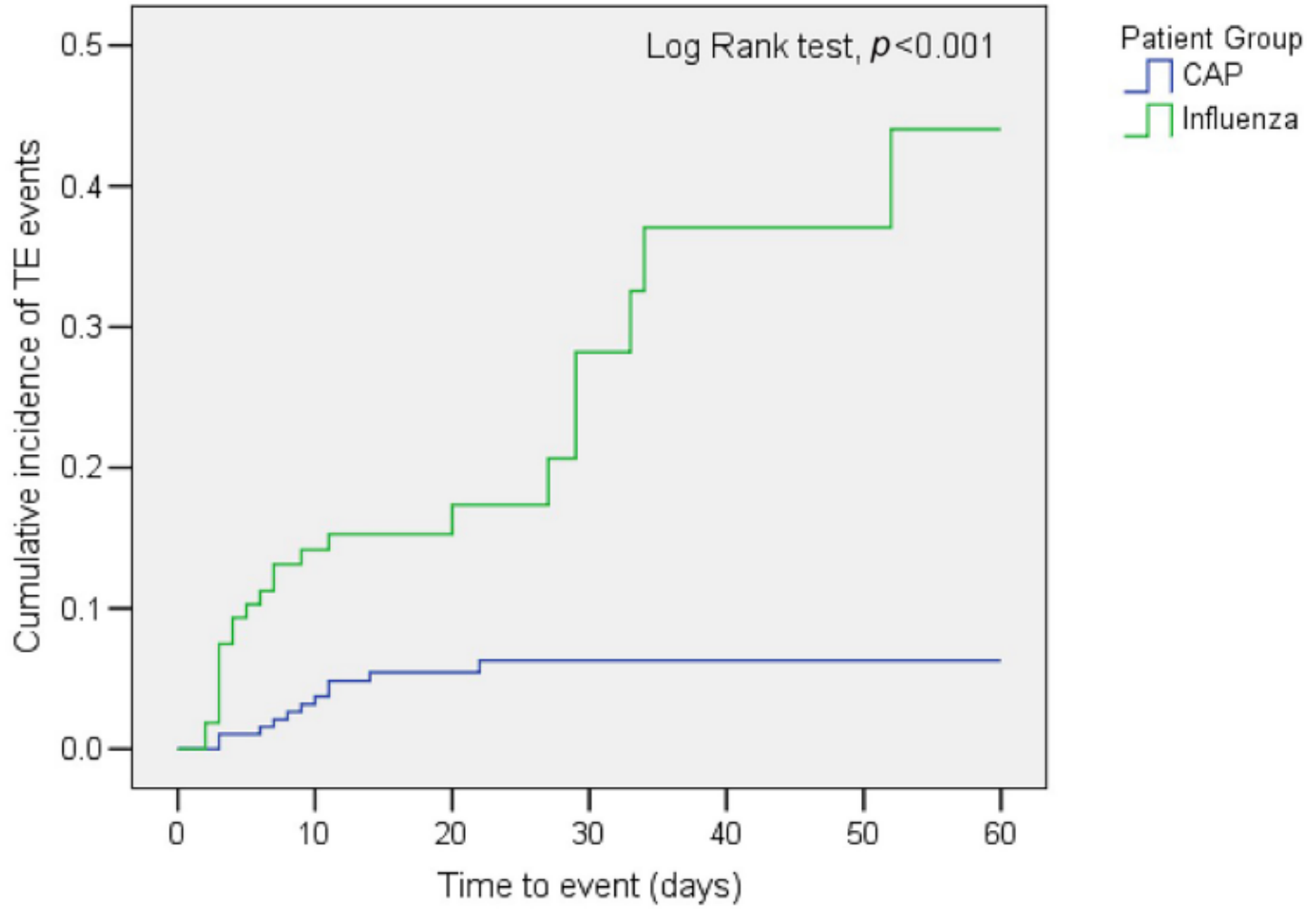


FIGURE 2 | Time to the occurrence of thromboembolic events in the patients with severe influenza or severe noninfluenza CAP admitted to the ICUs.

Influenza and Other Respiratory Viruses, 2024; 18:e13354

Thromboembolism

TABLE 4 | Impacts of acute TE events on patients' outcomes.

	Severe influenza		
	With TE events $n=23$	**Without TE events $n=85$**	***p*-value**
Use of mechanical ventilation	23 (100%)	51 (60%)	<0.001*
Length of mechanical ventilation (days)	20.52 ± 13.98	15.44 ± 16.78	0.009*
ICU stay (days)	34.47 ± 28.53	14.44 ± 8.54	<0.001*
Hospital stay (days)	26.87 ± 26.03	21.64 ± 16.78	0.707
ICU mortality	5 (21.7%)	8 (9.4%)	0.07864
28-day mortality	7 (30.43%)	13 (15.29%)	0.097
90-day mortality	11 (47.83%)	13 (15.29%)	0.001*

