

Immunocompromised Hosts in the ICU

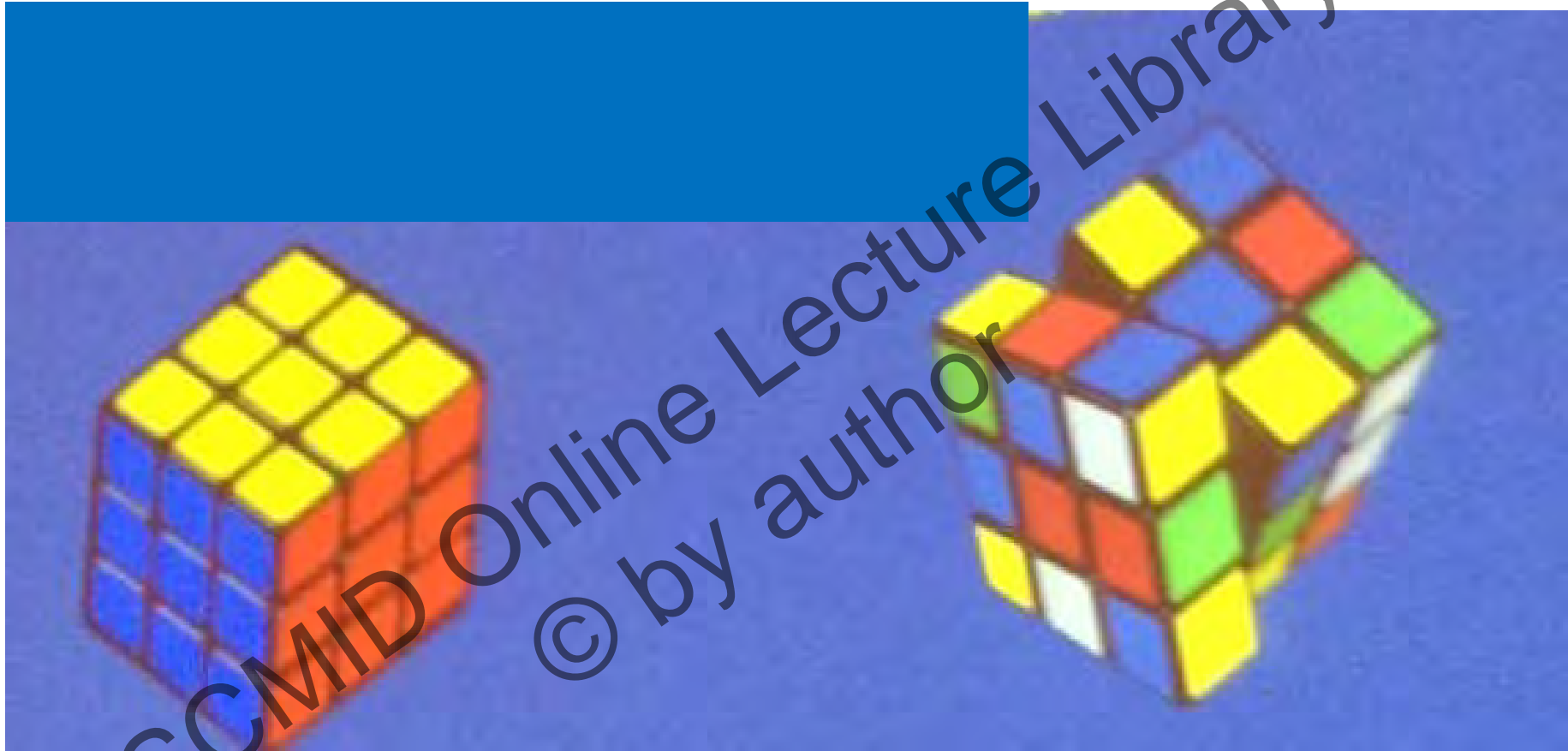
Current Challenges

Francesco G. De Rosa

Associate Professor, Infectious Diseases

Vice Director, Dept. of Medical Sciences

University of Turin, Italy



Normal Host

**Immunocompromised
Patients**

Immunodeficiencies & Associated Pathogens

Defect	Pathogen
Granulocytopenia	Gram-positiv cocci, <i>S. aureus</i> , CNS, Viridans group Streptococci, Granulicatella & Abiotrophia species, Enterococci, Gram-negative bacilli, <i>E. coli</i> , <i>P. aeruginosa</i> , <i>K. pneumoniae</i> , Enterobacter & Citrobacter species
Tegument damaged: CVC-related	CNS, <i>S. aureus</i> , <i>S. maltophilia</i> , <i>P. aeruginosa</i> , Acinetobacter species, Corynebacteria, Candida & Rhizopus species,
Oral mucositis	Viridans group Streptococci, Abiotrophia & Granulicatella species, Capnocytophaga, Fusobacterium, Rothia mucilaginosa, <i>Candida spp.</i> , HSV
Gut mucosal barrier injury	<i>E. coli</i> , <i>P. aeruginosa</i> , CNS, Enterococci, <i>Candida spp.</i>
Neutropenic enterocolitis	<i>Clostridium spp.</i> (septicum, tertium), <i>S. aureus</i> , <i>P. aeruginosa</i>

