Rôle de la réanimation dans la prise en charge des urgences hématologiques

Frédéric Pène

Réanimation Médicale, Hôpital Cochin, AP-HP

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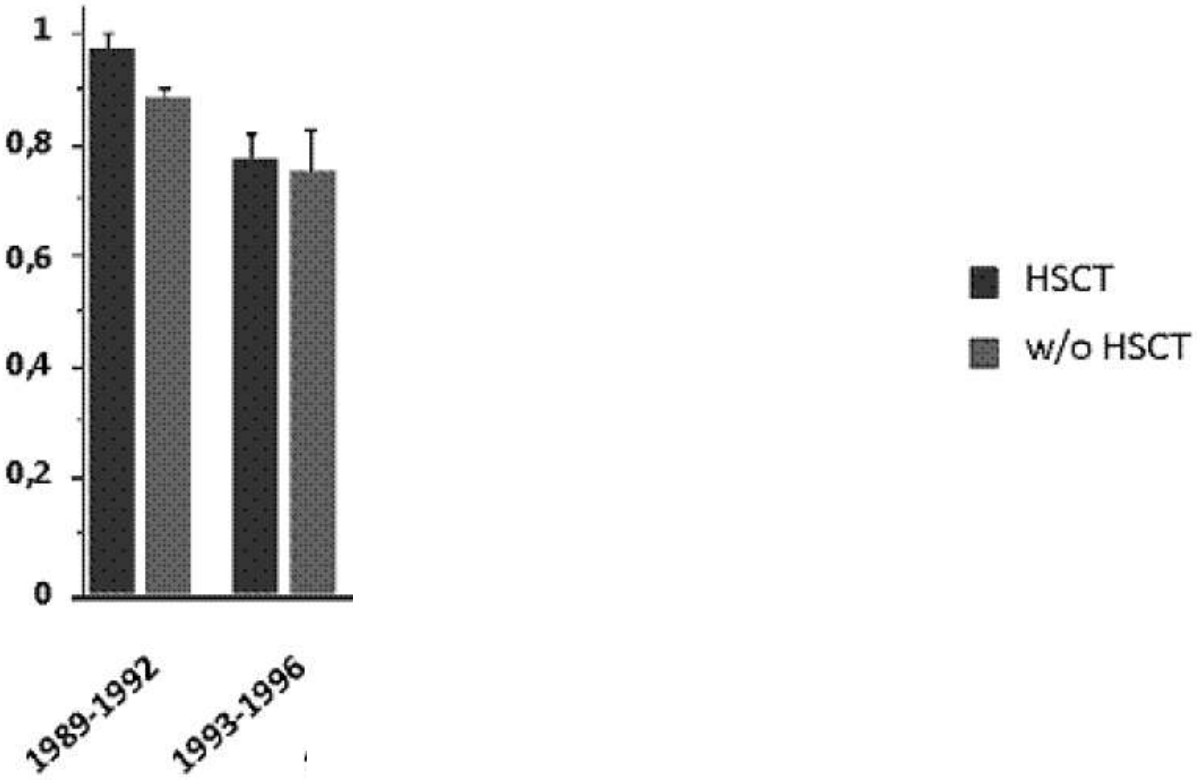
Causes for ICU admission in cancer patients

- Acute respiratory failure
- Severe sepsis and septic shock
- Bleeding
- Metabolic complications
  - Tumor lysis syndrome
  - Malignant hypercalcemia
  - Acute renal failure
- Coma
- Monitoring of high-risk procedures

Annals of Intensive Care
a SpringerOpen Journal
2011

Intensive care of the cancer patient: recent achievements and remaining challenges

Elie Azoulay[1,2*], Marcio Soares[3,4], Michael Darmon[5], Dominique Benoit[6], Stephen Pastores[7] and Bekele Afessa[8]



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Intensive care of the cancer patient: recent achievements and remaining challenges

Elie Azoulay[1,2*], Marcio Soares[3,4], Michael Darmon[5], Dominique Benoit[6], Stephen Pastores[7] and Bekele Afessa[8]

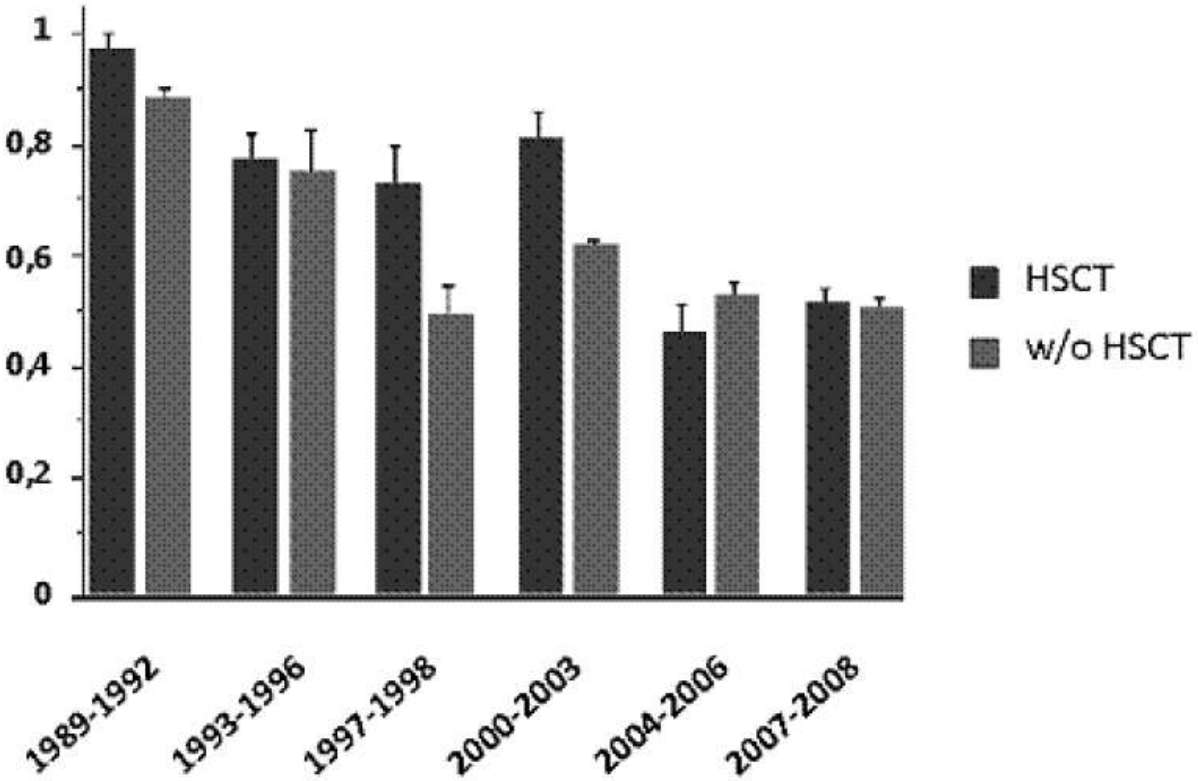
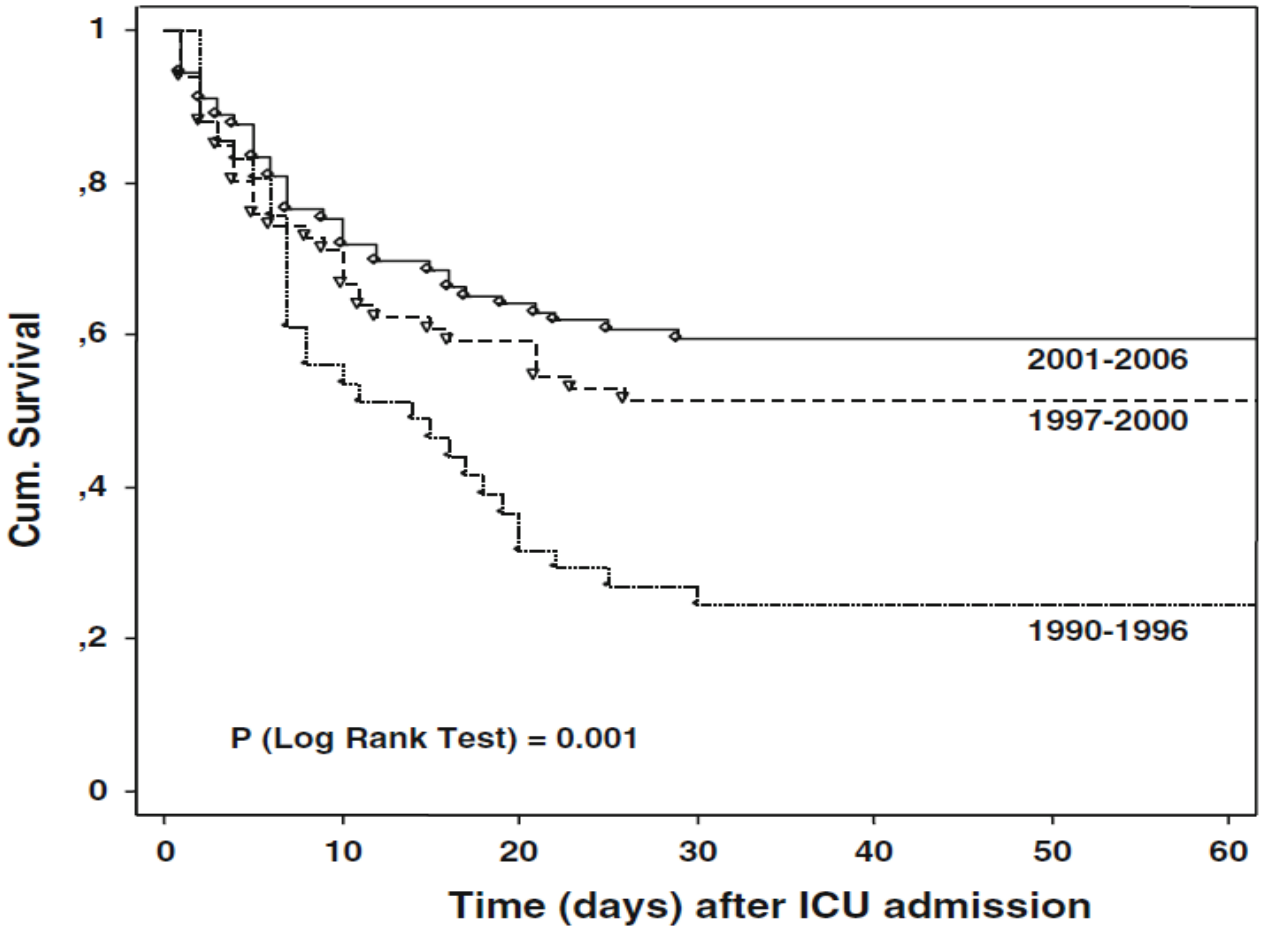


Figure 1 Trends of mortality in critically ill cancer patients during the past two decades. Unadjusted hospital mortality rates in critically ill cancer patients by year of study publication (clear gray). Unadjusted ICU mortality rates in bone marrow transplant recipients by year of study publication (dark gray).

Why did the outcome of critically ill cancer patients improve over time?

- **Advances in cancer treatments**
  - **Therapeutic intensification (high-dose chemotherapy and HSCT)**
  - **Specific targeted treatments**
  - **Monitoring of residual disease in asymptomatic patients (molecular fusion transcripts)**
  - **Surgical advances**

Continuous improvement of hematological patients in the ICU: the example of multiple myeloma



Bortezomib and imids

Autologous SCT

Combination chemotherapy

Peigne, Intensive Care Med 2009

Why did the outcome of critically ill cancer patients improve over time?