Influenza and Other Respiratory Viruses, 2024; 18:e13354

Case Sharing



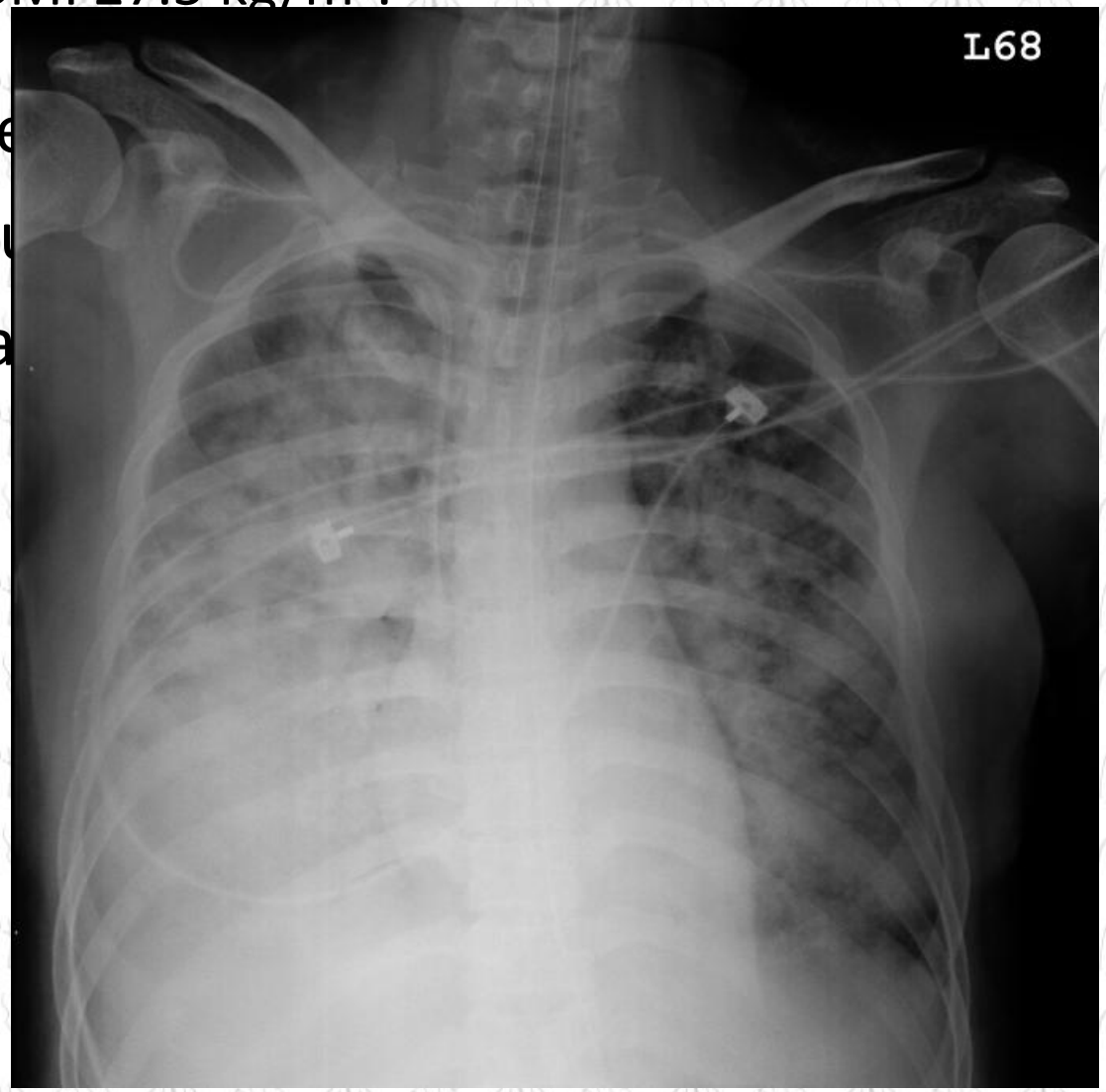
32F

October, 2025

T2DM poor control (last HbA1c: 8.5%), HTN. BMI 27.5 kg/m^2.

- Fever, cough, general soreness and we
- Contact history: father-in-law, colleagu
- Cluster history: she and her kids all ha

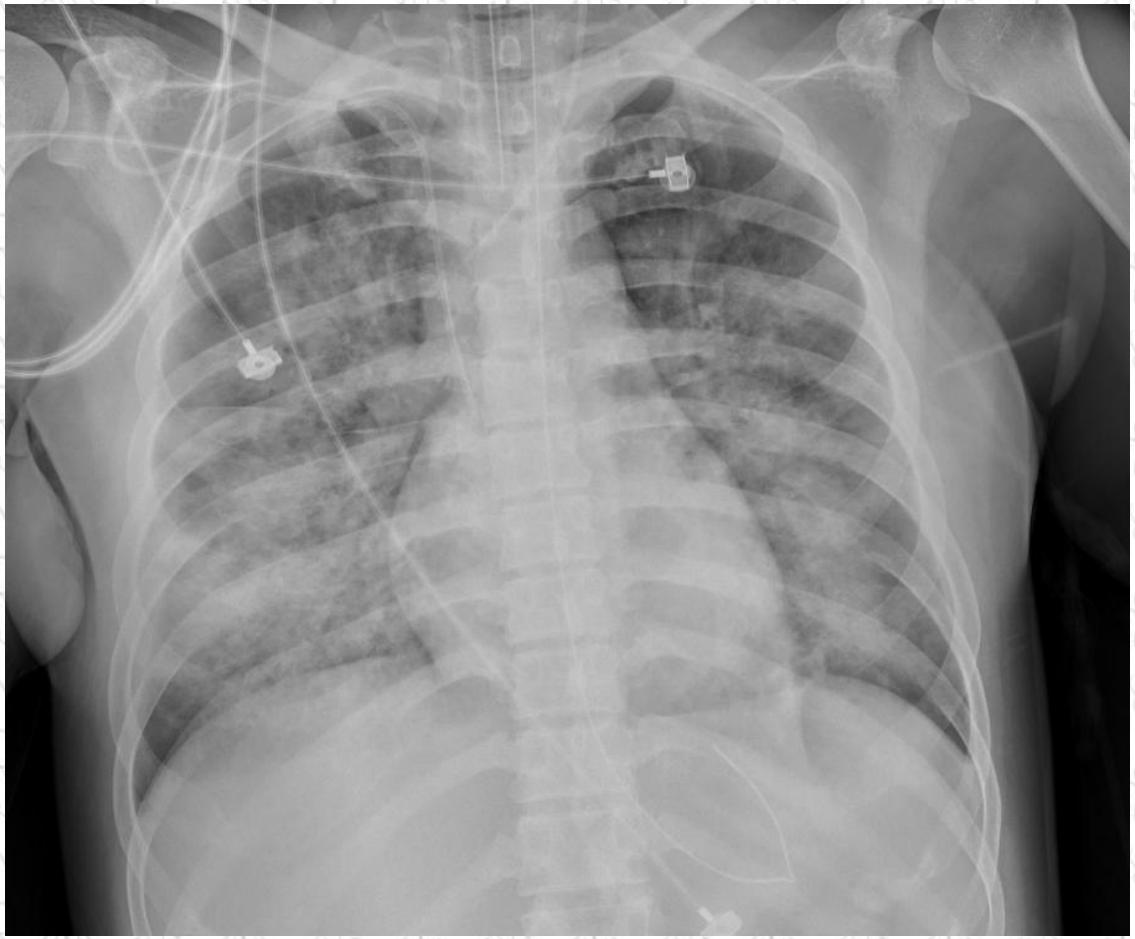
- Gasping at arrival.
- Influenza A rapid test: positive.