Immunodeficiencies & Associated Pathogens

Defect	Pathogen
Impaired cellular immunity	HSV, CMV, Respiratory viruses <i>Mycobacterium tuberculosis</i> , <i>Listeria monocytogenes</i> , <i>Nocardia</i> species, Non-tuberculous mycobacteria <i>Pneumocystis jirovecii</i> , <i>Aspergillus</i> spp., <i>Cryptococcus</i> spp., <i>Histoplasma capsulatum</i> , <i>Coccidioides</i> species, <i>Penicillium marneffeii</i> , <i>Toxoplasma gondii</i>
Impaired humoral immunity	<i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i>
Compromised spleen function	<i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i> , <i>Neisseria meningitidis</i>

Immunocompromised Patients

- Cancer
- Neutropenic Vs. deficit cell/mediated immunity
 - Allogenic HSCT
 - Multiple myeloma
 - Solid Organ Transplant
 - Liver Vs. Kidney Vs. Heart Vs. Lung
- HIV / AIDS
- Monoclonal Antibodies, Rheumatology
- Devices, ECMO....
- Epidemiology of Resistance
- Viral Infections
 - CMV, HSV, Resp. Viruses, H1N1

Challenges

- **Immunosuppression**
 - Infectious risk
- **Admission**
 - Not delayed
- **Support**
 - ECMO.....
- **Diagnosis**
 - Diagnostic strategies
- **Treatment**
 - Pharmacology
- **Stewardship**

