UPEC
UNIVERSITÉ PARIS-EST CRÉTEIL
FACULTÉ
DE MÉDECINE

CARMAS
CArdiovascular and Respiratory
Manifestations of Acute lung
injury and Sepsis

SDRA sans facteur de risque classique: une entité à part?

Nicolas de Prost
Réanimation Médicale,
Hôpital Henri Mondor, Créteil

- Qu’est-ce que le SDRA ?
  - Historique
  - Données histologiques
  - Définitions
- Approche histologique: DAD *vs* «ARDS mimickers»
- SDRA sans facteur de risque:
  - Données épidémiologiques
  - Quelles investigations ?
  - Mesures thérapeutiques spécifiques

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Description initiale

- 12 patients: SDRA de causes pulmonaires et extra-pulmonaires
  - PEEP : 3/5 survivants
  - ZEEP: 2/7 survivants
- Nécropsie (n=7):
  - poumon hépatisé, congestif
  - Œdème pulmonaire
  - Hémorragie alvéolaire
  - *Mbnes hyalines* chez 6 patients

ACUTE RESPIRATORY DISTRESS IN ADULTS

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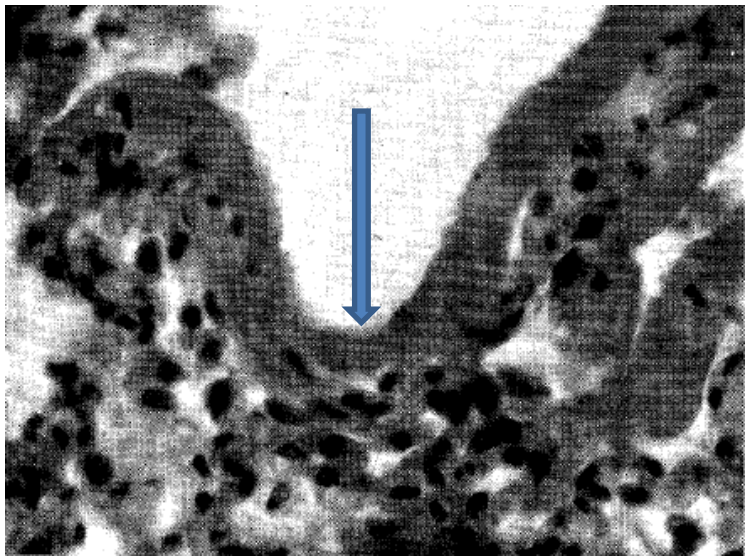

The Lancet, 1967

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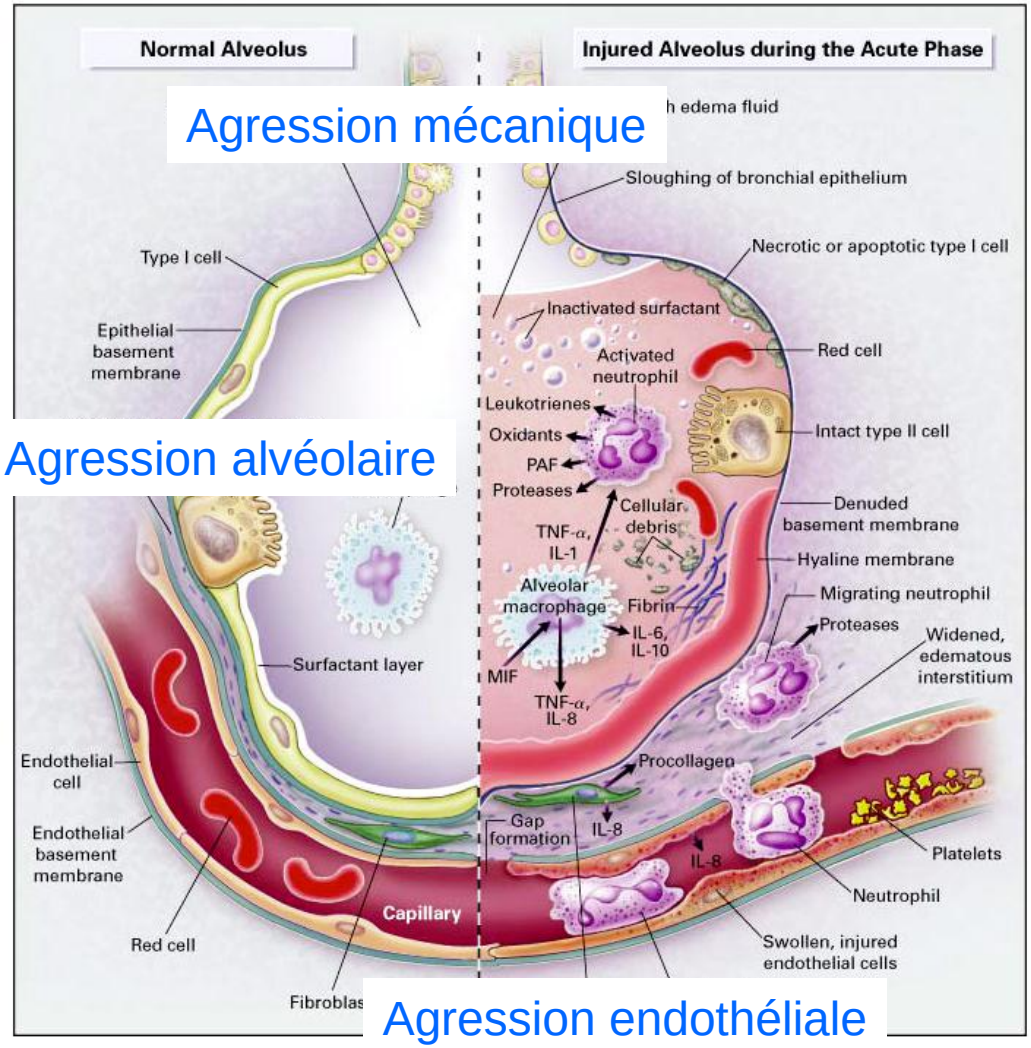
La forme la plus grave d'œdème pulmonaire lésionnel

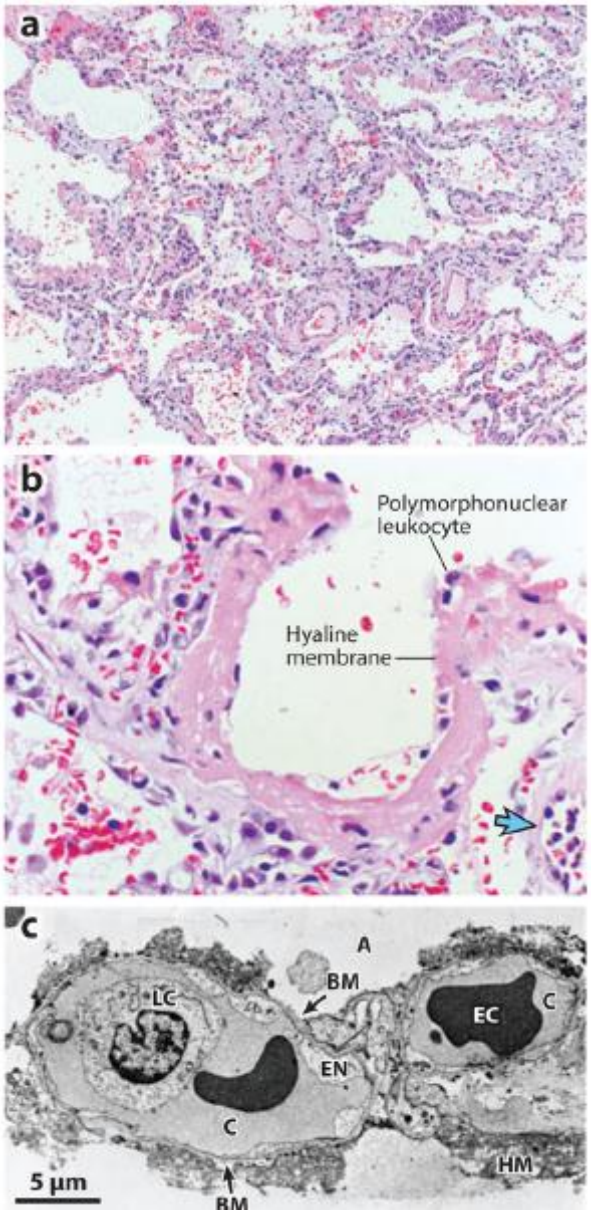
- Trouble de perméabilité de la barrière alvéolo-capillaire
- Infiltrat par des cellules mononucléées
- Réaction inflammatoire pulmonaire
- Atteinte microvasculaire
- Inactivation du surfactant
- Dysfonction des mécanismes de résorption de l'œdème alvéolaire