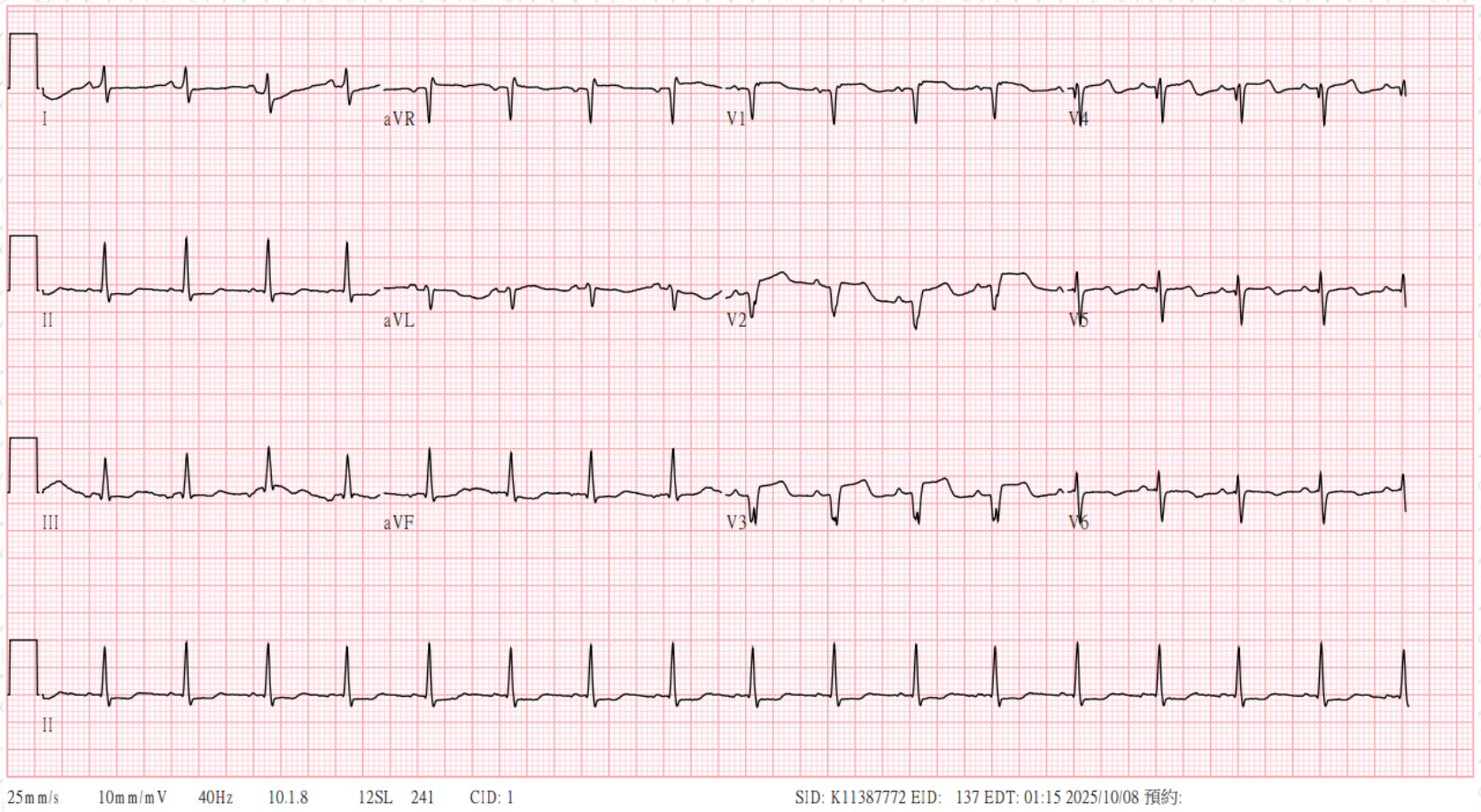


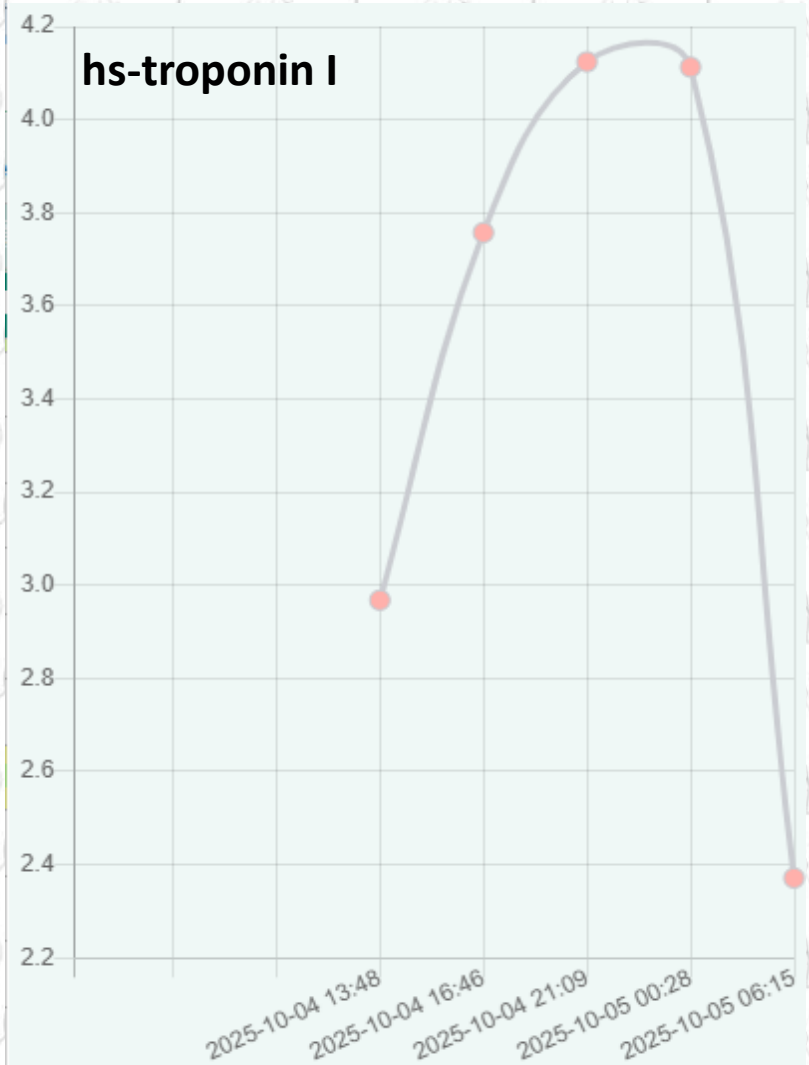
Transferred for VV-ECMO

收縮壓	舒張壓	脈搏	呼吸	體溫	SPO2	GCS
103	73	99	30	37.7	71	3

Blood Gas			
pH:	7.41		(7.35-7.45)
pCO2:	25 *	mmHg	(35.0-45.0)
pO2:	73 *	mmHg	(75.0-100.0)
HCO3-act:	15.8 *	mmol/L	(18.0-23.0)
tCo2:	16.6 *	mmol/L	(22.0-29.0)
BEvt:	-7.7	mmol/L	(-2.0) - 3.0
O2SAT.:	95	%	(95-98)
Hct:	29	%	
FiO2(採檢輸入):	1.0		(0.21-1)
PaO2/FIO2 :	73 *	mmHg(kPa)	(400-500)
Na :	139	mmol/L	(136-146)
K :	3.8	mmol/L	(3.5-5.1)