Signs of marrow failure

Storm cloud of infection

Granulo-rise

Initial
empiric
therapy

Modifications
and antifungal
therapy

GO

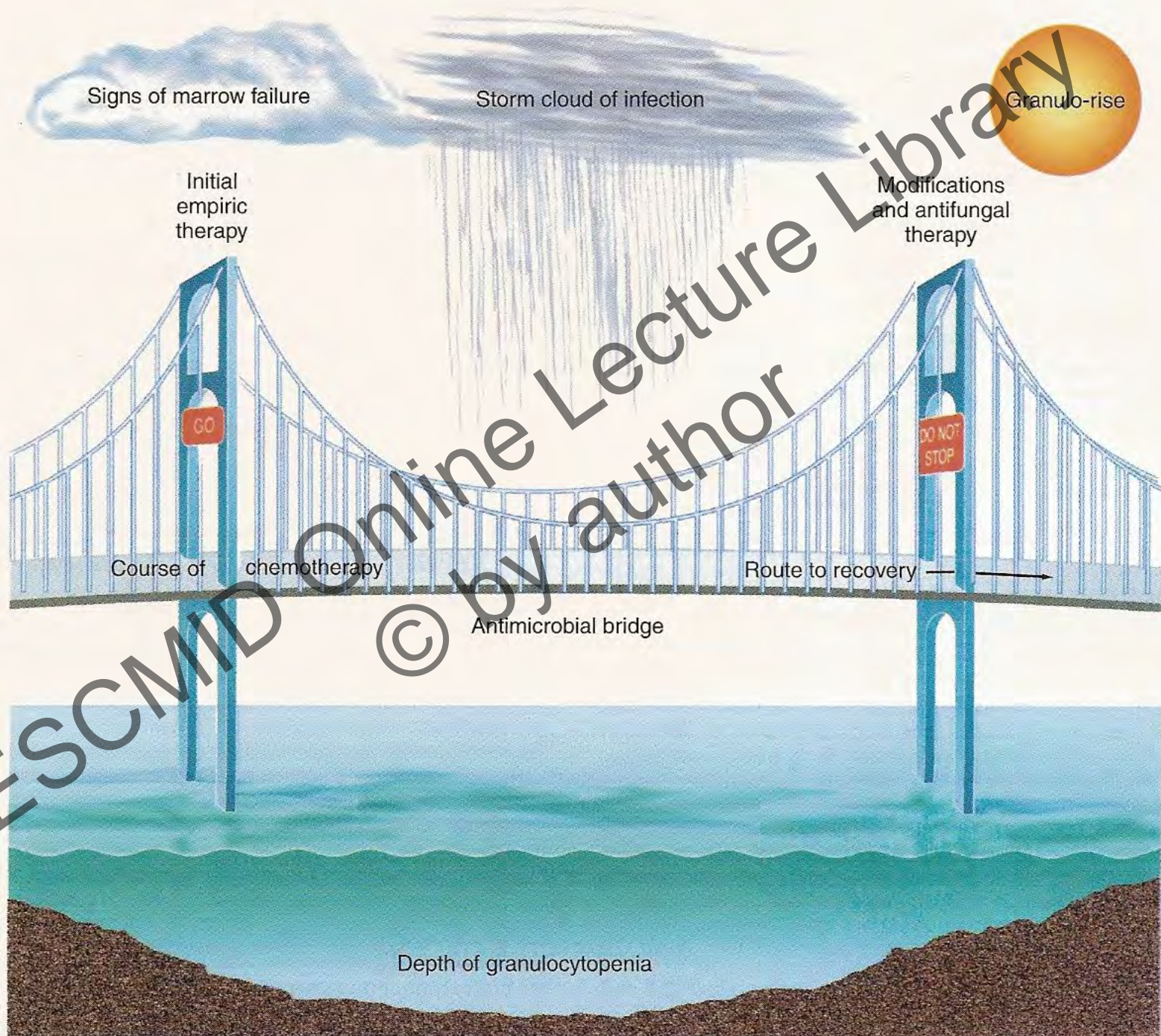
DO NOT
STOP

Course of
chemotherapy

Route to recovery

Antimicrobial bridge

Depth of granulocytopenia



ESCMID Online Lecture Library
© by author

Sepsis Severe or Septic Shock

Outcome According to Immune Status and Immunodeficiency Profile

Violaine Tolsma, MD; Carole Schwebel, MD, PhD; Elie Azoulay, MD, PhD; Michael Darmon, MD, PhD; Bertrand Souweine, MD, PhD; Aurélien Vesin, MSc; Dany Goldgran-Toledano, MD; Maxime Lugosi, MD; Samir Jamali, MD; Christine Cheval, MD; Christophe Adrie, MD, PhD; Hatem Kallel, MD; Adrien Descorps-Declere, MD; Maité Garrouste-Orgeas, MD, PhD; Lila Bouadma, MD, PhD; and Jean-François Timsit, MD, PhD

