



Management of acute respiratory failure (ARF) in immunocompromised patients

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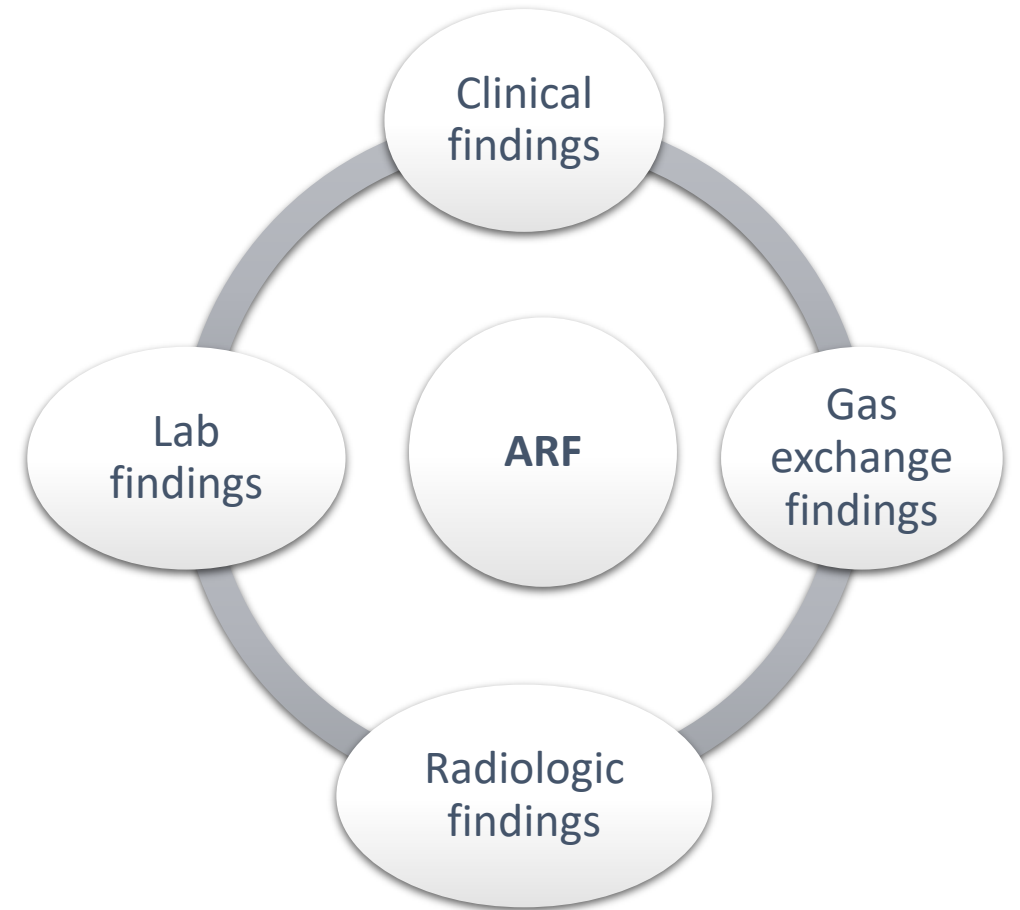
No Conflict of Interest regarding the presentation ...

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Acute Respiratory Failure

- Severe form of acute organ dysfunction characterized by impaired gas-exchange
 - $\text{PaO}_2/\text{FiO}_2 < 300$; $\text{SpO}_2/\text{FiO}_2 < 315$
- De novo / acute hypoxemic / Type 1 respiratory failure is the predominant type of ARF in immunocompromised patients
- Management
 - Restoration of oxygenation, and decrease the work of breathing
 - Appropriate diagnosis
 - Prediction
 - Diagnostic confirmation
 - Appropriate therapy of the underlying pathology



- Growing number of adults have immune dysfunction
 - Up to 5% of the general population are cancer survivors
 - Transplantation is on the rise
 - Immunosuppressant drugs and immunotherapy are used more
- ARF occurs in up to half of patients with hematological malignancies (AML and allogeneic HSCT) and 15% of those with solid tumours (lung cancer) or solid organ transplantation (heart and lung), with a mortality of 50%
- Immunosuppressed patients comprise 1/3rd of ICU admissions
 - > 3 mo or > 0.5 mg/kg/day steroid use
 - Other immunosuppressive agent use
 - Solid organ transplant patients
 - Chemotherapy for solid tumors within last 5 years
 - Hematologic malignancy
 - Primary immunodeficiencies

Acute respiratory failure in immunocompromised adults

Elie Azoulay, Djamel Mokart, Achille Kouatchet, Alexandre Demoule, Virginie Lemiale

Lancet Respir Med 2019;
7: 173-86

Diagnosis of severe respiratory infections in immunocompromised patients

Intensive Care Med (2020) 46:298-314

Elie Azoulay^{1,2}, Lene Russell³, Andry Van de Louw⁴, Victoria Metaxa⁵, Philippe Bauer⁶, Pedro Povoa⁷, José Garnacho Montero⁸, Ignacio Martín Loeches⁹, Sangeeta Mehta¹⁰, Kathryn Puxty¹¹, Peter Schellongowski¹², Jordi Rello^{13,14}, Djamel Mokart¹⁵, Virginie Lemiale¹ and Adrien Mirouse^{1,2} on behalf of the Nine-i Investigators

Main causes of ARF in the immunocompromised host

- Disease related
 - Leukemic infiltration
 - Leukostasis
 - Lysis pneumopathy
 - Recovery phase of neutropenia
- Infections
- Treatment related
- Diffuse alveolar hemorrhage
- Cardiogenic pulmonary edema

Factors associated with mortality include ...

1. Factors reflecting **severity of ARF and associated organ dysfunctions**
 - Degree of hypoxemia ($\text{PaO}_2/\text{FiO}_2$), tachypnea and respiratory distress
 - SOFA score
2. Factors related to the **initial oxygenation** and ventilation strategy
 - Patients requiring ≥ 6 L/min O_2 or $\text{FiO}_2 > 40\%$ \rightarrow \uparrow intubation and hospital mortality (40%)
 - **HFNO or NIV failure**; Need for **invasive mechanical ventilation**
3. Factors related to the underlying disease and comorbid conditions
 - **Older age, frailty** or **poor performance** status
 - **Degree of immunosuppression**
4. Factors related to the cause of acute respiratory failure
 - **Invasive fungal infection** or **unknown cause** has worst prognosis
 - Cardiogenic pulmonary edema has the best prognosis
5. Factors related to **delayed ICU admission**

Acute hypoxemic respiratory failure in immunocompromised patients: the Efraim multinational prospective cohort study

Elie Azoulay^{1*}, Peter Pickkers², Marcio Soares³, Anders Perner⁴, Jordi Rello⁵, Philippe R. Bauer⁶, Andry van de Louw⁷, Pleun Hemelaar², Virginie Lemiale¹, Fabio Silvio Taccone⁸, Ignacio Martin Loeches^{9,10}, Tine Sylvest Meyhoff⁴, Jorge Salluh³, Peter Schellongowski¹¹, Katerina Rusinova¹², Nicolas Terzi¹³, Sangeeta Mehta¹⁴, Massimo Antonelli¹⁵, Achille Kouatchet¹⁶, Andreas Barratt-Due¹⁷, Miia Valkonen¹⁸, Precious Pearl Landburg¹⁹, Fabrice Bruneel²⁰, Ramin Brandt Bukan²¹, Frédéric Pène²², Victoria Metaxa²³, Anne Sophie Moreau²⁴, Virginie Souppart¹, Gaston Burghi²⁵, Christophe Girault²⁶, Ulysses V. A. Silva²⁷, Luca Montini¹⁵, François Barbier²⁸, Lene B. Nielsen^{29,30}, Benjamin Gaborit³¹, Djamel Mokart³² and Sylvie Chevret³³ for the Efraim investigators and the Nine-I study group

Intensive Care Med (2017) 43:1808–1819

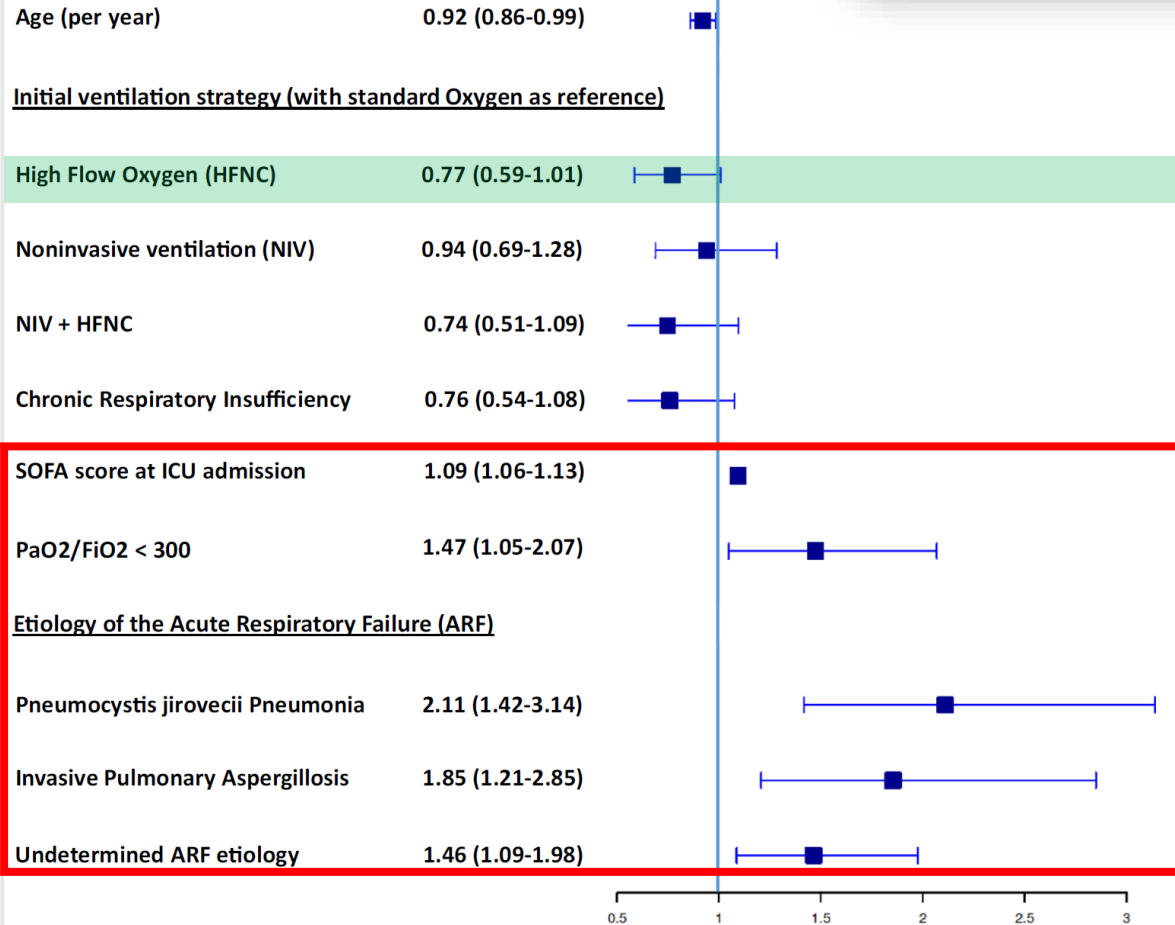
- 1611 patients
 - Hematological malignancies 52%
 - Solid tumors 35%
 - Systemic diseases 17%
 - Solid organ transplantation 9%
- Main etiologies
 - Bacterial 30%
 - Viral 15%
 - Fungal 15%
 - Undetermined 13%
- On admission 37% were intubated
- 57% not intubated
 - Standard O₂ 54%
 - HFNC 20%
 - NIV 17%
 - NIV+HFNC 9%
- ICU mortality 32%,
- Hospital mortality 44%
- 90-day mortality 56%