- **Advances in cancer treatments**
  - **Therapeutic intensification (high-dose chemotherapy and HSCT)**
  - **Specific targeted treatments**
  - **Monitoring of residual disease in asymptomatic patients (molecular fusion transcripts)**
  - **Surgical advances**

- **Supportive care**
  - **Fast metabolic control of hyperuricaemia (rasburicase)**
  - **Preventive or pre-emptive treatment of infections**
    - **Hematopoietic growth factors**
    - **Early detection of microbial patterns (ELISA, PCR)**
    - **New antimicrobial treatments (antifungal drugs)**

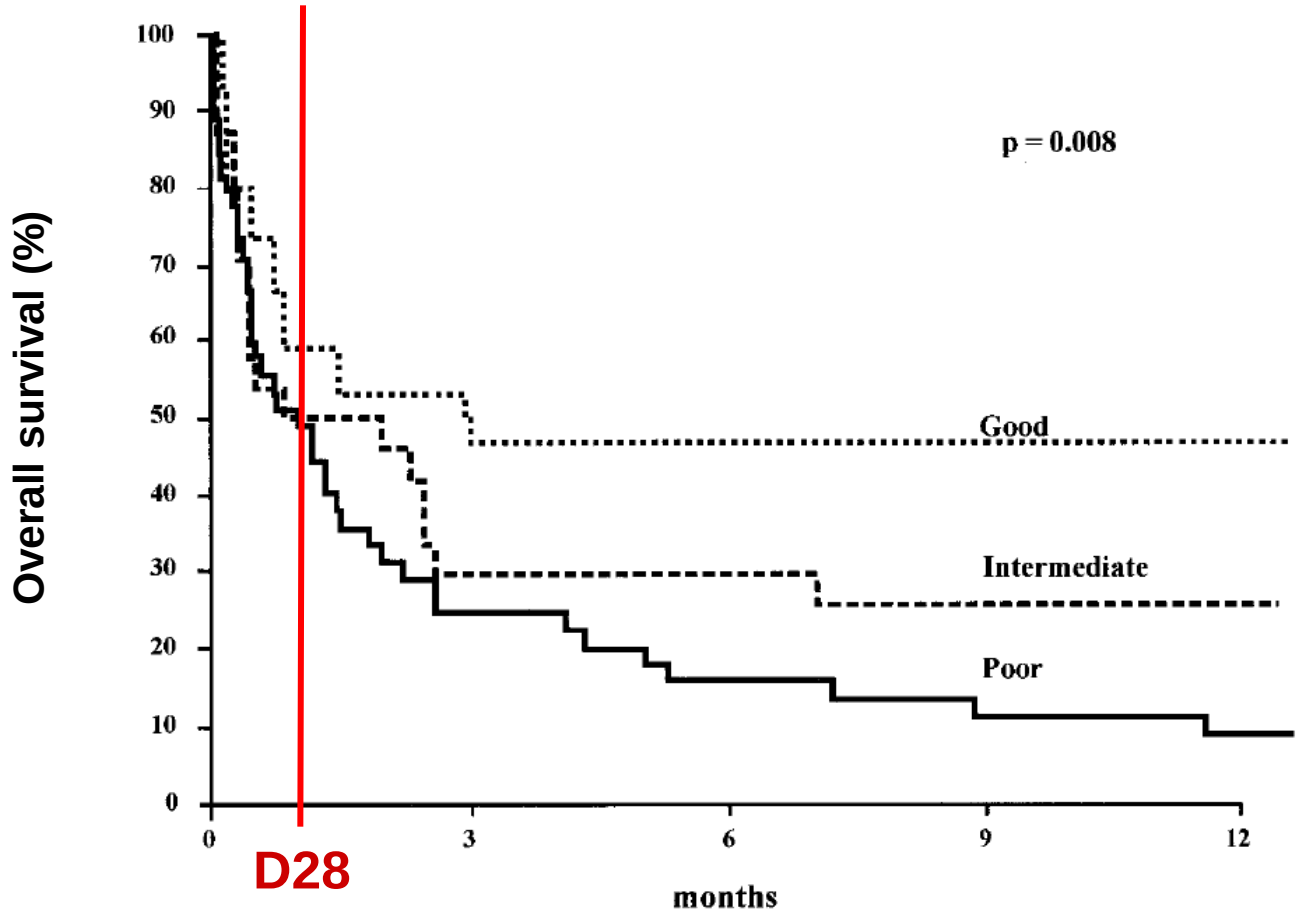
- **Indications and management of intensive care**
  - **Close collaborations between ICU physicians and hemato-oncologists**
  - **Early admission policy**
  - **Improvements in management of organ failures**

Prognostic factors of critically ill cancer patients

- Age
- Performance status
- Malignancy stage

Prognosis of hematologic malignancies does not predict intensive care unit mortality

Paul B. Massion, MD; Alain M. Dive, MD, PhD; Chantal Doyen, MD; Pierre Bulpa, MD; Jacques Jamart, MD; André Bosly, MD, PhD; Etienne Installé, MD



Crit Care Med, 2002

Prognostic factors of critically ill cancer patients

- Age
- Performance status
- Malignancy stage
- Allogeneic hematopoietic stem cell transplantation
- Neutropenia
- Bacterial complication
- Organ failures
- Volumes of admissions
- Delayed ICU admission

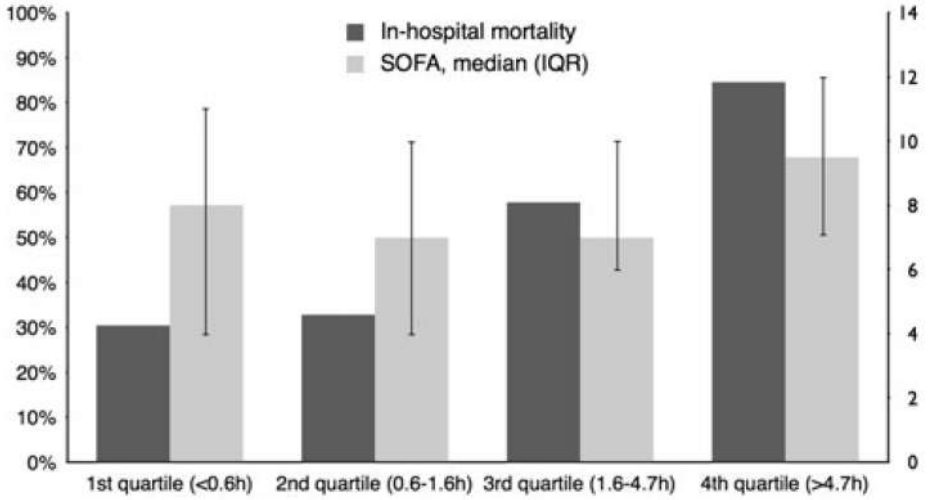
Intensive Care Med
DOI 10.1007/s00134-012-2594-0

ORIGINAL

Early intervention on the outcomes in critically ill cancer patients admitted to intensive care units

Jae-Uk Song
Gee Young Suh
Hye Yun Park
So Yeon Lim
Seo Goo Han
Yeh Rim Kang
O Jung Kwon
Sookyoung Woo
Kyeongman Jeon

MET criteria[a]	Number of patients (%)
Airway and breathing	
Acute respiratory distress: respiratory rate ≤ 8 or ≥ 30 breaths/min	86 (43)
Acute hypoxia: oxygen saturation derived from pulse oximetry <90 % for 5 min, despite previous oxygen administration	106 (53)
Acute hypercapnia and acute acidosis: arterial carbon dioxide pressure >50 mm Hg and pH <7.3	38 (19)
Upper airway obstruction: stridor or use of respiratory accessory muscle	40 (20)
Circulation	
Unexplained hypotension: systolic blood pressure <90 mmHg	91 (46)
Acute chest pain	4 (2)
Bradycardia or tachycardia: heart rate <50 or >130 beats/min	97 (49)
Arrhythmia with symptom	21 (11)
Neurology	
Sudden mental change or unexplained agitation	46 (23)
Seizure	9 (5)



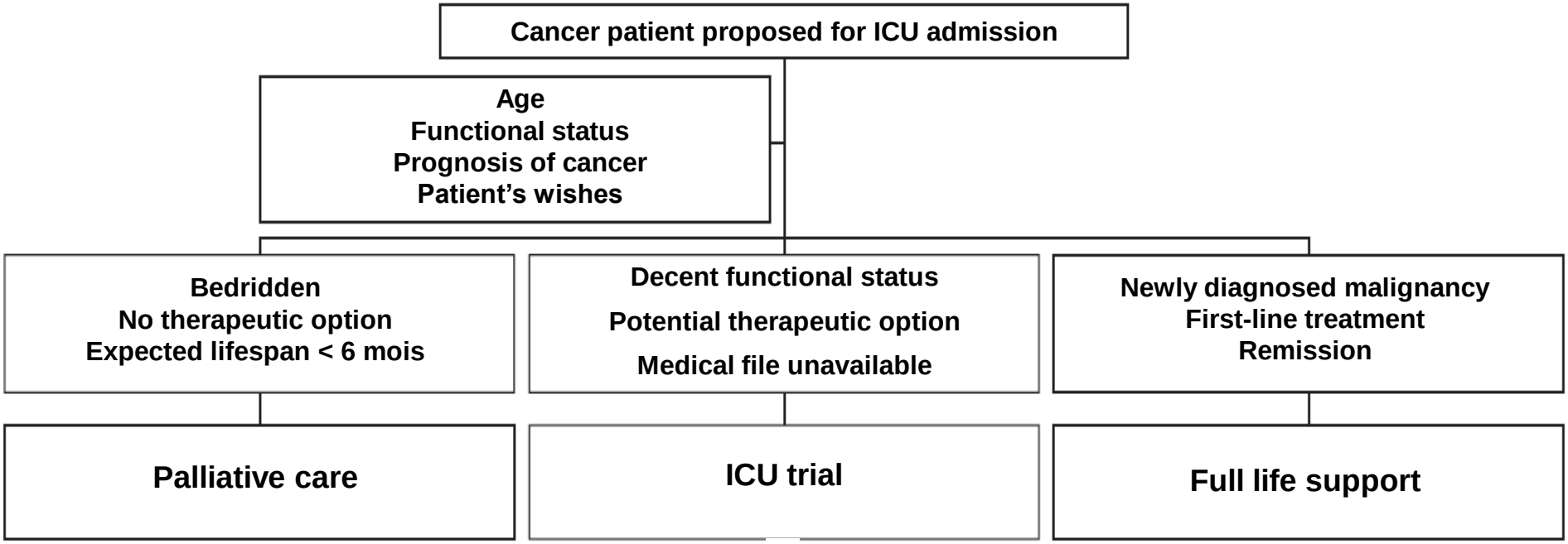
in-hospital mortality

OR per hour to intervention

1.4 [1.2-1.7], p<0.001

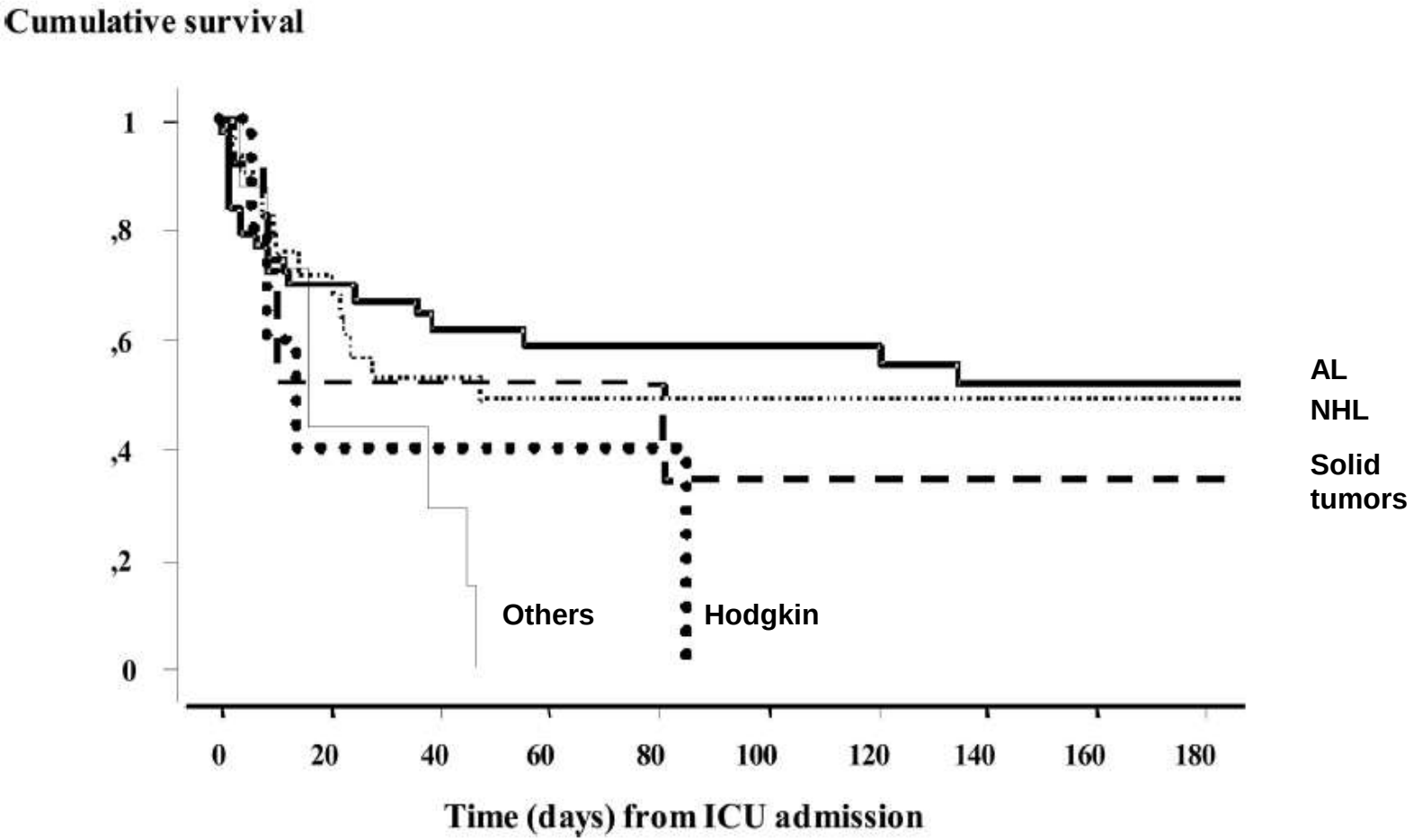
Élie Azoulay
Bekele Afessa

The intensive care support of patients with malignancy: do everything that can be done