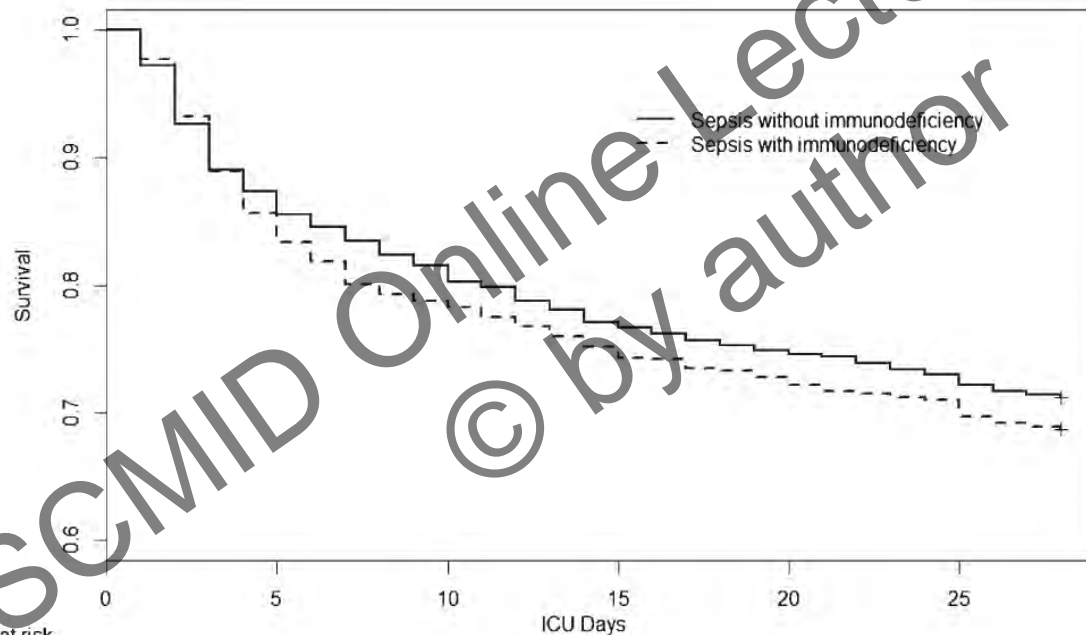
RESULTS: Among the 1,981 included patients, 607 (31%) were immunocompromised (including nonneutropenic solid tumor [19.6%], nonneutropenic hematologic malignancies [26.3%], and all-cause neutropenia [28%]). Compared with immunocompetent patients, immunocompromised patients were younger, with less comorbidity, were more often admitted for medical reasons, and presented less often with septic shock. The D28 crude mortality was 31.3% in immunocompromised patients and 28.8% in immunocompetent patients ($P = .26$). However, after adjustment for other prognostic factors, immunodeficiency was an independent risk factor for death at D28 (subdistribution hazard ratio [sHR], 1.37; 95% CI, 1.12-1.67). The immunodeficiency profiles independently associated with death were AIDS (sHR = 1.9), nonneutropenic solid tumor (sHR = 1.8), nonneutropenic hematologic malignancies (sHR = 1.4), and all-cause neutropenia (sHR = 1.7).

CONCLUSIONS: Immunodeficiency is common in patients with severe sepsis or septic shock. Despite a similar crude mortality, immunodeficiency was associated with an increased risk of short-term mortality after multivariate analysis. Neutropenia and specific, but not all, profiles of immunodeficiency were independently associated with an increased risk of death.

Sepsis Severe or Septic Shock

Outcome According to Immune Status and Immunodeficiency Profile

Violaine Tolsma, MD; Carole Schwebel, MD, PhD; Elie Azoulay, MD, PhD; Michael Darmon, MD, PhD; Bertrand Souweine, MD, PhD; Aurélien Vesin, MSc; Dany Goldgran-Toledano, MD; Maxime Lugosi, MD; Samir Jamali, MD; Christine Cheval, MD; Christophe Adrie, MD, PhD; Hatem Kallel, MD; Adrien Descorps-Declere, MD; Maité Garrouste-Orgeas, MD, PhD; Lila Bouadma, MD, PhD; and Jean-François Timsit, MD, PhD