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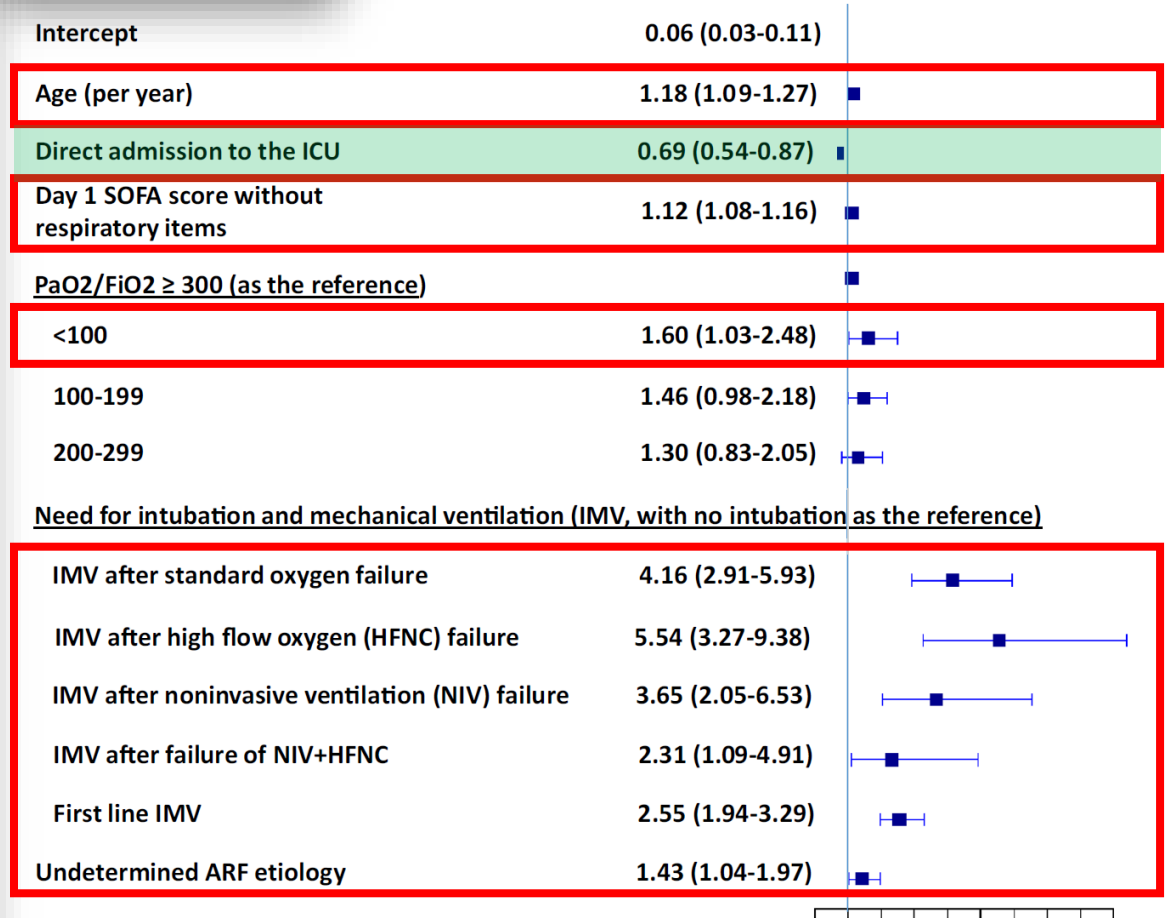
Intensive Care Med (2017) 43:1808–1819

Hazard Ratios (95% Confidence Intervals)



Increased risk of intubation and mechanical ventilation

Odds Ratios (95% Confidence Intervals)



Increased risk of hospital mortality

ICU-acquired pneumonia in immunosuppressed patients with acute hypoxemic respiratory failure: A post-hoc analysis of a prospective international cohort study

Journal of Critical Care 63 (2021) 243–245

Ignacio Martin-Loeches, MD^{a,b,*}, Michael Darmon, MD^{c,1}, Alexandre Demoule, MD^d, Massimo Antonelli, MD^{e,f}, Peter Schellongowski, MD^g, Peter Pickkers, MD^h, Marcio Soares, MDⁱ, Jordi Rello, MD^j, Philippe Bauer^k, Andry van de Louw, MD^l, Virgine Lemiale, MD^c, David Grimaldi, MD^m, Martin Balik, MDⁿ, Sangeeta Mehta, MD^o, Ac Kouatchet, MD^p, Andreas Barratt-Due, MD^q, Miiia Valkonen, MD^r, Jean Reignier, MD^s, Victoria Metaxa, MD^t, Anne Sophie Moreau, MD^u, Gaston Burghi, MD^v, Djamel Mokart, MD^w, Elie Azoulay, MD^c, For the Efraim investigators and the Nine-I study group

- ICU-AP occurred in 10% of patients
- Hospital mortality was 15% in ICU-AP group vs 7% in no ICU-AP group (p<0.001)
- Vasopressors (OR 2.22 [1.46–3.39]) and invasive mechanical ventilation vs HFNC at day 1 (OR 2.12 [1.07–4.20]) were associated with increased risk of ICU-AP
- ICU-AP was independently associated with mortality (HR 1.48 [1.14–1.91]; P=0.003)

| | Incidence of respiratory events | Need for ICU admission | Hospital respiratory mortality |
|--|---------------------------------|------------------------|--------------------------------|
| Haematological malignancies | | | |
| Acute myeloid leukaemia ^{5,18-23} | 22-84% | 66% | 45% |
| Acute lymphoblastic leukaemia ^{18,22,23} | 7-18.5% | 12-15% | 38.5% |
| Lymphoproliferative diseases ⁵ | 8% | 8% | 40-50% |
| Myelodysplastic syndrome ¹⁸ | 29.4% | 20% | 17% |
| Autologous haemopoietic stem cell therapy ^{24,25} | 3-28% | 42% | 3-55% |
| Allogeneic haemopoietic stem cell therapy ^{26,27} | 24-30% | 50% | 51% |
| Prolonged neutropenia ^{6,28} | 8-29.5% | 11-16% | 5-12% |
| Solid tumours | | | |
| Lung cancer ^{29,30} | 26-50% | 100% | 11.2-60% |
| Other solid tumours ^{5,30,31} | 0.7-10.3% | 100% | 6.1-55% |
| Patients on immunotherapy ^{32,33} | 1.3-3.6% | 1.3%* | .. |
| Solid organ transplantation | | | |
| Lung transplantation ³⁴ | 14% | All | 65% |
| Heart transplantation ³⁵ | 12.5% | All | 76.5% |
| Kidney transplantation ^{36,37} | 3.3-4.8% | All | 16.4-22.5% |

Acute respiratory failure in immunocompromised adults

Characteristics and outcomes of patients with acute myeloid leukemia admitted to intensive care unit with acute respiratory failure: a post-hoc analysis of a prospective multicenter study

Annals of Intensive Care (2023) 13:79

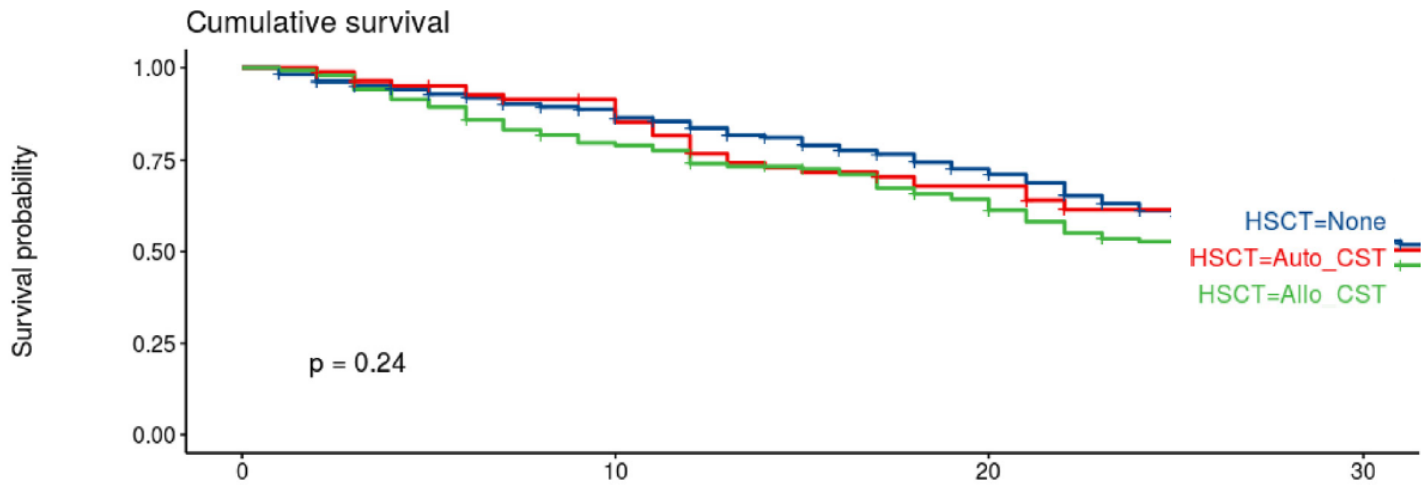
Carolina Secreto^{1,8*}, Dara Chean², Andry van de Louw³, Achille Kouatchet⁴, Philippe Bauer⁵, Marco Cerrano¹, Etienne Lengliné⁶, Colombe Saillard⁷, Laurent Chow-Chine⁸, Anders Perner⁹, Peter Pickkers¹⁰, Marcio Soares¹¹, Jordi Rello^{12,13}, Frédéric Pène¹⁴, Virginie Lemiale¹⁵, Michael Darmon¹⁵, Sofiane Fodil¹⁵, Ignacio Martin-Loeches¹⁶, Sangeeta Mehta¹⁷, Peter Schellongowski¹⁸, Elie Azoulay¹⁵ and Djamel Mokart⁸

- Post-hoc analysis of EFRAIM study on AML patients
- **Hospital mortality 46.8%**
- Variables independently associated with mortality
 - **ECOG performance status ≥ 2** (OR = 2.79, $p = 0.04$)
 - **Cough** (OR = 2.94, $p = 0.034$)
 - Use of **vasopressors** (OR = 2.79, $p = 0.044$)
 - **Leukemia-specific pulmonary involvement [namely leukostasis, pulmonary infiltration by blasts or acute lysis pneumopathy** (OR = 4.76, $p = 0.011$)]
 - **Liver SOFA score** (OR = 1.85, $p = 0.014$)
- Focal alveolar chest X-ray pattern was associated with survival (OR = 0.13, $p = 0.001$)
- 3 clusters according to clinical, biological and radiological features were identified:
 - **Cluster 1 “leukemic cluster”**, isolated, milder ARF
 - **Cluster 2 “pulmonary cluster”**, symptomatic, highly oxygen-requiring, severe ARF with diffuse radiological findings (mortality OR = 2.48, $p = 0.04$)
 - **Cluster 3 “inflammatory cluster”**, multiorgan failures in addition to ARF (OR = 3.49, $p = 0.006$)

Acute Respiratory Failure Outcomes in Patients with Hematologic Malignancies and Hematopoietic Cell Transplant: A Secondary Analysis of the EFRAM Study

Transplantation and Cellular Therapy 27 (2021) 78.e1–78.e6

Laveena Munshi^{1,*}, Michael Darmon², Marcio Soares³, Peter Pickkers⁴, Philippe Bauer⁵, Anne-Pascale Meert⁶, Ignacio Martin-Loeches^{7,8}, Thomas Staudinger⁹, Frederic Pene¹⁰, Massimo Antonelli^{11,12}, Andreas Barratt-Due¹³, Alexandre Demoule¹⁴, Victoria Metaxa¹⁵, Virginie Lemiale¹⁶, Fabio Taccone¹⁷, Djamel Mokart¹⁸, Elie Azoulay¹⁶, Sangeeta Mehta¹ On Behalf of the EFRAM Investigators



Multivariable Logistic Regression Analysis Demonstrating the Association Between HM without HCT versus Autologous HCT or Allogeneic HCT and Hospital Mortality

| Variable | OR | 95% CI | P Value |
|---------------------------|-----------|-----------|---------|
| ECOG status 0 | Reference | — | — |
| ECOG status 1 | 1.30 | .77-2.18 | .32 |
| ECOG status 2 | 2.25 | 1.29-3.93 | .04 |
| ECOG status 3 | 5.33 | 2.86-9.94 | <.001 |
| BAL performed | 1.35 | 1.02-1.56 | .04 |
| Vasopressors | 2.76 | 1.83-4.15 | <.001 |
| Renal replacement therapy | 3.07 | 1.90-4.94 | <.001 |
| Age (per 1 yr) | 1.02 | 1.00-1.03 | .03 |
| HM no HCT | Reference | — | — |
| Autologous HCT | 1.07 | .57-2.03 | .83 |
| Allogeneic HCT | .99 | .60-1.66 | .98 |
| Other etiologies | Reference | — | — |
| Fungal infection | 1.43 | .68-3.01 | .34 |
| Undetermined ARF | 1.29 | .70-2.40 | .42 |

Etiologies and Outcome of Patients with **Solid Tumors** Admitted to ICU with Acute Respiratory Failure: A Secondary Analysis of the EFRAIM Study

Benguerfi et al. Respiratory Care 2023;68:740-748

- 529 had solid tumors: **33% lung cancer**, 21% breast cancer 10%, GI cancer 9%
- Cause of admission: **bacterial or viral infection 42%**; cancer or treatment related 16%; extrapulmonary sepsis 12%, fungal infection 4%, unknown 12%
- **Hospital mortality rate 46%**. Independent factors related with mortality
 - **Chronic cardiac failure** OR 1.78 [1.09–2.92]
 - **Lung cancer** OR 2.50 [1.51–4.19]
 - **Day 1 SOFA** OR 1.97 [1.32-2.96]
 - Non-infectious etiologies OR 0.32 [0.16–0.61]

Etiologies and Outcomes of Acute Respiratory Failure in Solid Organ Transplant Recipients: Insight Into the EFRAIM Multicenter Cohort

Messika, et al. Transplantation Proceedings, 52, 2980e2987 (2020)