Adapted from Azoulay & Afessa, Intensive Care Med 2005

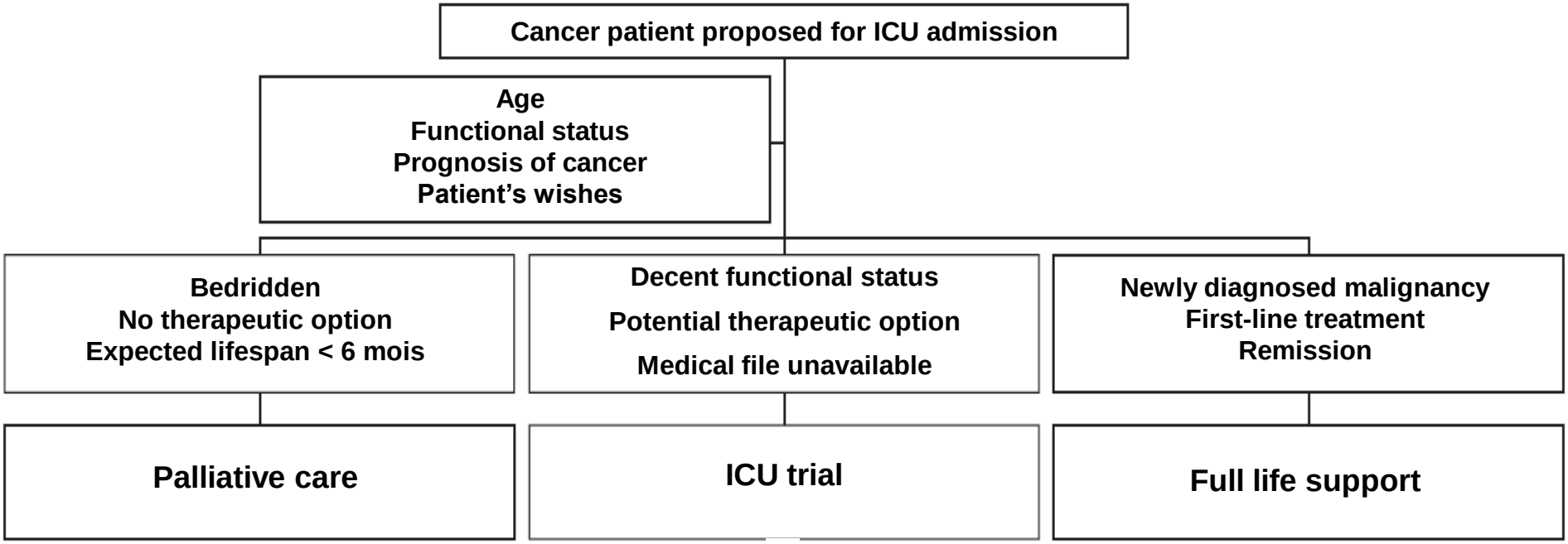
Malignancy-related organ failures: benefit of chemotherapy in the ICU



Darmon, Crit Care Med 2005

Élie Azoulay
Bekele Afessa

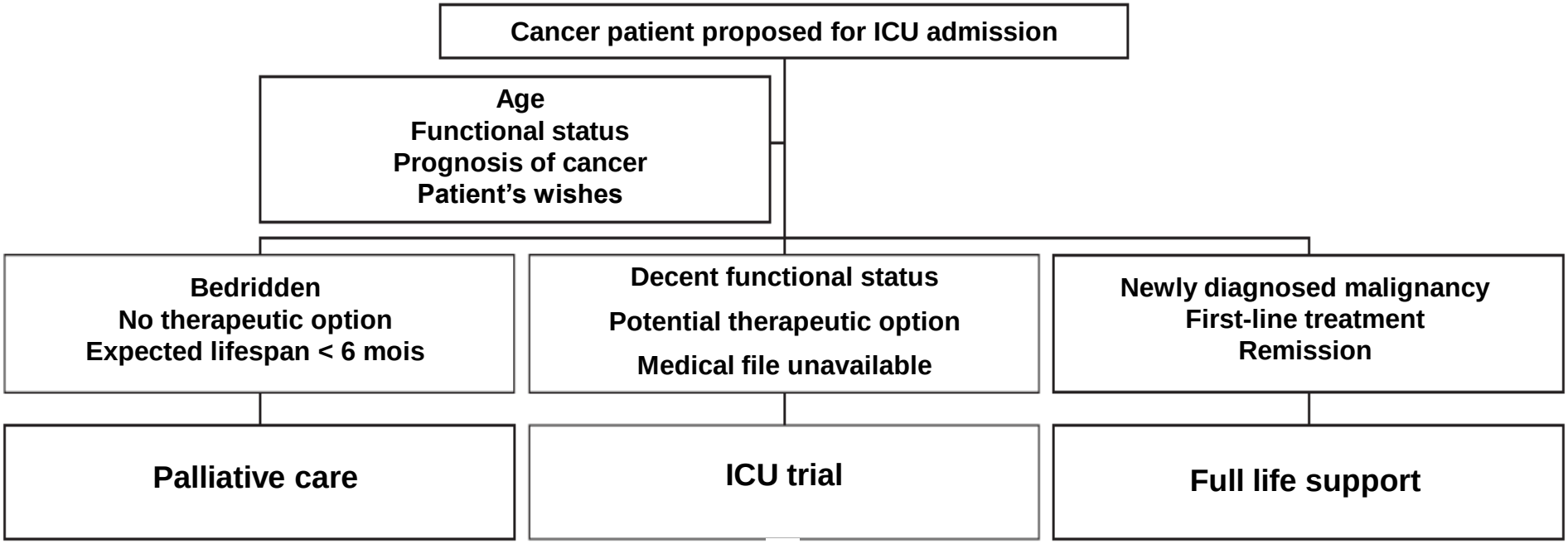
The intensive care support of patients with malignancy: do everything that can be done



Adapted from Azoulay & Afessa, Intensive Care Med 2005

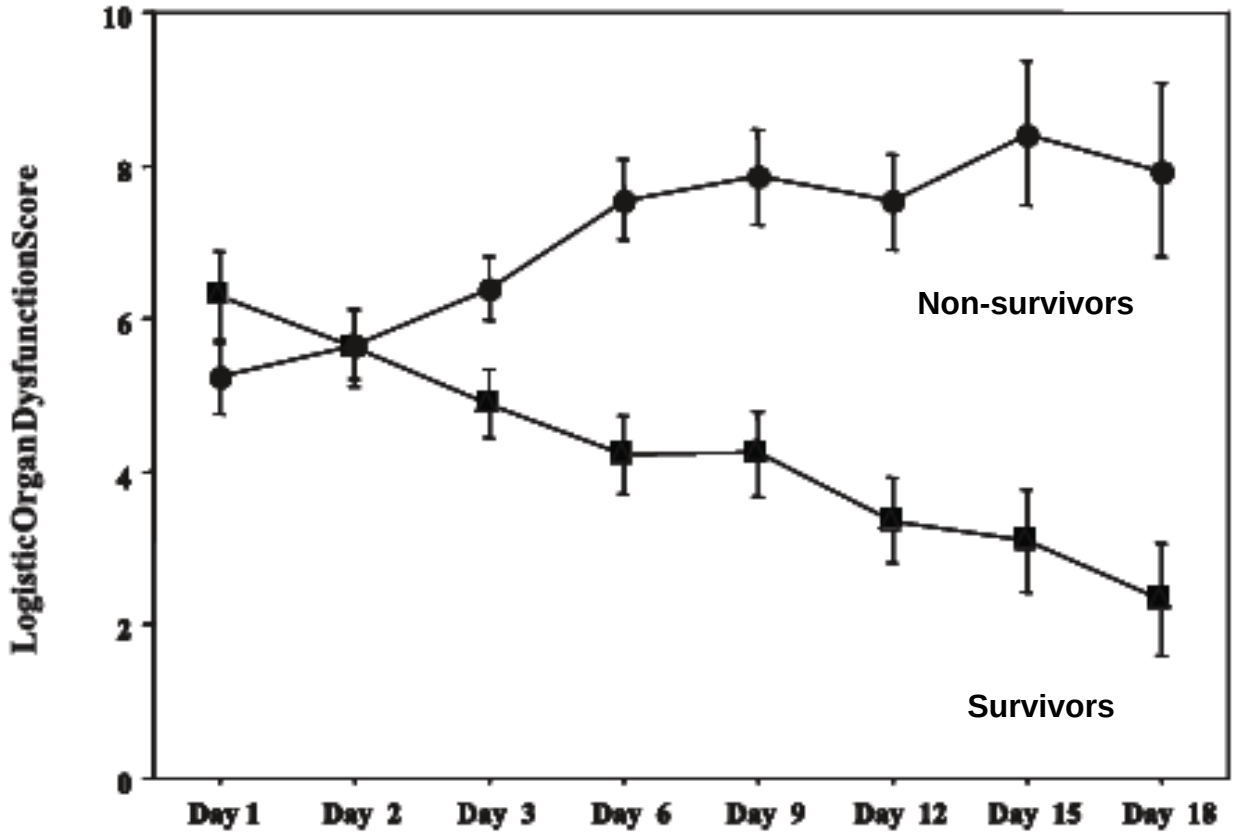
Élie Azoulay
Bekele Afessa

The intensive care support of patients with malignancy: do everything that can be done

