Does High-Dose Steroid Therapy Improve Prognosis in AE of ILD?

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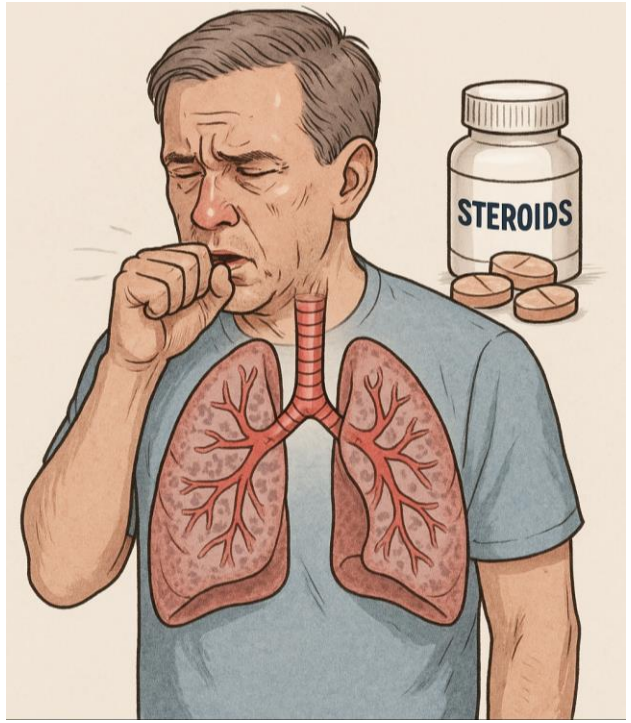


Epidemiology and prognosis

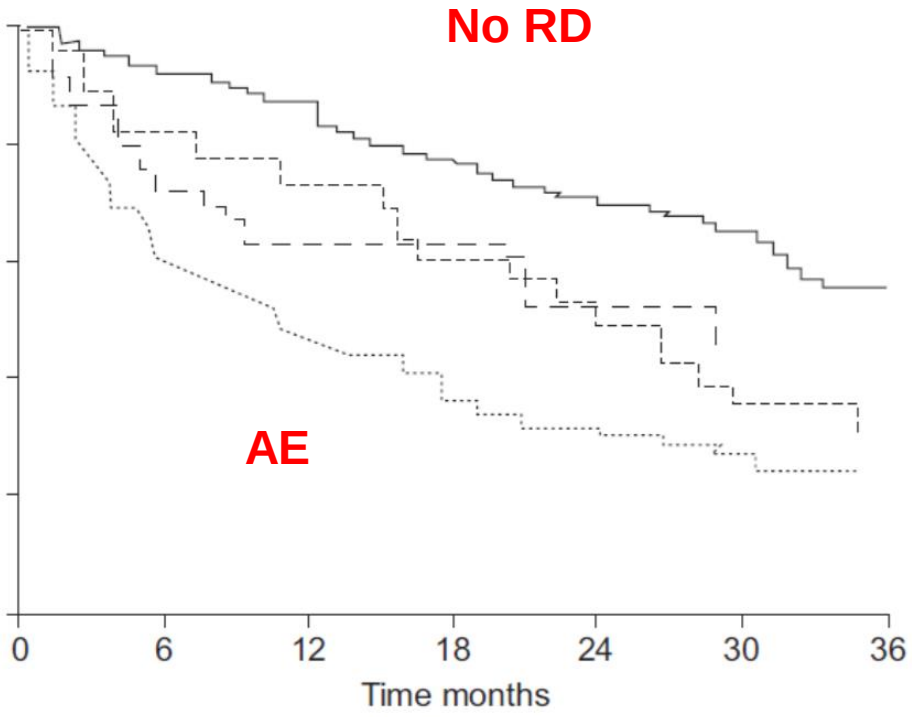
Acute exacerbation of idiopathic pulmonary fibrosis: incidence, risk factors and outcome

J.W. Song, S-B. Hong, C-M. Lim, Y. Koh and D.S. Kim

Retrospective study
1990-2009
461 patients with IPF (269 cases were biopsy-proven)

Incidence[#]	AE[¶]	RD
1-yr	58 (14.2)	97 (23.0)
2-yr	71 (18.8)	124 (31.2)
3-yr	75 (20.7)	134 (35.4)

	AE	No RD
Median survival time	15.5 months	60.6 months
5 year survival rate	18.4%	50%

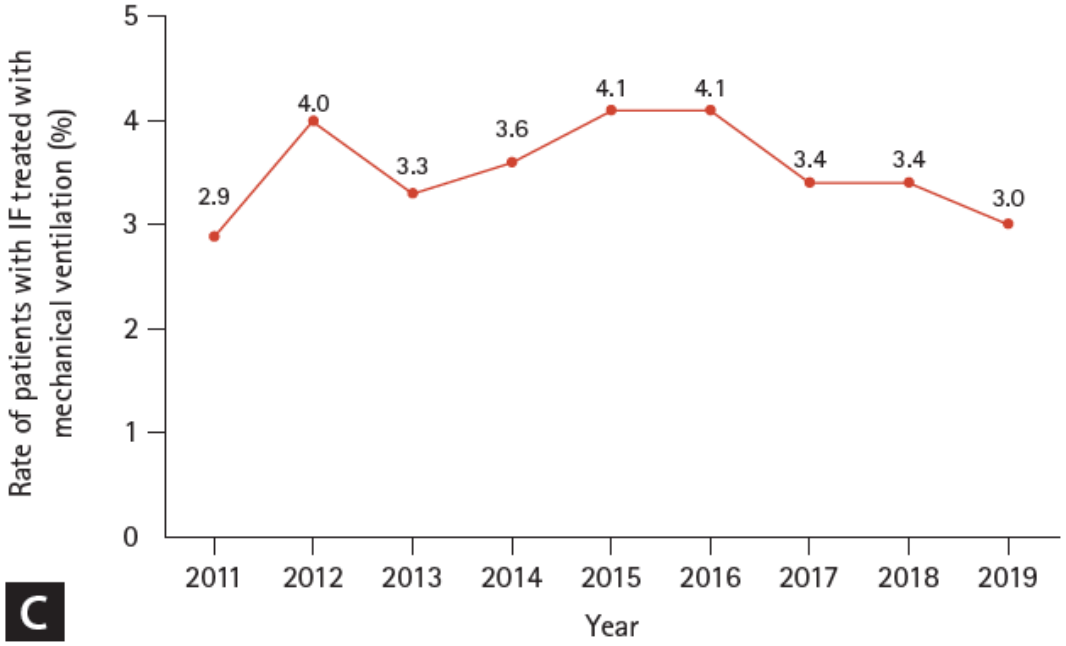


Eur Respir J 2011; 37: 356–363

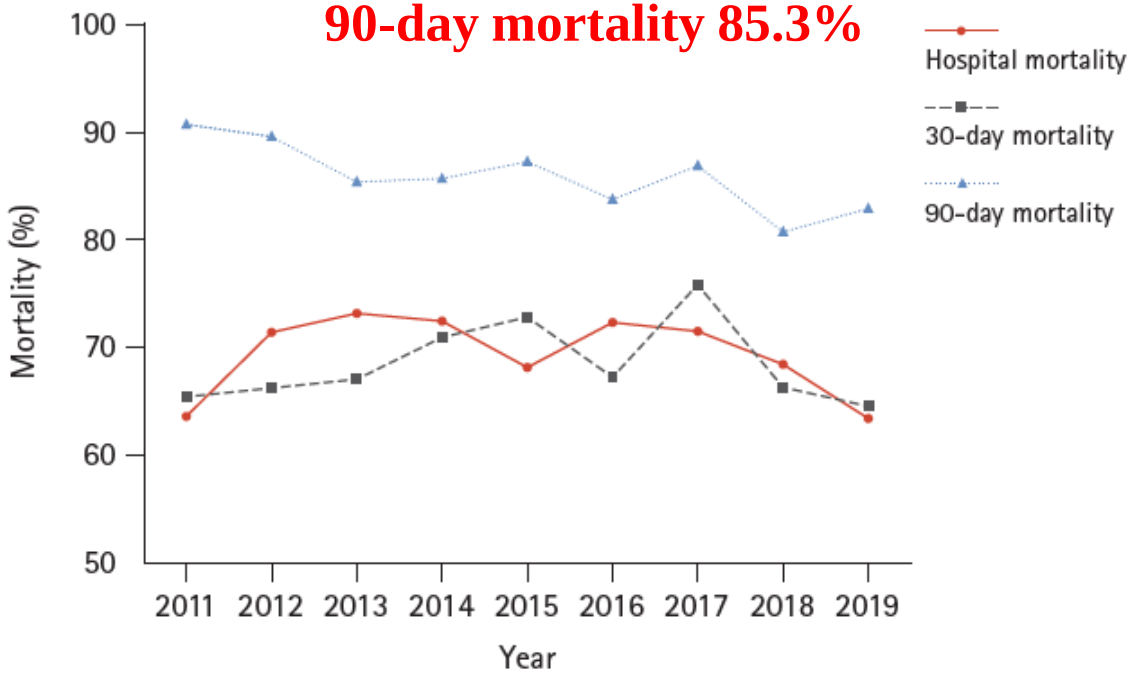
Mechanical ventilation in patients with idiopathic pulmonary fibrosis in Korea: a nationwide cohort study

Jae Kyeom Sim[1], Seok Joo Moon[2], Juwhan Choi[1], Jee Youn Oh[1], Young Seok Lee[1], Kyung Hoon Min[1], Gyu Young Hur[1], Sung Yong Lee[1], and Jae Jeong Shim[1]

[1]Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul; [2]Smart Health-Care Center, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Korea



Overall 69.4%
30-day mortality 68.7%
90-day mortality 85.3%



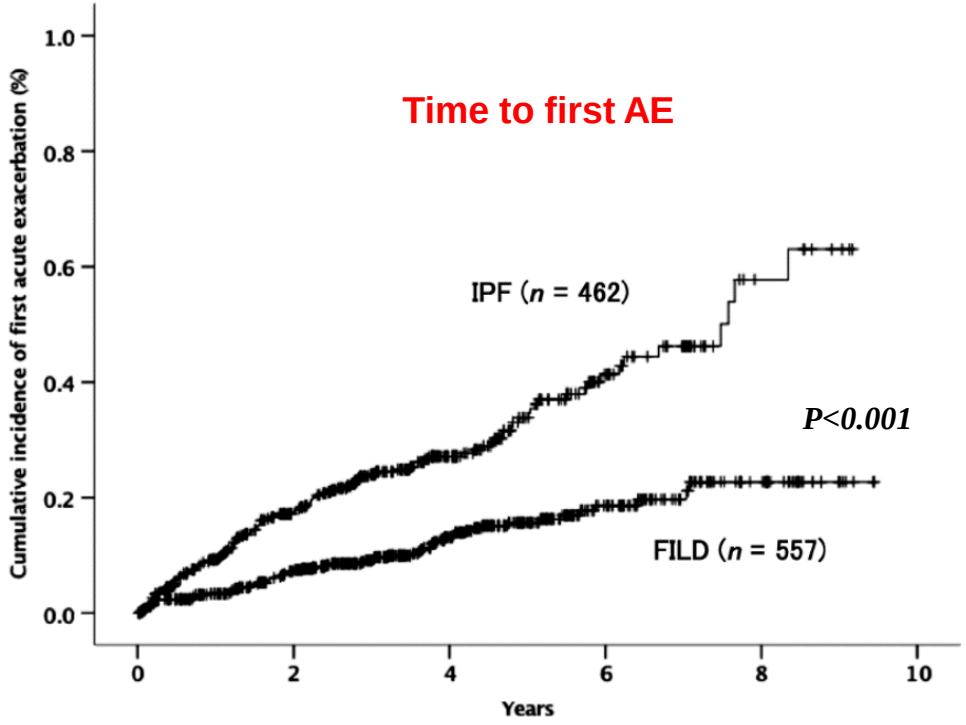
KJIM 2024; 39: 295-305

Acute exacerbations of fibrotic interstitial lung diseases

Atsushi SUZUKI,[1,2] Yasuhiro KONDOH,[1] Kevin K. BROWN,[3] Takeshi JOHKOH,[4] Kensuke KATAOKA,[1] Junya FUKUOKA,[5] Tomoki KIMURA,[1] Toshiaki MATSUDA,[1] Toshiki YOKOYAMA,[1] Jun FUKIHARA,[2] Masahiko ANDO,[6] Tomonori TANAKA,[7] Naozumi HASHIMOTO,[2] Koji SAKAMOTO[2] AND Yoshinori HASEGAWA[2,8]