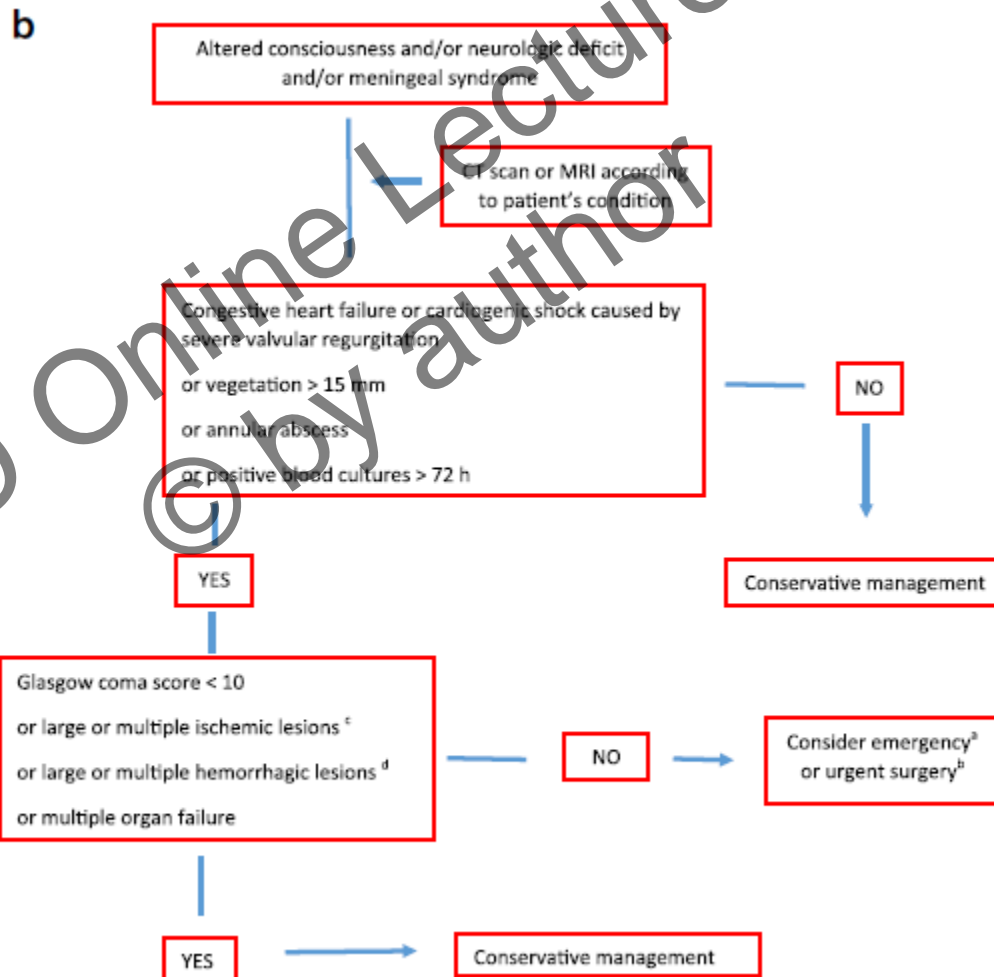


No. of patients at risk	0	5	10	15	20	25
Sepsis without immun.	1374	1200	1121	1059	1029	1002
Sepsis with immun.	607	520	478	456	442	431

Figure 3 – Kaplan-Meier survival curve between d 1 and d 28 according to the immune status. Immun = immunodeficiency.