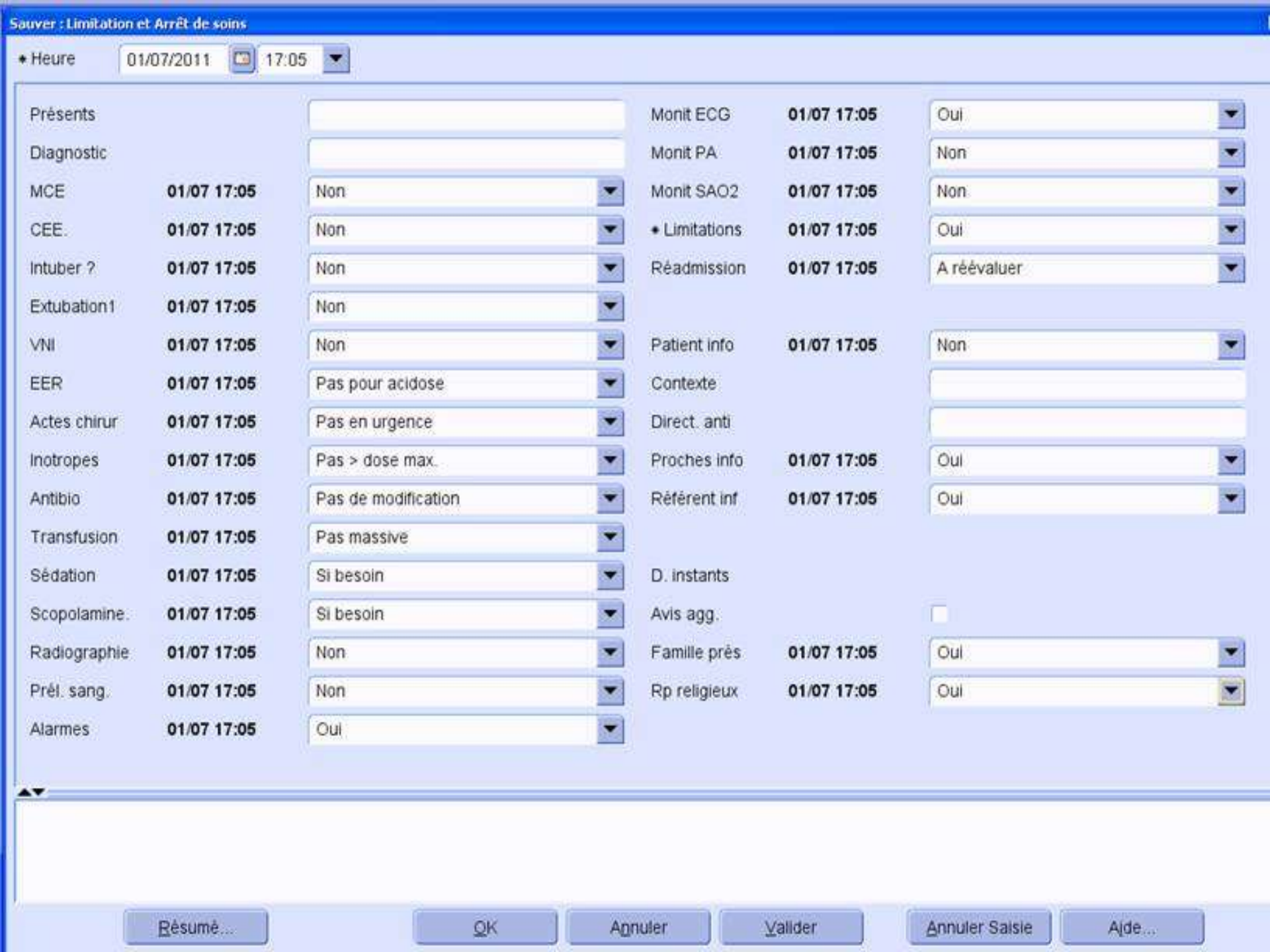


Adapted from Azoulay & Afessa, Intensive Care Med 2005

The ICU trial: the benefit of the doubt



Lecuyer, Crit Care Med 2007


Sauver : Limitation et Arrêt de soins
• Heure
01/07/2011
17:05
Présents
Diagnostic
MCE 01/07 17:05 Non
CEE. 01/07 17:05 Non
Intuber ? 01/07 17:05 Non
Extubation1 01/07 17:05 Non
VNI 01/07 17:05 Non
EER 01/07 17:05 Pas pour acidose
Actes chirur 01/07 17:05 Pas en urgence
Inotropes 01/07 17:05 Pas > dose max.
Antibio 01/07 17:05 Pas de modification
Transfusion 01/07 17:05 Pas massive
Sédation 01/07 17:05 Si besoin
Scopolamine. 01/07 17:05 Si besoin
Radiographie 01/07 17:05 Non
Prél. sang. 01/07 17:05 Non
Alarmes 01/07 17:05 Oui
Monit ECG 01/07 17:05 Oui
Monit PA 01/07 17:05 Non
Monit SAO2 01/07 17:05 Non
• Limitations 01/07 17:05 Oui
Réadmission 01/07 17:05 A réévaluer
Patient info 01/07 17:05 Non
Contexte
Direct. anti
Proches info 01/07 17:05 Oui
Référent inf 01/07 17:05 Oui
D. instants
Avis agg.
Famille près 01/07 17:05 Oui
Rp religieux 01/07 17:05 Oui
Résumé...
OK
Annuler
Valider
Annuler Saisie
Aide...

Réanimation (2010) 19, 699–705

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RECOMMANDATIONS

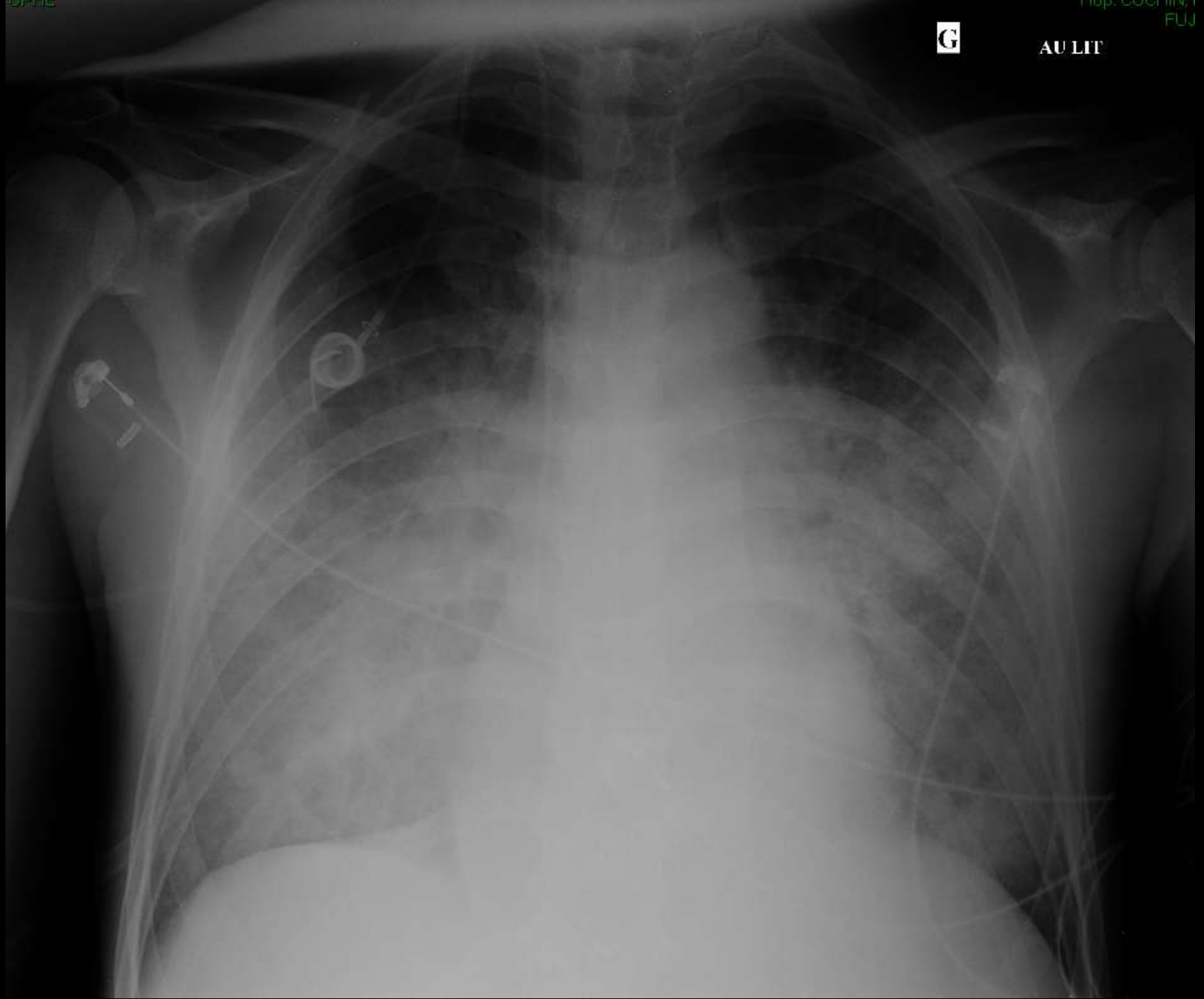
Aspects cliniques et éthiques du transfert en réanimation des patients porteurs d'hémopathies malignes

Clinical and ethical aspects of admission in intensive care unit of patients with malignant hemopathies

La commission d'éthique de la société française d'hématologie (SFH)[1], la société de réanimation en langue française (SRLF)[1], le groupe francophone de réanimation et urgences pédiatriques (GFRUP)[1]

A 67 yo male patient

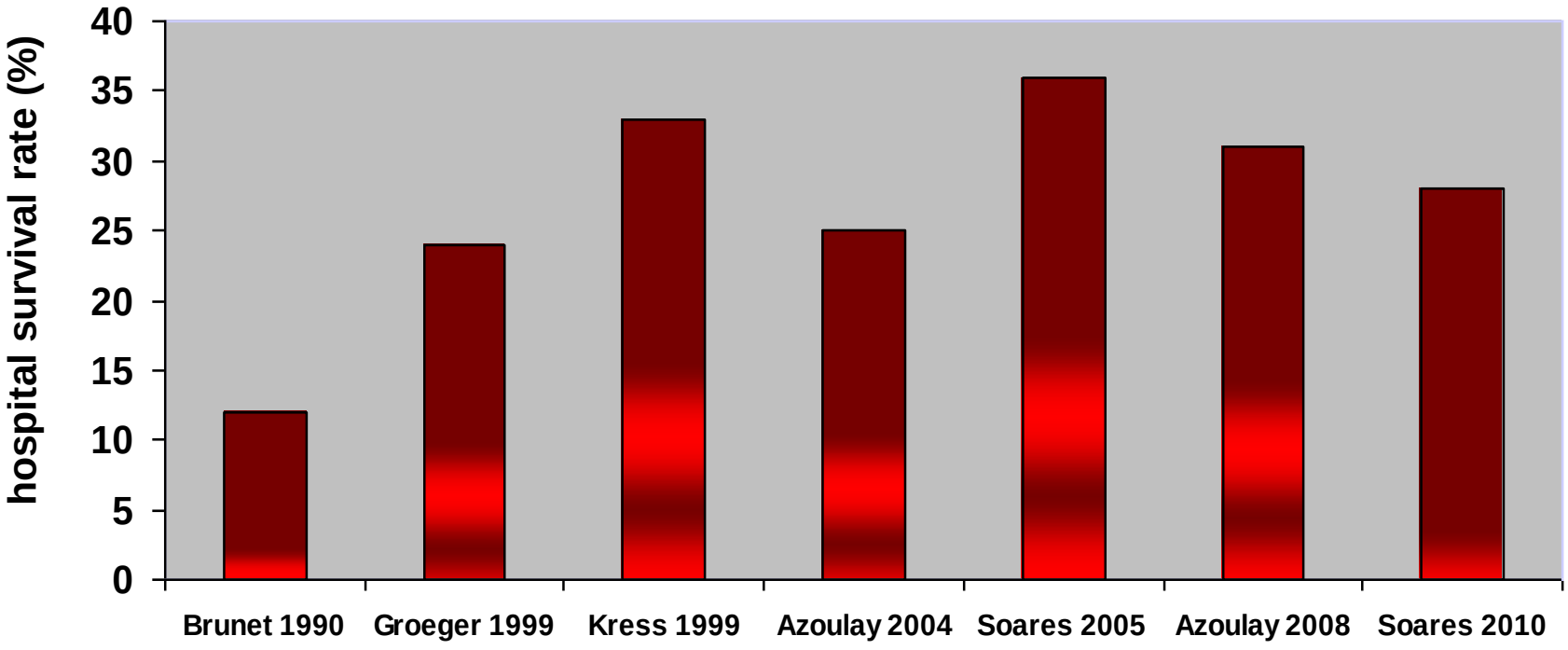
- Non-Hodgkin large B-cell lymphoma stage IV (bone marrow)
- Malnutrition with impaired functional status (PS 2)
- Good clinical response after 2 courses of chemo R-CHOP
- Following the 3rd course of chemotherapy
- Day 8: febrile neutropenia empirically treated with amoxicillin-clavulanic acid + ciprofloxacin
- Day-15: acute respiratory failure (SpO_2 93% with O_2 6 L/min)
- Blood cell count: WBC 2100/mm^3, Hb 8.6 g/dL, PLT 75000/mm^3


G
AU LIT

Relevant questions

- **Should this patient be admitted to the ICU?**
- **Ventilatory management?**
- **Diagnostic procedures?**

Survival trends of mechanically ventilated cancer patients



Non-invasive ventilation

NONINVASIVE VENTILATION IN IMMUNOSUPPRESSED PATIENTS WITH PULMONARY INFILTRATES, FEVER, AND ACUTE RESPIRATORY FAILURE

GILLES HILBERT, M.D., DIDIER GRUSON, M.D., FRÉDERIC VARGAS, M.D., RUDDY VALENTINO, M.D., GEORGES GBIKPI-BENISSAN, M.D., MICHEL DUPON, M.D., JOSY REIFFERS, M.D., AND JEAN P. CARDINAUD, M.D.