Total ILD (n=1019)	IPF (n=462)	NSIP (n=22)	CHP (n=29)	CTD-ILD (n=205)	UC-ILD(CR) (n=209)	UC-ILD(CRP) (n=92)
FU period (years)	2.9 (1.3-4.6)	5.4 (2.5-7.9)	3.3 (2.1-5.8)	3.9 (2.6-5.6)	2.9 (1.2-4.7)	4.1 (3.1-5.8)
Number of AE (%)	124 (27%)	2 (9%)	7 (24%)	27 (13%)	20 (10%)	13 (14%)

Time to first AE



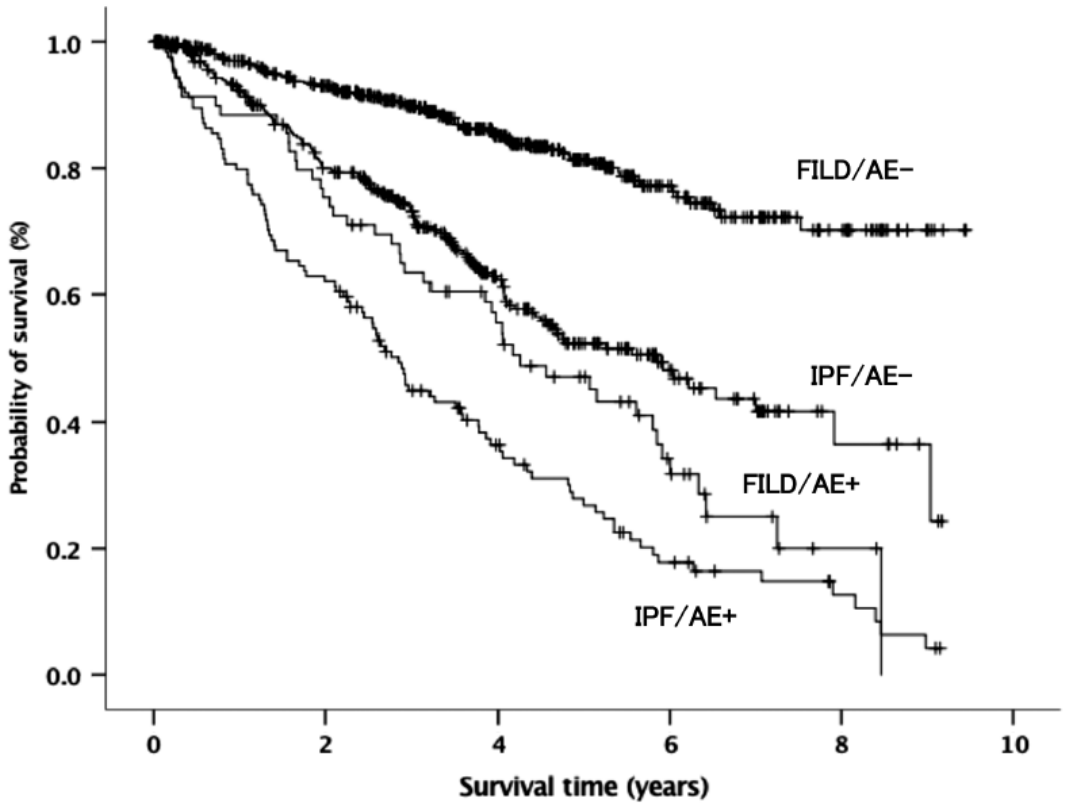
No. of patients (AE)

IPF	0	40	71	92	99	109	117	120	123	124
FILD	0	18	36	44	56	62	66	67	69	69

	Incidence of AE
IPF	8.38 per 100 patient-yrs
F-ILD	3.21 per 100 patient-yrs

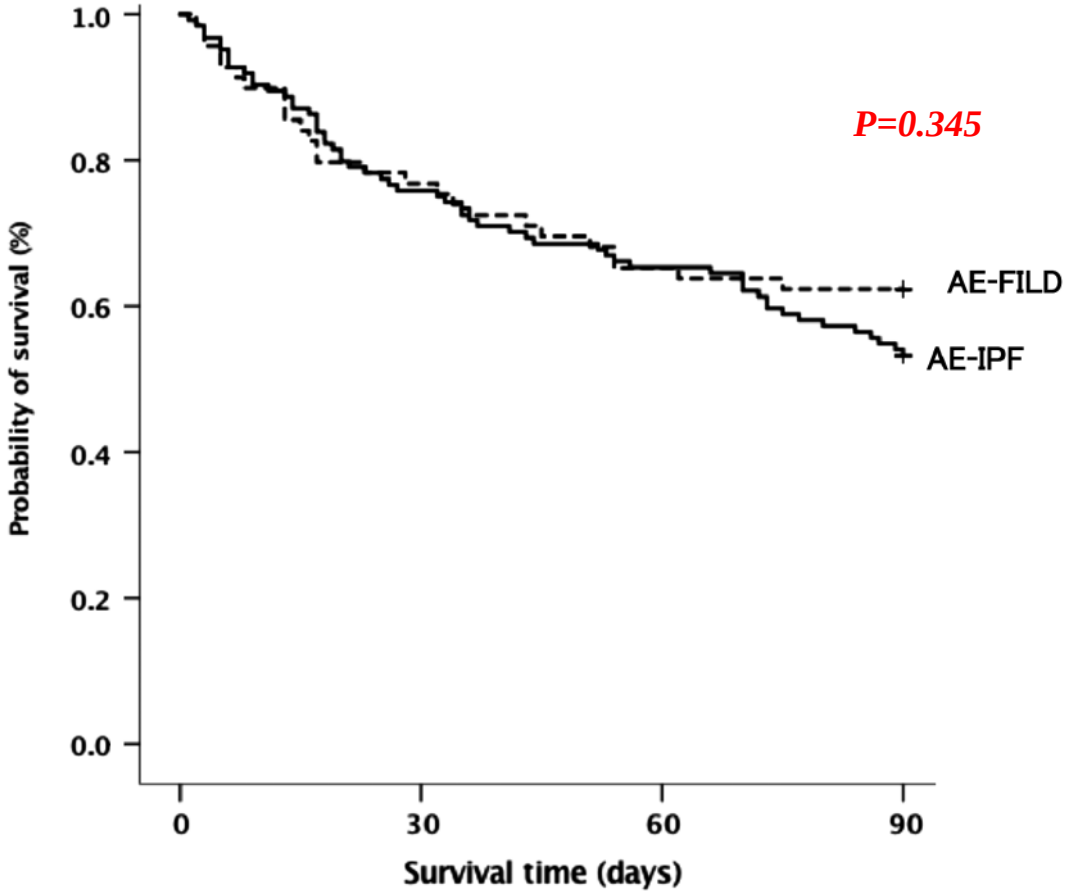
Respirology 2020; 25: 525-534

Impact of AE on overall survival



Number at risk					
FILD/AE−	488	387	217	88	29
IPF/AE−	338	230	110	37	7
FILD/AE+	69	52	34	14	2
IPF/AE+	124	77	36	15	6

90-day survival after AE



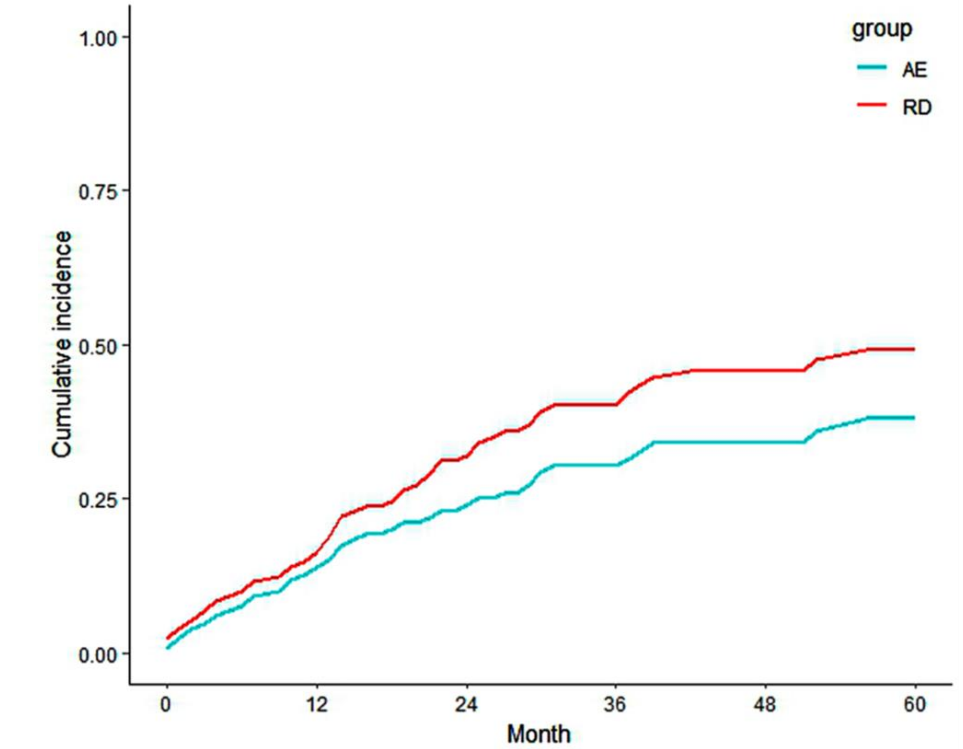
No. of patients				
AE-FILD	69	53	45	43
AE-IPF	124	94	81	66