Bedside echo: global hypokinesia, EF around 40%.

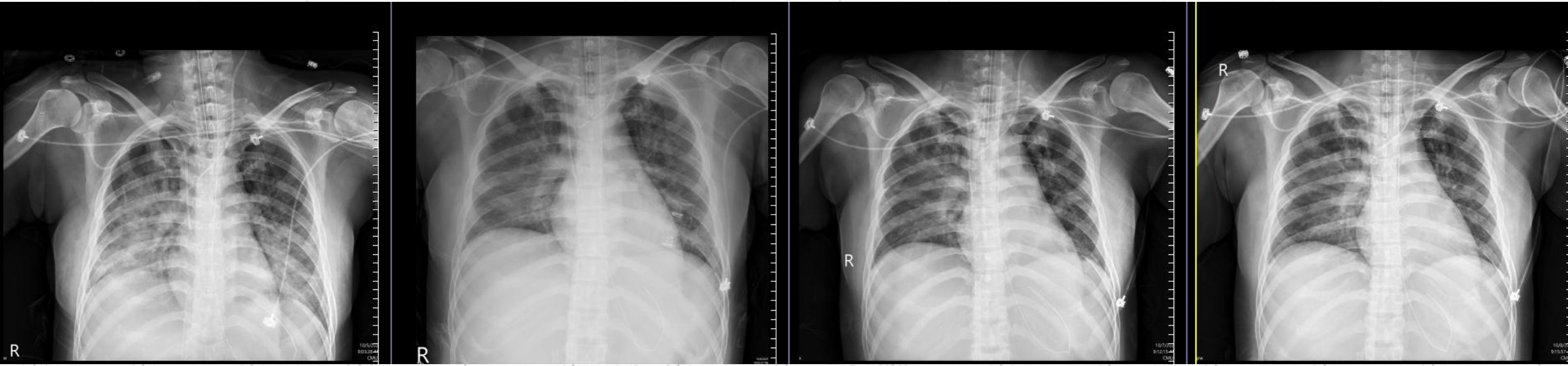
Initial diagnosis

- **Influenza A pneumonia with ARDS**, hypoxic respiratory failure s/p ETT with MV, then VV-ECMO.
- Heart failure, secondary MI or myocarditis related.

Treatment

- **Peramivir** for 5 days.
- Piperacillin/Tazobactam and levofloxacin for severe CAP coverage.
- Lung protective strategy for ARDS.

Hospital day 2 | Hospital day 3 | Hospital day 4 | Hospital day 5



Piperacillin/Tazobactam

Levofloxacin

S.endotracheal tube Culture

報告內容：
嗜氧報告：
No growth to date
Gram stain:Not found
Neutrophil:2+
Epithelium cell:<1/100x

Remove ECMO

Echocardiography (Hospital day 5)

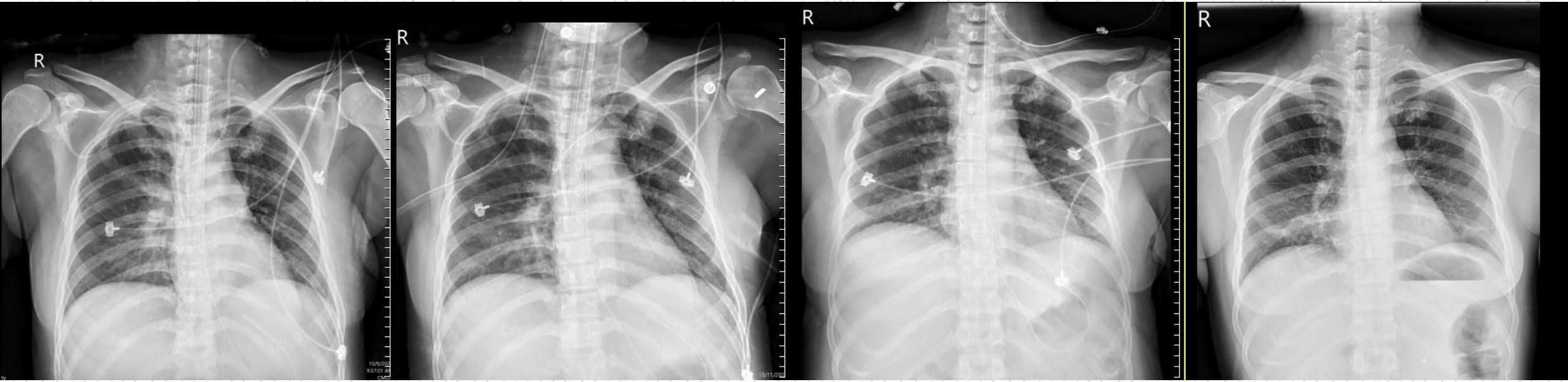
- LV apical hypokinesia with borderline LV contractility. EF: 52.5%.
- Grade I diastolic dysfunction.
- Mild MR/PR/TR.

Hospital day 6

Hospital day 8

Hospital day 10

4 days after discharge



Extubation

Hospital day 15
Discharge

Final diagnosis

- **Influenza A pneumonia with ARDS**, hypoxic respiratory failure s/p ETT with MV, then VV-ECMO.
- Heart failure, secondary MI related.

66M, heavy smoker

November, 2025

CAD s/p PCI with stenting, HTN, COPD under triple therapy. BMI 40.1 kg/m^2.

- Productive cough for 2 days, fever and SOB for 1 day.
- Contact history: grandson had URI symptoms 1 week ago.