- 142 were SOT recipients; **kidney 51%**, lung 23%, liver 20%, heart 5%
- **Invasive diagnostic strategy was more frequently performed in lung transplant recipients with a trend toward a higher rate of bacterial etiology in lung than kidney transplant recipients**
- **ICU survival 75%, hospital survival 63%, 90-day survival 55%**; although statistically not significant lung tx patients had the worst prognosis
- **SOFA score** (OR 1.19 [1.06-1.33] and **ECOG ≥ 3** 4.26 [0.91-20.06])

Assessing the cause of ARF at the bedside

- D **D**uration of respiratory symptom
- I **I**mmunosuppression type
- R **R**adiological pattern (CXR, lung USG ...)
- E **E**xperience of clinician regarding similar cases
- C **C**linical findings
- T **T**omography (HRCT)

Acute respiratory failure in immunocompromised adults

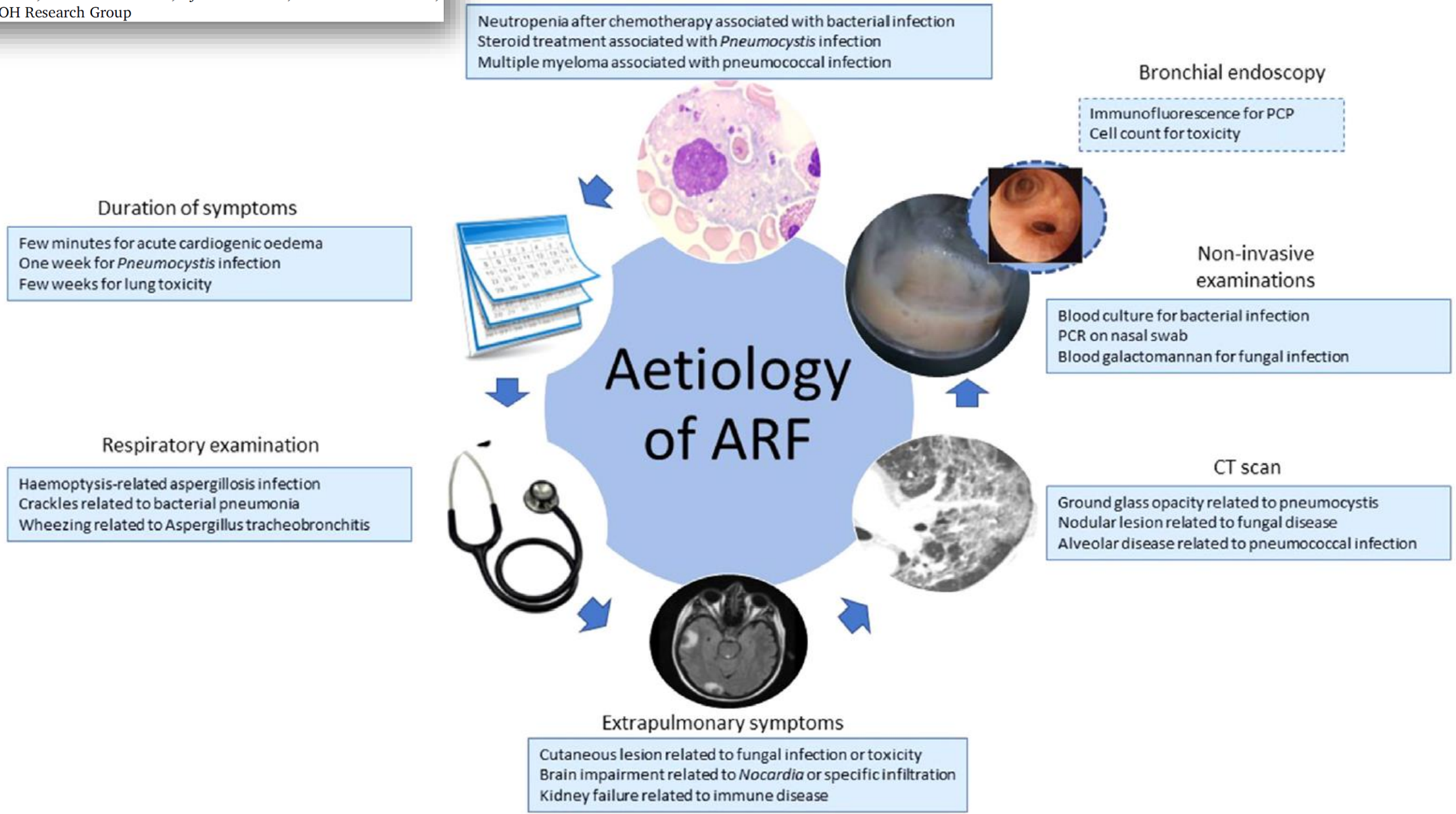
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*Lancet Respir Med 2019;
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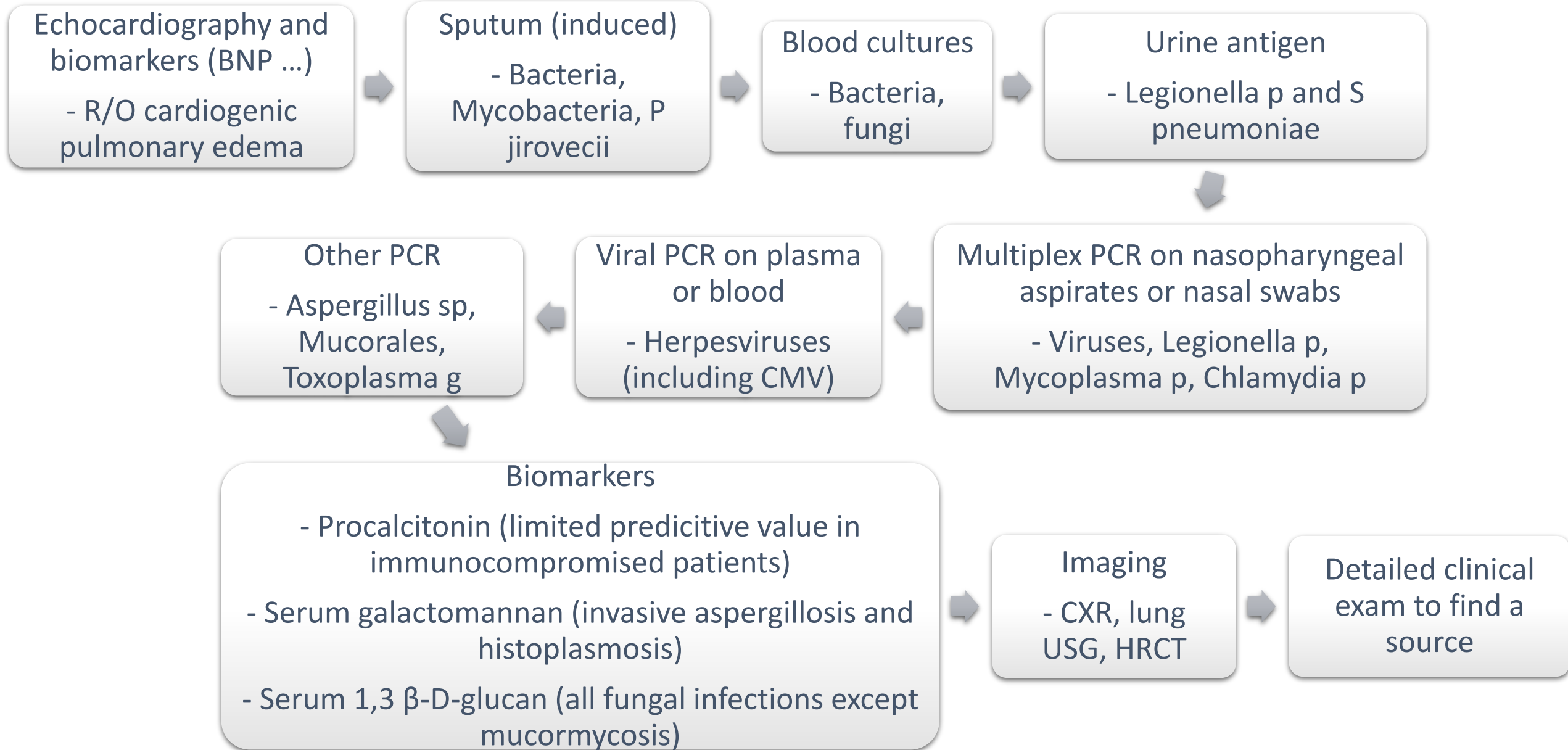
Oxygenation strategy during acute respiratory failure in immunocompromised patients

Journal of Intensive Medicine 1 (2021) 81–89

Virginie Lemiale^{1,*}, Elise Yvin¹, Achille Kouatchet², Djamel Mokart³, Alexandre Demoule⁴, Guillaume Dumas¹, Grrr-OH Research Group



Diagnostic algorithm

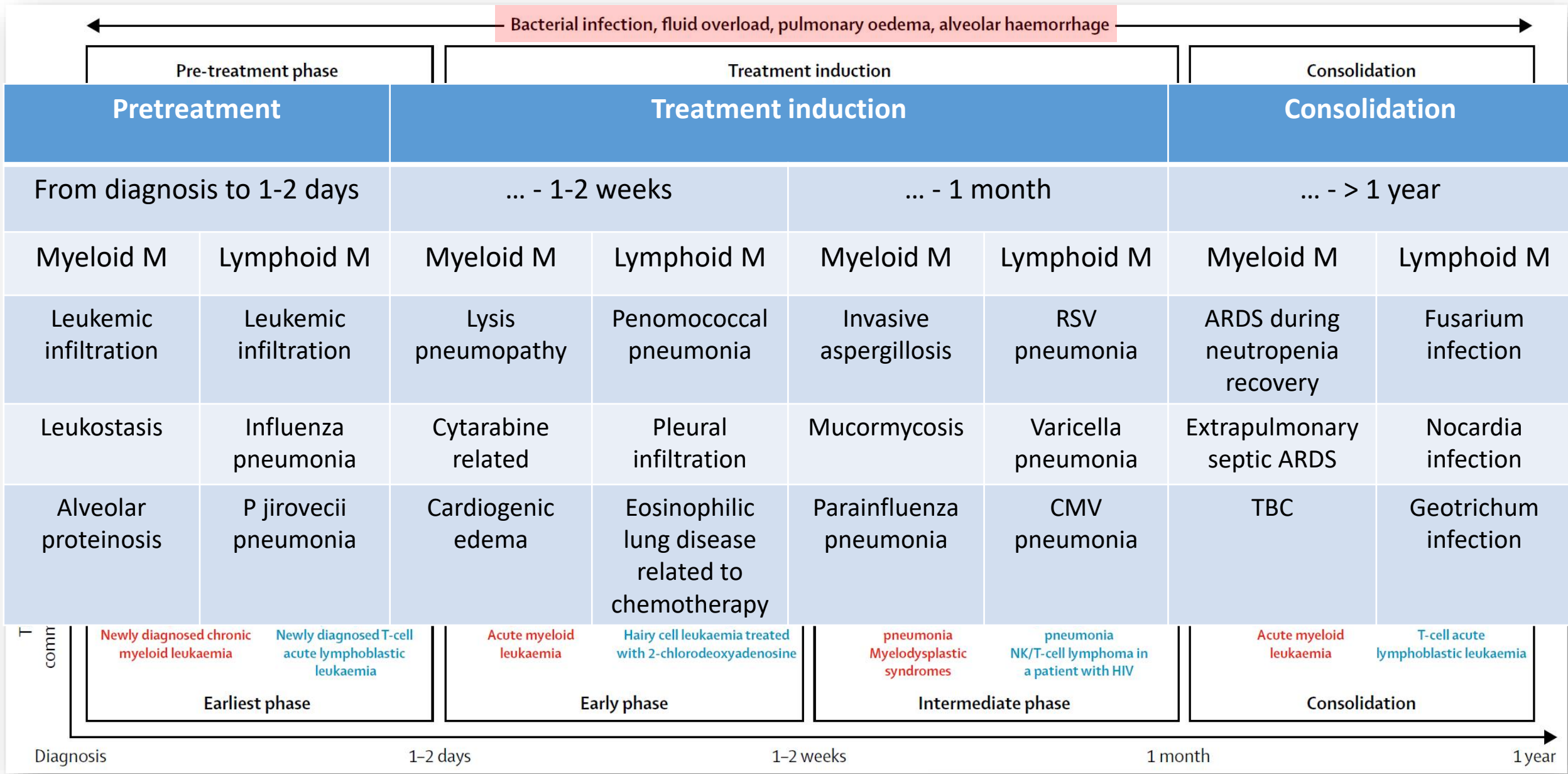


Diagnosis and outcome of acute respiratory failure in immunocompromised patients after bronchoscopy