Michel Wolff
Bruno Mourvillier
Romain Sonnevile
Jean-François Timsit

My paper 10 years later: infective endocarditis in the intensive care unit



Our Epidemiological Comments

- KPC wave....
 - Future agenda, Future Microbiol 2015
- High rate of MDR GNR in H1N1 infected patients with ARDS treated with ECMO
 - ICM 2013
- Save the tube
 - Carbapenemase
 - *C. difficile*
 - Candida
 - Clin Infect Dis 2015

K. pneumoniae Carbapenemase (KPC)- producing *K. pneumoniae*

- Is this an epidemiological issue?
 - Yes
- Is this a transplant issue?
 - Do not know
- Is this a critical issue?
 - Yes
- Is this a critical issue in transplant patients?
 - Yes

Invasive Fungal Infections

- Prophylaxis
 - Limited role for Candida
 - More caution for solid organ transplant recipients
- Pre-emptive treatment
 - Need beta-glucan
- Empiric treatment
 - Pros and cons
- Definite treatment
 - Need diagnosis

Mortality of Invasive Candidiasis

Difficult to Detect
Easy to Cure

Easy to Detect
Difficult to Cure

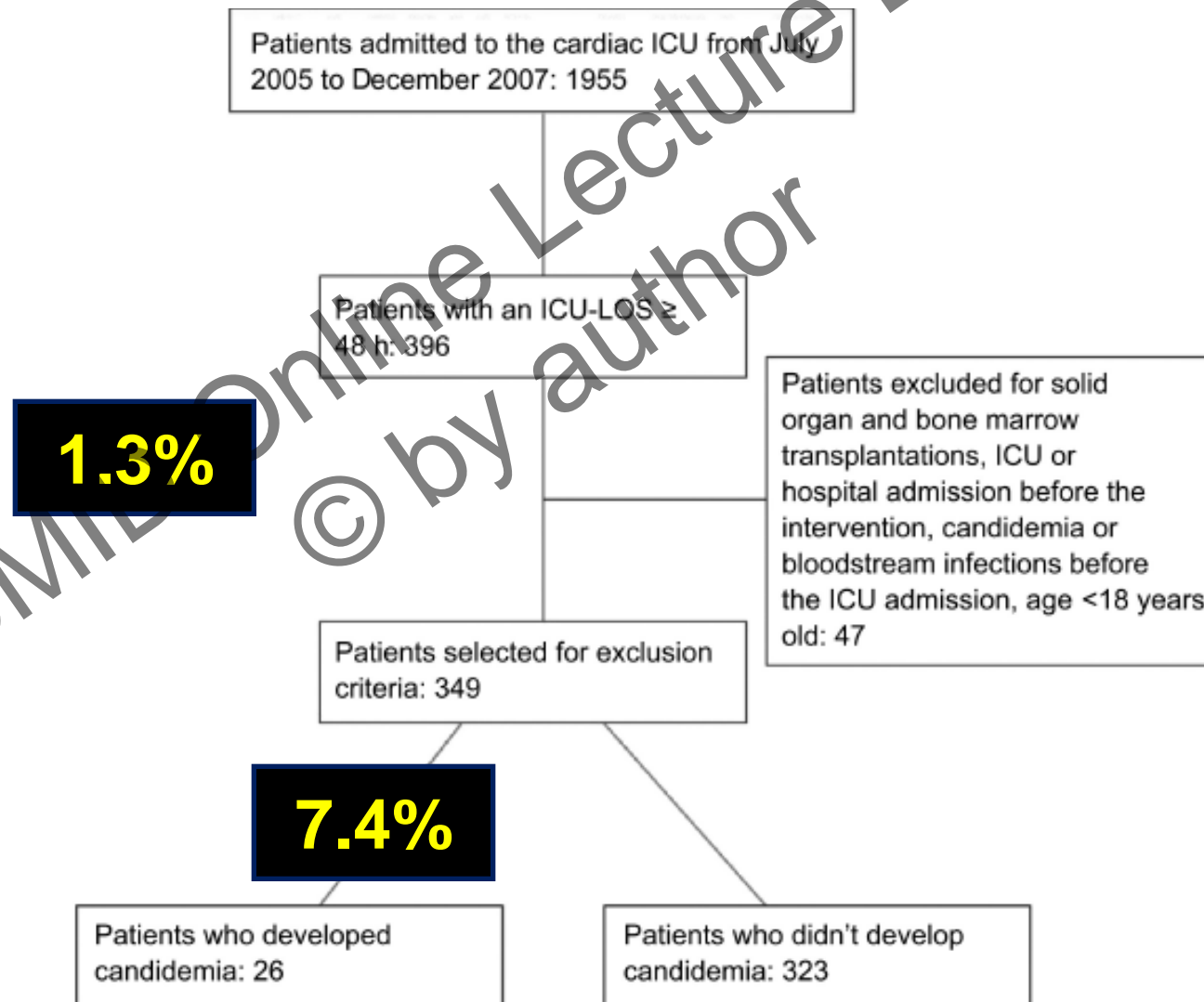
-

+



Candidemia After Cardiac Surgery In The ICU: An Observational Study

Pasero D et al *Interact CardioVasc Thorac Surg* 2011;12:374-378



Aspergillus in the Lower Respiratory Tract of Immunocompetent Critically Ill Patients

Lugosi M et al J Infect 2014; 69(3): 284-92

- 66 cases (5 with **definite** invasive pulmonary aspergillosis (IPA), 18 with probable IPA, and 43 colonisations) were matched to 330 controls
- **Independent risk factors** for at least one Aspergillus-positive respiratory-tract specimen were:
 - SAPSII at admission [OR, 1.10; 95%CI, 1.00-1.21]
 - ARDS [OR, 2.64; 95%CI, 1.29-5.40]
 - Long-term steroid therapy [OR, 4.77; 95%CI, 1.49-15.23]
 - Steroid therapy started in the ICU [OR, 11.03; 95%CI, 4.40-27.67]
 - Bacterial infection [OR, 2.73; 95%CI, 1.37-5.42]
- **The risk of death**, compared to the controls, was not higher
 - In the cases overall [HR, 0.66; 95%CI, 0.41-1.08; p = 0.1]