Respirology 2020; 25: 525-534

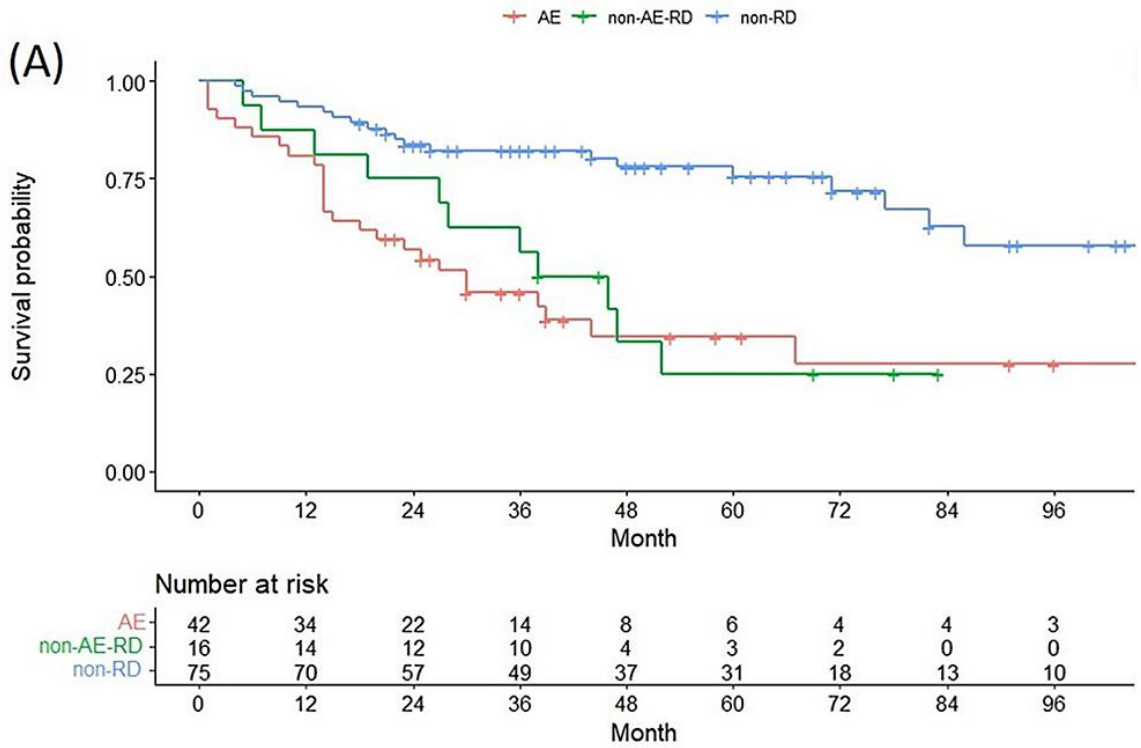
Acute exacerbation of progressive pulmonary fibrosis: incidence and outcomes

Min Jee Kim[1†], Jiyoul Yang[1†] and Jin Woo Song[1*]

	SSc-ILD	SJS-ILD	RA-ILD	Fibrotic HP	iNSIP
No (%)	18 (13.5)	10 (7.5)	57 (42.9)	28 (21.1)	20 (15)



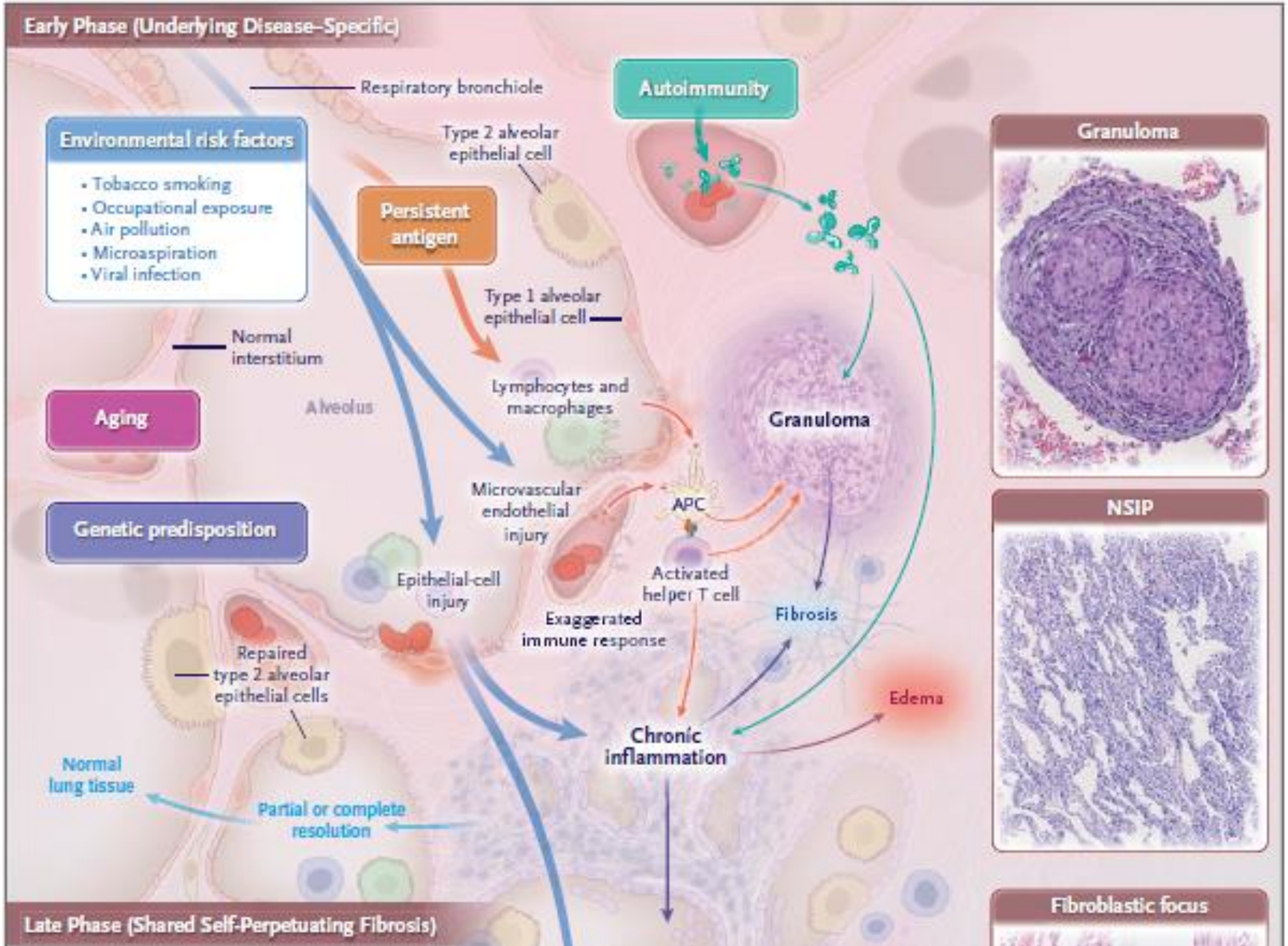
	1-year	5-year
RD	16.4%	49.2%
AE	12.5%	38%



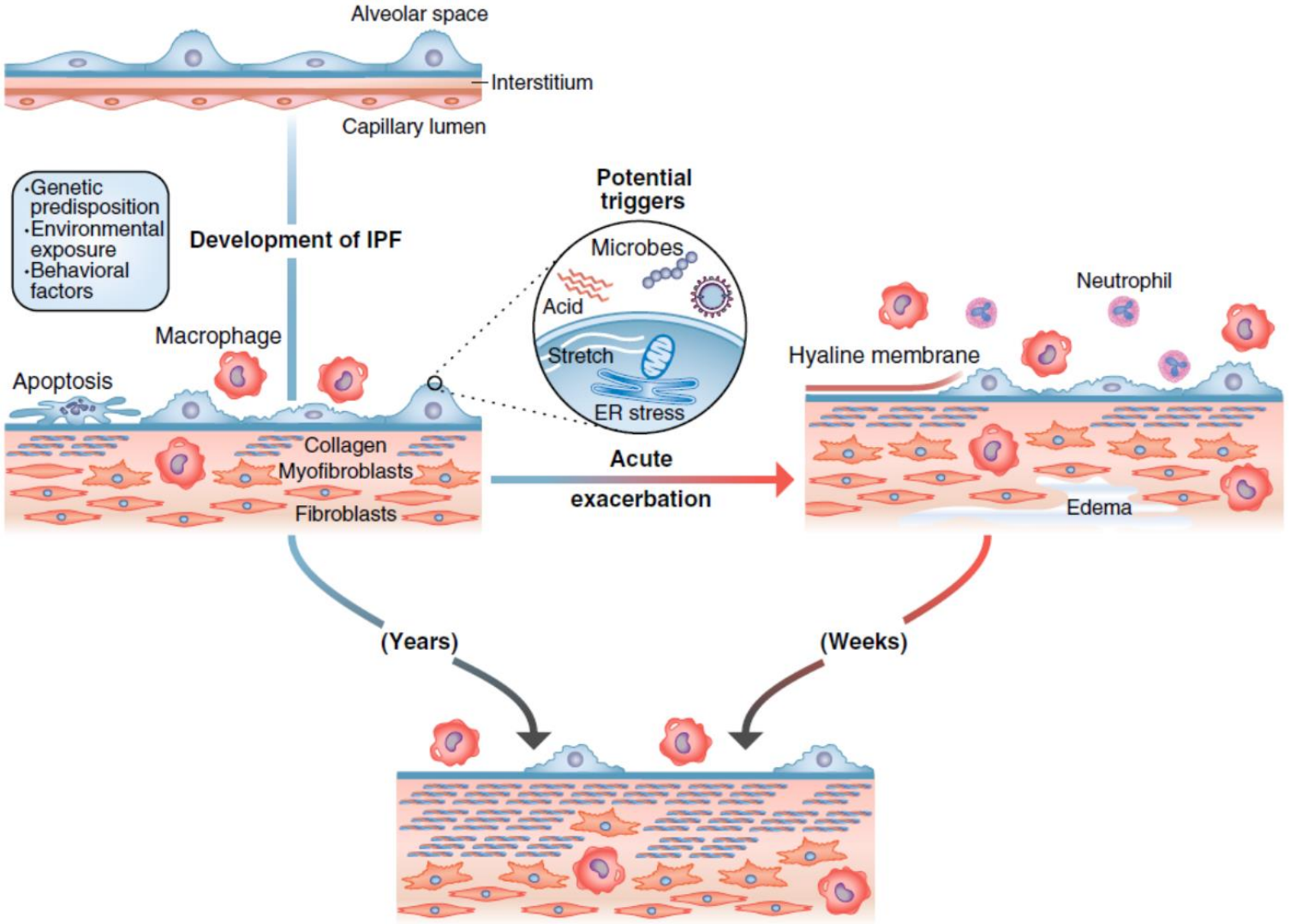
	1 year (%)	3 year (%)	5 year (%)
Non-RD	12	19.8	32.7
AE group	21.4	65.6	86.2
Non-AE RD	12.9	62.3	75