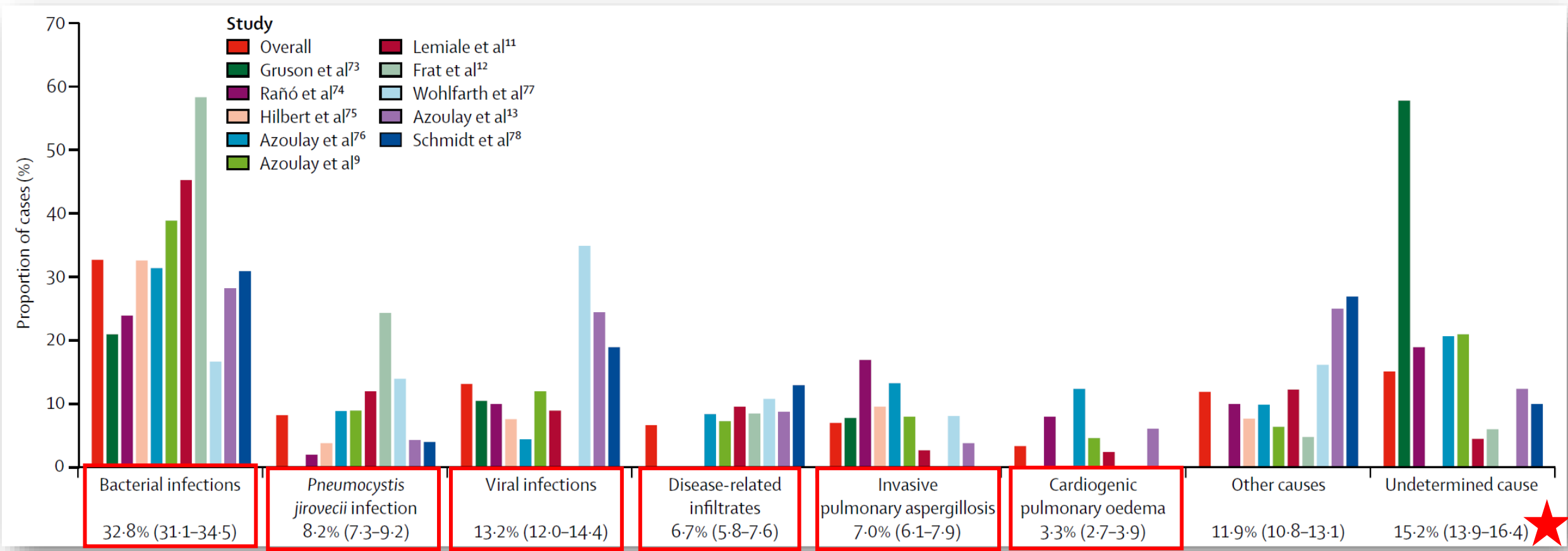
Eur Respir J 2019; 54: 1802442

Philippe R. Bauer¹, Sylvie Chevret², Hemang Yadav¹, Sangeeta Mehta³, Peter Pickkers⁴, Ramin B. Bukan⁵, Jordi Rello⁶, Andry van de Louw⁷, Kada Klouche⁸, Anne-Pascale Meert⁹, Ignacio Martin-Loeches^{10,11}, Brian Marsh¹², Lorenzo Socias Crespi¹³, Gabriel Moreno-Gonzalez¹⁴, Nina Buchtele¹⁵, Karin Amrein¹⁶, Martin Balik¹⁷, Massimo Antonelli¹⁸, Martine Nyunga¹⁹, Andreas Barratt-Due²⁰, Dennis C.J.J. Bergmans²¹, Angélique M.E. Spoelstra-de Man²², Anne Kuitunen²³, Florent Wallet²⁴, Amélie Seguin²⁵, Victoria Metaxa²⁶, Virginie Lemiale²⁷, Gaston Burgh²⁸, Alexandre Demoule²⁹, Thomas Karvunidis³⁰, Antonella Cotoia³¹, Pål Klepstad³², Ann M. Møller³³, Djamel Mokart³⁴ and Elie Azoulay²⁷ for the Efrain investigators and the Nine-I study group³⁵

- **Performed in 39% of patients** who had mostly hematological malignancy and a higher severity of illness score
- Achieved a **diagnosis in 27%** of patients and resulted in a **management change in 38%** of patients
- Associated with **worsening of respiratory status in 11%** of patients
- Rate of **undiagnosed causes was 13%**
- Associated with **higher ICU (40% vs 28%; p<0.0001) and hospital mortality (49% vs 41%; p=0.003)**
- Associated with **increased risk of hospital mortality (OR 1.4 [1.1–1.8] after propensity score matching)**



Acute respiratory failure in immunocompromised adults



Acute respiratory failure in immunocompromised adults

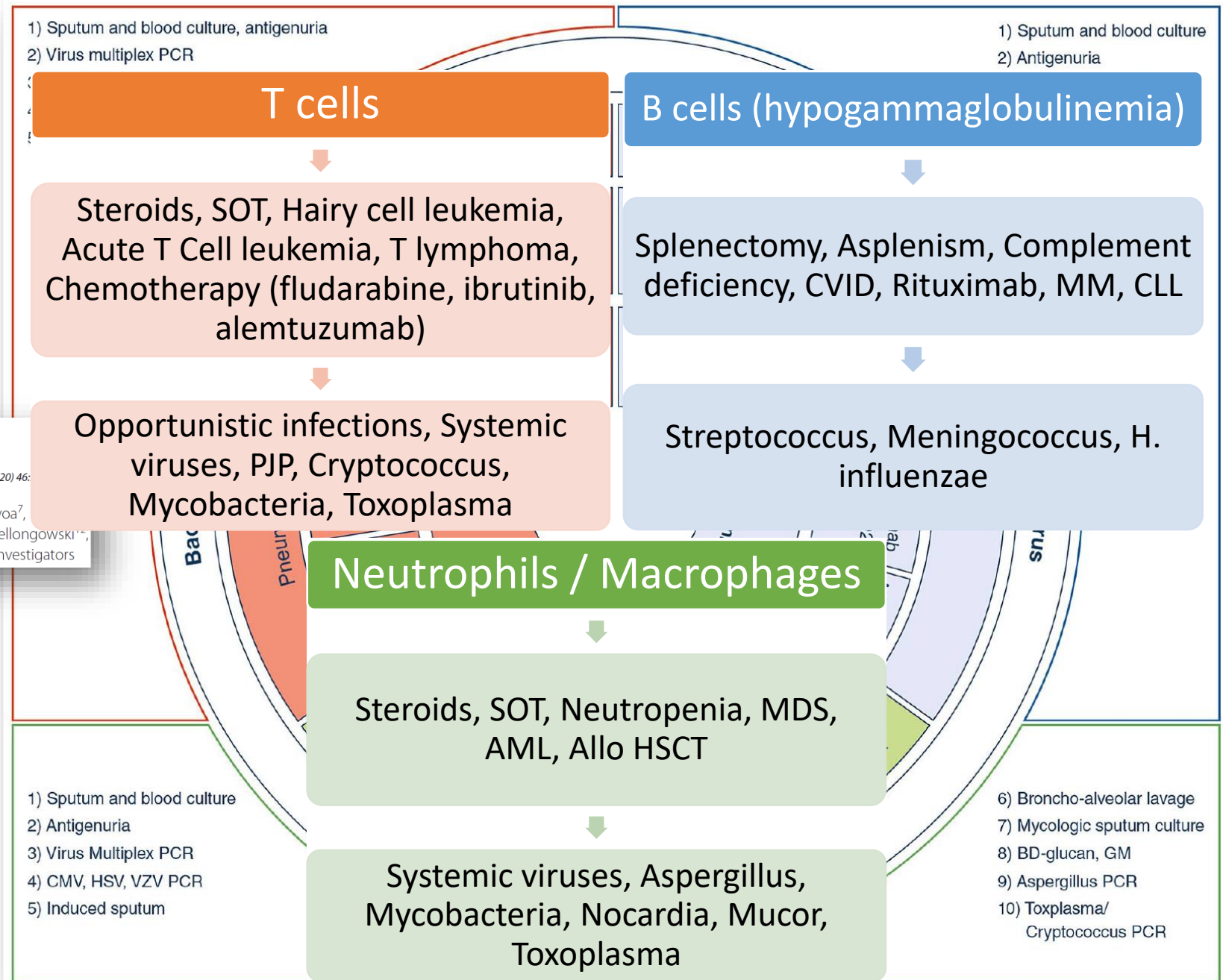
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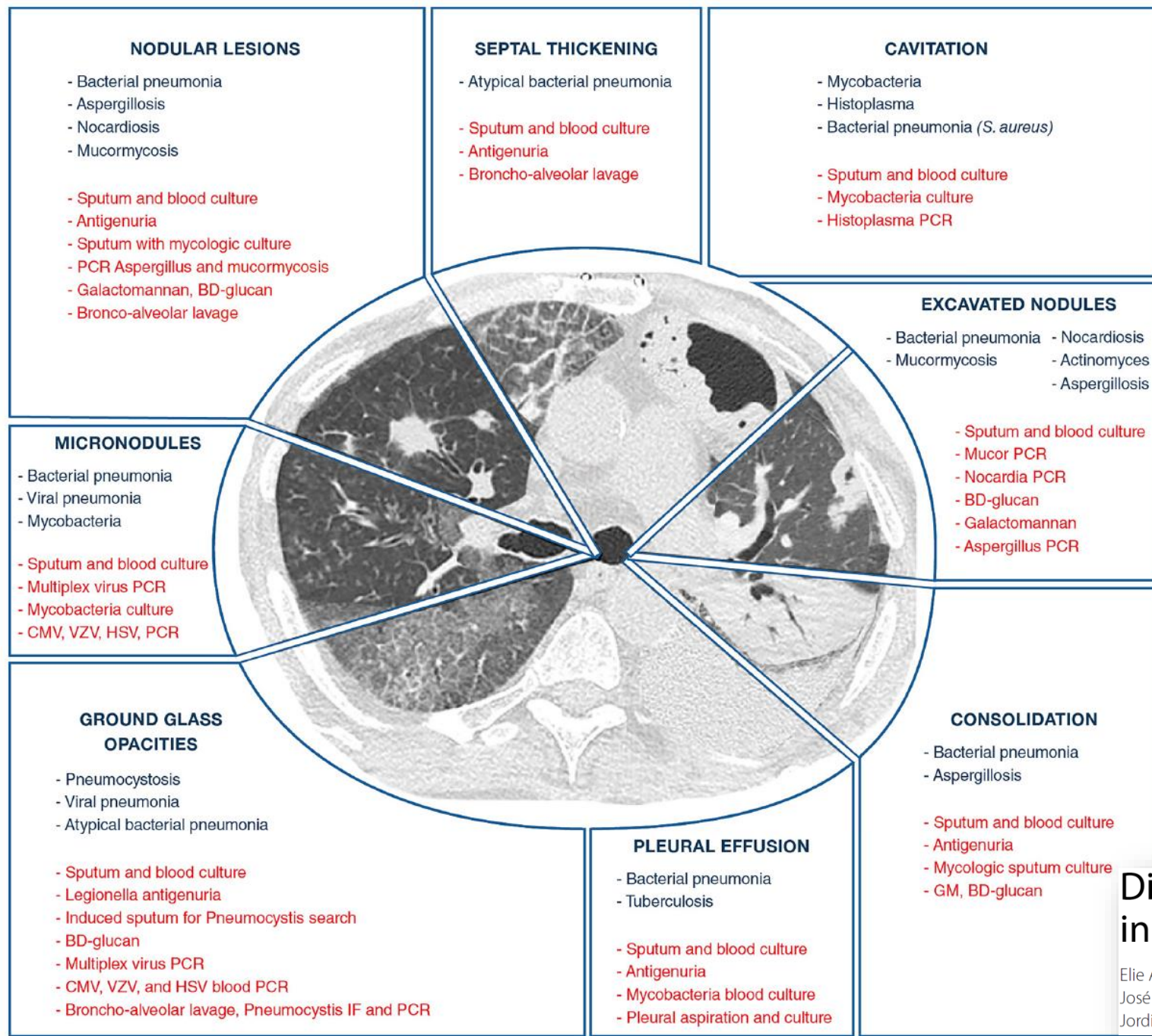
Lancet Respir Med 2019; 7: 173-86

Diagnosis of severe respiratory infections in immunocompromised patients

Intensive Care Med (2020) 46:

Elie Azoulay^{1,2*}, Lene Russell³, Andry Van de Louw⁴, Victoria Metaxa⁵, Philippe Bauer⁶, Pedro Povoas⁷, José Garnacho Montero⁸, Ignacio Martin Loeches⁹, Sangeeta Mehta¹⁰, Kathryn Puxty¹¹, Peter Schellongowski¹², Jordi Rello^{13,14}, Djamel Mokart¹⁵, Virginie Lemiale¹ and Adrien Mirouse^{1,2} on behalf of the Nine-i Investigators