Ware & Matthay, *N Engl J Med* 2000

Avec une signature anatomo-pathologique

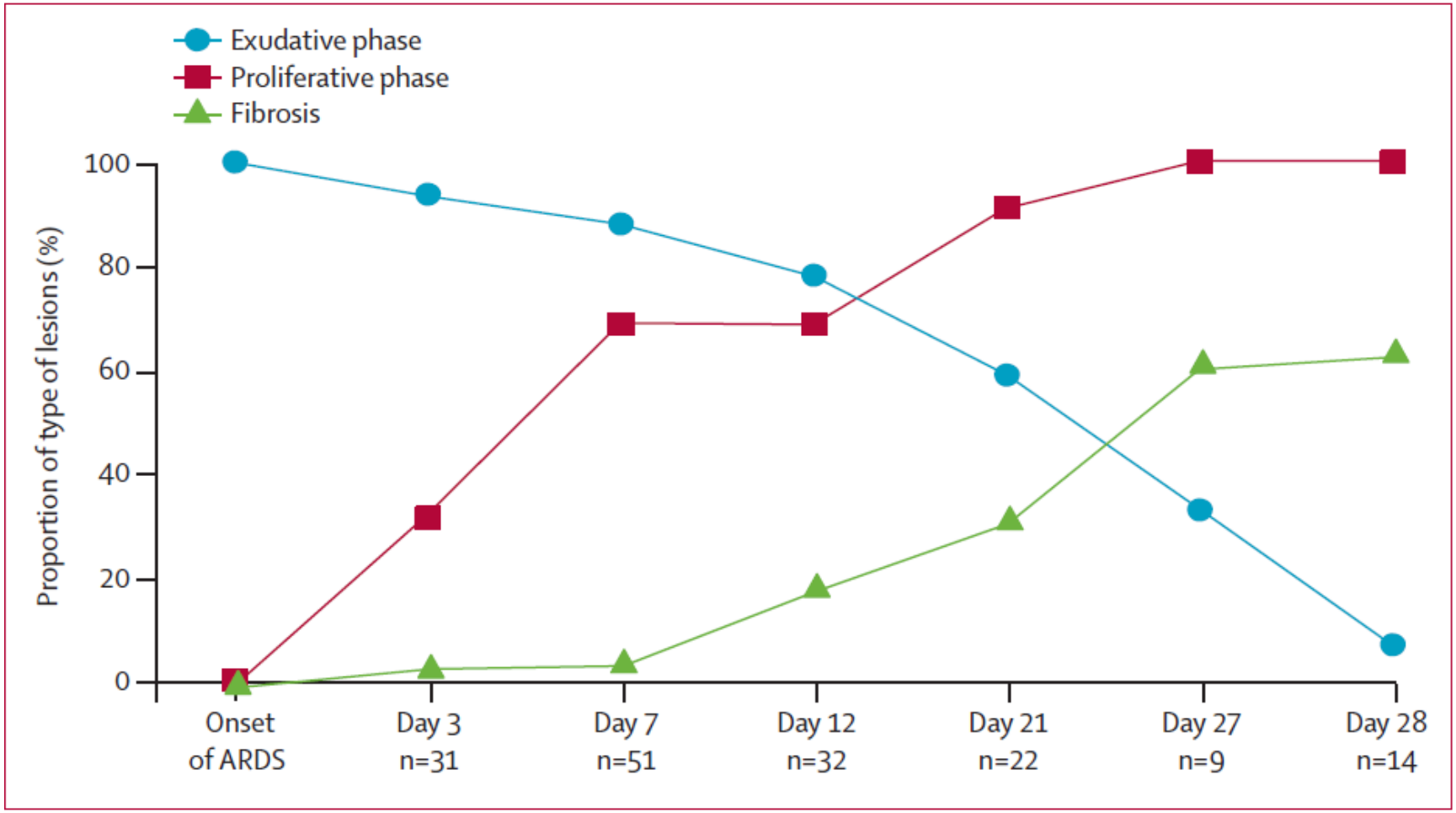
- Dommage alvéolaire diffus:
  - Membranes hyalines
  - Œdème pulmonaire
  - Hémorragie alvéolaire
  - Infiltrats inflammatoires à PNN
  - Épaississement barrière alvéolo-capillaire



Matthay, *Ann Rev Pathol* 2011

Bachofen and Weibel, *Am Rev Resp Dis* 1977

Des lésions évolutives



Thille et al, *Lancet Resp Med* 2013

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Critères diagnostiques

Conference Report

The American-European Consensus Conference on ARDS

Definitions, Mechanisms, Relevant Outcomes, and Clinical Trial Coordination

GORDON R. BERNARD, ANTONIO ARTIGAS, KENNETH L. BRIGHAM, JEAN CARLET, KONRAD FALKE, LEONARD HUDSON, MAURICE LAMY, JEAN ROGER LEGALL, ALAN MORRIS, ROGER SPRAGG, and the Consensus Committee

	Délai	Oxygénation	RX thorax	PAOP
ALI	Survenue brutale	$PaO_2/FiO_2 \leq 300$ mmHg (quel que soit le niveau de PEEP)	Infiltrats bilatéraux	≤18 mmHg Pas d'IVG
SDRA	Survenue brutale	$PaO_2/FiO_2 \leq 200$ mmHg (quel que soit le niveau de PEEP)	Infiltrats bilatéraux	≤18 mmHg Pas d'IVG

Am J Resp Crit Care Med 1994

Comparison of Clinical Criteria for the Acute Respiratory Distress Syndrome with Autopsy Findings

- Recherche de DAD chez 382 patients autopsiés:
  - ARDS (AECC): 33%
  - DAD: 29%

Critères cliniques sans DAD (n=43):

- Pneumonie: n=32
- HIA: n=4
- OAP: n=3
- EP: n=3
- Fibrose post chimio: n=1

Patients	Clinical Criteria for ARDS		No Clinical Criteria for ARDS		Sensitivity (95% CI), %†	Specificity (95% CI), %‡
	Diffuse Alveolar Damage, *n*	No Diffuse Alveolar Damage, *n*	Diffuse Alveolar Damage, *n*	No Diffuse Alveolar Damage, *n*		
All patients (*n* = 382)	84	43	28	227	75 (66–82)	84 (79–88)
Patients with risk factors for ARDS (*n* = 284)	84	43	27	130	76 (67–83)	75 (68–81)
Patients with pulmonary risk factors (*n* = 106)	27	19	17	43	61 (47–74)	69 (57–79)
Patients with extrapulmonary risk factors (*n* = 178)	57	24	10	87	85 (75–92)	78 (70–85)

Esteban, *Ann Intern Med* 2004

Analysis	Sensitivity (95% CI)	*p* Value vs. AECC	Specificity (95% CI)	*p* Value vs. AECC
Primary				
AECC definition	0.83 (0.72–0.95)	—	0.51 (0.41–0.61)	—
LIS >2.5	0.74 (0.61–0.87)	.34	0.77 (0.69–0.86)	<.001
Delphi definition	0.69 (0.55–0.83)	.07	0.82 (0.75–0.90)	<.001
Secondary (*a priori*)				
AECC + PEEP 10[a]	0.69 (0.55–0.83)	.03	0.79 (0.71–0.87)	<.001
AECC + CXR air space[b]	0.83 (0.72–0.95)	1.00	0.65 (0.55–0.74)	<.001
LIS >2.5 with dynamic compliance[c]	0.88 (0.78–0.98)	.69	0.64 (0.54–0.73)	.10
Secondary (*post hoc*)				
LIS >2.5 + AECC[d]	0.62 (0.47–0.77)	.004	0.87 (0.80–0.93)	<.001
LIS >2.5 + Delphi[e]	0.60 (0.45–0.74)	.006	0.88 (0.81–0.94)	<.001

Série autopsique (n=138)

Variable	No. (%) of Patients		
	AECC Positive	LIS Positive	Delphi Positive
Total	47	22	17
Pneumonia	22 (46.8)	13 (59.1)	10 (58.8)
Pulmonary embolism	10 (21.3)	5 (22.7)	5 (29.4)
Cardiogenic pulmonary edema	5 (10.6)	1 (4.5)	1 (5.9)
No significant pulmonary pathological findings	18 (38.3)	6 (27.3)	5 (29.4)

Ferguson, *Crit Care Med* 2005

SDRA: définition de Berlin

Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

	Acute Respiratory Distress Syndrome
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging[a]	Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation[b]	
Mild	200 mm Hg < PaO_2/FIO_2 ≤ 300 mm Hg with PEEP or CPAP ≥5 cm H_2O[c]
Moderate	100 mm Hg < PaO_2/FIO_2 ≤ 200 mm Hg with PEEP ≥5 cm H_2O
Severe	PaO_2/FIO_2 ≤ 100 mm Hg with PEEP ≥5 cm H_2O