Respiratory Research 2024; 25:415

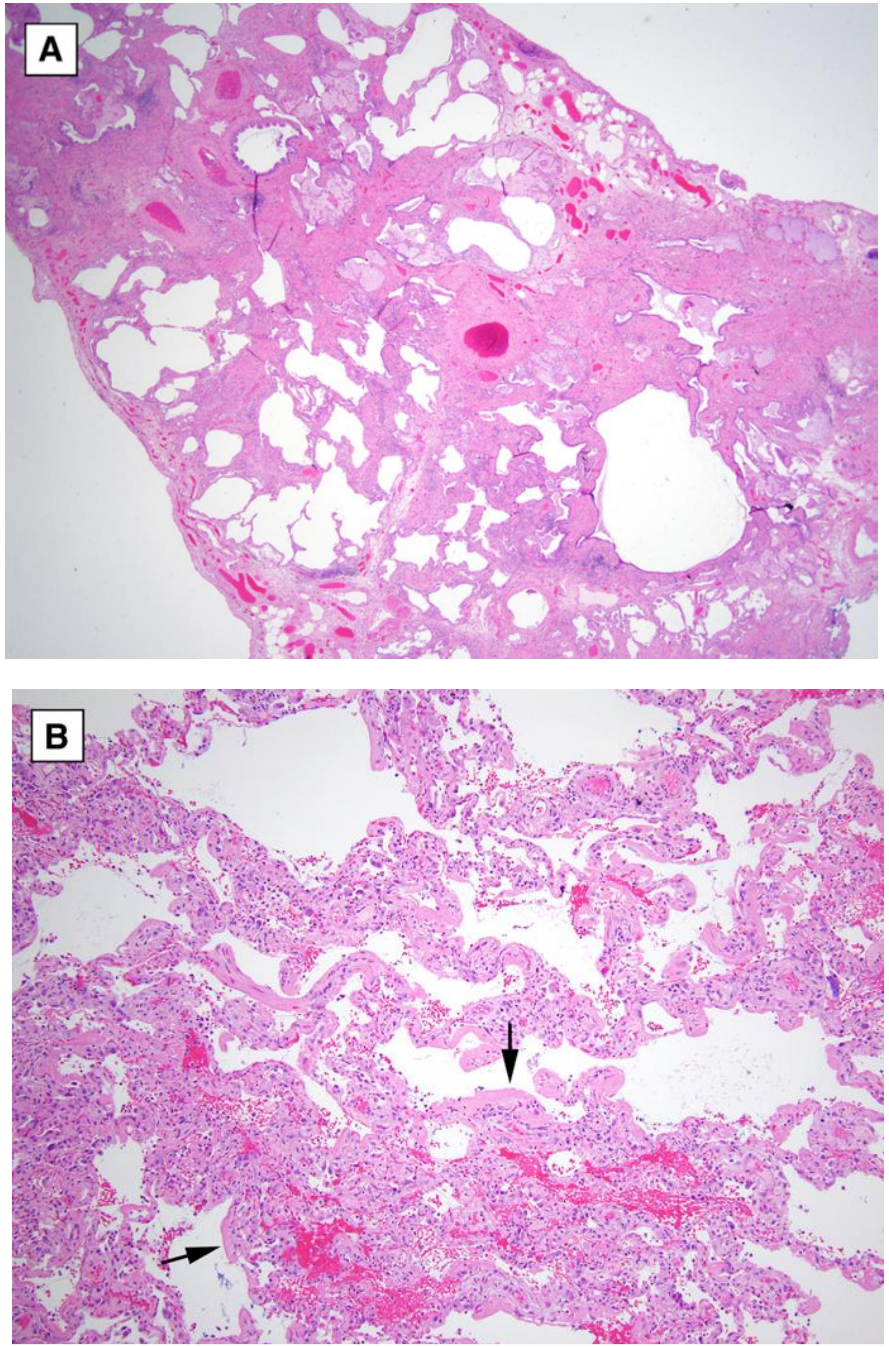
Pathogenesis and Pathology



NEJM 2020; 383: 958-68



AJRCCM 2016; 194: 265-275

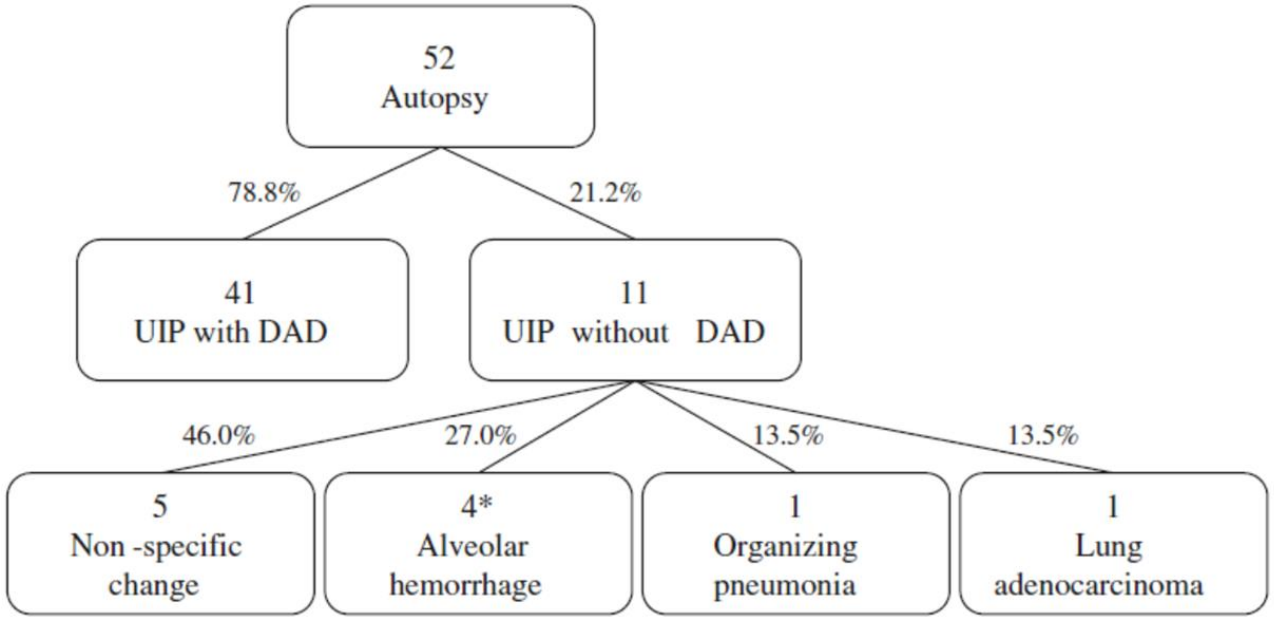


AJRCCM 2007; 176: 636-643

Autopsy analyses in acute exacerbation of idiopathic pulmonary fibrosis

Keishi Oda[1], Hiroshi Ishimoto[1], Sohsuke Yamada[2], Hisako Kushima[3], Hiroshi Ishii[4], Tomotoshi Imanaga[5], Tatsuhiko Harada[6], Yuji Ishimatsu[6], Nobuhiro Matsumoto[7], Keisuke Naito[1], Kazuhiro Yatera[1], Masamitsu Nakazato[7], Jun-ichi Kadota[3], Kentaro Watanabe[4], Shigeru Kohno[6] and Hiroshi Mukae[1*]

Pathological findings	No. (%)
UIP pattern	52 (100)
Diffuse alveolar damage	41 (78.8)
Alveolar hemorrhage	15 (28.8)
Organizing pneumonia	1 (1.9)
Pulmonary thromboembolism	9 (17.3)
Lung cancer	6 (11.5)
Bronchopneumonia	15 (28.8)
Bacterial infection	6 (11.5)
Fungal infection	7 (13.5)
Cytomegalovirus infection	6 (11.5)



Respiratory Research 2014; 15:109

Definition and Diagnosis

Acute exacerbation of IPF

Definition

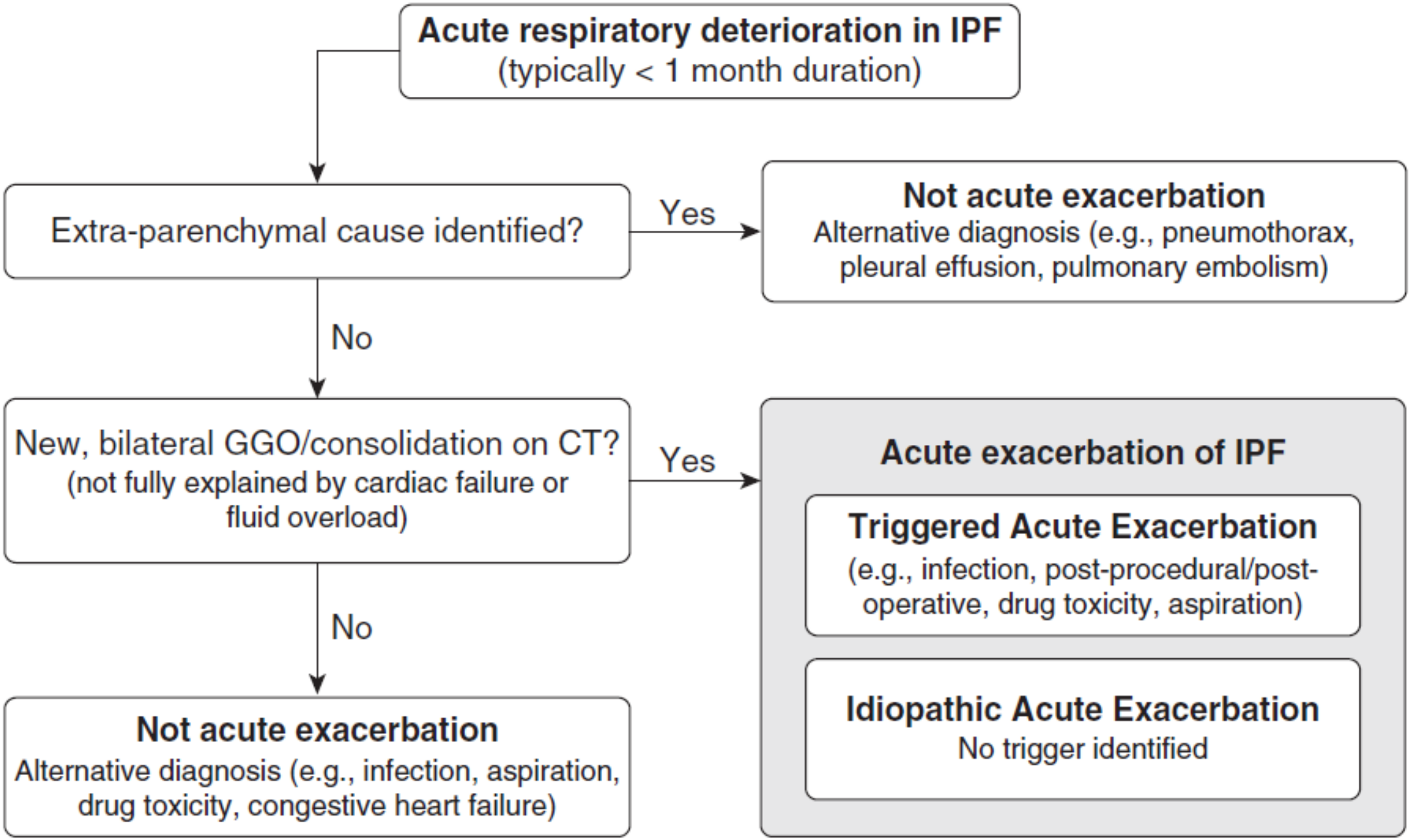
An acute, clinically significant respiratory deterioration characterized by evidence of

Definition and diagnostic criteria for non-IPF AE-ILD (?)