 - In the subgroups with definite IPA [HR, 1.60; 95%CI, 0.43-5.94; p = 0.48] probable IPA [HR, 0.84; 95%CI, 0.28-2.50; p = 0.76], or colonisation [HR, 0.58; 95%CI, 0.33-1.02; p = 0.06]
 - In cases who received antifungal therapy, mortality was not lower than in untreated cases [HR, 0.67; 95%CI, 0.36-1.24; p = 0.20].

Invasive fungal infection among hematopoietic stem cell transplantation patients with mechanical ventilation in the intensive care unit

Chen-Yiu Hung^{1,2,3†}, Kuo-Chin Kao^{1,2,3†}, Po-Nan Wang⁴, Han-Chung Hu^{1,2,3}, Meng-Jer Hsieh^{1,2,3}, Jui-Ying Fu^{1,2,3}, Chih-Hao Chang^{1,2,3}, Li-Fu Li^{1,2,3}, Chung-Chi Huang^{1,2,3}, Ying-Huang Tsai^{1,2,3} and Cheng-Ta Yang^{1,2,3*}

Abstract

Background: Invasive fungal infection (IFI) is associated with high morbidity and high mortality in hematopoietic stem cell transplantation (HSCT) patients. The purpose of this study was to assess the characteristics and outcomes of HSCT patients with IFIs who are undergoing MV at a single institution in Taiwan.

Methods: We performed an observational retrospective analysis of IFIs in HSCT patients undergoing mechanical ventilation (MV) in an intensive care unit (ICU) from the year 2000 to 2009. The characteristics of these HSCT patients and risk factors related to IFIs were evaluated. The status of discharge, length of ICU stay, date of death and cause of death were also recorded.

Results: There were 326 HSCT patients at the Linkou Chang-Gung Memorial Hospital (Taipei, Taiwan) during the study period. Sixty of these patients (18%) were transferred to the ICU and placed on mechanical ventilators. A total of 20 of these 60 patients (33%) had IFIs. Multivariate analysis indicated that independent risk factors for IFI were admission to an ICU more than 40 days after HSCT, graft versus host disease (GVHD), and high dose corticosteroid ($p < 0.01$ for all). The overall ICU mortality rate was 88% (53 of 60 patients), and was not significantly different for patients with IFIs (85%) and those without IFIs (90%, $p = 0.676$).