Abbreviations: CPAP, continuous positive airway pressure; FIO_2, fraction of inspired oxygen; PaO_2, partial pressure of

JAMA 2012

Facteurs de risque « communs »

DIRECTS	INDIRECTS
Pneumonie	Sepsis non pulmonaire
Inhalation de liquide gastrique	Polytraumatisme
Inhalation de fumée	Transfusion
Contusion pulmonaire	Brulures
Noyade	Pancréatite
Vascularite pulmonaire (?)	Choc non cardiogénique
	Intoxication médicamenteuse

Ranieri, *JAMA* 2012; Ferguson, *Intensive Care Med* 2013

Comparison of the Berlin Definition for Acute Respiratory Distress Syndrome with Autopsy

Arnaud W. Thille[1,3], Andrés Esteban[1], Pilar Fernández-Segoviano[2], José-Maria Rodriguez[2], José-Antonio Aramburu[2], Oscar Peñuelas[1], Irene Cortés-Puch[1], Pablo Cardinal-Fernández[1], José A. Lorente[1], and Fernando Frutos-Vivar[1]

	Clinical Criteria for ARDS		No Clinical Criteria for ARDS		% Sensitivity (95% CI)	% Specificity (95% CI)
	+	−	+	−		
Using DAD as the reference standard						
Mild, moderate, or severe ARDS						
All patients with autopsy (n = 712)	159	197	19	337	89 (84–93)	63 (59–67)
Patients with risk factors for ARDS (n = 448)	159	197	4	88	98 (94–99)	31 (26–36)
Moderate or severe ARDS						
All patients with autopsy (n = 712)	153	154	25	380	86 (80–90)	71 (69–75)
Patients with risk factors for ARDS (n = 448)	153	154	10	131	94 (89–97)	46 (40–52)
Using DAD or pneumonia as the reference standard						
Mild, moderate, or severe ARDS						
All patients with autopsy (n = 712)	262	94	49	307	84 (80–88)	77 (72–80)
Patients with risk factors for ARDS (n = 448)	262	94	37	55	88 (83–91)	37 (30–45)
Moderate or severe ARDS						
All patients with autopsy (n = 712)	234	73	77	328	75 (70–80)	82 (78–85)
Patients with risk factors for ARDS (n = 448)	234	73	40	101	85 (81–89)	58 (51–65)

- Meilleure Se et moins bonne Sp que pour définition AECC

Am J Resp Crit Care Med 2013

Définition de Berlin et autopsie

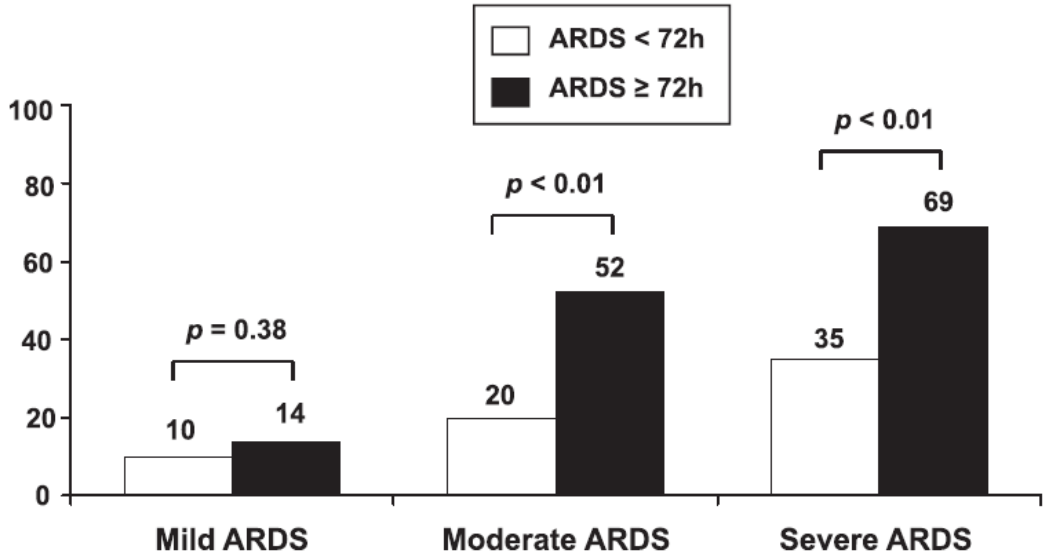

Figure 4. Proportion of patients with acute respiratory distress syndrome (ARDS) with diffuse alveolar damage (DAD) on autopsy examination according to severity and duration of time during which patients met clinical criteria of ARDS before autopsy examination. The proportion of DAD was higher in patients with moderate and severe ARDS who met clinical criteria for ARDS during more than 72 hours, and reached 69% in patients with severe ARDS of more than 72 hours.

Thille, AJRCCM 2013

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Intensive Care Med
DOI 10.1007/s00134-015-4046-0

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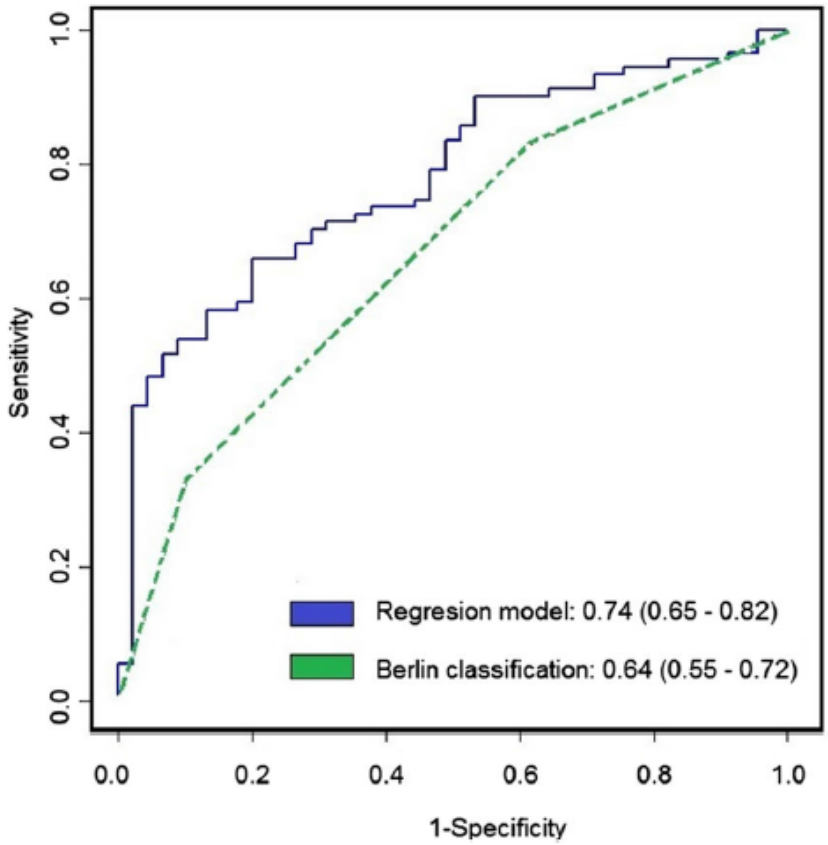
Acute respiratory distress syndrome in patients with and without diffuse alveolar damage: an autopsy study

Comparaison du phénotype clinique de patients ayant les critères de SDRA avec *DAD +* (n=49) ou *DAD-* (n=100) à l'autopsie

Facteurs associés à DAD

PaO_2/FiO_2 ratio	0,99 [0,98-0,99]	P<0,01
Cdyn	0,94 [0,89-0,98]	P<0,01
Age	0,97 [0,95-0,99]	P<0,01



Discussion

We report for the first time in ARDS non-survivors different clinical characteristics depending on the underlying histology. These findings provide support to the concept that the presence of DAD defines a specific subphenotype within patients with the clinical diagnosis of ARDS.