consolidation superimposed on a background pattern consistent with UIP pattern

- **Deterioration not fully explained by cardiac failure or fluid overload**

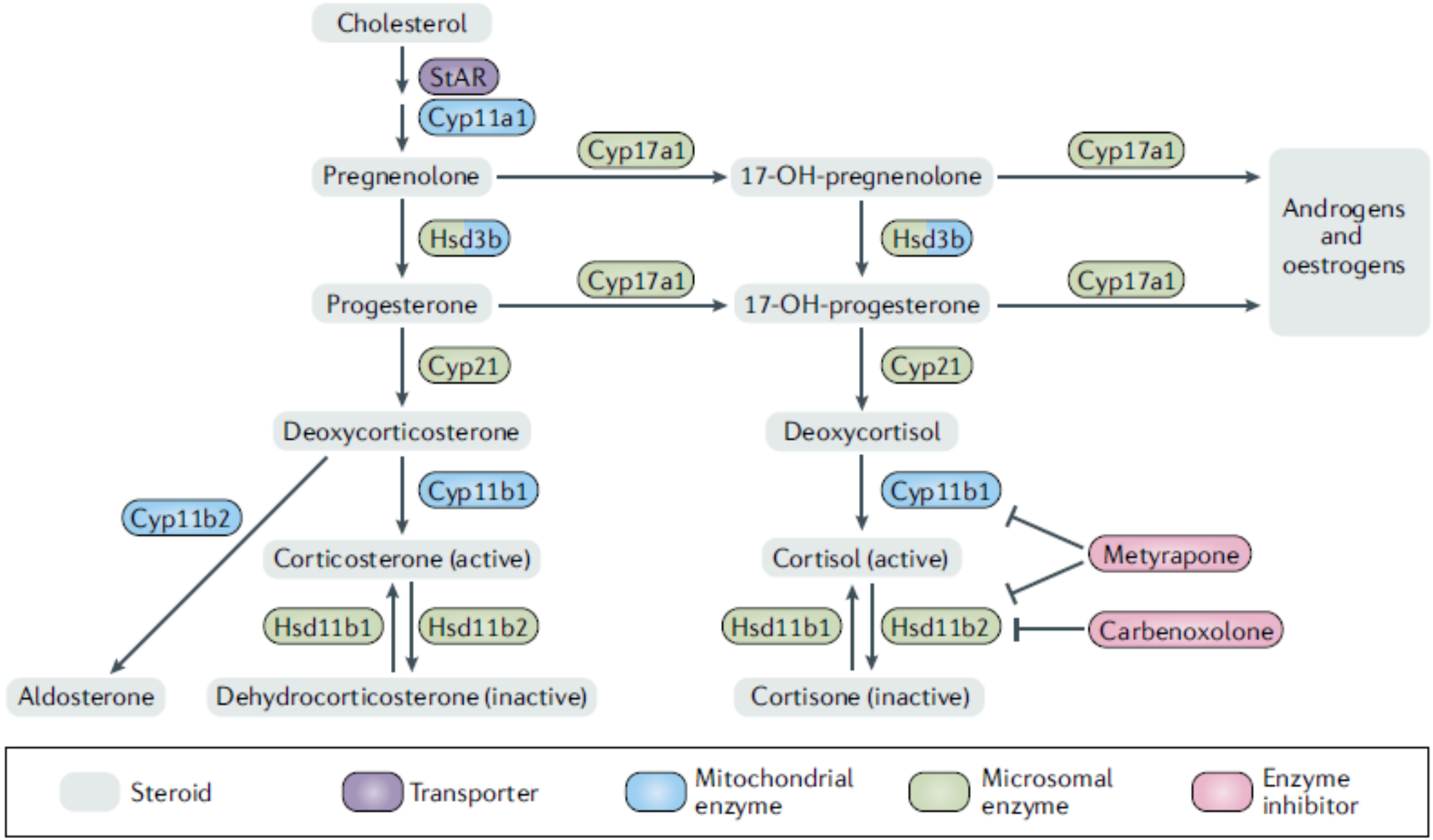
AJRCCM 2016; 194 (3): 265-275



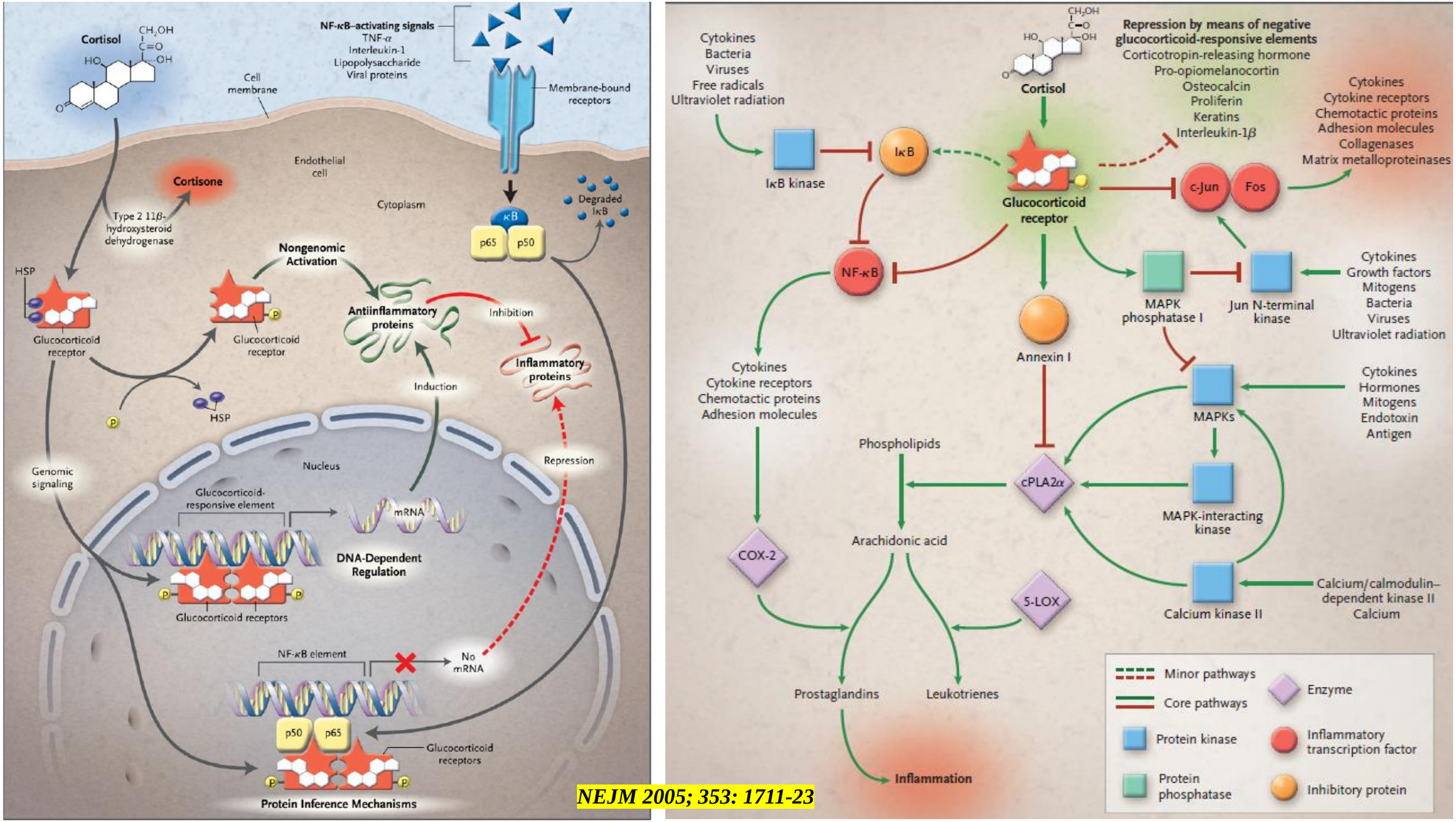
AJRCCM 2016; 194 (3): 265-275

Corticosteroid

- **Properties: mechanism of action, dose**



Nat Rev Immunol 2021; 23: 233



NEJM 2005; 353: 1711-23

Primary effects of glucocorticoids

Anti-inflammatory	**Inhibit inflammation** **1) blocking the action of inflammatory mediators (transrepression)** **2) inducing anti-inflammatory mediators (transactivation)**
Immunosuppressive	**Suppress delayed hypersensitivity reactions by directly affecting T-lymphocytes**
Anti-proliferative	**Inhibition of DNA synthesis and epidermal cell turnover**
Vasoconstrictive	**Inhibit the action of histamine and other vasoconstrictive mediators**

Allergy, Asthma & Clinical Immunology 2013, 9:30

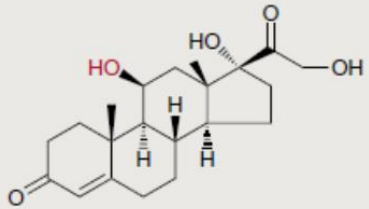
Side Effects of High-Dose or Prolonged Glucocorticoid Therapy

Tissue	Side Effects
Adrenal gland	Adrenal atrophy, Cushing's syndrome
Cardiovascular system	Dyslipidemia, hypertension, thrombosis, vasculitis
Central nervous system	Changes in behavior, cognition, memory, and mood (i.e., glucocorticoid-induced psychoses), cerebral atrophy
Gastrointestinal tract	Gastrointestinal bleeding, pancreatitis, peptic ulcer
Immune system	Broad immunosuppression, activation of latent viruses
Integument	Atrophy, delayed wound healing, erythema, hypertrichosis, perioral dermatitis, petechiae, glucocorticoid-induced acne, striae rubrae distensae, telangiectasia
Musculoskeletal system	Bone necrosis, muscle atrophy, osteoporosis, retardation of longitudinal bone growth
Eyes	Cataracts, glaucoma
Kidney	Increased sodium retention and potassium excretion
Reproductive system	Delayed puberty, fetal growth retardation, hypogonadism

NEJM 2005; 353: 1711-23

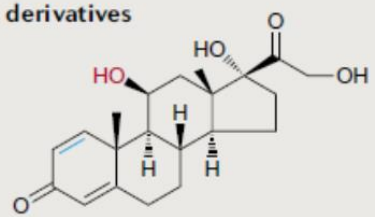
Short acting

Endogenously derived

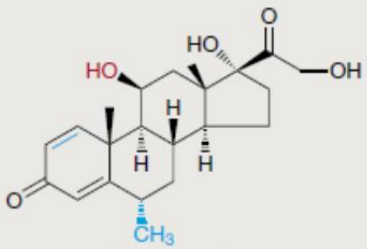


Cortisol (hydrocortisone)

Synthetic derivatives

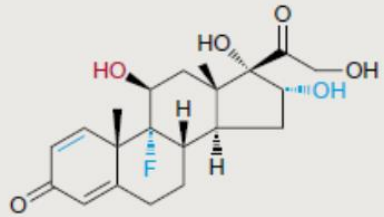


Prednisolone



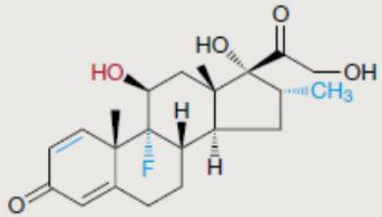
Methylprednisolone

Intermediate acting

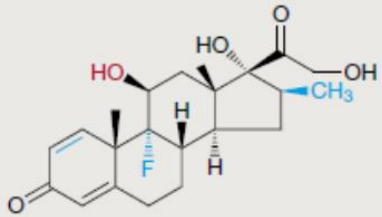


Triamcinolone

Long acting



Dexamethasone



Betamethasone

Nat Rev Rheumatology 2020; 16: 133-144

Glucocorticoid	Antiinflammatory potency[b]	Mineralcorticoid potency	Half-life in hours
Cortisol	1	1	8–12
Prednisone[a]	4	0.8	18–36
methylprednisolone[b]	5	0.5	18–36
Betamethasone	25	0.01	> 36
Dexamethasone	25	0.01	> 36