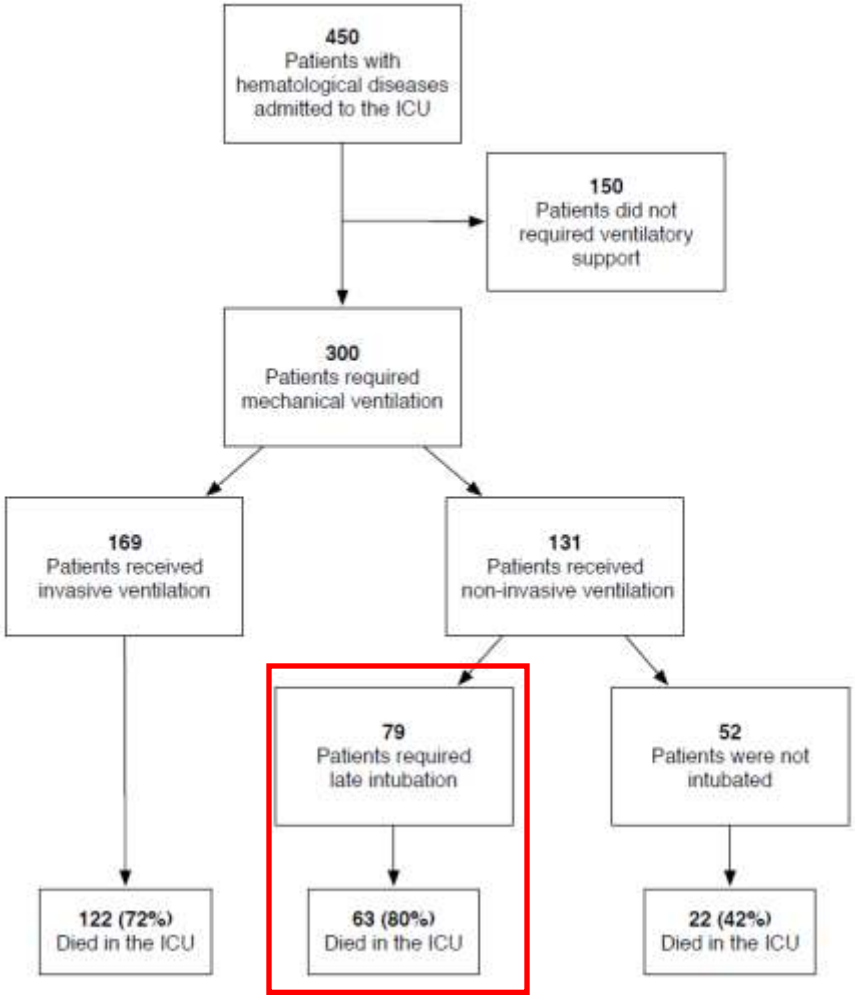
OUTCOME	NONINVASIVE-VENTILATION GROUP (N=26)	STANDARD-TREATMENT GROUP (N=26)	P VALUE
Intubation — no./total no. (%)	12/26 (46)	20/26 (77)	0.03
Immunosuppression from hematologic cancer and neutropenia	8/15 (53)	14/15 (93)	0.02
Drug-induced immunosuppression	3/9 (33)	5/9 (56)	0.32
Immunosuppression from the acquired immunodeficiency syndrome	1/2 (50)	1/2 (50)	0.83
Initial improvement in PaO_2:FiO_2 — no. (%)	12 (46)	4 (15)	0.02
Sustained improvement in PaO_2:FiO_2 without intubation — no. (%)	13 (50)	5 (19)	0.02
Death in the ICU — no./total no. (%)†	10/26 (38)	18/26 (69)	0.03
Immunosuppression from hematologic cancer and neutropenia	7/15 (47)	13/15 (87)	0.02
Drug-induced immunosuppression	3/9 (33)	4/9 (44)	0.50
Immunosuppression from the acquired immunodeficiency syndrome	0/2	1/2 (50)	0.50
Total duration of any ventilatory assistance — days			
Among all patients	6±3	6±5	0.59
Among survivors	5±2	3±5	0.12
Length of ICU stay — days			
Among all patients	7±3	9±4	0.11
Among survivors	7±3	10±4	0.06
Death in the hospital — no./total no. (%)	13/26 (50)	21/26 (81)	0.02
Immunosuppression from hematologic cancer and neutropenia	8/15 (53)	14/15 (93)	0.02
Drug-induced immunosuppression	4/9 (44)	6/9 (67)	0.32
Immunosuppression from the acquired immunodeficiency syndrome	1/2 (50)	1/2 (50)	0.83

N Engl J Med 2001

CRITICAL CARE
2012

Ventilatory support in critically ill hematology patients with respiratory failure

Rosario Molina[1], Teresa Bernal[2], Marcio Borges[3], Rafael Zaragoza[4], Juan Bonastre[5], Rosa María Granada[6], Juan Carlos Rodriguez-Borregán[7], Karla Núñez[8], Iratxe Seijas[9], Ignacio Ayestaran[10] and Guillermo M Albaiceta[1,11,12*], for the EMEHU study investigators[13]



	OR	95% confidence interval	*P*
APACHE-II	1.06	1.02-1.10	0.002
Congestive heart failure on admission	0.26	0.08-0.85	0.026
Shock on admission	1.69	0.86-3.33	0.131
NIMV as first ventilatory approach	0.32	0.15-0.67	0.003
NIMV failure	5.74	2.40-13.73	<0.001
Allogeneic HSCT	6.78	1.78-25.85	0.005

Intensive Care Med (2004) 30:965–971
DOI 10.1007/s00134-004-2237-1

BRIEF REPORT

Didier Gruson
Frederic Vargas
Gilles Hilbert
Nam Bui
Thierry Maillot
Thierry Mayet
Odile Pillet
Genevieve Chene
Georges Gbikpi-Benissan

Predictive factors of intensive care unit admission in patients with haematological malignancies and pneumonia

Parameters at the onset of the clinical evidence of pneumonia (in haematology ward)	Survivors (n=38)	Non-survivors (n=15)	P value
Age, years, mean±SD	50±13	48±16	0.75
Type of treatment			
Chemotherapy, n (%)	17 (45)	9 (60)	0.19
Transplantation	21 (55)	6 (40)	
Pathologic chest auscultation, n patients (%)	18 (47)	8 (53)	0.68
No. of involved quadrants on first chest X-ray	1.2±0.8	2.4±1.1	<0.001
Initial PaO2 at the first blood gas analysis, mmHg	79±18	59±22	0.001
Initial level of nasal oxygen supplementation, l/min	1.3±1.7	3.9±2.4	<0.001
Positive blood culture, n patients (%)	11 (29)	6 (40)	0.6
Gram-negative bacilli isolated in blood cultures	3 (8)	5 (33)	0.056
Presence of hepatic failure, n patients (%)	3 (7)	12 (80)	0.01

If O_2 > 3 L/min

Diagnostic bronchoscopy in hematology and oncology patients with acute respiratory failure: Prospective multicenter data*

Elie Azoulay, MD, PhD; Djamel Mokart, MD; Antoine Rabbat, MD; Frédéric Pene, MD; Achille Kouatchet, MD; Fabrice Bruneel, MD; François Vincent, MD; Rebecca Hamidfar, MD; Delphine Moreau, MD; Ismaël Mohammedi, MD; Geraldine Epinette, MS; Gaëtan Beduneau, MD; Vincent Castelain, MD; Arnaud de Lassence, MD†; Didier Gruson, MD; Virginie Lemiale, MD; Benoît Renard, MD; Sylvie Chevret, MD, PhD; Benoît Schlemmer, MD

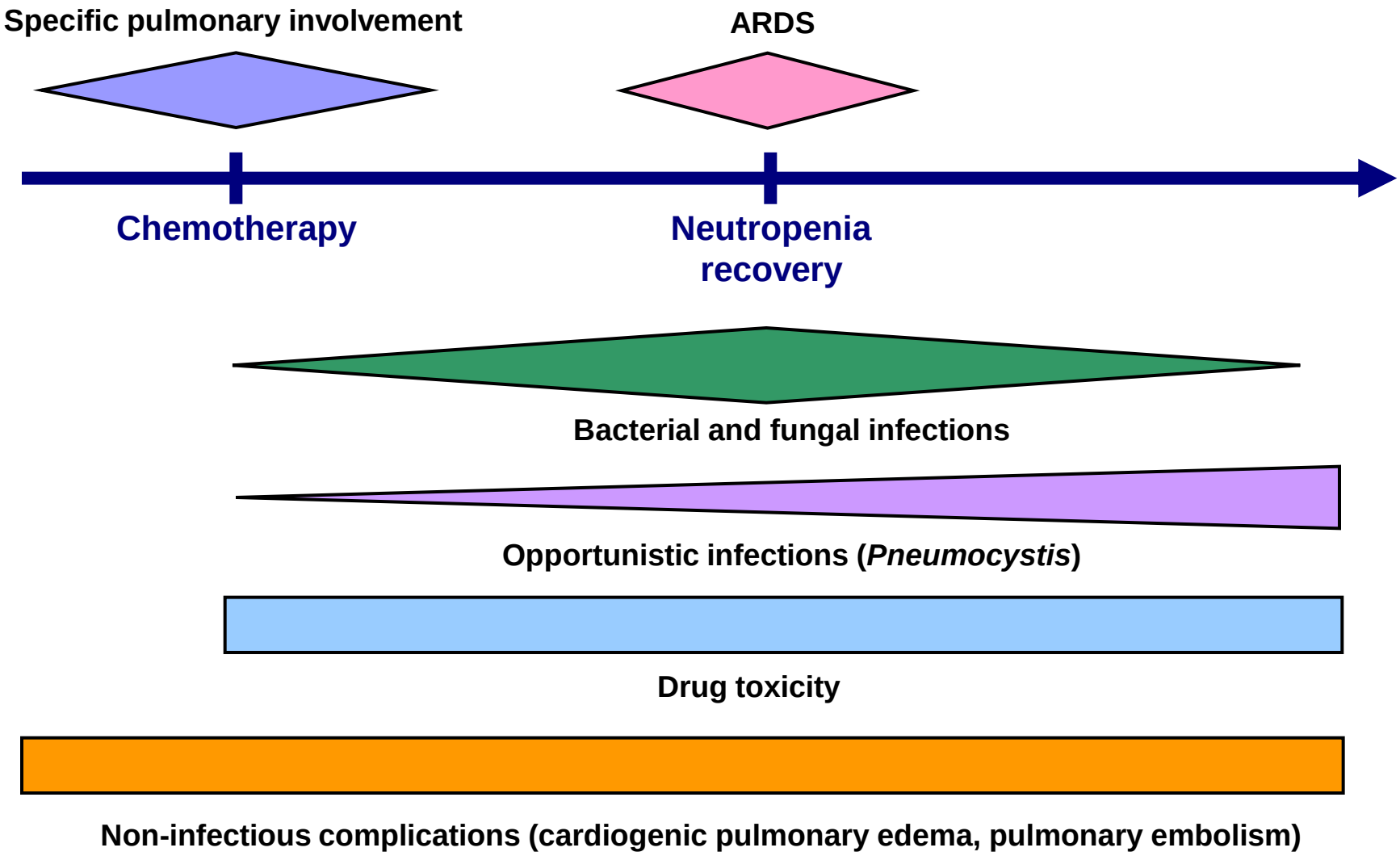
	Odds-ratio	95% Confidence Interval	*p* Value
Related to the malignancy			
Remission of the malignancy	0.30	0.09–0.93	.03
Allogeneic bone marrow or stem cell transplantation	5.95	1.48–23.90	.01
Related to the cause of acute respiratory failure			
Admission during neutropenia recovery	0.13	0.03–0.57	.006
Undetermined diagnosis	8.65	1.39–53.56	.02
Related to the need for life-sustaining interventions			
Need for conventional mechanical ventilation	8.18	1.16–57.36	.03
Need for vasopressors	5.09	1.07–24.18	.04

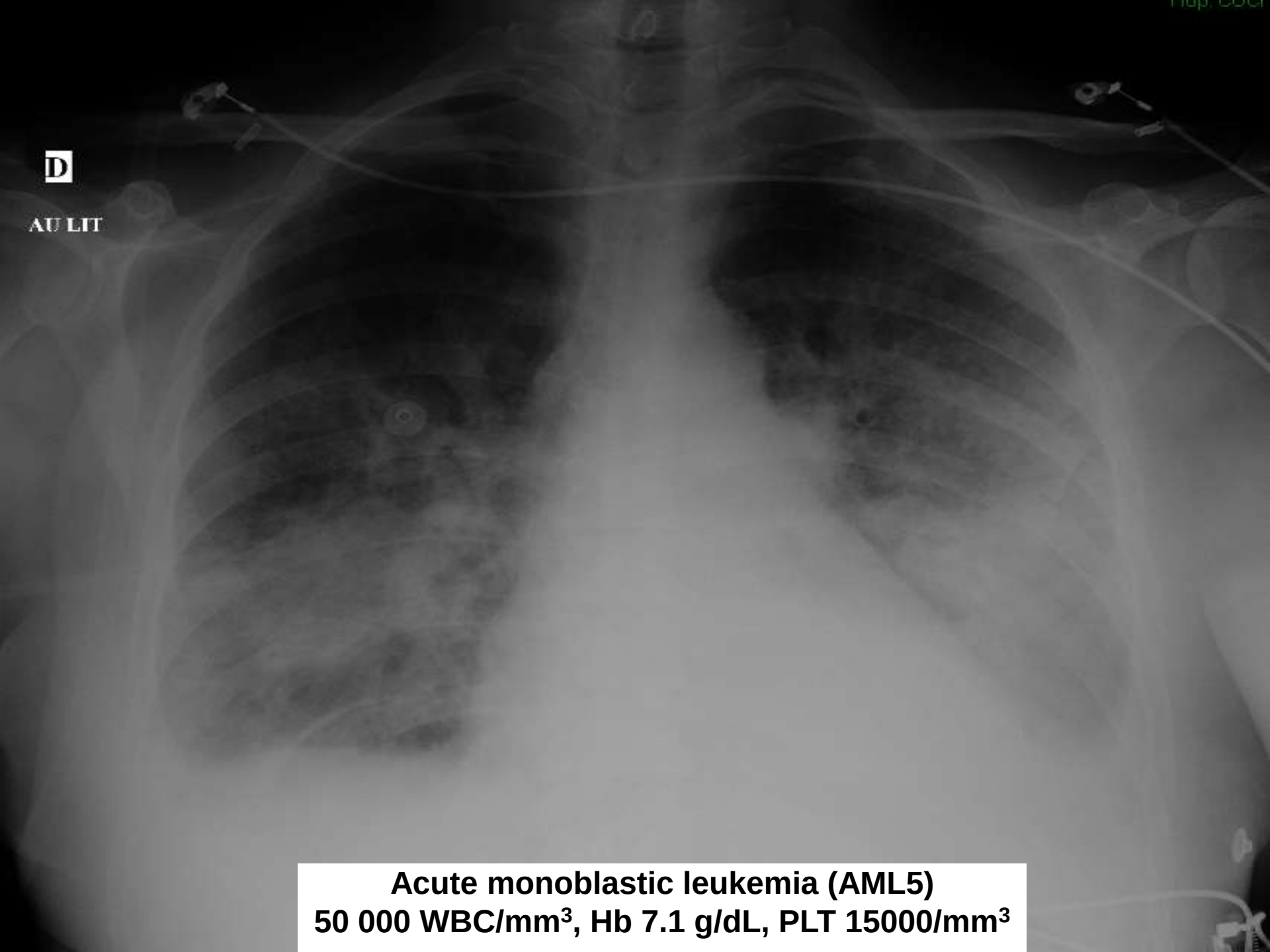
Crit Care Med 2008

The 4 steps of diagnosis

- **Appraisal of the clinical history**
- **Clinical picture**
- **Lung imaging**
- **Microbiological investigations**