Intensive Care Med 2015

Intensive Care Med
DOI 10.1007/s00134-014-3583-2

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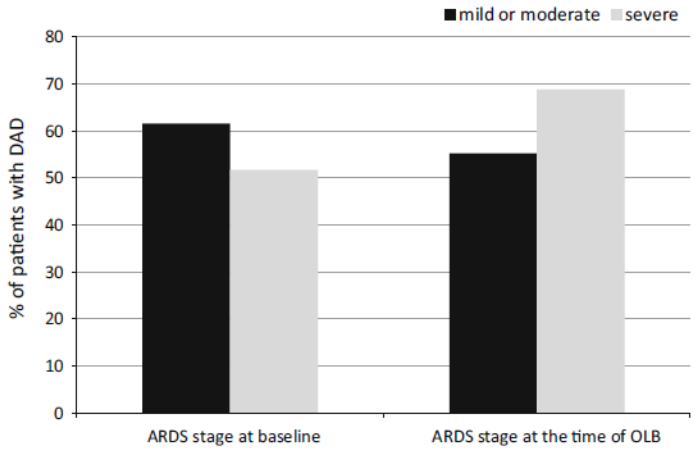
Open lung biopsy in nonresolving ARDS frequently identifies diffuse alveolar damage regardless of the severity stage and may have implications for patient management

DAD+ chez 58% (n=48/83) patients avec SDRA

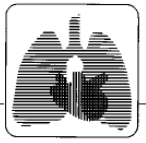
Diffuse alveolar damage	48
No diffuse alveolar damage	35
Interstitial lung fibrosis	13
Pneumonia	4
Organizing pneumonia	9
Cancer	3
Alveolar hemorrhage	5
Normal	1



	DAD +	DAD -	p
Sévérité SDRA *Léger* *Modéré* *Sévère*	 4 (8) 33 (69) 11 (23)	 7 (20) 23 (66) 5 (14)	NS
PaO_2/FiO_2 ratio	129	155	<0,05
P*plateau*	28	23	<0,01

In patients with nonresolving ARDS the use of steroids may be considered after ongoing infection has been ruled out. A large randomized controlled trial failed to demonstrate improvements in patient survival with steroids as compared to placebo [8]. Given the prevalence of DAD found on OLBs in nonresolving ARDS in the present study, it is unlikely that steroids would improve lung function. The only pathological diagnosis that is steroid-sensitive in this setting, other than a specific ARDS-causing immunological disease, is organizing

Intensive Care Med 2014



clinical investigations in critical care

The Role of Open-Lung Biopsy in ARDS*

Sanjay R. Patel, MD; Dimitri Karmpaliotis, MD; Najib T. Ayas, MD; Eugene J. Mark, MD; John Wain, MD, FCCP; B. Taylor Thompson, MD; and Atul Malhotra, MD

Diagnoses	No.
DAD	23
Acute phase	5
Fibroproliferative phase	18
Specific infection	8
Diffuse alveolar hemorrhage	5
BOOP	5
Bronchiolitis	3
Culture-negative purulent pneumonia	2
Drug reaction	2
Pulmonary lymphoma	2
Lymphangitic tumor	1
Organizing pneumonia	1
Desquamative interstitial pneumonia	1
Hypersensitivity pneumonitis	1
Chronic eosinophilic pneumonia	1
Allergic bronchopulmonary aspergillosis	1
Pulmonary edema	1

Chest 2004

"Imitators" of the ARDS*

Implications for Diagnosis and Treatment

Marvin I. Schwarz, MD, FCCP; and Richard K. Albert, MD, FCCP

Table 1—*Acute Noninfectious Diffuse Parenchymal Lung Diseases and Their Underlying Histology, Etiology, and BAL Cellular Content*

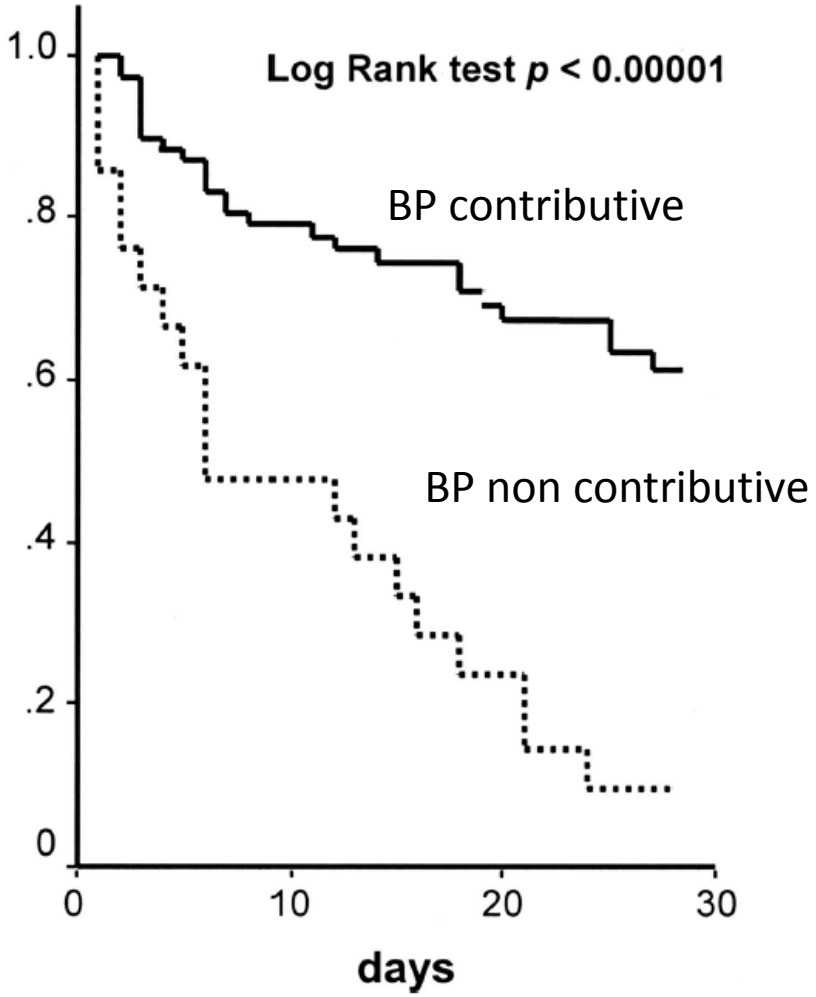
AIP	
	Organizing diffuse alveolar damage
	Idiopathic (Hamman-Rich syndrome), CVD, cytotoxic drugs, infections
	Neutrophilia (> 10%)
AEP	
	Eosinophilic infiltration and diffuse alveolar damage
	Idiopathic, drugs
	Eosinophilia (> 25%)
Acute BOOP	
	Organizing pneumonia,
	Idiopathic, CVD, drugs, radiation, infections
	Neutrophilia, and sometimes lymphocytosis (< 25%), eosinophilia (< 25%)
DAH	
	Pulmonary capillaritis, bland hemorrhage, diffuse alveolar damage
	Vasculitides, CVD, ABMA disease, coagulopathies, diffuse infections (partial list)
	RBCs, hemosiderin-laden macrophages
Acute HP	
	Granulomatous and cellular pneumonitis with diffuse alveolar damage
	Environmental and workplace antigens
	Lymphocytosis (> 25%) and sometimes neutrophilia (< 10%)

A contributive result of open-lung biopsy improves survival in acute respiratory distress syndrome patients

Laurent Papazian, MD; Christophe Doddoli, MD; Bruno Chetaille, MD; Yaël Gernez, MD; Xavier Thirion, MD; Antoine Roch, MD; Yannis Donati, MD; Marilyne Bonnety, MD; Christine Zandotti, MD; Pascal Thomas, MD

100 biopsies pulmonaires réalisées chez 100 patients atteints de SDRA

Result of OLB	No.
Fibrosis	16
Fibrosis and infection	29
Infection	28
Diffuse alveolar damage	13
Miscellaneous	
Systemic lupus erythematosus	2
Bronchioloalveolar carcinoma	1
Amiodarone toxicity	2
Intra-alveolar hemorrhage	1
Allograft rejection	1
Drug toxicity	2
Rheumatoid lung and mycobacterial infection	1
Acute eosinophilic pneumonia	1
Carcinomatous lymphangitis	2
Microangiitis	1



Crit Care Med 2007

Limites des études histologiques

- Etudes rétrospectives
- Faible effectif
- Biais de sélection des patients (OLB/autopsie)
- Effet centre (chirurgie thoracique)

- Données peu « généralisables » et difficilement utilisables pour le clinicien

Ten diseases that may be mistaken for ARDS

Table 1 lists ten clinical entities that may be mistaken for ARDS. While it is beyond the scope of this brief report to outline a diagnostic approach to all of these entities, we offer a few observations from clinical experience. While some entities may present in an accelerated time course of several–many days, which would be consistent with the time course for ARDS, more typically they present with a longer time course. This should raise suspicion that the clinical problem is something other than ARDS. Another clinical clue is the absence of a known clinical risk factor for ARDS; or if a clinical risk factor has been identified and treated appropriately (for example, pneumonia),

Guerin, *Intensive Care Med* 2015

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Intensive Care Med
DOI 10.1007/s00134-015-4064-y