Pulm Ther (2023) 9:329–344

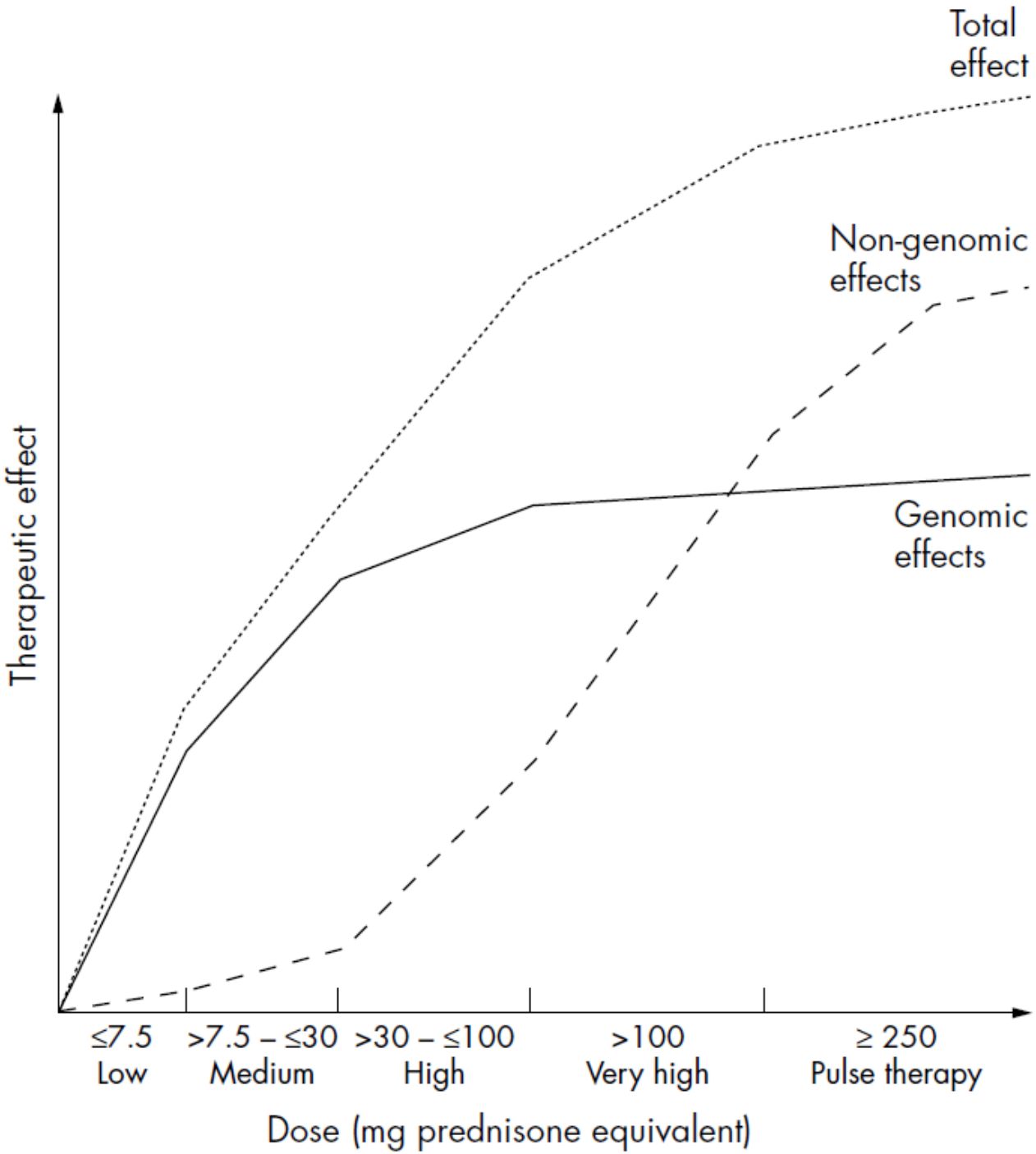
Standardised nomenclature for glucocorticoid dosages and glucocorticoid treatment regimens: current questions and tentative answers in rheumatology

F Buttgereit, J A P da Silva, M Boers, G-R Burmester, M Cutolo, J Jacobs, J Kirwan, L Köhler, P van Riel, T Vischer, J W J Bijlsma

Relationship between clinical dosing and cellular actions of glucocorticoids

Terminology*	Clinical application†	Genomic actions (receptor saturation)‡§	Nongenomic actions§	
			Nonspecific	cGCR-mediated
Low dose (≤7.5 mg/day)	Maintenance therapy for many rheumatic diseases	+ (<50%)	–	?
Medium dose (>7.5 to ≤30 mg/day)	Initial treatment for primary chronic rheumatic diseases	++ (>50 to <100%)	(+)	(+)
High dose (>30 to ≤100 mg/day)	Initial treatment for subacute rheumatic diseases	++(+) (almost 100%)	+	+
Very high dose (>100 mg/day)	Initial treatment for acute and/or potentially life-threatening exacerbations of rheumatic diseases	+++ (almost 100%)	++	+(+?)
Pulse therapy (≥250 mg for 1 or a few days)	For particularly severe and/or potentially life-threatening forms of rheumatic diseases	+++ (100%)	+++	+(++?)

Ann Rheum Dis 2002;61:718–722



Ann Rheum Dis 2002;61:718–722

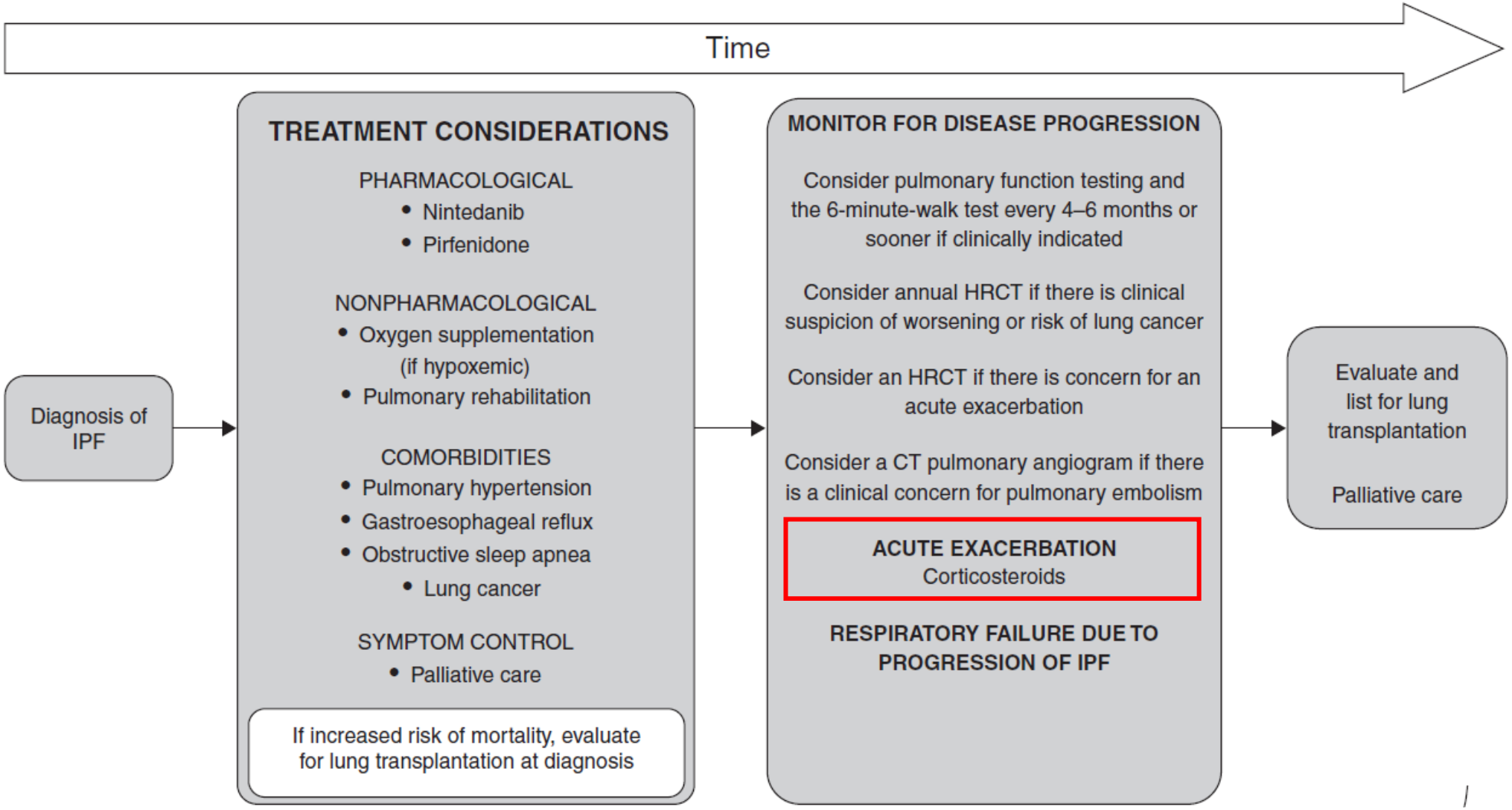
Corticosteroid

- **Properties: Clinical efficacy of high dose steroid**

Early Intervention Can Improve Clinical Outcome of Acute Interstitial Pneumonia*

Gee Young Suh, MD;† Eun Hae Kang, MD;† Man Pyo Chung, MD; Kyung Soo Lee, MD; Joungho Han, MD; Masanori Kitaichi, MD; and O Jung Kwon, MD

Study objectives: **To report on our experience with acute interstitial pneumonia (AIP) in which patients underwent early diagnostic procedures and received mechanical ventilation with a "lung-protective" strategy and early institution of immunosuppressive therapy.**
Design: **A retrospective chart review.**
Setting: **A tertiary referral hospital.**
Participants: **Ten patients with AIP who presented with idiopathic ARDS and showed diffuse alveolar damage on surgical lung biopsy specimens from July 1995 to March 2004.**
Measurements and results: **The median age of patients was 65.5 years (age range, 38 to 73 years). Patients presented with a median duration of severe dyspnea of 9.5 days (range, 2 to 34 days) at the hospital visit. All patients required mechanical ventilation beginning at median time of hospital day 1 (range, hospital day 0 to 5), which continued for a median duration of 9.5 days (range, 4 to 98 days). Patients received ventilation in the pressure assist-control mode with a median tidal volume of 6.97 mL/kg (range, 6.05 to 8.86 mL/kg) and median positive end-expiratory pressure of 11 cm H_2O (range, 8 to 16 cm H_2O). An aggressive diagnostic workup for respiratory infection, including BAL at a median time of hospital day 2 (range, hospital day 1 to 5) was performed. High-dose steroid pulse therapy was initiated on median hospital day 3.5 (range, hospital day 1 to 8), while surgical lung biopsy was performed on median hospital day 4 (range, hospital day 2 to 7). Eight patients (80%) survived to hospital discharge.**
Conclusion: **Earlier intervention, such as an aggressive diagnostic approach, mechanical ventilation with lung-protective strategy, and the early institution of immunosuppressive may improve clinical outcome in patients with AIP.** ***(CHEST 2006; 129:753–761)***



- **Weak recommendation, very low-quality evidence**
- **No published or planned RCTs for AE-IPF**
- **Expert opinion, no specific guidance on dose, route and duration**

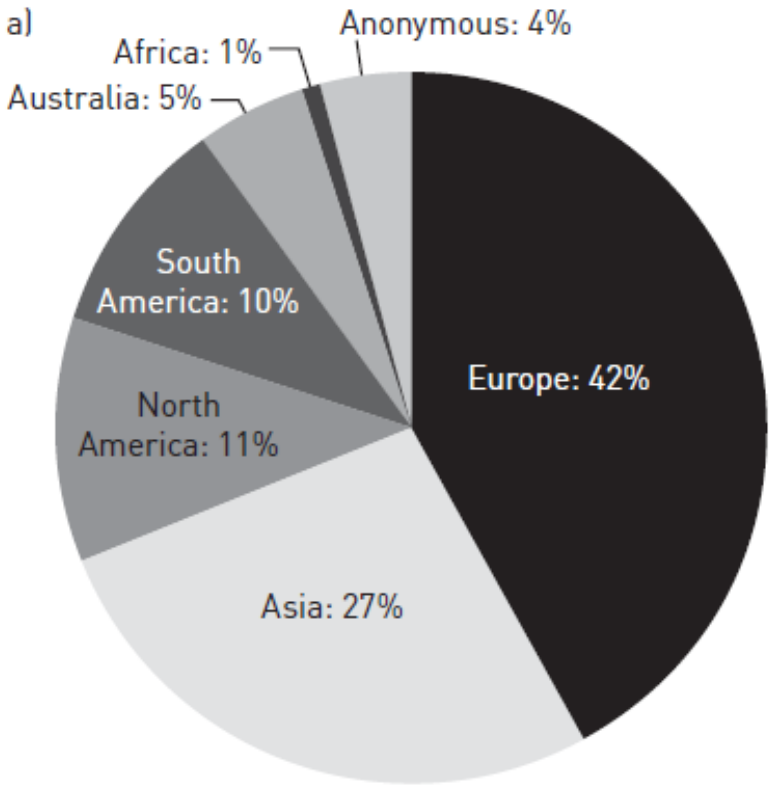
AJRCCM 2011; 183: 788-824
AJRCCM 2022; 205: 18-47

급성악화의 치료에 대한 현재까지의 보고는 주로 증례보고나 후향적 코호트 분석연구로 근거가 매우 부족하여 적절한 치료는 아직 정립되지 않았다. 호흡곤란이나 저산소증에 대한 산소투여와 같은 보존적 처치가 일반적으로 시행되고 있다. 그러나 기관삽관 및 인공호흡기 치료는 예후가 불량하여 제한적으로 치료가 가능한 폐손상의 유발원인이 있는 경우나 폐이식을 고려하는 경우 외에 추천되지 않는다.