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Table 3 Community-acquired respiratory virus (CARV)

| Type | Family | Genus | Virus |
|----------------|------------------------|---|--|
| RNA viruses | Orthomyxoviridae | <i>Influenza A</i> | All Influenza A subtypes |
| | | <i>Influenza B</i> | Influenza B |
| | Paramyxoviridae | <i>Rubulavirus</i> | Human parainfluenza virus type 2 (PIV-2) Human parainfluenza virus type 4a (PIV-4a) Human parainfluenza virus type 4b (PIV-4b) |
| | | <i>Respirovirus</i> | Human parainfluenza virus type 1 (PIV-1) Human parainfluenza virus type 3 (PIV-3) |
| | Pneumoviridae | <i>Metapneumovirus</i> | Human metapneumovirus (hMPV) |
| | | <i>Orthopneumovirus</i> | Human orthopneumovirus/Respiratory syncytial virus A (RSV-A) Human orthopneumovirus/Respiratory syncytial virus B (RSV-B) |
| Coronaviridae | <i>Betacoronavirus</i> | Middle East respiratory syndrome-related coronavirus (MERS-CoV) Severe acute respiratory syndrome-related coronavirus (SARS-CoV) Human coronavirus NL63 Human coronavirus 229E Human coronavirus HKU1 Human coronavirus OC43 | |
| Picornaviridae | <i>Enterovirus</i> | Enterovirus A-L Rhinovirus A, B, C | |

Table 4 Systemic viruses responsible for pneumonia in immunocompromised patients

| Virus type | Source | Extra-respiratory manifestations | Diagnosis |
|--------------------|--|---|--|
| HSV (HSV-1, HSV-2) | Donor transmission to transplant recipient Reactivation in T-cell defects | Skin and genital eruption Encephalitis, esophagitis, Keratitis | PCR (blood, BAL, tissue) Tissue culture Serology Histopathology |
| VZV | Donor transmission to transplant recipient Reactivation in T-cell defects | Varicella, herpes zoster Encephalitis, cerebellitis, hepatitis, myelitis Herpes zoster ophthalmicus | PCR Direct fluorescent antibody testing Viral culture Histopathology |
| CMV | Donor transmission to transplant recipient Reactivation in T-cell defects | Esophagitis, gastritis, colitis Retinitis, encephalitis, myelitis, polyradicu- lopathy Neutropenia | PCR (blood, BAL) Histopathology Serology |
| Adenovirus | Reactivation | Hemorrhagic cystitis, nephritis Colitis, hepatitis, encephalitis | Viral culture (nasal, blood, urine, CSF, tissues) EIA, Immunofluorescence, PCR, serology Histopathology |

Diagnosis of severe respiratory infections in immunocompromised patients

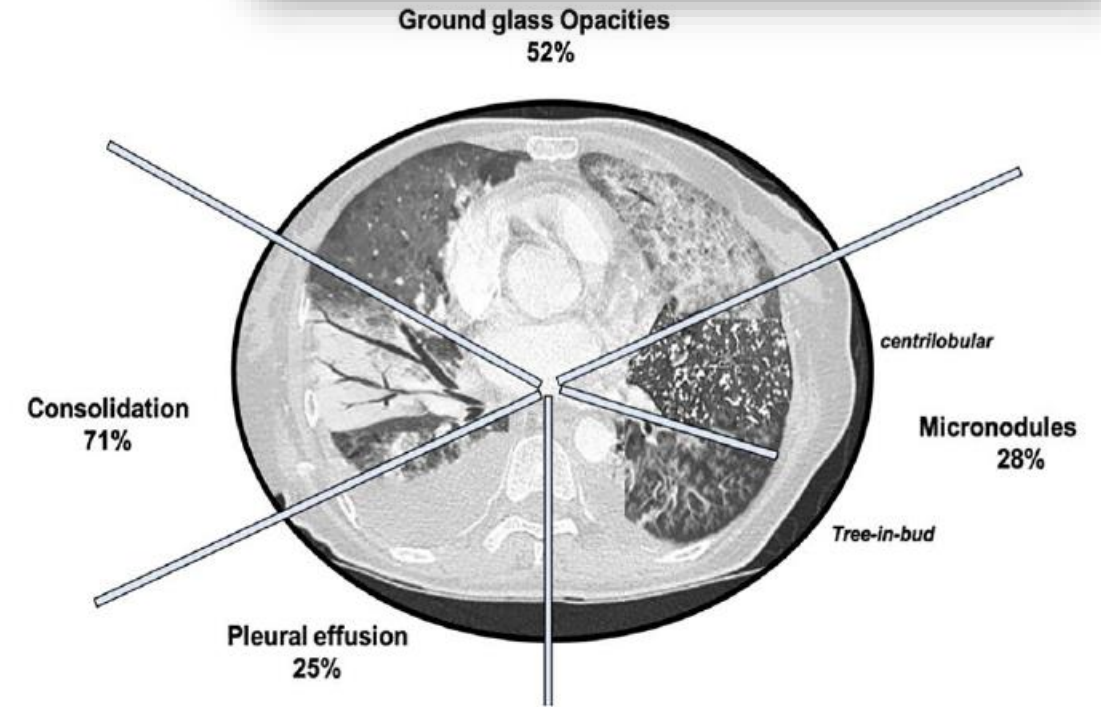
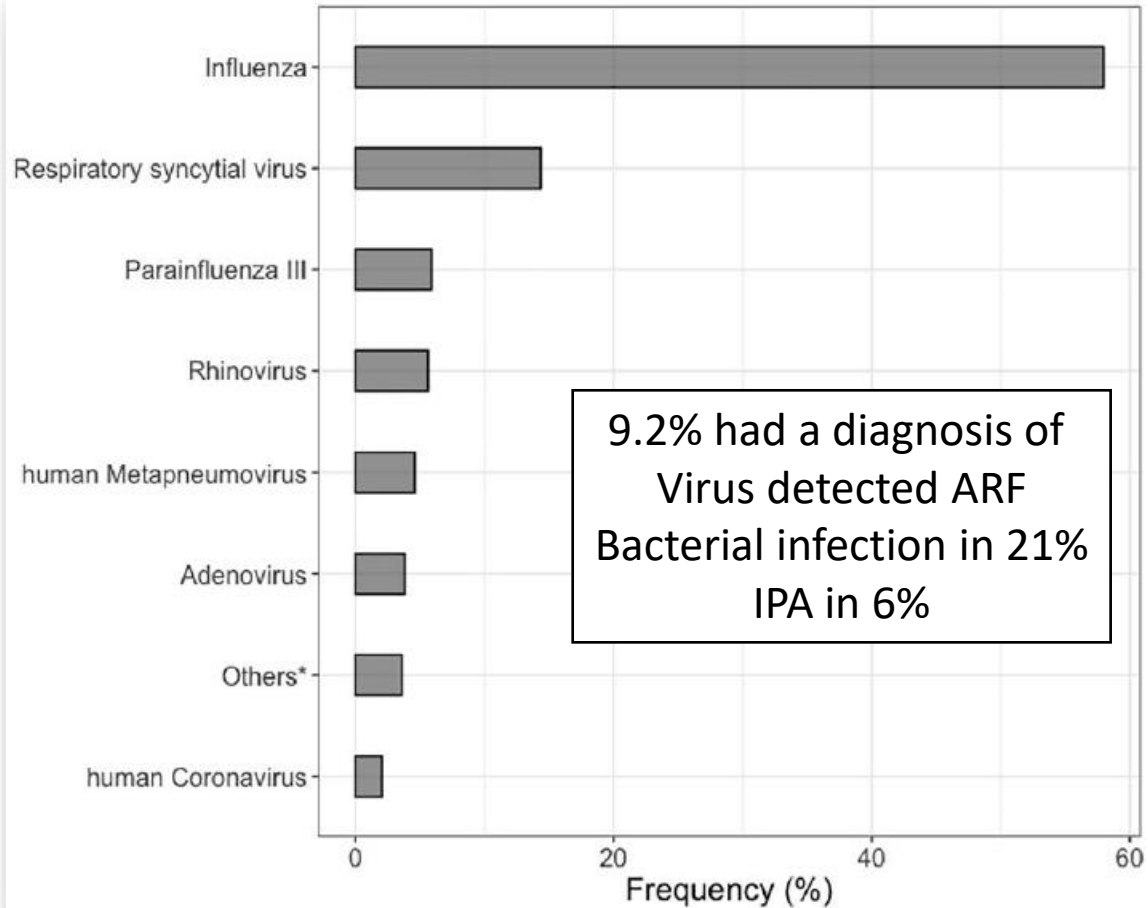
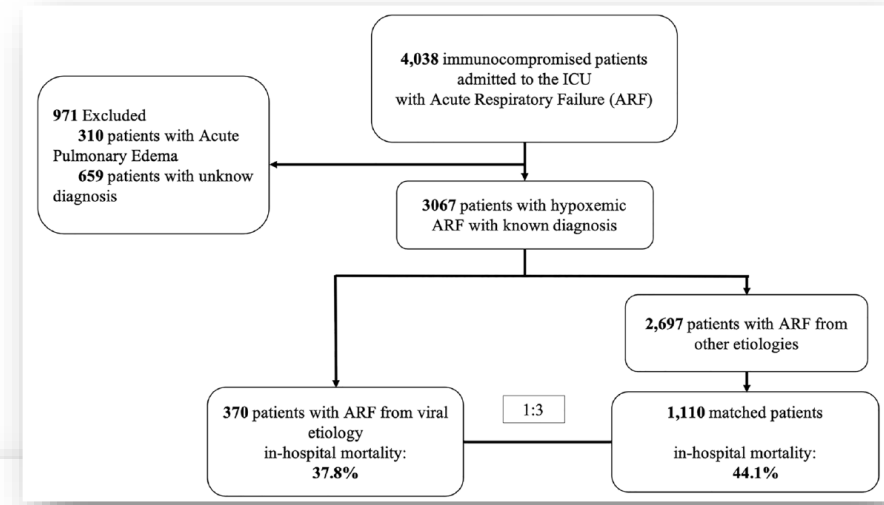
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Prognosis of critically ill immunocompromised patients with virus-detected acute respiratory failure

Guillaume Dumas^{1*}, Maxime Bertrand^{2,3}, Virginie Lemiale^{2,3}, Emmanuel Canet⁴, François Barbier⁵, Achille Kouatchet⁶, Alexandre Demoule⁷, Kada Klouche⁸, Anne-Sophie Moreau⁹, Laurent Argaud¹⁰, Florent Wallet¹¹, Jean-Herlé Raphalen¹², Djamel Mokart¹³, Fabrice Bruneel¹⁴, Frédéric Pène^{15,16} and Elie Azoulay^{2,3}

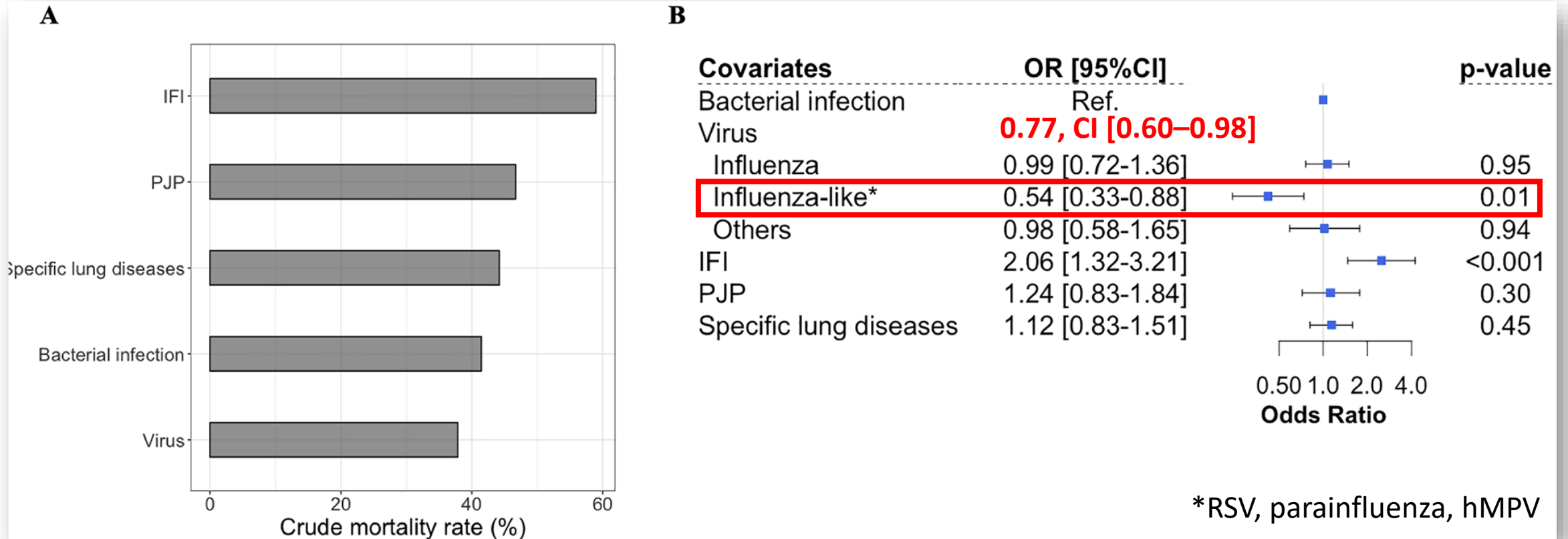
Annals of Intensive Care (2023) 13:101



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Annals of Intensive Care (2023) 13:101

Crude in-hospital mortality rate 38%



Invasive fungal infections

- *Pneumocystis jirovecii*
- *Aspergillus* spp
- *Cryptococcus* spp
- *Mucorales*
- *Fusarium*