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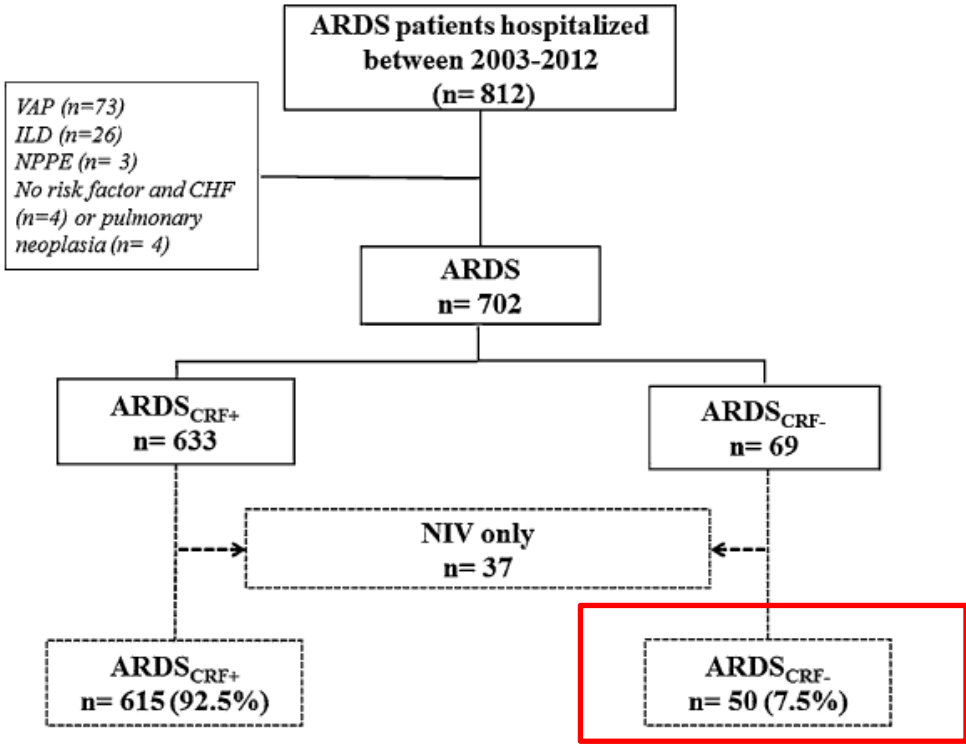
Acute respiratory distress syndrome mimickers lacking common risk factors of the Berlin definition

- Etude rétrospective bicentrique
- Objectifs: déterminer la *prévalence* et les *étiologies* des SDRA sans FDR de Berlin



Causes

Immunes	18
Médicamenteuse	13
Idiopathiques	7
Autres	12

Intensive Care Med 2015

Variables	ARDS patients with CRF (n=615)		ARDS patients with no CRF (n=50)		p
Age, years	61	[47-72]	66	[50-75]	0.33
Male gender, n (%)	410	(67)	37	(74)	0.30
Time between first respiratory symptoms and ICU admission, days	2	[0-5]	13	[4-30]	<0.0001
Worsening of respiratory symptoms-admission, days	1	[0-2]	2	[2-4]	<0.0001
Severity criteria during the first 48 hours of ICU admission					
SAPS II	55	[39-73]	40	[31-53]	<0.0001
LOD score	10	[6-13]	4	[3-8]	<0.0001
Shock, n (%)	494	(80)	22	(44)	<0.0001
PaO_2/FiO_2 ratio, mmHg	104	[73-150]	94	[72-138]	0.14
Berlin classification of ARDS, n (%)					0.13
mild	56	(9)	2	(4)	
moderate	263	(43)	17	(34)	
severe	296	(48)	31	(62)	
Outcome variables					
Duration of ICU stay, days	13	[6-23]	13	[8-24]	0.50
Ventilator-free days at day 60, days	0	[0-47]	0	[0-37]	0.059
ICU Mortality, n (%)	327	(53)	33	(66)	0.088
Rescue maneuvers during ICU stay, n (%)					
Neuromuscular blocking agents	550	(89)	46	(92)	0.63
Nitric oxide inhalation	188	(31)	21	(42)	0.099
Prone postition	174	(28)	16	(32)	0.59
ECMO	17	(3)	2	(4)	0.62
Non pulmonary organ failures during ICU stay, n (%)					
Shock	530	(86)	41	(82)	0.40
Hemodialysis	207	(34)	20	(40)	0.65
Corticosteroid therapy	92	(15)	42	(84)	<0.0001

Facteurs associés à la mortalité hospitalière

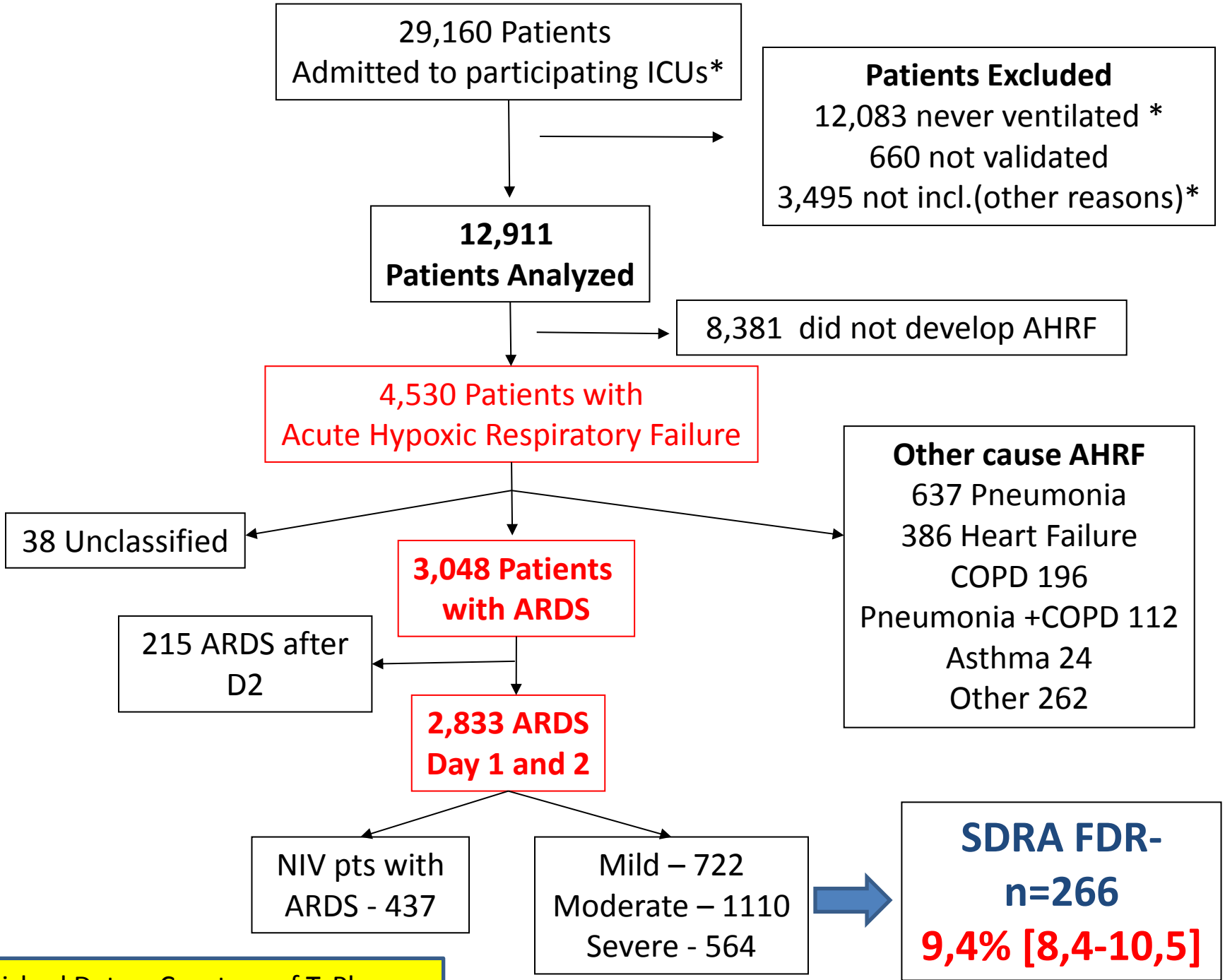
	n	Death n (%)	Univariate analysis		Multivariable analysis	
			OR (95% CI)	P	OR (95% CI)	P
SAPS II	665	-	1.03 [1.02-1.04]	<0.0001	1.03 [1.02-1.04]	<0.0001
LODS	665	-	1.14 [1.10-1.18]	<0.0001	1.09 [1.04-1.06]	<0.0001
Shock						
Yes	516	299 (58)	1.99 [1.37-2.88]	<0.0001	-	
No	149	61 (41)	1			
Absence of ARDS CRF						
Yes	50	33 (66)	1.69 [0.92-3.09]	0.091	**2.06 [1.02-4.18]**	**0.044**
No	615	327 (53)	1			
Berlin classification with shock						
mild	58	31 (53)	1			
moderate	280	126 (45)	1.66 [0.49-5.56]	0.41		
severe	327	203 (62)	4.65 [1.36-15.94]	0.014	2.04 [1.41-2.95]	<0.001
Age	665	-	1.02 [1.01-1.03]	<0.001	1.02 [1.01-1.03]	0.004
NIV duration	665	-	1.17 [1.04-1.32]	0.009	1.46 [1.24-1.71]	<0.001
No bacterial infection						
Yes	306	189 (62)	1.78 [1.30-2.42]	<0.001	1.47 [1.03-2.11]	0.033
No	359	171 (48)	1			