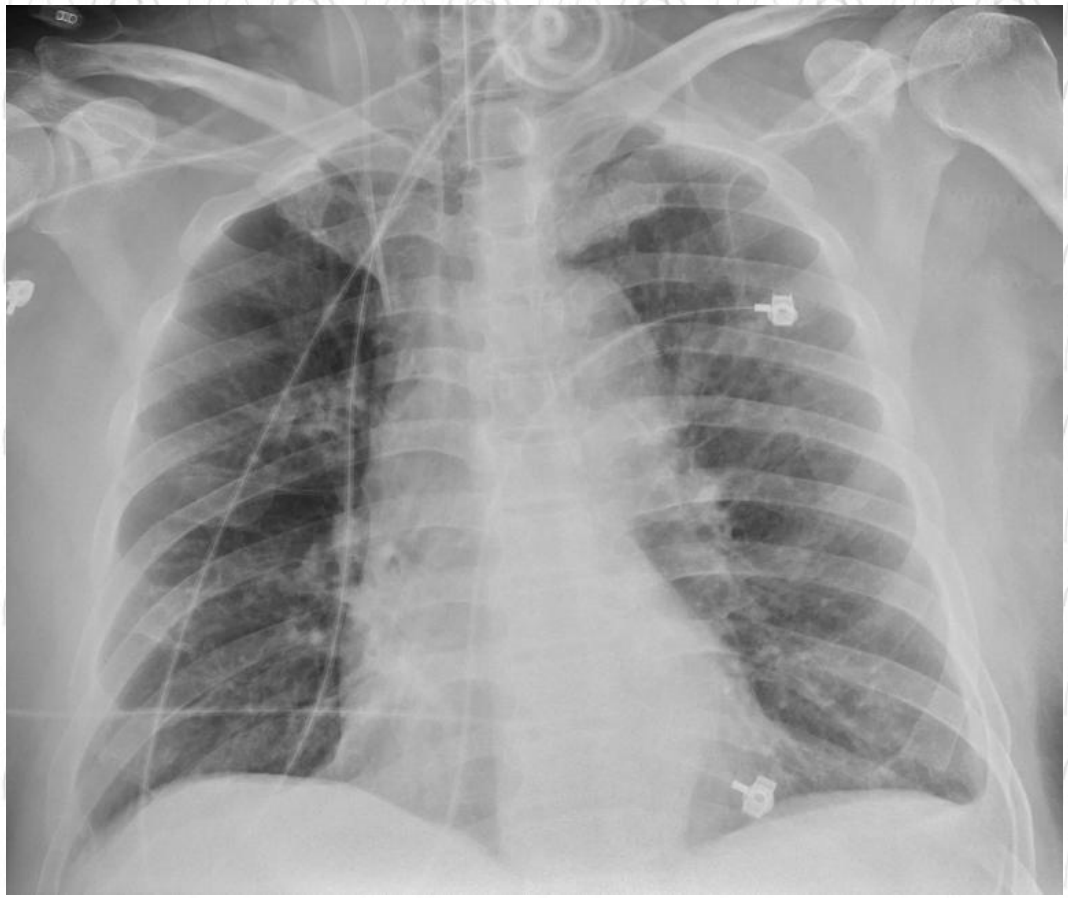
- Gasping at arrival.
- Bilateral wheezing breathing sound.

收縮壓	舒張壓	脈搏	呼吸	體溫	SPO2	GCS
202	105	140	40			15

Blood Gas

pH:	7.11 *		(7.35-7.45)
pCO2:	97 *	mmHg	(35.0-45.0)
pO2:	86	mmHg	(75.0-100.0)
HCO3-act:	30.8 *	mmol/L	(18.0-23.0)
tCo2:	33.8 *	mmol/L	(22.0-29.0)
BEvt:	-1.1	mmol/L	(-2.0) - 3.0
O2SAT.:	92 *	%	(95-98)
Hct:	>65	%	
FiO2(採檢輸入):	1		(0.21-1)
PaO2/FIO2 :	86 *	mmHg(kPa)	(400-500)
Na :	136	mmol/L	(136-146)
K :	4.1	mmol/L	(3.5-5.1)

檢驗項目	報告內容
Influenza A antigen：	Positive *



Initial diagnosis

- **Influenza A infection** complicated with **COPD AE**, hypercapnic respiratory failure s/p ETT with MV

Treatment

- **Peramivir** STAT
- Amoxicillin/Clavulanic acid for COPD AE empiric coverage
- Methylprednisolone, bronchodilator and full sedation for COPD AE

Hospital day 11

- Extubation followed by BiPAP



Hospital day 12

- Left leg swelling.

- Left femoral vein DVT.
- On heparin pump.
- Family hesitating about IVC filter and thrombectomy.



Hospital day 16

Pulmonary embolism

- PEA…
- s/p ECPCR 41mins





Hospital day 24

- Right thalamic ICH, with IVH and mild secondary SAH.
- Hypoxic-ischemic encephalopathy.