Acute respiratory failure in malignancies

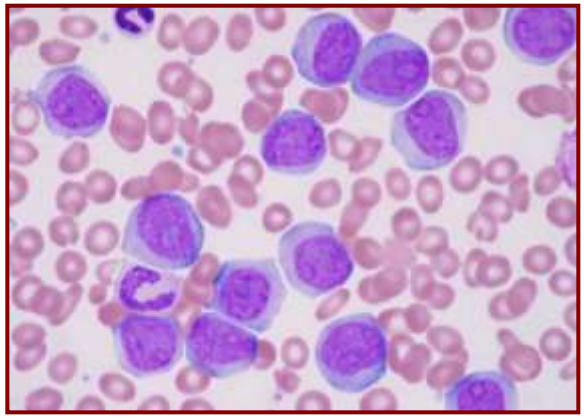




Acute monoblastic leukemia (AML5)
50 000 WBC/mm^3, Hb 7.1 g/dL, PLT 15000/mm^3

Specific disease-related pulmonary complications

- Lung infiltration
- Leukostasis
- Acute cell lysis pneumopathy
- Compression
- Hemoptysis
- Pleural effusion



Chemotherapy
corticosteroids

Chemotherapy,
endoluminal prothesis

Drainage

Arterial embolisation

Pulmonary involvement in patients with malignancies

Infections

- Bacterial infections
  - Common pyogenic bacteria
    - Streptococcus pneumoniae
    - Staphylococcus aureus
    - Haemophilus influenzae
    - *Pseudomonas aeruginosa* and Enterobacteriaceae
  - Intracellular bacteria
    - Legionella pneumophilia
    - Chlamydia and Mycoplasma pneumoniae
  - Other bacteria
    - Actinomyces israeli
    - *Nocardia* spp.
- *Pneumocystis jirovecii*
- Invasive fungal Infections
  - Molds
    - Aspergillosis
    - Emerging mycotic infections: trichosporosis, fusariosis, zygomycetes
  - Yeasts
    - Lung involvement during candidemia
  - Endemic fungal infections
    - Histoplasmosis, coccidioidomycosise, blastomycosis
- Viral infections (primary infections or reactivations)
  - Seasonal respiratory viruses
    - Influenzae, parainfluenzae, rhinovirus
    - Respiratory syncytial virus
  - Herpes virus
    - Cytomegalovirus, herpes virus, zoster virus and HHV6
  - Other viruses: adenovirus
- Mycobacterial infections
  - Tuberculosis and atypical mycobacteria

Noninfectious causes

- Cardiogenic pulmonary edema
- Capillary leak syndrome
- Lung infiltration
- Drug-induced toxicity
- Alveolar hemorrhage
- Transfusion-related acute lung injury
- Radiation-induced lung damage
- Alveolar proteinosis
- Diffuse alveolar damage
- Bronchiolitis
- Cryptogenic organized pneumonia
- Second malignancy

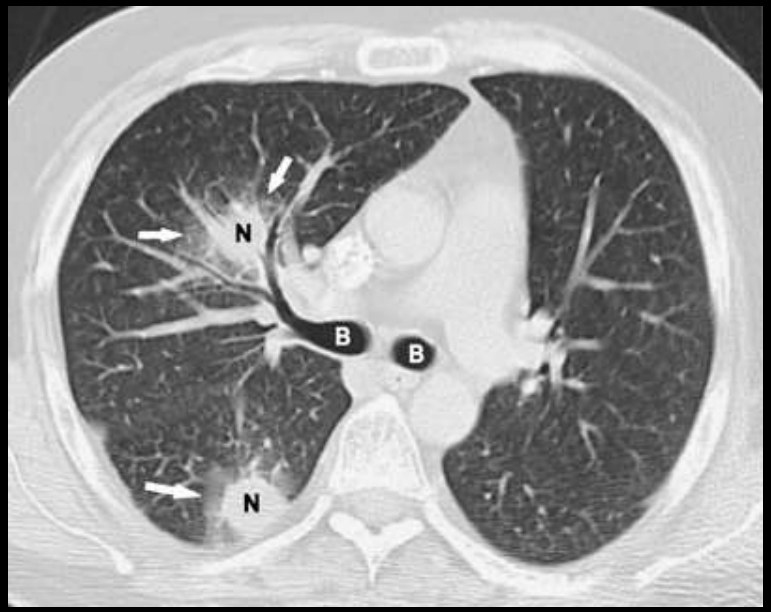
Intensive Care Med
DOI 10.1007/s00134-006-0129-2 2006

REVIEW

Élie Azoulay
Benoît Schlemmer

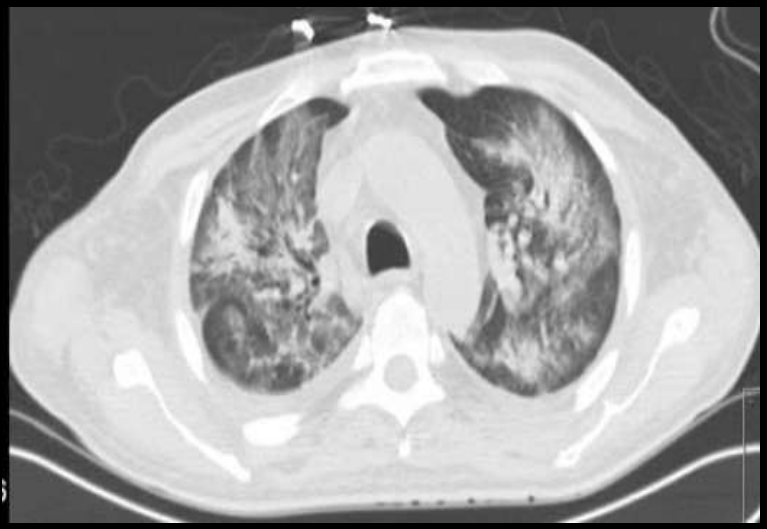
Diagnostic strategy in cancer patients with acute respiratory failure

Diagnosis	Deficiencies	Main infections
Acute myeloid leukemia	Phagocytosis Cell-mediated immunity	Bacteria Yeasts
Acute lymphocytic leukemia	Phagocytosis Cell-mediated immunity	Bacteria Yeasts, herpes viruses, *P. jirovecii*
Lymphomas	Cell-mediated immunity	*P. jirovecii* , yeasts, bacteria, encapsulated bacteria
Myelomas	Immunoglobulins	Encapsulated bacteria
Chronic lymphocytic leukemia	Phagocytosis Cell-mediated immunity	Encapsulated bacteria Intracellular organisms
Chronic myeloid leukemia	Phagocytosis	Bacteria
Solid cancer	Compression, obstruction, ulceration	Bacteria
Bone marrow transplantation	Phagocytosis Cell-mediated immunity Immunoglobulins	Bacteria Encapsulated bacteria Yeasts, *P. jirovecii*
Associated condition	Asplenia in general associated with defect in immunoglobulins, altered phagocytosis and cell-mediated immunity	Encapsulated bacteria



Halo sign

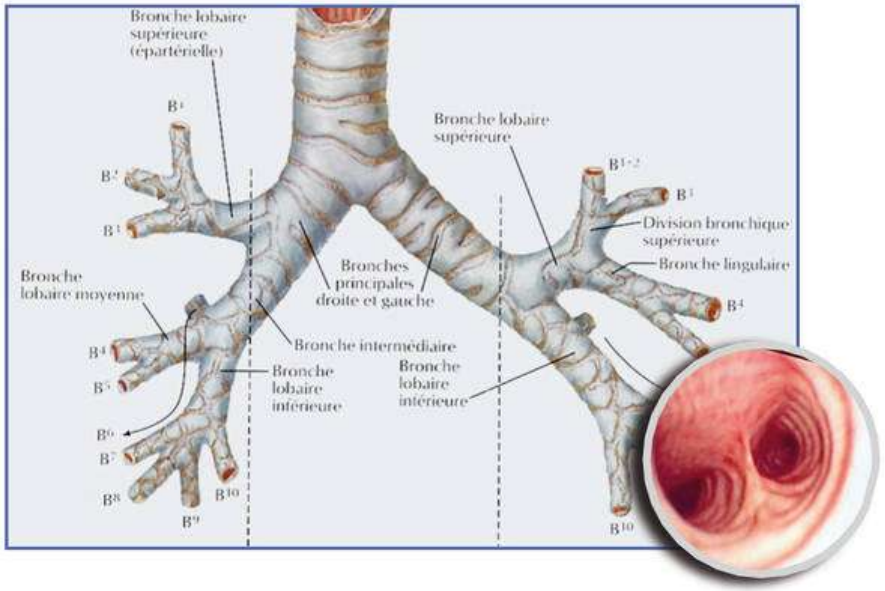
Air crescent



Ground-glass opacities

Reversed halo sign

Indications for fiberoptic bronchoscopy and broncho-alveolar lavage?



Intensive Care Med
DOI 10.1007/s00134-006-0129-2 2006

REVIEW

Élie Azoulay
Benoît Schlemmer

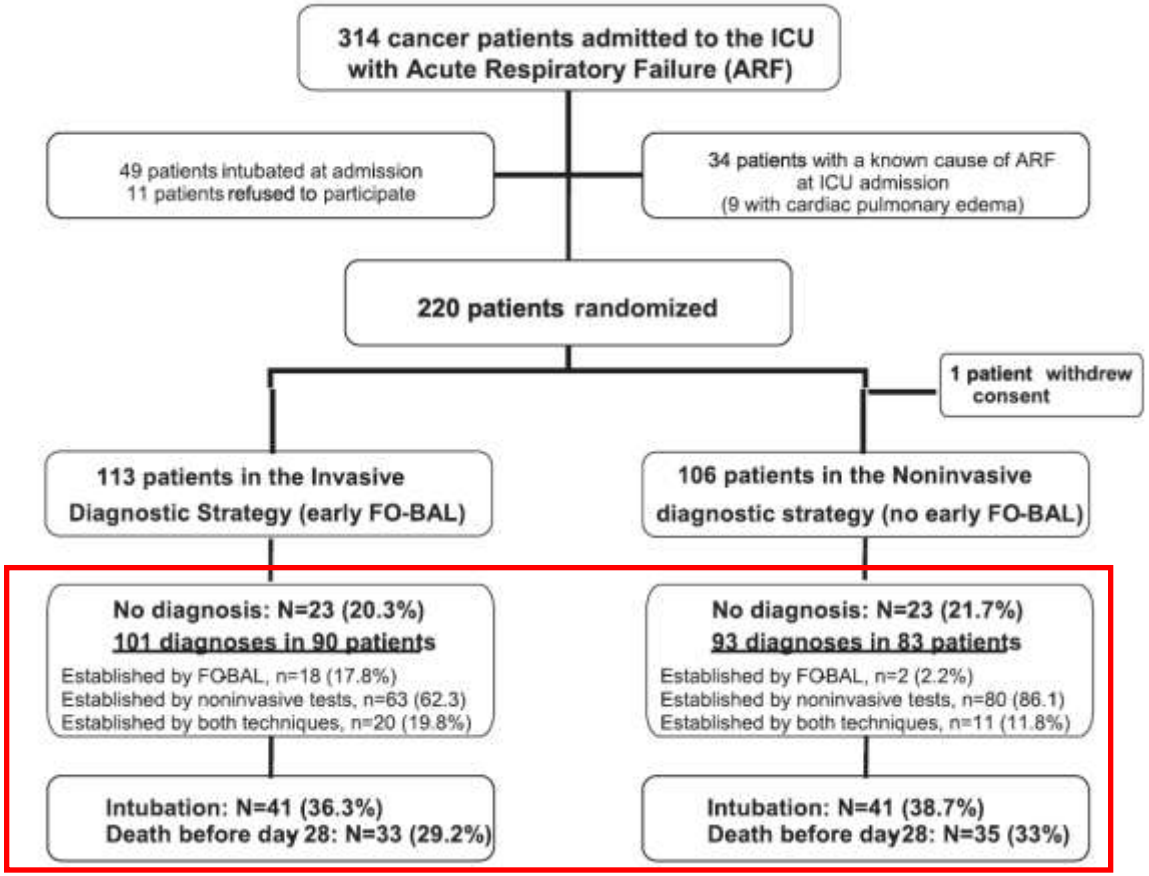
Diagnostic strategy in cancer patients with acute respiratory failure