Gibelin, *Intensive Care Med* 2015

Etude ASteRoID: ArdS with no Risk factor from the berlIn Definition

données préliminaires

- Etude ancillaire de l'étude Lung Safe
- Objectif: déterminer la prévalence et le pronostic du SDRA sans FDR (définition de Berlin)

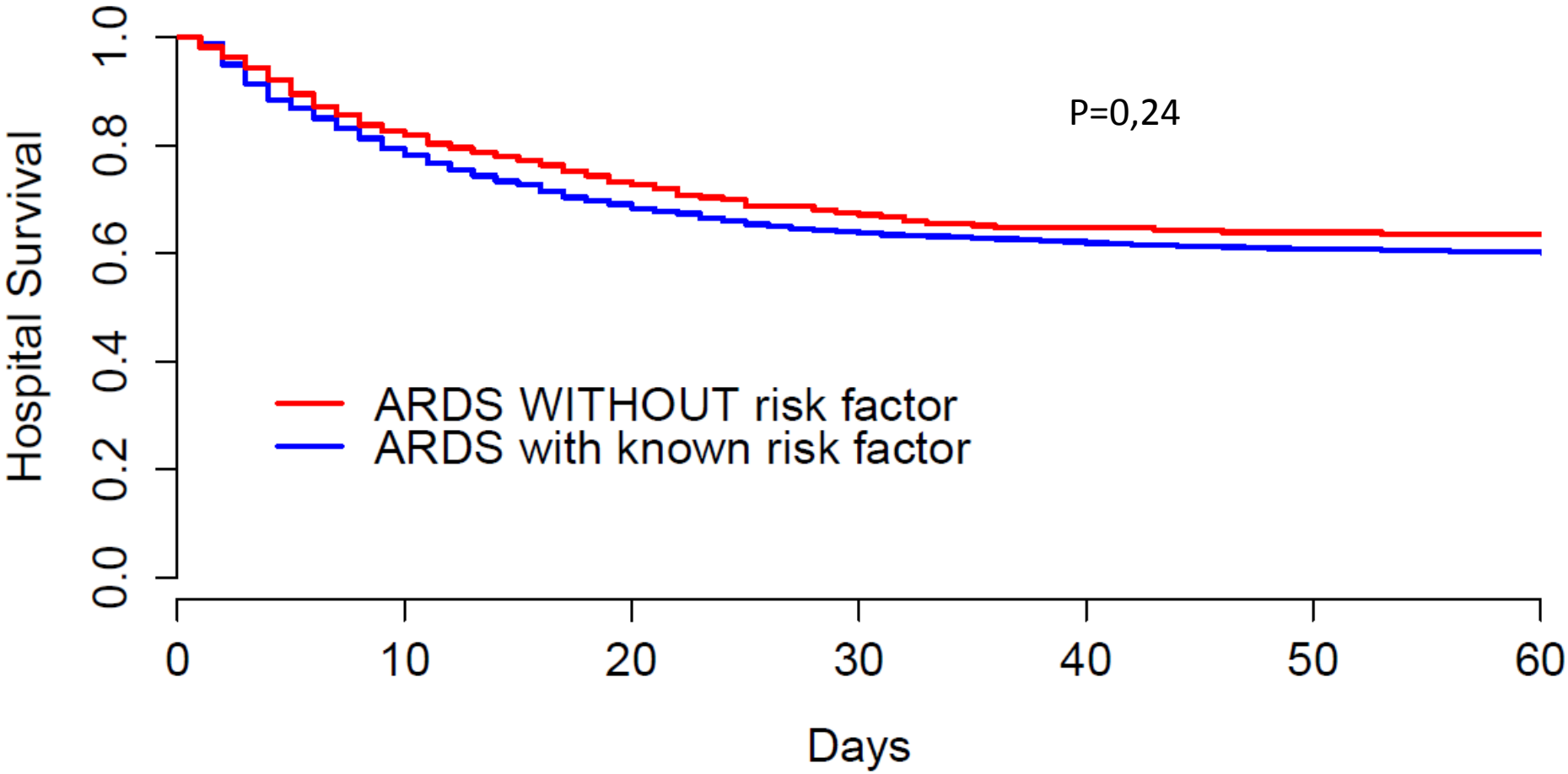

29,160 Patients
Admitted to participating ICUs*
Patients Excluded
12,083 never ventilated *
660 not validated
3,495 not incl.(other reasons)*
12,911
Patients Analyzed
8,381 did not develop AHRF
4,530 Patients with
Acute Hypoxic Respiratory Failure
Other cause AHRF
637 Pneumonia
386 Heart Failure
COPD 196
Pneumonia +COPD 112
Asthma 24
Other 262
38 Unclassified
3,048 Patients
with ARDS
215 ARDS after
D2
2,833 ARDS
Day 1 and 2
NIV pts with
ARDS - 437
Mild – 722
Moderate – 1110
Severe - 564
SDRA FDR-
n=266
9,4% [8,4-10,5]
Unpublished Data – Courtesy of T. Pham

Asteroid: caractéristiques à l'admission

	SDRA FDR + (n=2550)	SDRA FDR – (n=266)	p
Age	63 [50-74]	68 [57-76]	<0.0001
Sexe masculin, %	1570 (61.6)	162 (60.9)	0,88
BPCO, %	522 (20.5)	83 (31.2)	<0.0001
Diabète, %	542 (21.2)	73 (27.4)	0.025
IRC, %	241 (9.4)	45 (16.9)	0.0002
Immunodépression, %	538 (21,1)	49 (18,4)	0.35
PaO_2/FiO_2, mm Hg	122 [84-169]	130 [94-185]	0.004
Sévérité SDRA *Léger* *Modéré* *Sévère*	 462 (20,4) 1095 (48,3) 710 (31,3)	 52 (24,9) 101 (48,3) 56 (26,8)	0,21
Crs, mL/cmH2O	31 [24-43]	35 [23-42]	0.21
SOFA	9 [6-12]	8 [6-11]	0.0004
SOFA non respiratoire	6 [3-9]	5 [2-8]	0.0002

Asteroid: évolution

	SDRA FDR + (n=2550)	SDRA FDR – (n=266)	p
Durée VM, jours	8 [4-15]	6 [3-16]	0.12
Nbre jours sans VM J28, jours	10 [0-22]	11 [0-24]	0.073
Décubitus ventral, %	193 (7.6)	12 (4.5)	0.089
ECMO, %	72 (2.8)	9 (3.4)	0.74
Corticoïdes H72, %	354 (13,9)	52 (19,0)	0,016
Sédation	1954 (76,6)	178 (66,9)	0.0006
Durée de séjour réa, jours	10 [5-18]	8 [4-19]	0.097
Durée de séjour hôpital, jours	17 [8-31]	14 [8-28]	0.20
Mortalité réanimation, %	890 (35)	77 (29)	0,060
Mortalité hospitalière, %	1021 (40)	97 (36)	0,27
Cause du décès			0,047
Hémodynamique	337 (38)	24 (32)	
Respiratoire	364 (41)	40 (53)	
Hépatique	50 (6)	1 (1)	
Neurologique	98 (11)	7 (9)	
Rénale	27 (3)	1 (1)	


Hospital Survival
0.0
0.2
0.4
0.6
0.8
1.0
P=0,24
ARDS WITHOUT risk factor
ARDS with known risk factor
0
10
20
30
40
50
60
Days

- Qu’est-ce que le SDRA ?
  - Historique
  - Données histologiques
  - Définitions
- Approche histologique: DAD *vs* «ARDS mimickers»
- SDRA sans facteur de risque:
  - Données épidémiologiques
  - Quelles investigations ?
  - Mesures thérapeutiques spécifiques

Intensive Care Med
DOI 10.1007/s00134-015-4120-7

EDITORIAL

Jean-Louis Vincent
Carlos Santacruz

Do we need ARDS?