Expired…



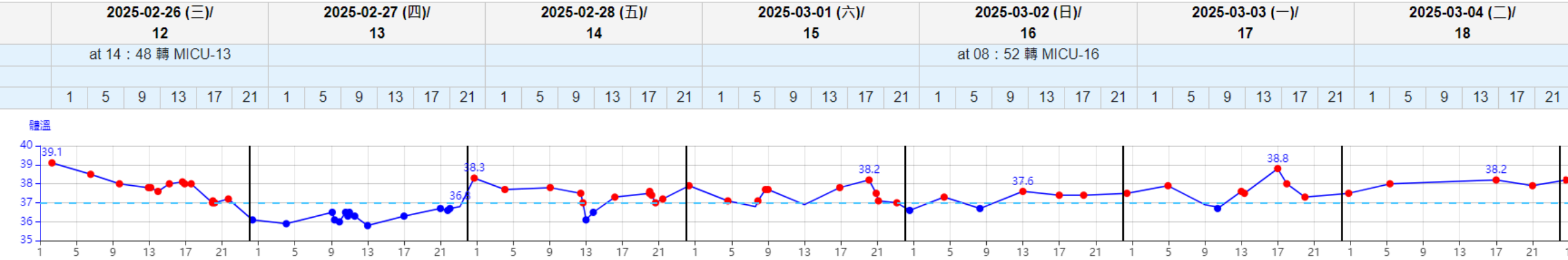
36M

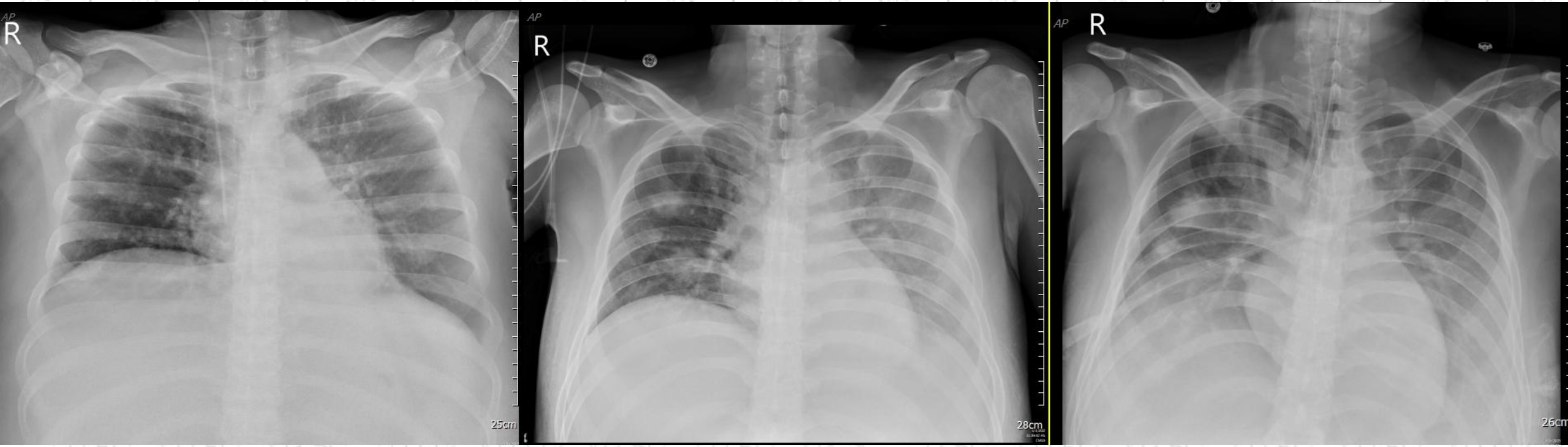
Feb, 2025

New-diagnosed anaplastic large cell lymphoma

- Just receive 1st BV-CHP and brentuximab.
- Admitted to ICU due to tumor lysis syndrome, improved after supportive care.
- VRE bacteremia, catheter infection related.

- **Unresolved fever with progressive dyspnea!**





Gram's Stain

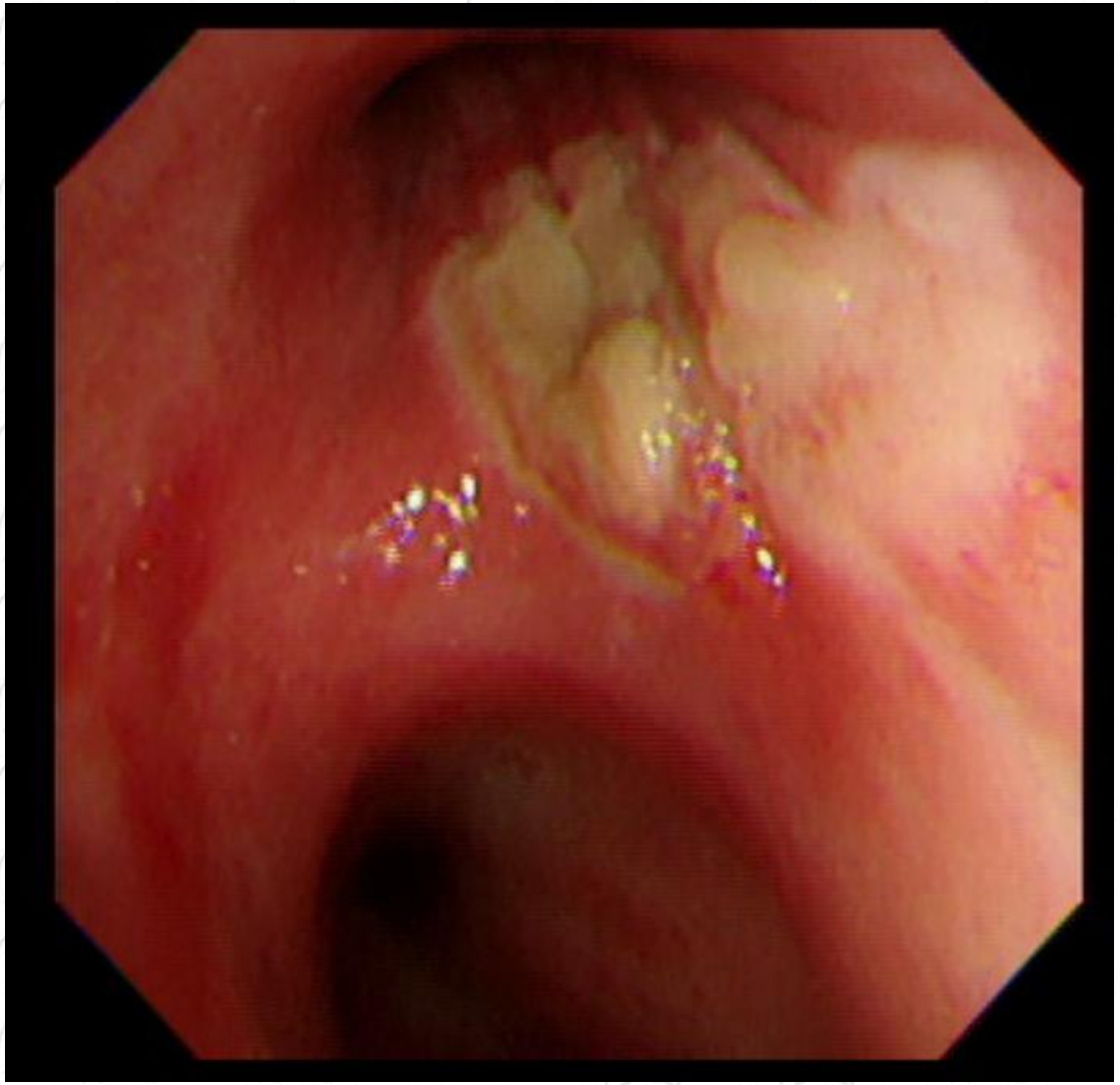
Gram stain:Not found

Neutrophil : 2+

Epithelium cell : 1-9/100x

Influenza A RNA :Positive

Peravimir for 5 days due to immunocompromising condition.