2011년과 2016년에 발표된 IPF의 진단 및 치료에 대한 국제 권고안에서는 급성악화 치료의 근간은 급성 폐손상에 대한 지지요법으로, 약물치료에 대한 근거는 부족하나 고용량의 스테로이드 요법을 우선적으로 시도해 보도록 하였다[1]. 스테로이드의 용량과 기간에 대해서는 정해진 기준은 없으나 methylprednisolone을 하루 500-1,000 mg을 3일간 투여하고 이후 천천히 감량하는 방식을 가장 많이 사용하고 있다[19].

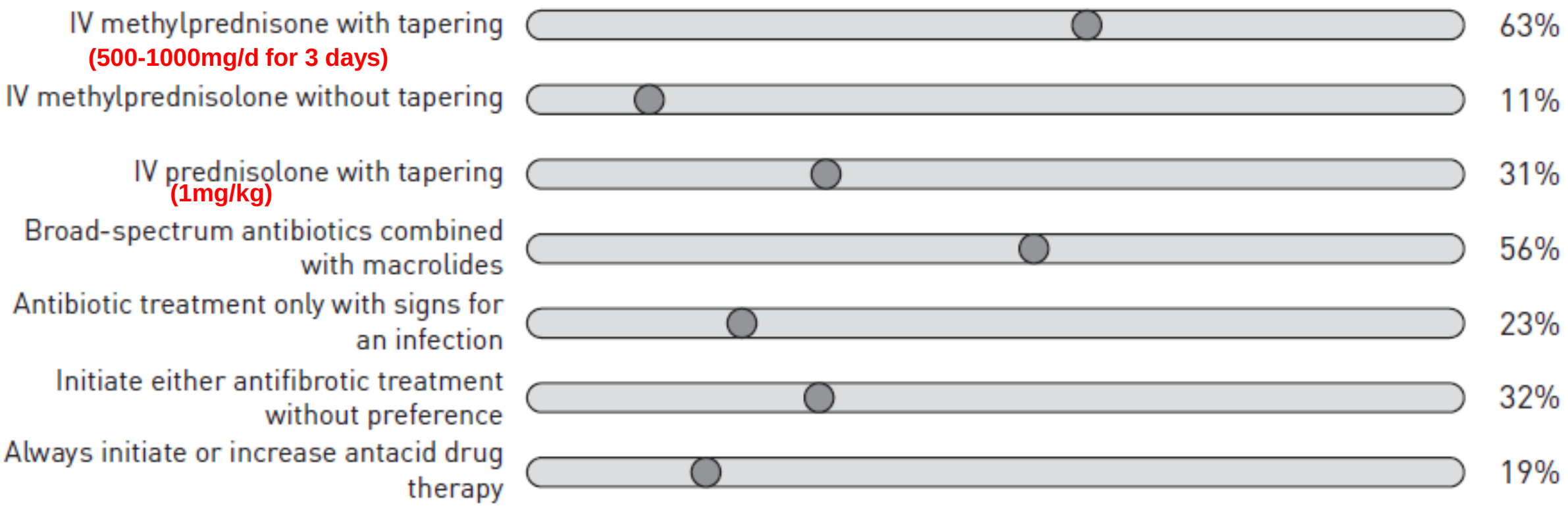
ILD 임상진료 지침
(2023년 1차 개정판)

Acute exacerbation of idiopathic pulmonary fibrosis: international survey and call for harmonisation



Eur Respir J 2020; 55: 1901760

Main drug management approaches worldwide



Eur Respir J 2020; 55: 1901760

Treatment during AE and in-hospital outcome of patients with AE according to treatment

Treatment regimen	Cases	Survival	p-value
Steroid pulse[#]	13 (14.4)	7 (53.8)	0.933
Steroid pulse[#] plus cytotoxic agent[¶]	8 (8.9)	4 (50.0)	
High-dose steroid[+]	46 (51.1)	19 (41.3)	
High-dose steroid[+] plus cytotoxic agent[¶]	14 (15.6)	11 (78.6)	
Low-dose steroid[§]	6 (6.7)	3 (50.0)	
Low-dose steroid[§] plus cytotoxic agent[¶]	1 (1.1)	1 (100.0)	
No treatment	2 (2.2)	0	
Total	90 (100)	45 (50)	

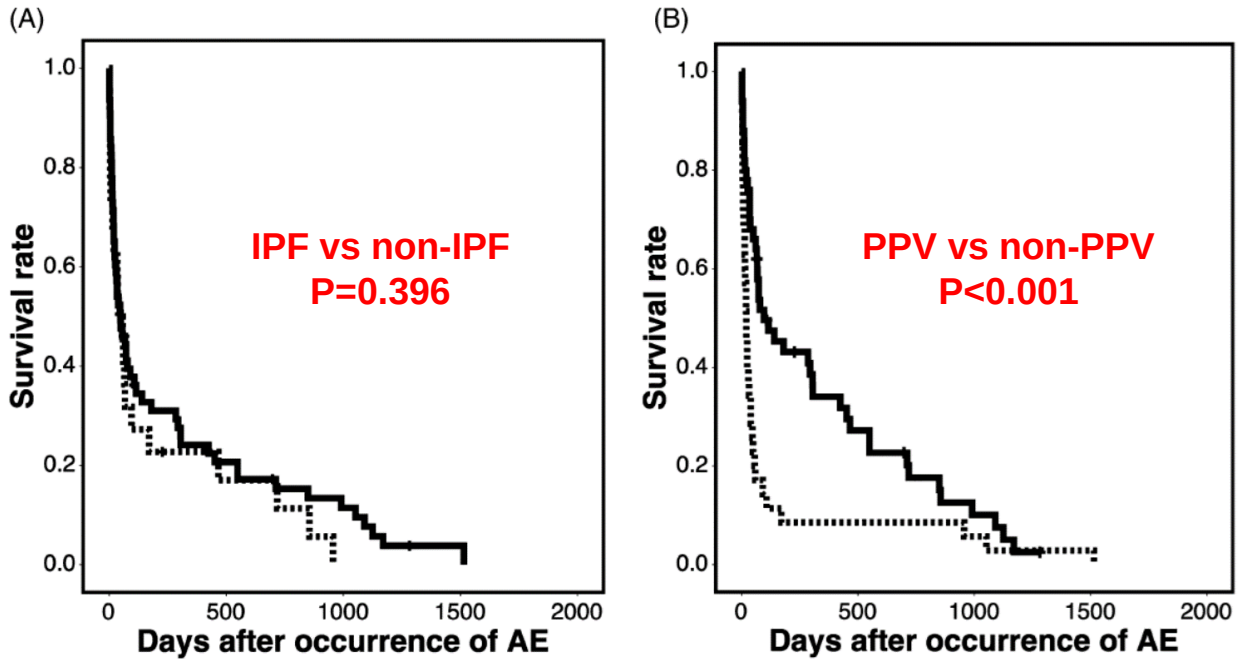
Data are presented as n (%) unless otherwise stated. [#]: steroid pulse was $\geqslant$500 mg·day^{-1} methylprednisolone for 3 days, followed by high-dose steroid; [¶]: cytotoxic agents were azathioprine, cyclosporine or cyclophosphamide; [+]: high-dose steroid was $\geqslant$0.5 mg·kg^{-1}·day^{-1} prednisolone; [§]: low-dose steroid was $\leqslant$0.5 mg·kg^{-1}·day^{-1} prednisolone.

Eur Respir J 2011; 37: 356–363

High-dose prednisolone after intravenous methylprednisolone improves prognosis of acute exacerbation in idiopathic interstitial pneumonias

Toru ARAI,[1,2] Kazunobu TACHIBANA,[2] Chikatoshi SUGIMOTO,[1] Yasushi INOUE,[2] Sayoko TOKURA,[2,3]
Tomohisa OKUMA,[4] Masanori AKIRA,[3] Masanori KITAICHI,[5] Seiji HAYASHI[2] AND Yoshikazu INOUE[1]

Retrospective study, 2004-2013
85 patients with AE-IIPs (IPF/non-IPF: 63/22 patients)
Positive pressure ventilation (PPV) (n=35), no PPV case (n =50)
High dose (≥ 0.6 mg/kg), (n=67) *vs* Low-dose prednisolone (n=18)



Parameters	HR	95% CI	*P*-value
All cases			
PMX-DHP (yes)	1.065	0.613–1.849	0.824
Initial PSL (high)†	0.775	0.454–1.323	0.350
Immunosuppressant (yes)	0.728	0.456–1.163	0.184
No PPV cases			
PMX-DHP (yes)	0.563	0.209–1.516	0.256
Initial PSL (high)†	0.429	0.204–0.903	0.026
Immunosuppressant (yes)	0.689	0.349–1.360	0.283
PPV cases			
PMX-DHP (yes)	1.087	0.543–2.174	0.814
Initial PSL dose (high)†	1.623	0.619–4.255	0.324
Immunosuppressant (yes)	0.937	0.468–1.879	0.855

Respirology 2017; 22: 1363-1370

Corticosteroid responsiveness in patients with acute exacerbation of interstitial lung disease admitted to the emergency department

Hye Jin Jang, Seung Hyun Yong, Ah Young Leem, Su Hwan Lee, Song Yee Kim, Sang Hoon Lee, Eun Young Kim, Kyung Soo Chung, Ji Ye Jung, Young Ae Kang, Young Sam Kim, Joon Chang & Moo Suk Park✉