The key message is that we must always try to find a cause for severe acute respiratory failure. Indeed, this is a concept that can be generalized to any severe disease, and is also true for other syndromes, like sepsis, shock or coma. Even brain death needs to have a defined cause. Finding the underlying cause of the severe respiratory failure can not only help guide treatment but may also lead to earlier discontinuation of life support if a non-reversible, terminal condition is identified.

Intensive Care Med 2015

"Imitators" of the ARDS*

Implications for Diagnosis and Treatment

radiographic criteria for ALI/ARDS. Some of these have distinct BAL characteristics and/or specific histologic findings. It is important to distinguish these from ALI/ARDS because most cases seem to respond to the early initiation of systemic corticosteroid therapy. In addition, studies evaluating novel

Chest 2004

SDRA modéré ou sévère (critères de Berlin)

Facteur de risque -

***Etape 1:* Bilan infectieux « approfondi »**

- Hémocultures, antigénuries légionelle et pneumocoque, sérologies des germes intra-cellulaires, PCR virale « multiplex », sérologie VIH.
- **Lavage broncho-alvéolaire** (LBA): bactériologie standard, virologie et cytologie pour les sujets immunocompétents + myco-parasitologie pour les immunodéprimés.

Facteur de risque +
Prise en charge habituelle

Etape 2: En l'absence de diagnostic et avant J5:

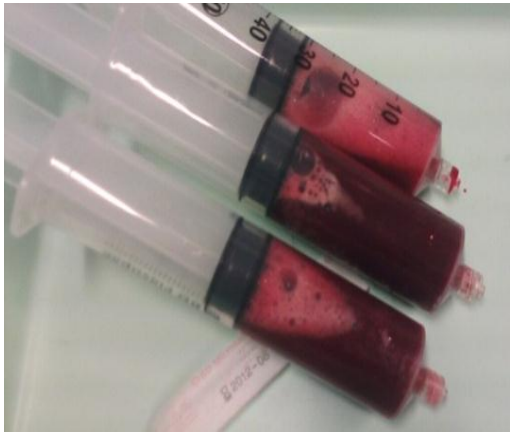
- Scanner thoracique coupes fines: verre dépoli, rayon de miel, adénomégalies, masse tumorale
- Bilan d'auto-immunité complet : facteur rhumatoïde, anticorps anti-CCP, facteurs anti-nucléaires, anticorps anti-DNA natif, anti-antigènes nucléaires solubles, ANCA, anticorps anti-synthétases , sérologies « éleveur d'oiseaux » et « poumon de fermier », enzyme de conversion de l'angiotensine, sérologies VHB, VHC
- Enquête médicamenteuse (pneumotox.com)
- Avis spécialisé: pneumologue, interniste, oncologue

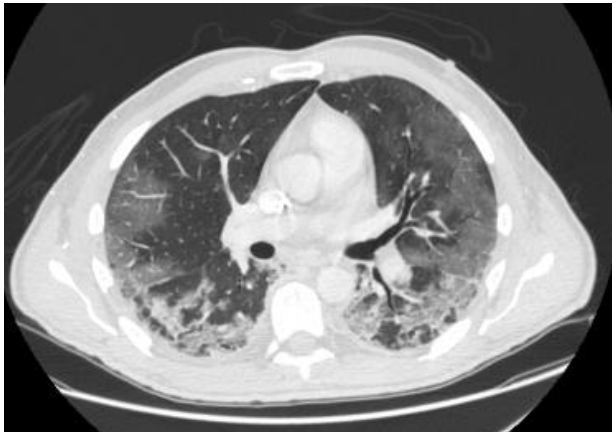
Immunosuppression?

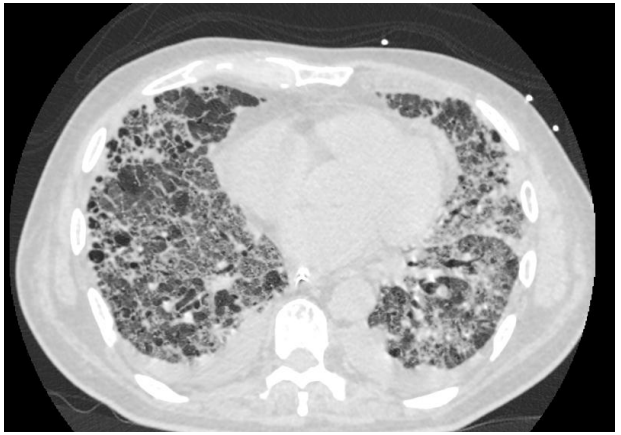
Etape 3 : Biopsie pulmonaire chirurgicale?

Apport des investigations complémentaires

	All		Non-survivors		Survivors		P
Bronchoalveolar lavage (BAL) fluid cytology, n	45		30		15		
Hemorrhagic, n (%)	9	(20)	2	(7)	7	(47)	0.003
Total cell count, 10^3/mL	226	[100-462]	210	[100-420]	450	[100-520]	0.42
Macrophages, %	33	[18-52]	35	[24-61]	14	[10-30]	0.016
Neutrophils, %	25	[9-47]	25	[15-53]	4	[0-34]	0.02
Lymphocytes, %	17	[5-45]	12	[5-36]	66	[11-87]	0.04







Gibelin, *Intensive Care Med* 2015

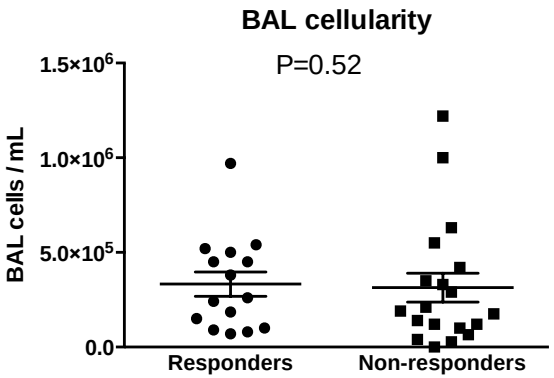
Facteurs associés à la mortalité chez les patients sans FDR

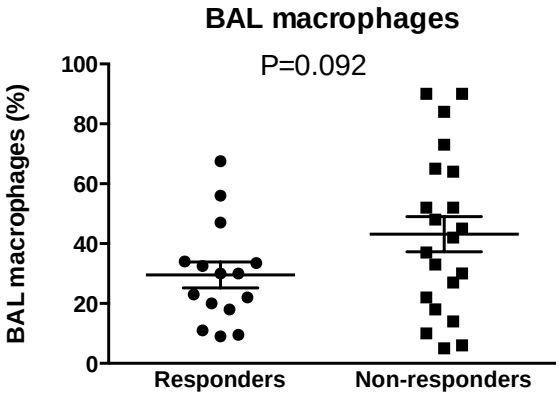
Réversibilité potentielle des lésions pulmonaires: établie par 3 experts en aveugle de l'évolution clinique, disposant de la cytologie du LBA et du scanner thoracique

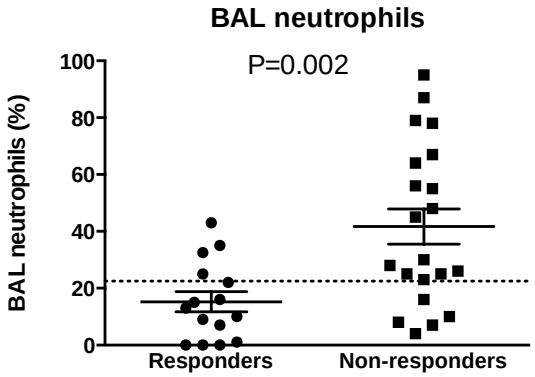
	N	Death n (%)	Univariate analysis		Multivariable analysis	
			OR (95% CI)	P	aOR (95% CI)	P
Non-invasive mechanical ventilation						
Yes	23	19 (83)	4.41 [1.18-16.45]	0.03		
No	27	14 (52)	1			
Presence of potentially reversible lung lesions						
Yes	19	8 (42)	0.16 [0.04-0.60]	0.007	**0.14 [0.03-0.62]**	**0.010**
No	28	23 (82)	1			
Plasma creatinine level > 140 µmol/L						
Yes	14	5 (36)	0.16 [0.04-0.61]	0.007	0.13 [0.02-0.65]	0.013
No	36	28 (78)	1			
LOD score	50	-	0.83 [0.68-1.01]	0.06		