FOB + BAL

Reference	*n*	Diagnosis	Diagnostic impact	Therapeutic impact
Stover et al. [96]	97	HM	66	–
Martin et al. [142]	100	HM	30	–
Xaubet et al. [143]	96	HM	49	31
Campbell et al. [144]	22	HM	55	–
Pisani et al. [145]	150	HM	39	–
Maschmeyer et al. [146]	46	Neutropenia	30	–
Cordonnier et al. [100]	56	Neutropenia	53	24
Cazzadori et al. [147]	142	HM	36	–
Von Eiff et al. [40]	90	HM	66	65
White et al. [3]	68	HM	31	24
Ewig et al. [28]	49	HM	31	16
Gruson et al. [18]	41	Neutropenia	63	28
Hilbert et al. [22]	24/46	HM	62	71
Murray et al. [2]	27	HM	33	28
Azoulay et al. [4]	203	HM	49.5	45.1
Pagano et al. [148]	127	HM	53	14
Jain et al. [82]	104	HM	56	–
Hohenadel et al. [81]	95	HM	30	–
Total	1537		46.2	34.6

Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure

Randomized Controlled Trial



Test/Infections

1. Imaging studies
   - Chest radiograph
   - High-resolution computed tomography
2. Echocardiography
3. Sputum examination for
   - Bacteria
   - *Candida* spp.
   - Other fungi
   - Tuberculosis
4. Induced sputum (*P. jiroveci*)
5. Nasopharyngeal aspirates
6. Blood cultures
7. Polymerase chain reaction test for
   - Herpes viridae
   - Cytomegalovirus
8. Circulating *Aspergillus* galactomanan
9. Serologic tests for
   - *Chlamydiae pneumoniae*
   - *Mycoplasma pneumoniae*
   - *Legionella pneumophila*
10. Urine antigen for
    - *Legionella pneumophila*
    - *Streptococcus pneumoniae*

Azoulay and coll., Am J Respir Crit Care Med 2010

RECOGNISE • RESUSCITATE • REFER

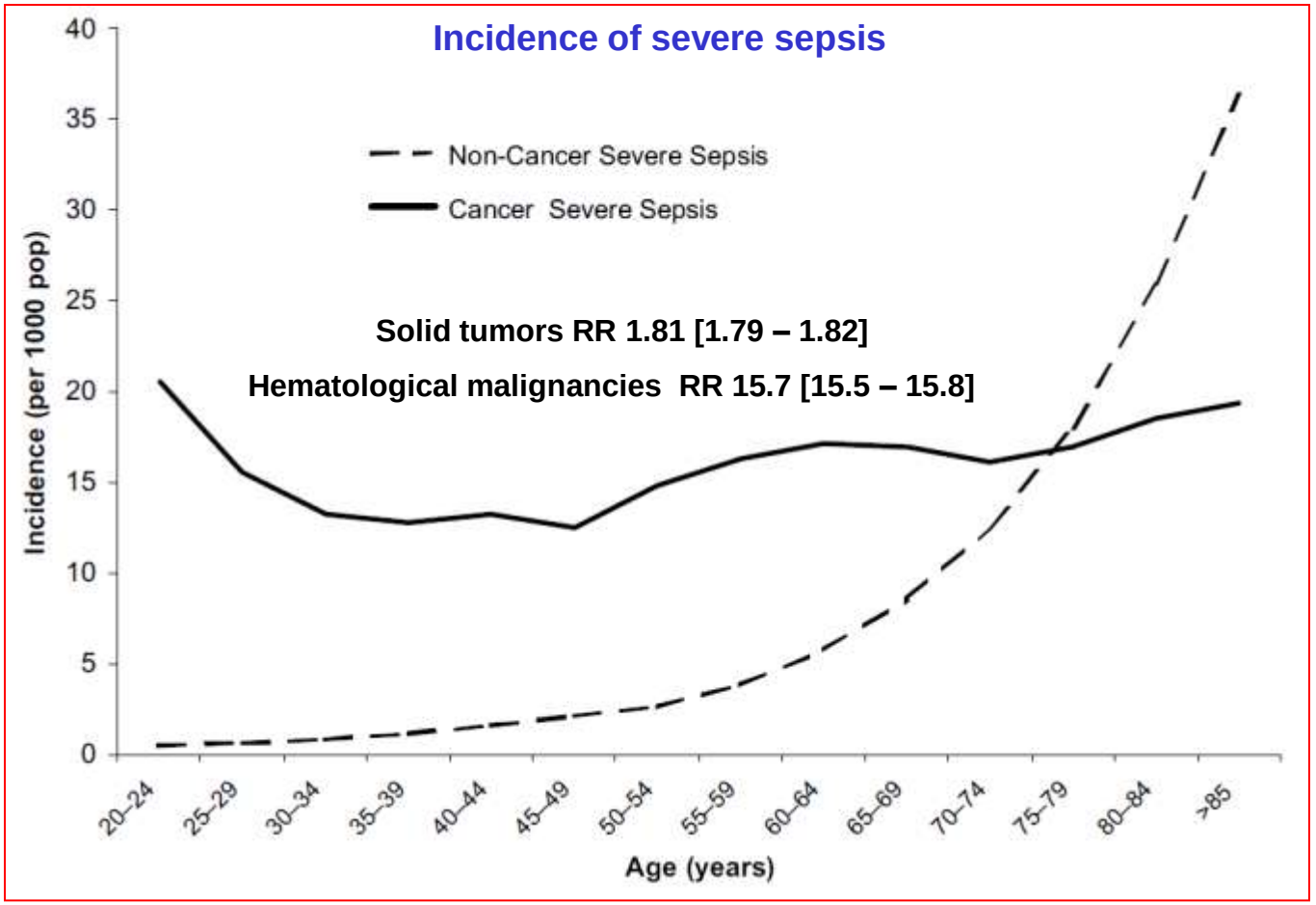
Research

Open Access

Hospitalized cancer patients with severe sepsis: analysis of incidence, mortality, and associated costs of care

Mark D Williams[1], Lee Ann Braun[2], Liesl M Cooper[3], Joseph Johnston[4], Richard V Weiss[5], Rebecca L Qualy[6] and Walter Linde-Zwirble[7]

Crit Care 2004



Research

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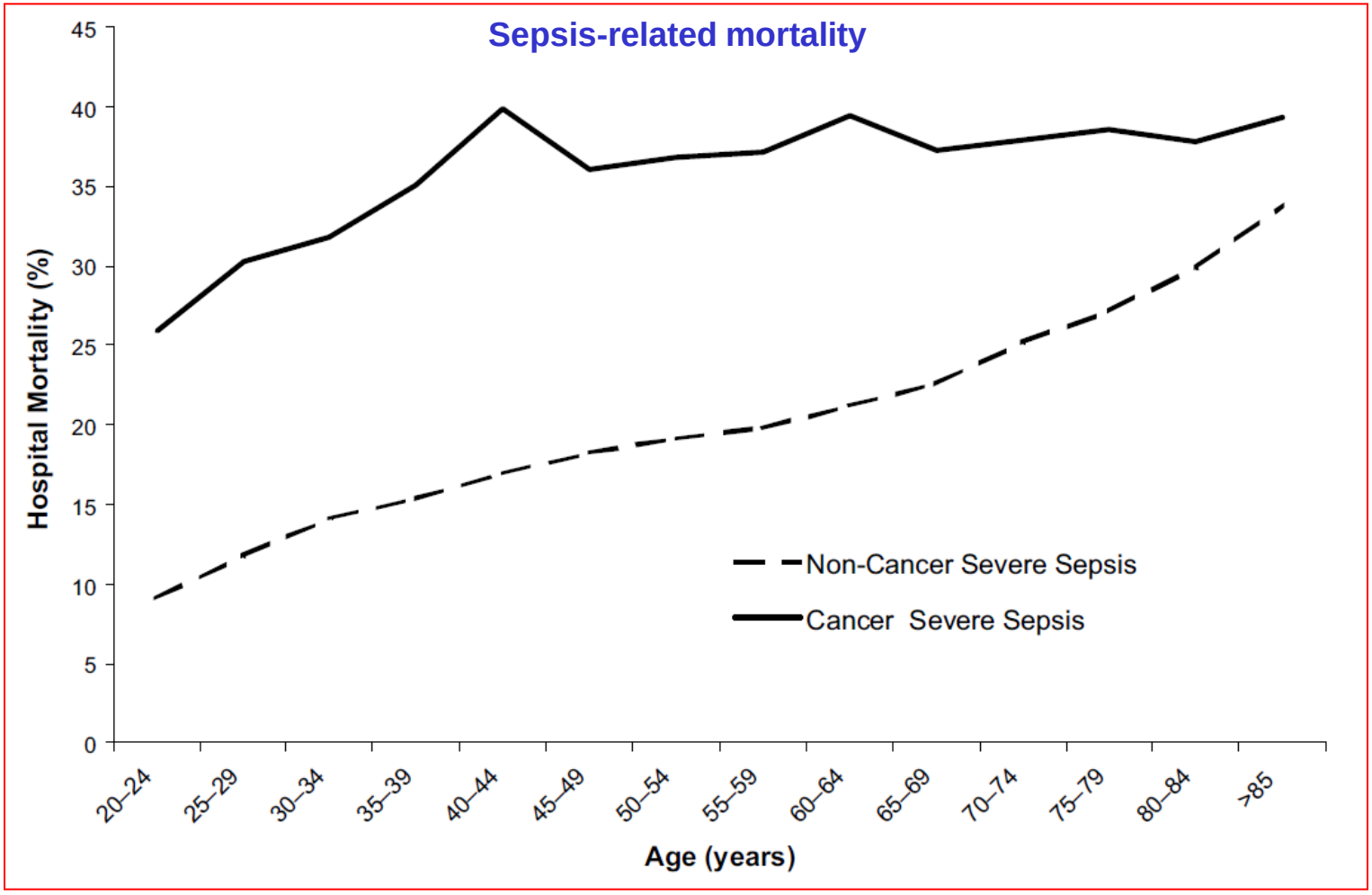
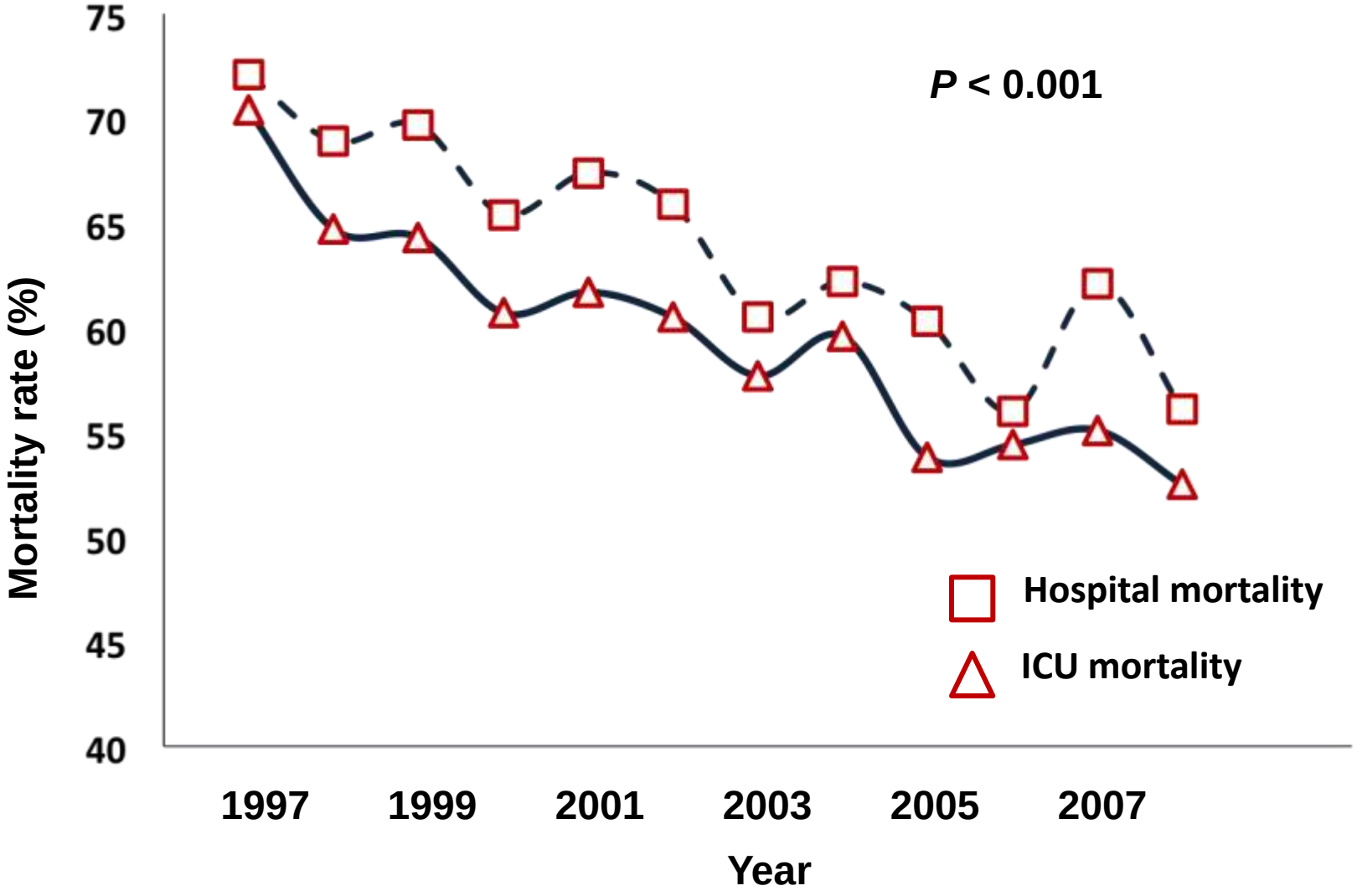