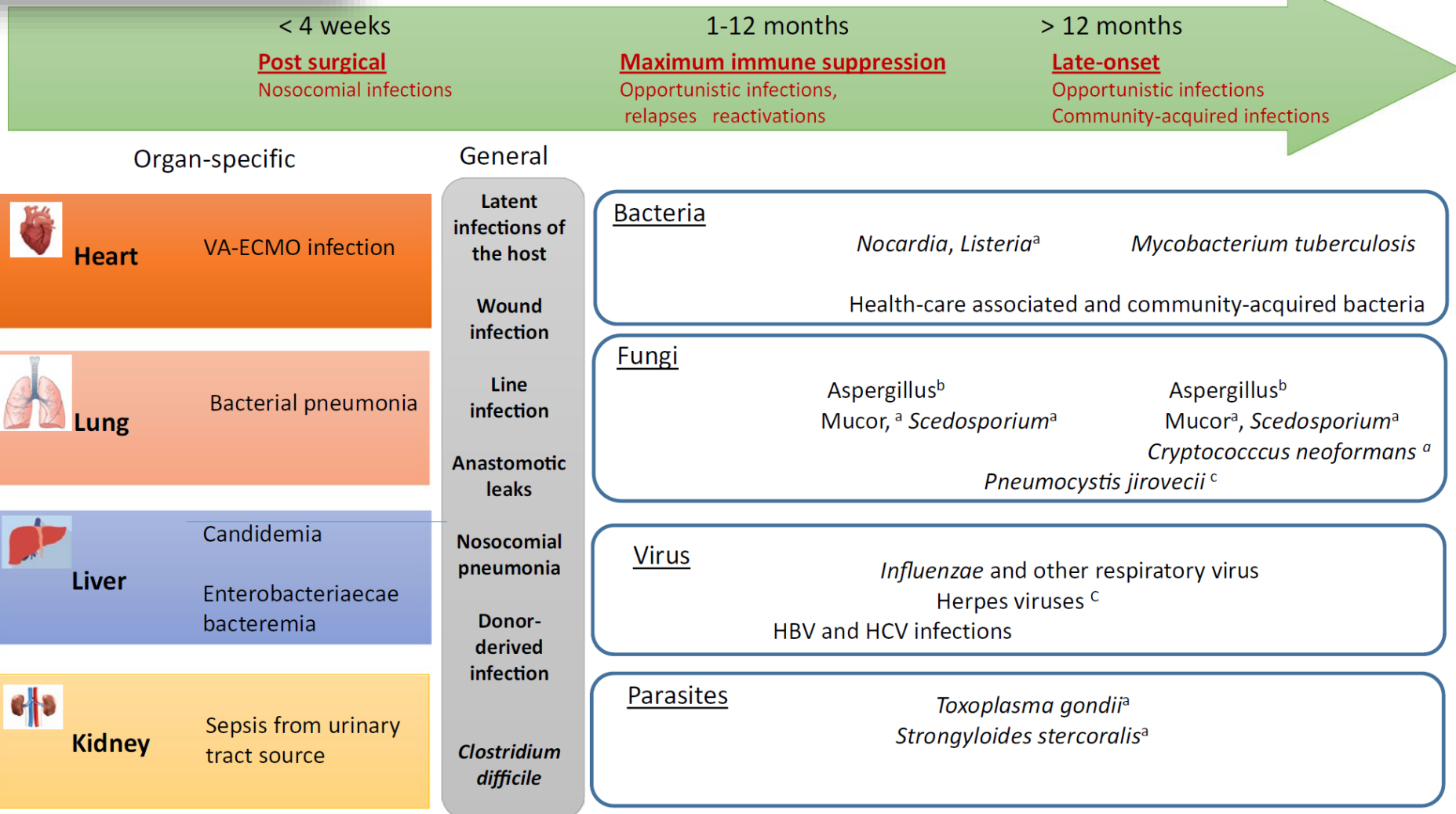
Parasitic infections

- *Toxoplasma gondii*
- *Strongyloides stercoralis*

Diagnostic and therapeutic approach to infectious diseases in solid organ transplant recipients

Intensive Care Med (2019) 45:573–591

Jean-François Timsit^{1,2*}, Romain Sonnevile^{3,4}, Andre C. Kalil⁵, Matteo Bassetti⁶, Ricard Ferrer⁷, Samir Jaber⁸, Fanny Lanternier^{9,10}, Charles-Edouard Luyt^{11,12}, Flavia Machado¹³, Malgorzata Mikulska¹⁴, Laurent Papazian¹⁵, Frédéric Pène^{16,17}, Garyphalia Poulakou¹⁸, Claudio Viscoli¹⁴, Michel Wolff¹⁹, Lara Zafrani²⁰ and Christian Van Delden²¹



a low incidence

b high incidence in lung Tx

c high incidence if no prophylaxis

Oxygenation and ventilation

- Earlier studies have shown higher mortality in immunocompromised patients who required IMV.
- However, more recent studies have revealed that failure of NIV or HFNO was associated with higher mortality, and even that early IMV was associated with improved survival, as IMV is a reflection of disease severity.

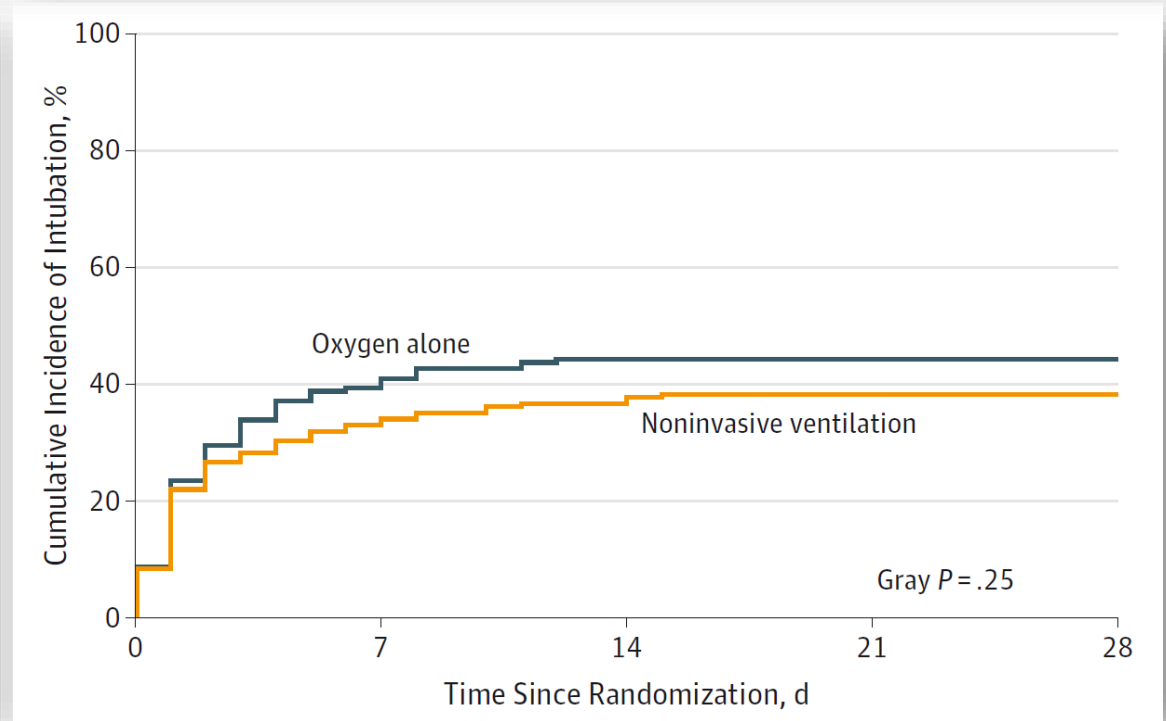
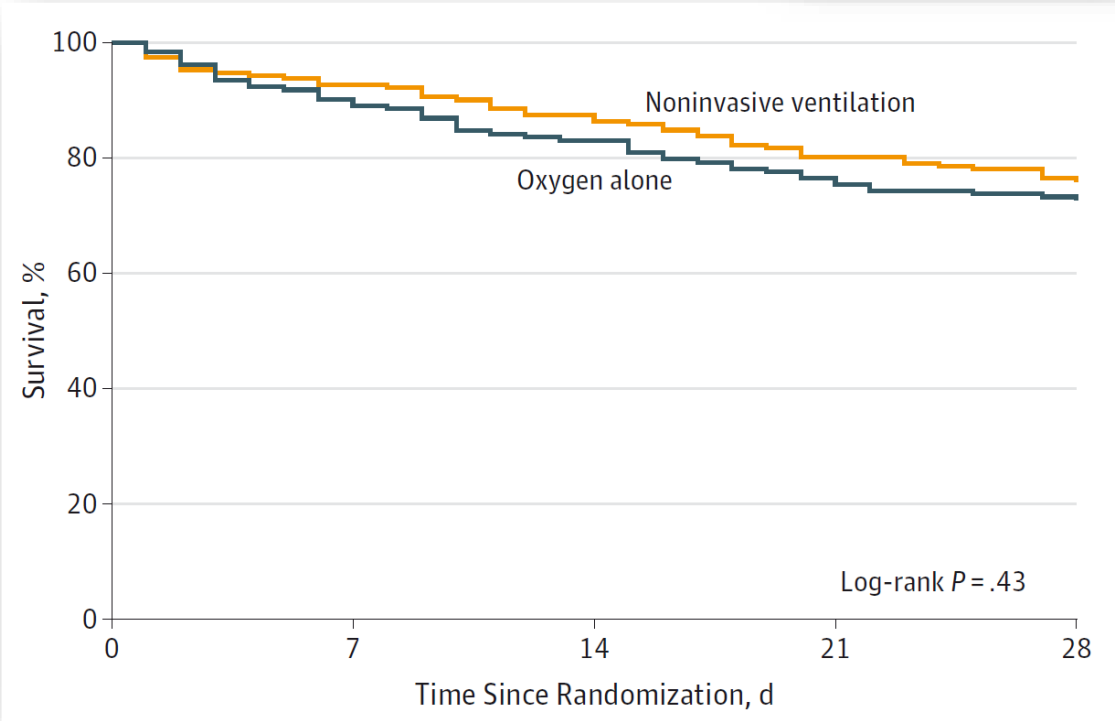
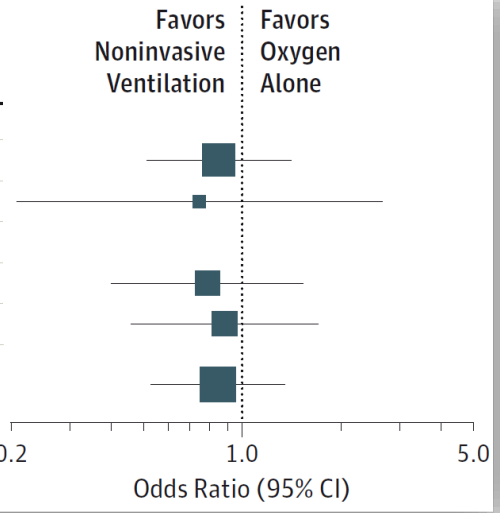
Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure

A Randomized Clinical Trial

JAMA. 2015;314(16):1711-1719.