報告內容：
Lung, RB3, biopsy, fungal infection.

描述：
The specimen submitted consists of a tissue fragment measuring 0.3x 0.2x0.1 cm. in size fixed in formalin.

Grossly, it is tan and elastic.

All for section.

Microscopically, it shows necrotic debris and fungal spores a nd hyphi which are highlighted by PAS and GMS staining. Please corr elate with clinical picture and culture result.

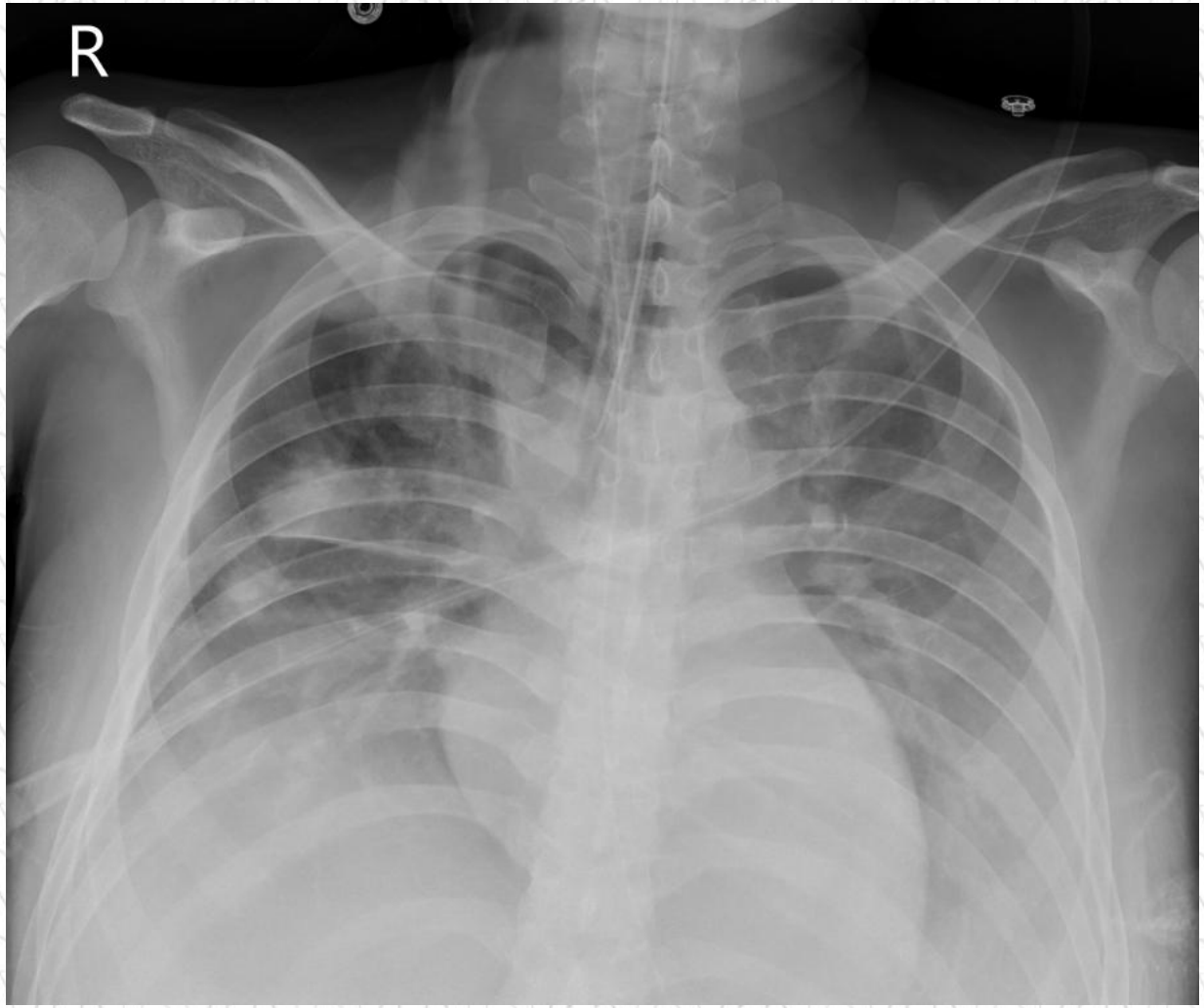
Aspergillus antigen(BAL):	Positive (9.4) (Negative,<0.5)