Survival to septic shock in cancer patients: the CUB-Réa network (n=3437)



Zuber, Crit Care Med 2012

Intensive Care Med (2008) 34:17–60
DOI 10.1007/s00134-007-0934-2

SPECIAL ARTICLE

Special Article

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Jean M. Carlet, MD; Julian Bion, MD; Margaret M. Parker, MD; Roman Jaeschke, MD; Konrad Reinhart, MD; Derek C. Angus, MD, MPH; Christian Brun-Buisson, MD; Richard Beale, MD; Thierry Calandra, MD, PhD; Jean-Francois Dhainaut, MD; Herwig Gerlach, MD; Maurene Harvey, RN; John J. Marini, MD; John Marshall, MD; Marco Ranieri, MD; Graham Ramsay, MD; Jonathan Sevransky, MD; B. Taylor Thompson, MD; Sean Townsend, MD; Jeffrey S. Vender, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; for the International Surviving Sepsis Campaign Guidelines Committee

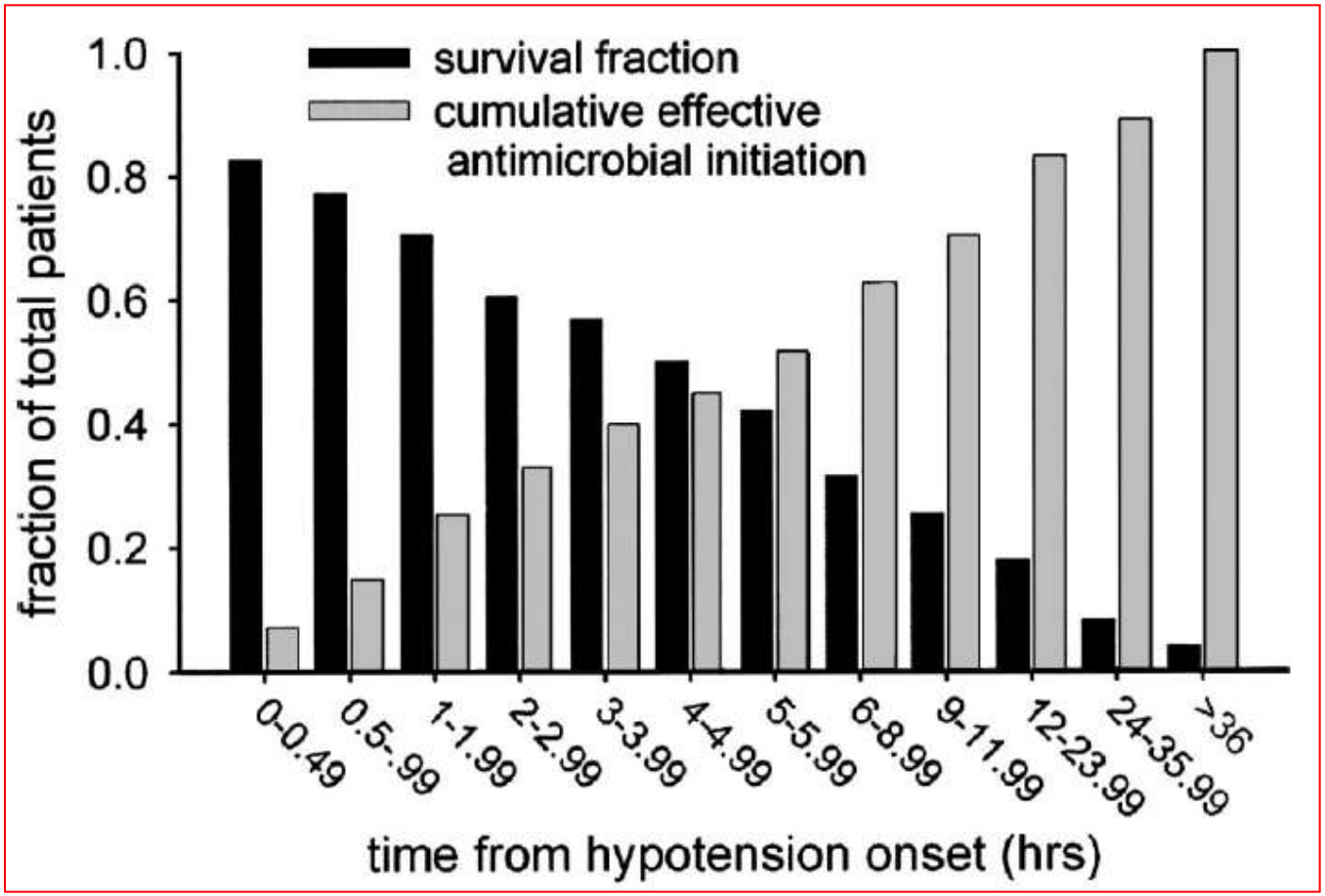
Crit Care Med 2008 Vol. 36, No. 1

Management of severe sepsis in the ICU: the cornerstones of the golden hours

- Collect blood cultures
- Early appropriate antibiotherapy
- Control of infection source
  - Removal of infected devices
  - Surgery

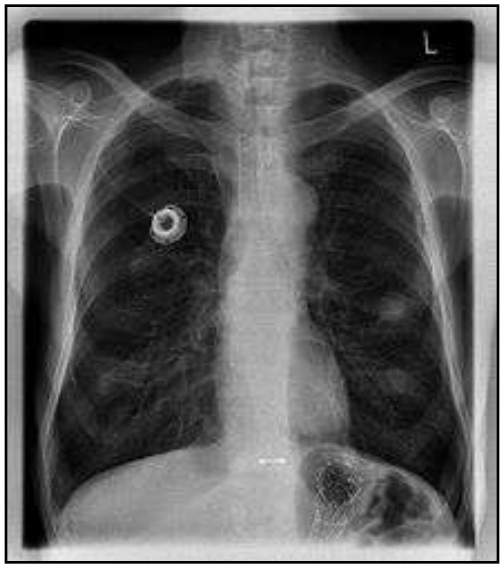
Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

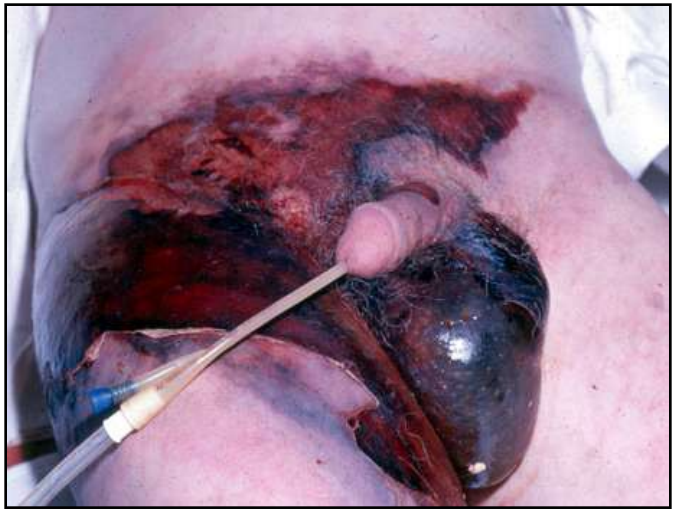
Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc



Crit Care Med 2006

Sites of infections in neutropenic patients





Management of severe sepsis in the ICU: the cornerstones of the golden hours

- Collect blood cultures
- Early appropriate antibiotherapy
- Control of infection source
  - Removal of infected devices
  - Surgery
- Early volume resuscitation
  - ≥ 20 mL/kg cristalloids
- Vasopressive support
  - Norepinephrine>epinephrine>dopamine
  - MAP > 65 mmHg

Management of severe sepsis in the ICU: doing less is better !!!

- **Resuscitation**
  - **Cristalloids rather than colloids**
  - **Restrictive fluid strategy**
- **Protective mechanical ventilation**
  - **V_T 6 mL/kg better than 12 mL/kg**
- **Restrictive transfusion strategy**
  - **Hb 70-90 g/L rather than 100-120 g/L**
- **Daily sedatives interruption**

Management of severe sepsis in the ICU: controversial issues

- Albumin resuscitation
- Intravenous immunoglobulin
- Glucose control and intensive insulin therapy
- Low-dose corticosteroids
- Type and timing of renal replacement therapy
- Anticoagulant treatment
- Platelet transfusion
- Pathophysiology-targeted treatments
- Immunity-enhancing treatments

Michael Darmon
Elie Azoulay
Corinne Alberti
Fabienne Fieux
Delphine Moreau
Jean-Roger Le Gall
Benoît Schlemmer

Impact of neutropenia duration on short-term mortality in neutropenic critically ill cancer patients

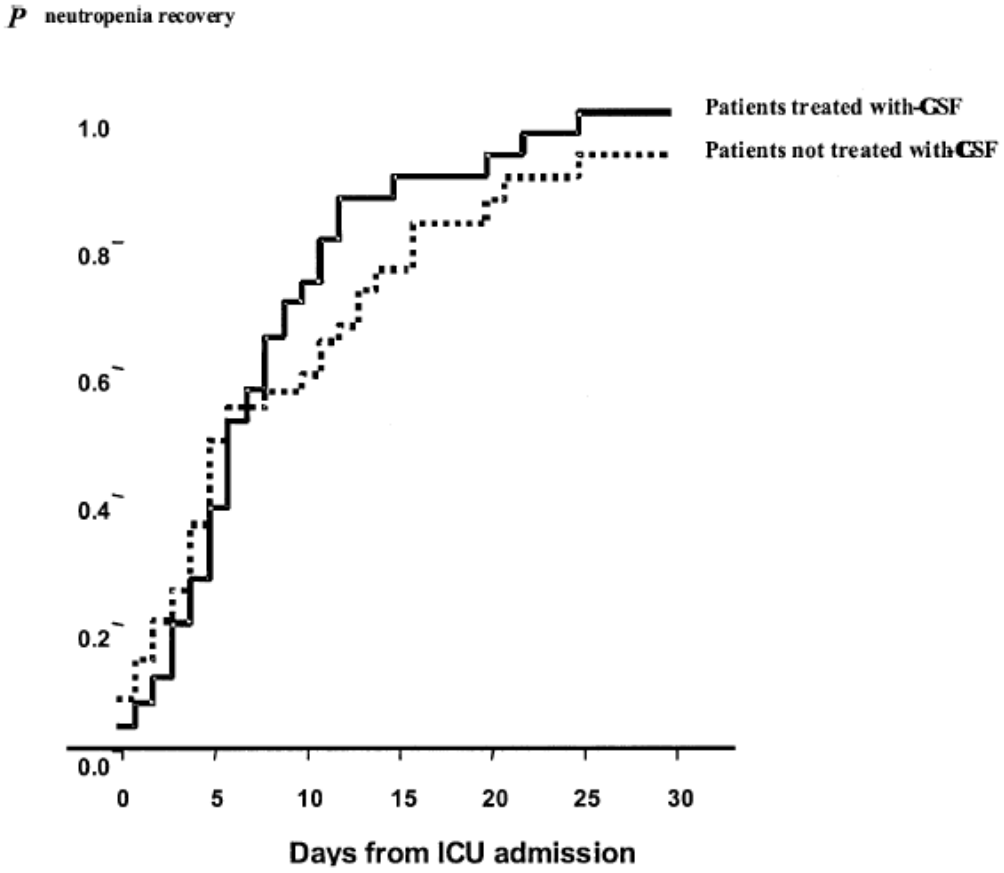


Fig. 1 Impact of G-CSF therapy on the likelihood of neutropenia recovery

Intensive Care Med 2002

Hematological patients in the ICU

- **Significant advances over the last decade**
- **Large ICU admission policy for early and aggressive management of organ failures**
- **Close collaborations between intensive care physicians and hematologists are needed**
- **Frequent reappraisal of expected benefits of intensive care**
- **Relevant endpoints: assessment of post-ICU outcomes of cancer patients (quality of life, maintenance of anticancer treatments, long-term overall and disease-free survival)**