Virginie Lemiale, MD; Djamel Mokart, MD; Matthieu Resche-Rigon, MD, PhD; Frédéric Pène, MD, PhD; Julien Mayaux, MD; Etienne Faucher, MD; Martine Nyunga, MD; Christophe Girault, MD, PhD; Pierre Perez, MD; Christophe Guitton, MD, PhD; Kenneth Ekpe, MD; Achille Kouatchet, MD; Igor Théodose, MS; Dominique Benoit, MD, PhD; Emmanuel Canet, MD; François Barbier, MD, PhD; Antoine Rabbat, MD; Fabrice Bruneel, MD; François Vincent, MD; Kada Klouche, MD, PhD; Kontar Loay, MD; Eric Mariotte, MD; Lila Bouadma, MD, PhD; Anne-Sophie Moreau, MD; Amélie Seguin, MD; Anne-Pascale Meert, MD, PhD; Jean Reignier, MD, PhD; Laurent Papazian, MD, PhD; Ilham Mehzeni, MD; Yves Cohen, MD, PhD; Maleka Schenck, MD; Rebecca Hamidfar, MD; Michael Darmon, MD, PhD; Alexandre Demoule, MD, PhD; Sylvie Chevret, MD, PhD; Elie Azoulay, MD, PhD; for the Groupe de Recherche en Réanimation Respiratoire du patient d'Onco-Hématologie (GRRR-OH)

| Source | No. of Deaths/Total No. | | Odds Ratio (95% CI) |
|---|-------------------------|-------------------------|---------------------|
| | Oxygen Alone | Noninvasive Ventilation | |
| Underlying Conditions | | | |
| Solid tumors or hematologic malignancies | 43/150 | 41/161 | 0.85 (0.51-1.40) |
| Immunosuppressive treatment or organ transplant | 7/33 | 5/30 | 0.74 (0.2-2.63) |
| Oxygen flow at randomization^b | | | |
| >9 L/min | 26/77 | 24/84 | 0.78 (0.4-1.53) |
| ≤9 L/min | 24/106 | 22/107 | 0.88 (0.46-1.70) |
| All patients | 50/183 | 46/191 | 0.84 (0.53-1.34) |

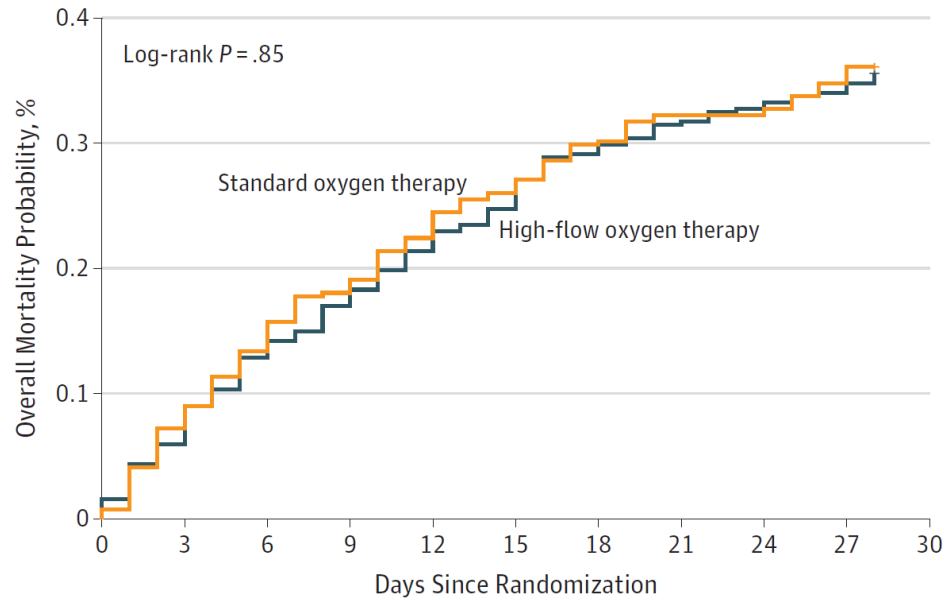


Effect of High-Flow Nasal Oxygen vs Standard Oxygen on 28-Day Mortality in Immunocompromised Patients With Acute Respiratory Failure

The HIGH Randomized Clinical Trial

JAMA. 2018;320(20):2099-2107.

Elie Azoulay, MD, PhD; Virginie Lemiale, MD; Djamel Mokart, MD, PhD; Saad Nseir, MD, PhD; Laurent Argaud, MD, PhD; Frédéric Pène, MD, PhD; Loay Kontar, MD; Fabrice Bruneel, MD; Kada Klouche, MD, PhD; François Barbier, MD, PhD; Jean Reignier, MD, PhD; Lilia Berrahil-Meksen, MD; Guillaume Louis, MD; Jean-Michel Constantin, MD, PhD; Julien Mayaux, MD; Florent Wallet, MD; Achille Kouatchet, MD; Vincent Peigne, MD; Igor Théodose, MS; Pierre Perez, MD; Christophe Girault, MD; Samir Jaber, MD, PhD; Johanna Oziel, MD; Martine Nyunga, MD; Nicolas Terzi, MD, PhD; Lila Bouadma, MD, PhD; Christine Lebert, MD; Alexandre Lautrette, MD, PhD; Naïke Bigé, MD, PhD; Jean-Herlé Raphalen, MD; Laurent Papazian, MD, PhD; Michael Darmon, MD, PhD; Sylvie Chevret, MD, PhD; Alexandre Demoule, MD, PhD



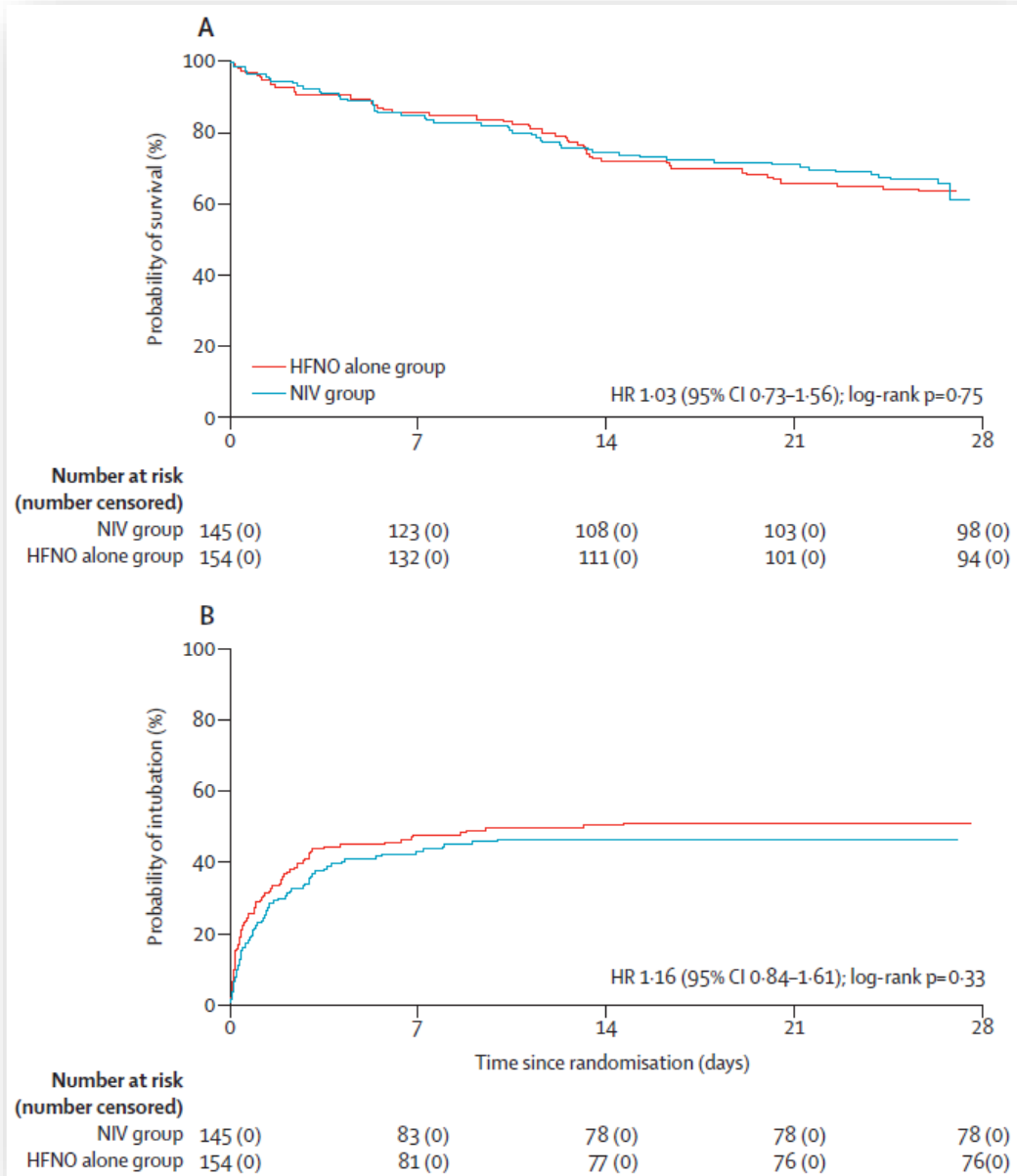
| Subset | Deaths at Day 28/Total No. of Patients | | Hazard Ratio (95% CI) | Favors High-Flow Nasal Oxygen Therapy | Favors Standard Oxygen Therapy |
|---|--|-------------------------|-----------------------|---------------------------------------|--------------------------------|
| | High-Flow Nasal Oxygen Therapy | Standard Oxygen Therapy | | | |
| ICU admission to randomization, d | | | | | |
| 0-1 | 120/321 | 118/330 | 0.95 (0.74-1.22) | | |
| ≥2 | 18/67 | 22/58 | 1.55 (0.83-2.90) | | |
| PaO ₂ : FIO ₂ ratio | | | | | |
| <200 | 99/237 | 95/251 | 0.89 (0.68-1.19) | | |
| ≥200 | 16/65 | 10/35 | 1.18 (0.54-2.60) | | |
| Oxygen flow at randomization, L/min | | | | | |
| ≤9 | 122/348 | 127/347 | 1.06 (0.83-1.36) | | |
| >9 | 16/40 | 13/41 | 0.76 (0.36-1.57) | | |
| Catecholamines | | | | | |
| No | 121/355 | 126/349 | 1.08 (0.84-1.39) | | |
| Yes | 17/33 | 14/39 | 0.62 (0.31-1.26) | | |
| Unknown diagnosis | | | | | |
| No | 99/297 | 95/303 | 0.93 (0.70-1.23) | | |
| Yes | 39/91 | 45/85 | 1.39 (0.90-2.13) | | |
| Hematologic malignancy | | | | | |
| No | 66/199 | 72/198 | 1.11 (0.79-1.55) | | |
| Yes | 64/167 | 65/181 | 0.94 (0.67-1.33) | | |
| All patients | 138/388 | 140/388 | 1.02 (0.81-1.29) | | |

Hazard Ratio (95% CI)

High-flow nasal oxygen alone or alternating with non-invasive ventilation in critically ill immunocompromised patients with acute respiratory failure: a randomised controlled trial

Lancet Respir Med 2022; 10: 641-49

Rémi Coudroy, Jean-Pierre Frat, Stephan Ehrmann, Frédéric Pène, Maxens Decavèle, Nicolas Terzi, Gwenaël Prat, Charlotte Garret, Damien Contou, Arnaud Gacouin, Jeremy Bourenne, Christophe Girault, Christophe Vinsonneau, Jean Dellamonica, Guylaine Labro, Sébastien Jochmans, Alexandre Herbland, Jean-Pierre Quenot, Jérôme Devaquet, Dalila Benzekri, Emmanuel Vivier, Saad Nseir, Gwenhaël Colin, Didier Thevenin, Giacomo Grasselli, David Bougon, Mona Assefi, Claude Guérin, Thierry Lherm, Achille Kouatchet, Stephanie Ragot, Arnaud W Thille, for the FLORALI-IM study group and the REVA Research Network*



| | HFNO alone group (n=154) | NIV group (n=145) | Hazard ratio (95% CI) | P _{interaction} |
|--|--------------------------|-------------------|-----------------------|--------------------------|
| All patients | 56/154 | 51/145 | 1.03 (0.73-1.56) | |
| Type of immunosuppression | | | | |
| Haematological malignancy or leucopenia or neutropenia | 31/81 | 22/75 | 1.37 (0.80-2.37) | 0.18 |
| Others | 25/73 | 29/70 | 0.82 (0.48-1.41) | |
| PaO₂/FiO₂ at inclusion | | | | |
| >200 mm Hg | 6/25 | 7/21 | 0.81 (0.26-2.51) | 0.50 |
| ≤200 mm Hg | 50/129 | 44/124 | 1.11 (0.74-1.66) | |
| Cause of respiratory failure | | | | |
| Confirmed diagnosis | 48/132 | 40/118 | 1.09 (0.71-1.65) | 0.87 |
| No diagnosis | 8/22 | 11/27 | 1.01 (0.40-2.56) | |