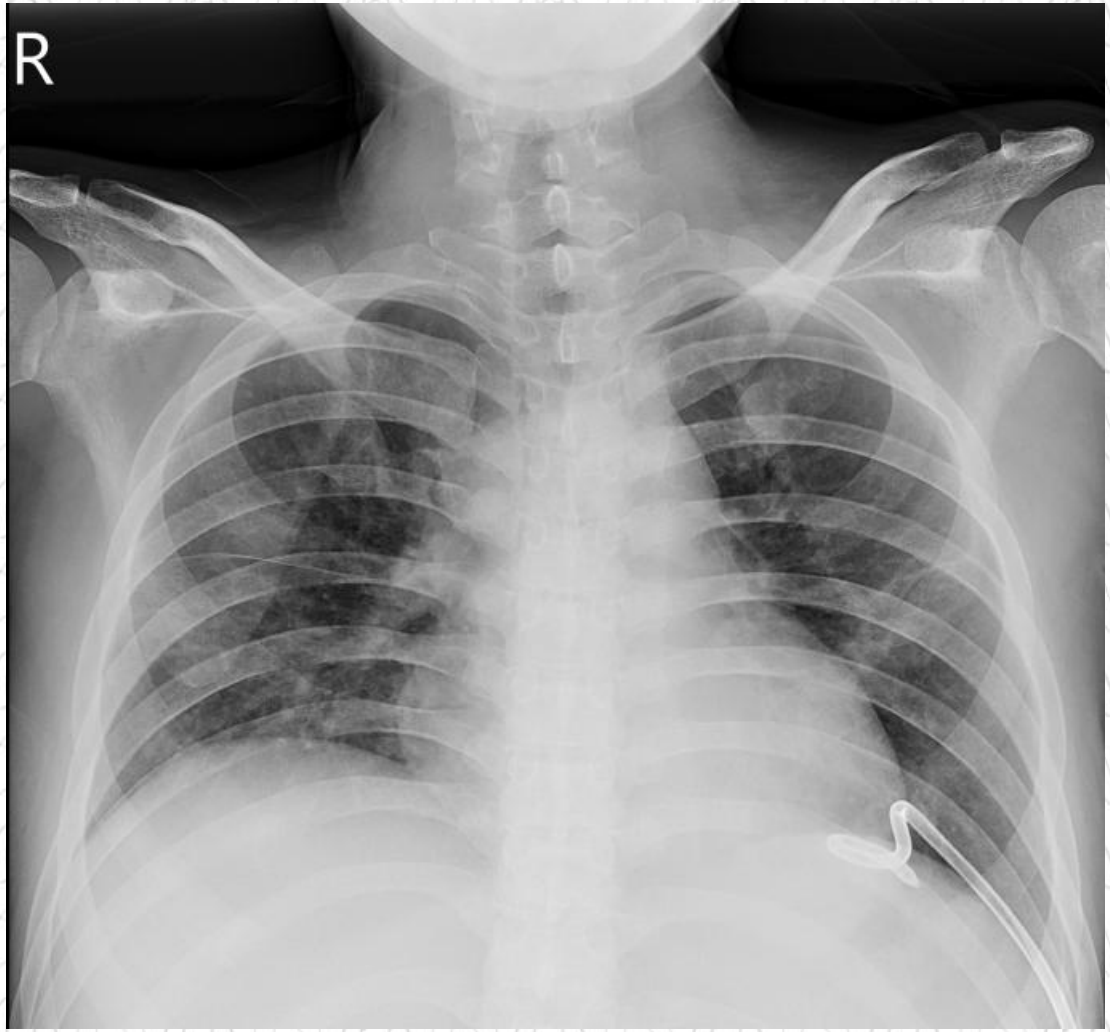
Sputum Fungus Culture
醫囑說明:檢體為BAL

報告內容：
Aspergillus fumigatus
Gram's stain:Mold

Diagnosis

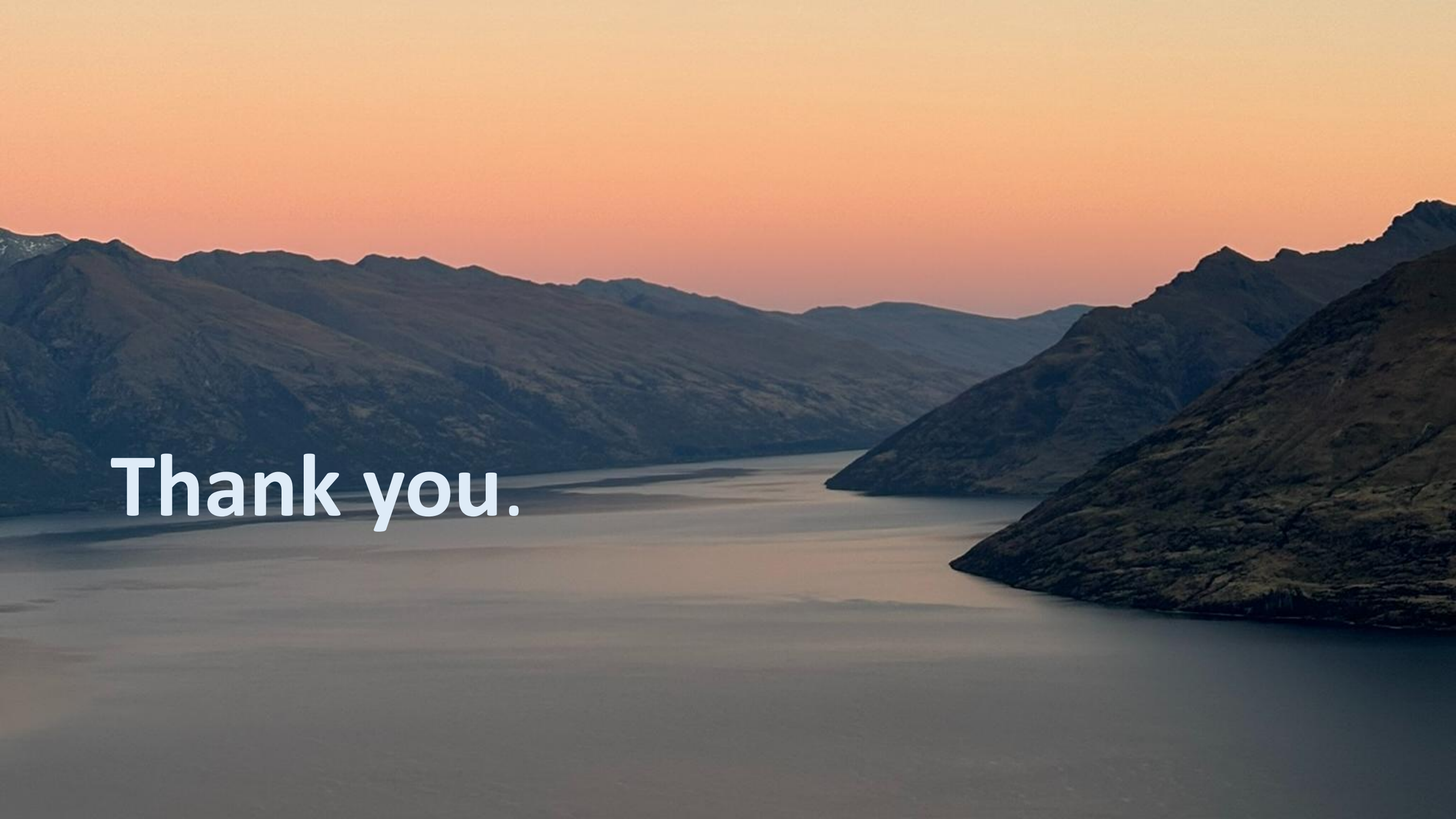
- Influenza A pneumonia with respiratory failure.
- Proven invasive pulmonary aspergillosis.


R


R

Take Home Message

- 流感病毒感染導致需要住院/加護醫療稱為流感重症。
- 盛行率與死亡率與盛行菌株以及是否流行期間相關。
- 高風險族群：65歲以上、免疫低下、肥胖、心血管疾病、神經疾病、慢性呼吸疾病、代謝性疾病、孕/產婦等。
- 治療以抗病毒藥物 (越早投藥越好) 與支持性療法為主。
- 常伴隨有細菌感染、麴黴菌感染、血栓事件需特別注意。


Thank you.