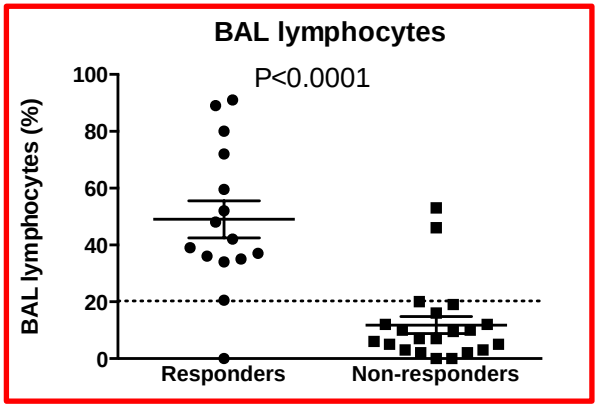
Gibelin, *Intensive Care Med* 2015

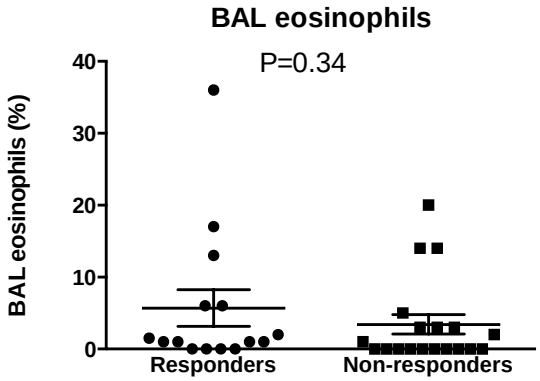
Apport de la cytologie du LBA

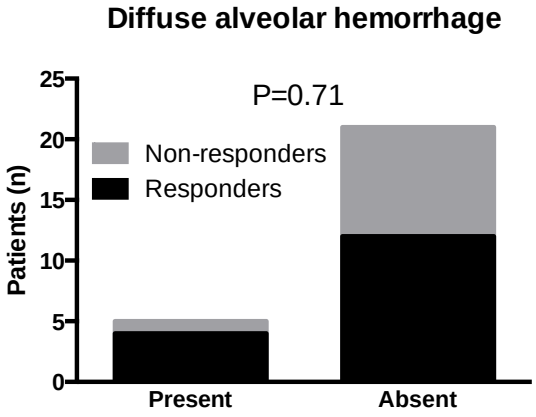




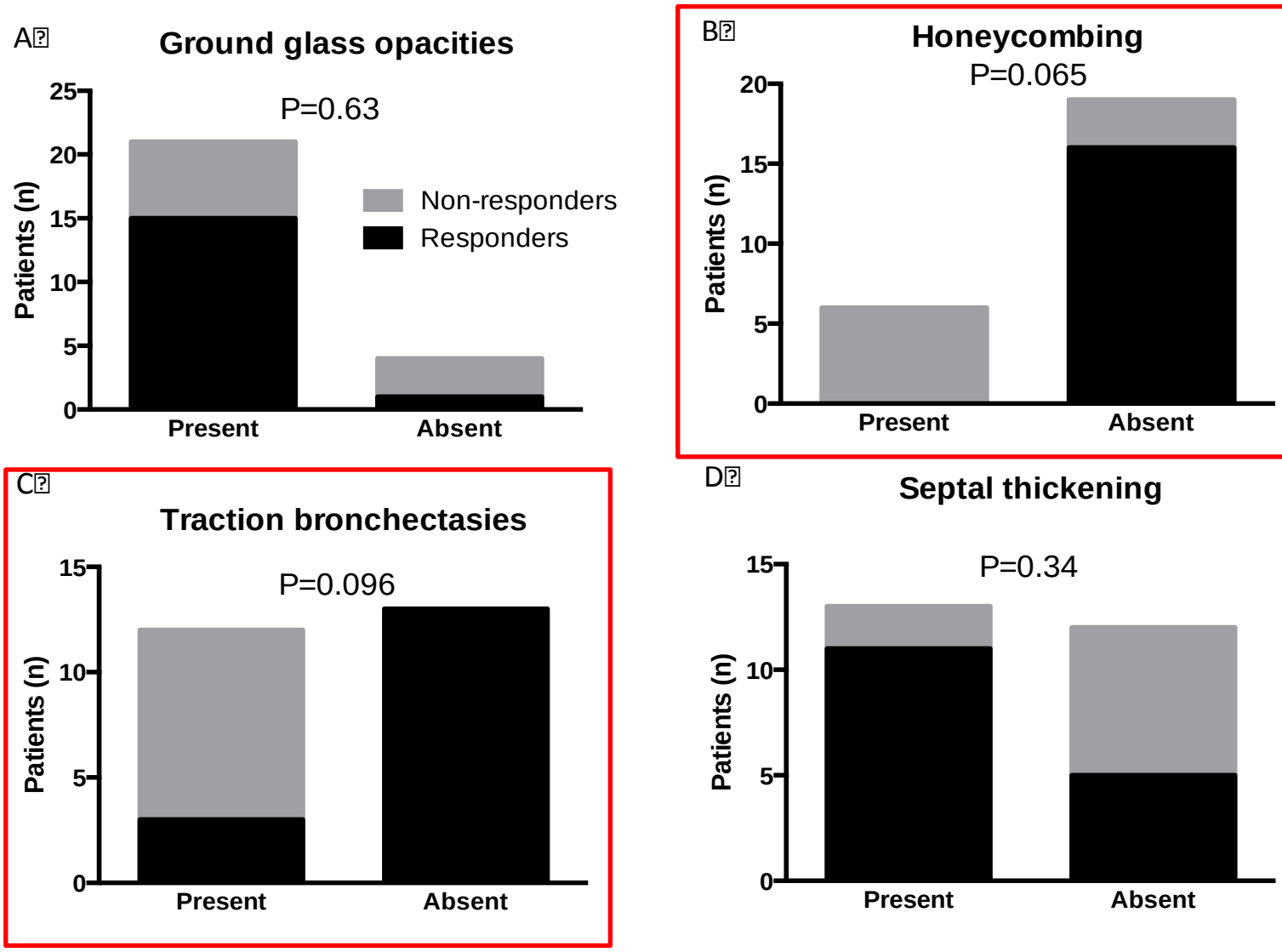








Apport de la tomodensitométrie thoracique



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PNP médicamenteuse (DALI)	Cause immune	Cause néoplasique	Idiopathique

PNEUMOTOX ON LINE

- Guidelines EULAR & ACR

Acute Interstitial Pneumonitis

Case Series and Review of the Literature

Drug	No.[a]	Drug	No.[a]
Amiodarone	14	Leuprorelin	0
Arsenic trioxide	0	Medroxyprogesterone	0
Basiliximab	0	Melphalan	2
Bleomycin	3	Methotrexate	11
Busulfan	0	Mitomycin C	1
Carmustine (BCNU)	1	Nitrofurantoin	0
Cyclophosphamide	10	Muromunab-CD3	0
Cyclosporine	4	Oxaliplatin	1
Cytarabine	5	Paclitaxel	3
Docetaxel	0	Pentostatin	0
Doxorubicin	8	Recombinant GM-CSF	0
Fludarabine	1	Rituximab	4
Gefitinib	0	Teniposide (VM-26)	0
Gemcitabine	2	Tretinoin/retinoic acid	0
Gold salts	0	Tumor necrosis factor	0
Immunglobulin	0	Vinblastine	3
Infliximab	1	Vincristine	5
IL-2	0	Vindesine	0
Irinotecan	3	Vinorelbine	0

- Vascularite à ANCA
- Goodpasture
- Connectivite

- Lymphangite K
- ADC pulmonaire lépidique
- Lymphome
- …

Biopsie pulmonaire chirurgicale?

- PAI
- BOOP
- ?

- **PEC multidisciplinaire**
- **Arrêt du(des) médicament(s) imputable(s)**
- **Immunosuppression (corticoïdes)**

- **PEC multidisciplinaire**
- **Immunosuppression (corticoïdes, cyclophosphamide)**
- **Echanges plasmatiques**

- **PEC multidisciplinaire**
- **Immunosuppression (corticoïdes)**
- **Ttt spécifique**

- **PEC multidisciplinaire**
- **Immuno-suppression (corticoïdes, cyclophosphamide)**

Dhokarh, *Chest* 2012

Mukhtyar *Ann Rheum Dis* 2009

Vourlekis, *Medicine* 2000

Conclusion

- La corrélation anatomo-clinique entre DAD et SDRA est médiocre
- Les SDRA secondaires à des entités histologiques autres que le DAD (*i.e.*, « *ARDS mimickers* ») ne sont pas exceptionnels
- Les SDRA sans FDR représentent un sous-groupe particulier de patients (~10%) ayant un phénotype clinique différent et des causes particulières souvent éligibles à une immunosuppression
- Un bilan étiologique (TDM, LBA) et un avis spécialisé devraient être réalisés en l'absence de FDR de Berlin et la biopsie pulmonaire chirurgicale en dernier recours