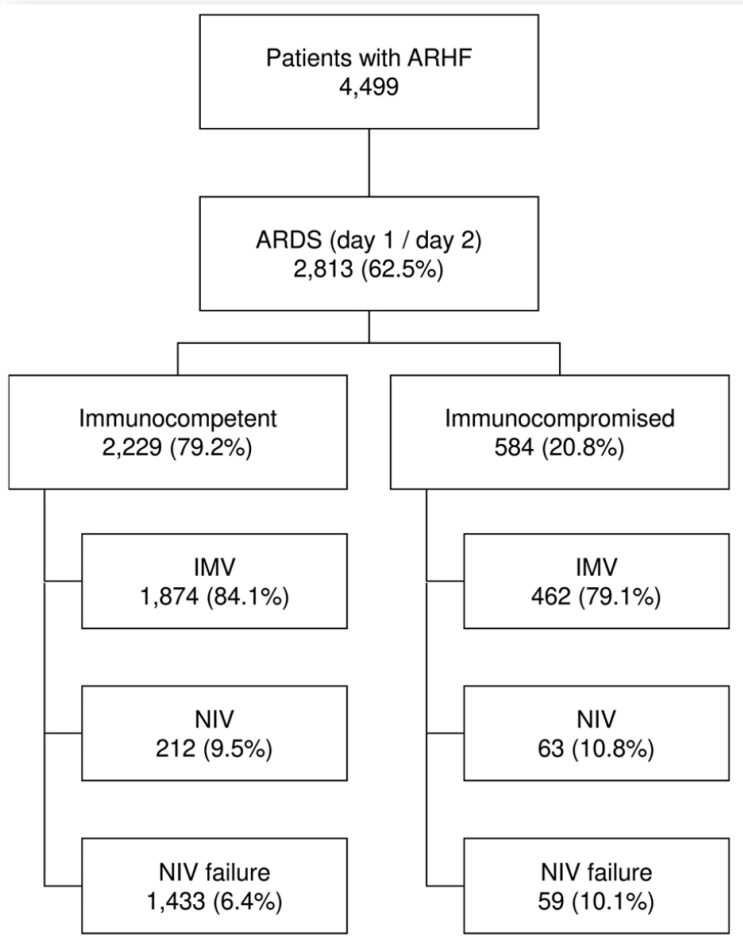
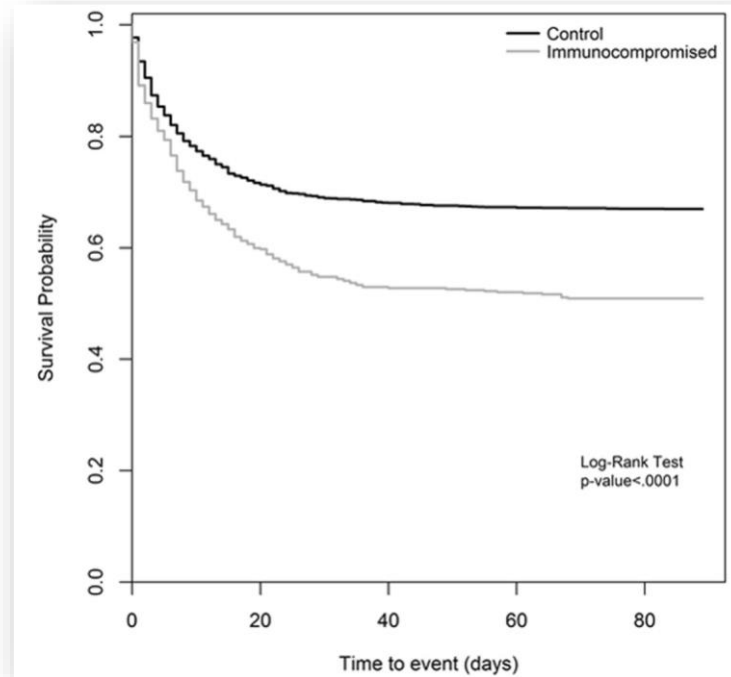
0.0 0.5 1 1.5 2.0 2.5 3.0

Favours HFNO alone Favours NIV

Immunocompromised patients with acute respiratory distress syndrome: secondary analysis of the LUNG SAFE database

Critical Care (2018) 22:157

Andrea Cortegiani^{1*}, Fabiana Madotto², Cesare Gregoretti¹, Giacomo Bellani^{3,4}, John G. Laffey^{5,6,7}, Tai Pham^{6,7}, Frank Van Haren^{8,9}, Antonino Giarratano¹, Massimo Antonelli¹⁰, Antonio Pesenti^{11,12}, Giacomo Grasselli¹¹, LUNG SAFE Investigators and the ESICM Trials Group



| | Control (n = 2229) | Study (n = 584) | p Value |
|---|-----------------------|--------------------|----------|
| ICU mortality ^b , n (%) | 698 (31.3) | 266 (45.5) | < 0.0001 |
| Hospital mortality ^c , n (%) | | 304 (52.4) | < 0.0001 |
| All patients | 804 (36.2) | | |

| | IMV (n = 462) | NIV (n = 63) | NIV failure (n = 59) | p Value |
|---|------------------|------------------------|-------------------------|---------|
| ICU mortality ^d , n (%) | 214 (46.3) | 18 (28.6) ^b | 34 (57.6) ^c | 0.0043 |
| Hospital mortality ^e , n (%) | | 25 (39.7) | 37 (62.7) ^c | 0.0362 |
| All patients | 242 (52.8) | | | |

Survival in Immunocompromised Patients Ultimately Requiring Invasive Mechanical Ventilation

Invasive Mechanical Ventilation

Am J Respir Crit Care Med Vol 204, Iss 2, pp 187–196, Jul 15, 2021

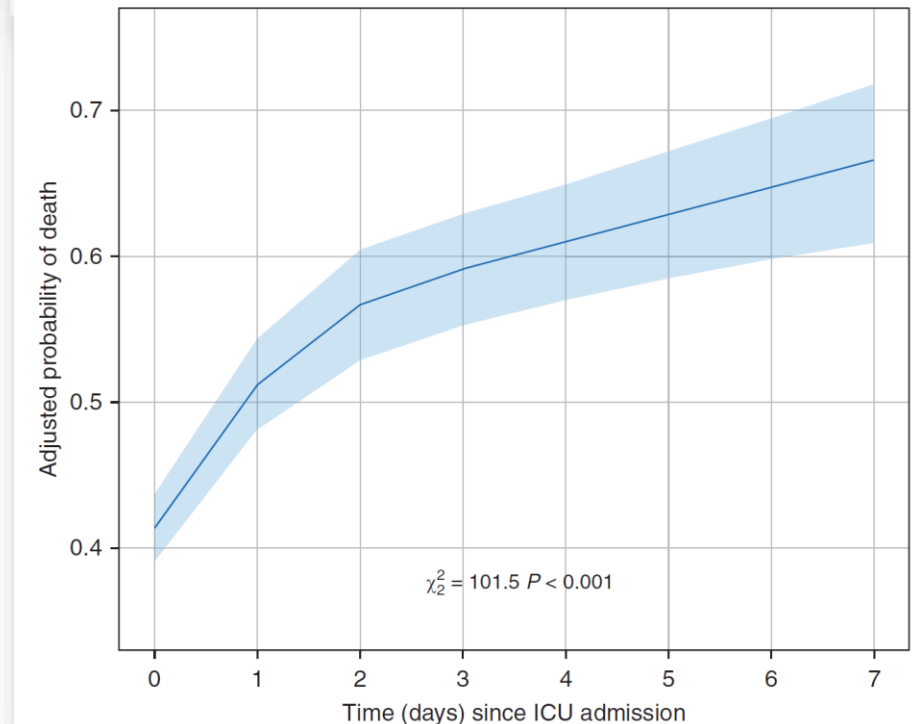
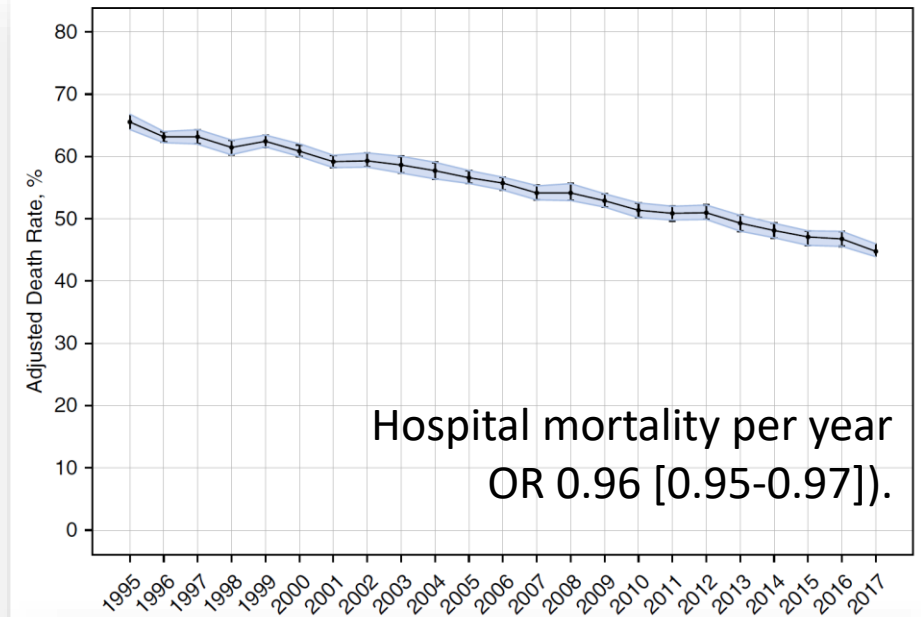
A Pooled Individual Patient Data Analysis

Guillaume Dumas^{1,2}, Virginie Lemiale^{1,2}, Nisha Rathi³, Andrea Cortegiani⁴, Frédéric Pène⁵, Vincent Bonny^{1,2}, Jorge Salluh⁶, Guillermo M. Albaiceta^{7,8}, Marcio Soares⁶, Ayman O. Soubani⁹, Emmanuel Canet¹⁰, Tarik Hanane¹¹, Achille Kouatchet¹², Djamel Mokart¹³, Pia Lebiez¹⁴, Melda Türkoğlu¹⁵, Rémi Coudroy^{16,17}, Kyeongman Jeon^{18,19}, Alexandre Demoule²⁰, Sangeeta Mehta²¹, Pedro Caruso²², Jean-Pierre Frat^{16,17}, Kuang-Yao Yang^{23,24}, Oriol Roca^{8,25,26}, John Laffey^{27,28}, Jean-François Timsit²⁹, Elie Azoulay^{1,2}, and Michael Darmon^{1,2}

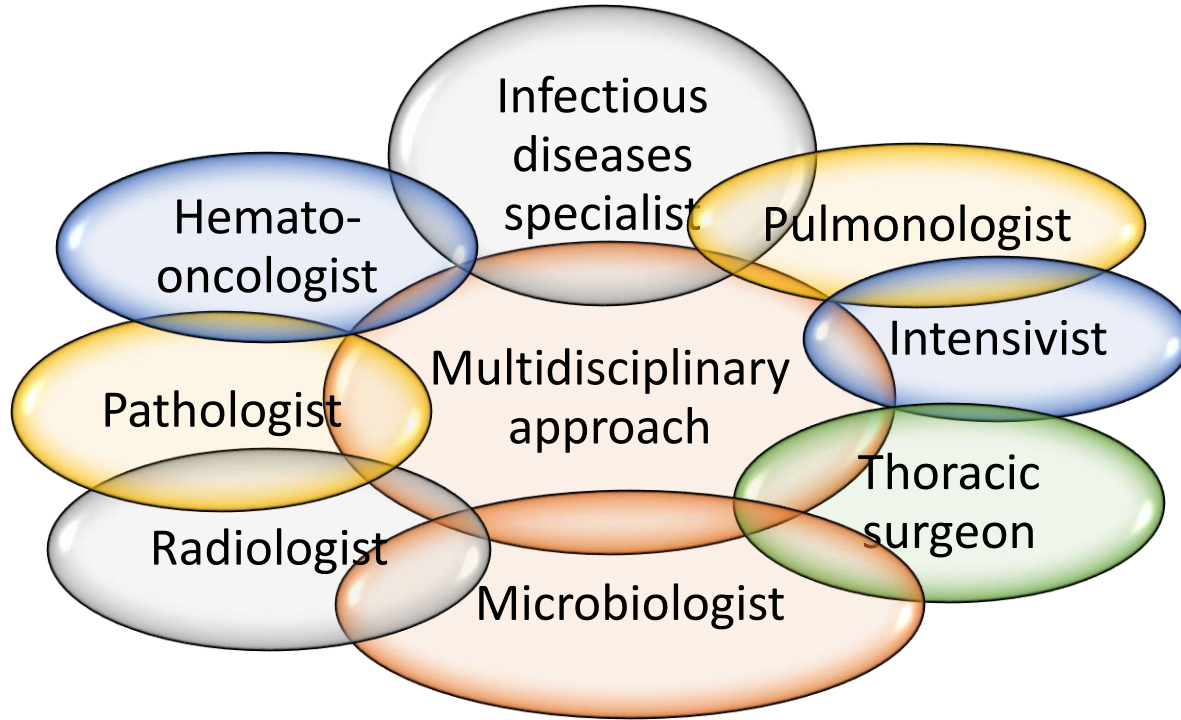
- 24 ICUs, 11,000+ pts
- 74% were intubated within 24 hours of ICU admission (early intubation)
- The crude mortality rate was 53%
- Mortality for **time from admission to intubation OR 1.38** [1.26-1.52]
- Mortality for **early intubation OR 0.83** [0.72-0.96]
- After propensity match, OR for **delayed intubation, 1.56** [1.44-1.70]

Table 2. Result of Regression Model Assessing Factors Independently Associated with Hospital Mortality, with Study as a Random Effect

| | OR (95% CI) | P Value |
|--|------------------|---------|
| Time to intubation, d* | 1.38 (1.26–1.52) | <0.001 |
| Age >60 yr | 1.73 (1.56–1.92) | <0.001 |
| Underlying disease | | |
| Nonmalignant immunosuppression | Ref. | |
| Solid tumor | 1.56 (1.34–1.81) | <0.001 |
| Hematological malignancy | 1.69 (1.38–2.05) | <0.001 |
| Respiratory etiology undetermined | 1.46 (1.10–1.94) | 0.01 |
| Pa _O ₂ /FiO ₂ | | |
| >300 mm Hg | Ref. | |
| 200–299 mm Hg | 1.32 (1.05–1.67) | 0.02 |
| 100–199 mm Hg | 1.56 (1.25–1.95) | <0.001 |
| <100 mm Hg | 2.26 (1.79–2.85) | <0.001 |
| Nonrespiratory SOFA score (by point) | 1.22 (1.20–1.24) | <0.001 |
| Year of admission | 0.96 (0.95–0.97) | <0.001 |



In conclusion ...



Try to avoid
undetermined
diagnosis !

Try to avoid
delayed ICU
admission !

Thank you ...