Conclusion: There was a high incidence of IFIs in HSCT patients requiring MV in the ICU in our study cohort. The independent risk factors for IFI are ICU admission more than 40 days after HSCT, GVHD, and use of high-dose corticosteroid.

Keywords: Invasive fungal infection (IFI), Hematopoietic stem cell transplantation (HSCT), Intensive care unit (ICU), Outcome assessment, Risk factor

Pharmacology

- Dosage
 - Obesity
 - ECMO
- Interactions
 - SOT
- Organ failure
 - Kidney
 - Liver
- Duration of treatment
- Strategies of deescalation

Conclusions

- Difficult to calculate the infectious risk
 - Beyond neutropenia and HIV and perhaps SOT
- Challenges are multiple
 - Diagnosis and diagnostic strategies
 - Treatment and treatment strategies
 -TDM
- Epidemiology is challenging
- Challenges begin outside the ICU

Great Challenges ...Patients...

- ECMO in HIV positive patients with pneumonia and ARDS
- Mucormycosis

ESCMID Online Lecture Library
© by author

ECMO & HIV / AIDS with ARDS

De Rosa FG et al BMC
Anesthesiology

- Three patients
- 2 PJP
 - 1 congenital HIV infection
 - 1 advanced naive
- 1 Legionella pneumonia in HIV/HCV
- All survived
- Two alive after one year
- One death after 90 days because of MDR *P. aeruginosa* septic shock

Clinical Features and Outcomes in Patients With Disseminated Toxoplasmosis Admitted to Intensive Care: A Multicenter Study

Matthieu Schmidt,¹ Romain Sonnevile,² David Schnell,³ Naïke Bigé,⁴ Rebecca Hamidfar,⁵ Nicolas Mongardon,⁶ Vincent Castelain,⁷ Keyvan Razazi,⁸ Antoine Marty,⁹ François Vincent,¹⁰ Martin Dres,¹¹ Stéphane Gaudry,¹² Charles Edouard Luyt,¹³ Vincent Das,¹⁴ Jean-Baptiste Micol,¹⁵ Alexandre Demoule,¹ and Julien Mayaux¹

¹Groupe Hospitalier Pitié-Salpêtrière Charles Foix, Service de Pneumologie et Réanimation Médicale, ²Université Paris Diderot, Sorbonne Paris Cité, Assistance Publique—Hôpitaux de Paris, Hôpital Bichat—Claude-Bernard, Service de Réanimation Médicale et des Maladies Infectieuses, ³Hôpital Saint-Louis, Service de Réanimation Médicale, and ⁴Hôpital Saint Antoine, Service de Réanimation Médicale, Paris; ⁵Hôpital Albert Michalon, Service de Réanimation Médicale, Grenoble; ⁶Hôpital Cochin, Service de Réanimation Médicale, Paris; ⁷Hôpital de Hautepierre, Service de Réanimation Médicale, Strasbourg; ⁸Hôpital Henri Mondor, Service de Réanimation Médicale, Créteil; ⁹Institut Gustave Roussy, Service de Réanimation Médico-Chirurgicale, Villejuif; ¹⁰Hôpital Avicenne, Service de Réanimation Médico-Chirurgicale, Bobigny; ¹¹Hôpital Kremlin Bicêtre, Service de Réanimation Médicale, Bicêtre; ¹²Hôpital Louis Mourier, Service de Réanimation Médico-Chirurgicale, Colombes; ¹³Groupe Hospitalier Pitié-Salpêtrière Charles Foix, Service de Réanimation Médicale, Paris; ¹⁴Centre Hospitalier Intercommunal André Grégoire, Service de Réanimation Médico-Chirurgicale, Montreuil; and ¹⁵Hôpital Gustave Roussy, Service d'Hématologie, Villejuif, France