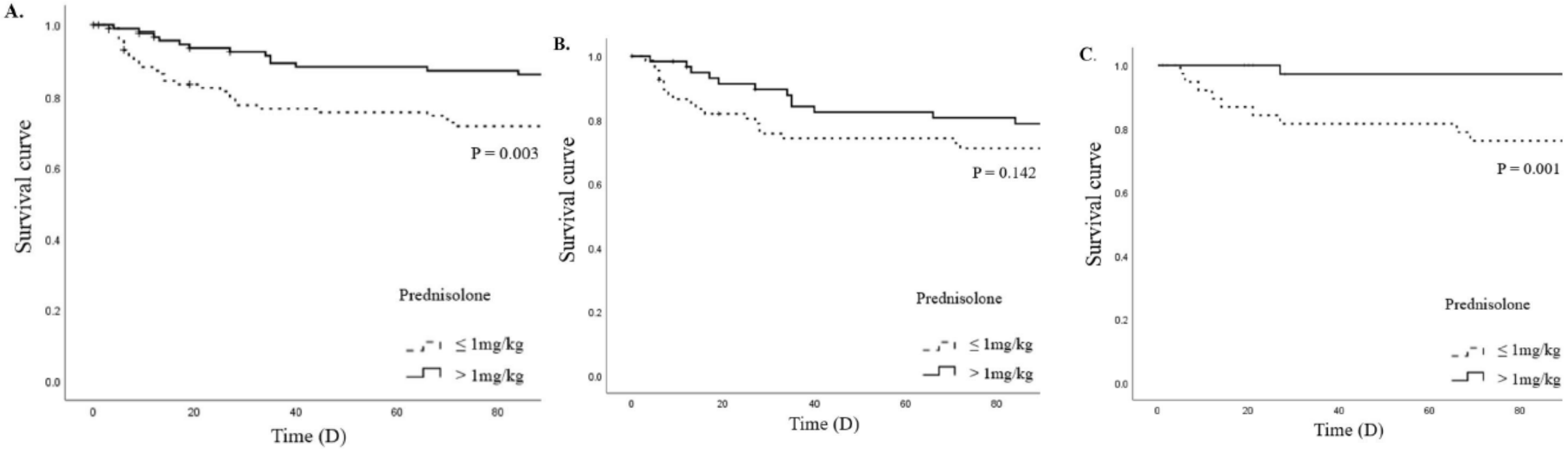
2016/1/1-2018/12/31, Retrospective single center study
182 patients with AE-ILD (117 IPF and 65 non-IPF admitted to ED)
Low dose (0.5-1mg/kg) *vs* high dose (>1mg/kg) prednisolone therapy

Risk factors related to 90-day mortality

Variable	Univariate			Multivariate		
	HR	95% CI	p-value	HR	95% CI	p-value
Age, years	0.993	0.968–1.019	0.603	0.989	0.957–1.009	0.200
Sex, male	1.228	0.624–2.415	0.552	0.777	0.377–1.599	0.493
Initial P/F ratio	0.998	0.998–1.001	0.241	0.995	0.992–0.999	0.006
FVC (%), predicted	0.994	0.975–1.014	0.540			
DLco (%), predicted	0.976	0.952–1.001	0.059			
Prednisolone > 1 mg/kg	0.380	0.193–0.747	0.005	0.221	0.102–0.480	< 0.001
Use of vasopressors within 3 days	1.852	0.881–3.890	0.104	1.451	0.630–3.340	0.382
Need for mechanical ventilator	3.877	2.068–7.267	< 0.001	4.205	2.059–8.589	< 0.001

Scientific Reports 2021; 11:5762

Kaplan–Meier survival curves according to corticosteroid use

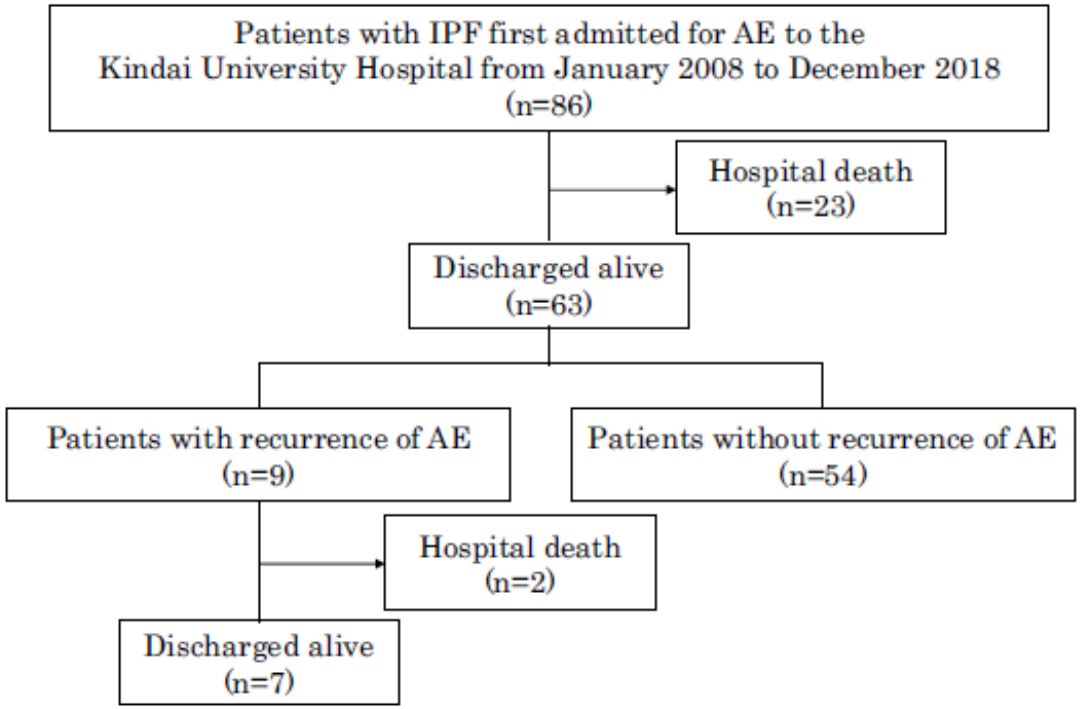


Total patients **IPF patients** **Non-IPF ILD patients**

Scientific Reports 2021; 11:5762

Initial therapeutic dose of corticosteroid for an acute exacerbation of IPF is associated with subsequent early recurrence of another exacerbation

Ryo Yamazaki, Osamu Nishiyama✉, Sho Saeki, Hiroyuki Sano, Takashi Iwanaga & Yuji Tohda



OR per 1 g increase in corticosteroid dose: 0.61, 95% confidence interval: 0.41–0.90, $p = 0.02$

Therapy	Patients with recurrence of AE n = 9	Patients without recurrence of AE n = 54	*p* Value
Total dose of corticosteroid over			
1 to 30 days			
mg/month	3133 ± 1990	5185 ± 2414	0.02
mg/kg/month	57.2 ± 37.7	93.5 ± 44.0	0.03
31 to 60 days			
mg/month	833 ± 238	809 ± 390	0.85
mg/kg/month	14.1 ± 5.2	13.9 ± 6.1	0.92
61 to 90 days			
mg/month	700 ± 212	597 ± 218[a]	0.19
mg/kg/month	11.8 ± 4.1	10.2 ± 3.5[a]	0.25
91 to 120 days			
mg/month	562 ± 212[b]	526 ± 195[a]	0.62
mg/kg/month	9.4 ± 3.6[b]	9.1 ± 3.5[a]	0.82
151 to 180 days			
mg/month	387 ± 186[c]	423 ± 162[d]	0.61
mg/kg/month	6.2 ± 2.9[c]	7.3 ± 3.1[d]	0.39
Immunosuppressive agent, n (%)	1 (11.1%)	19 (35.1%)	0.25
Antifibrotic agent			
Within 1 year after AE, n (%)	2 (22.2%)	6 (11.1%)	0.31

Scientific Reports 2021; 11:5782

Early corticosteroid dose tapering in patients with acute exacerbation of idiopathic pulmonary fibrosis

Keisuke Anan[1,2,3], Yuki Kataoka[1,3,4,5], Kazuya Ichikado[2], Kodai Kawamura[2], Takeshi Johkoh[6], Kiminori Fujimoto[7], Kazunori Tobino[8], Ryo Tachikawa[9], Hiroyuki Ito[10], Takahito Nakamura[11], Tomoo Kishaba[12], Minoru Inomata[13], Tsukasa Kamitani[14], Hajime Yamazaki[5], Yusuke Ogawa[1] and Yosuke Yamamoto[1*]

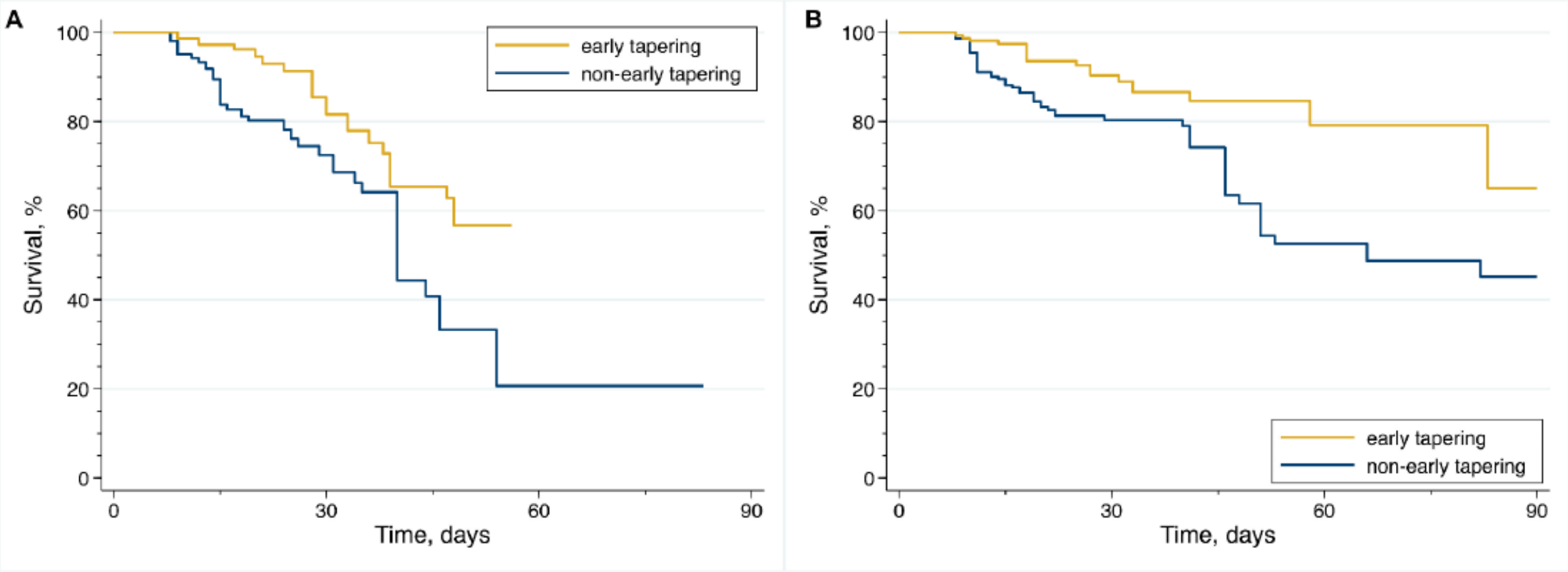
Retrospective cohort study
153 patients from 8 tertiary care hospital
229 patients from administrative cohort
Early tapering *vs* Non-early tapering
Definition of early tapering
Reduction in corticosteroid maintenance dose of > 10% within 2 weeks of admission

	Multi-center cohort data		Administrative cohort data	
	crude HR (95% CI)	adjusted HR (95% CI)	crude HR (95% CI)	adjusted HR (95% CI)
Univariate analysis	0.41 (0.22, 0.76)	–	0.65 (0.36, 1.18)	–
Main analysis (IPW-adjusted survival analysis)	–	0.37 (0.14, 0.99) *	–	0.27 (0.094, 0.83) †
Sensitivity analysis 1 (IPW-adjusted survival analysis) ††	–	0.28 (0.078, 0.98) *	–	0.35 (0.12, 1.04) †
Sensitivity analysis 2 (Cox proportional hazard model)	–	0.36 (0.18, 0.72) ¶	–	–
Sensitivity analysis 3 (Cox proportional hazard model)	–	0.41 (0.19, 0.87) §	–	0.59 (0.31, 1.13) §

Respiratory Research 2022; 23:291

Multicenter cohort

Administrative cohort



Respiratory Research 2022; 23:291

Pulse versus non-pulse corticosteroid therapy in patients with acute exacerbation of idiopathic pulmonary fibrosis

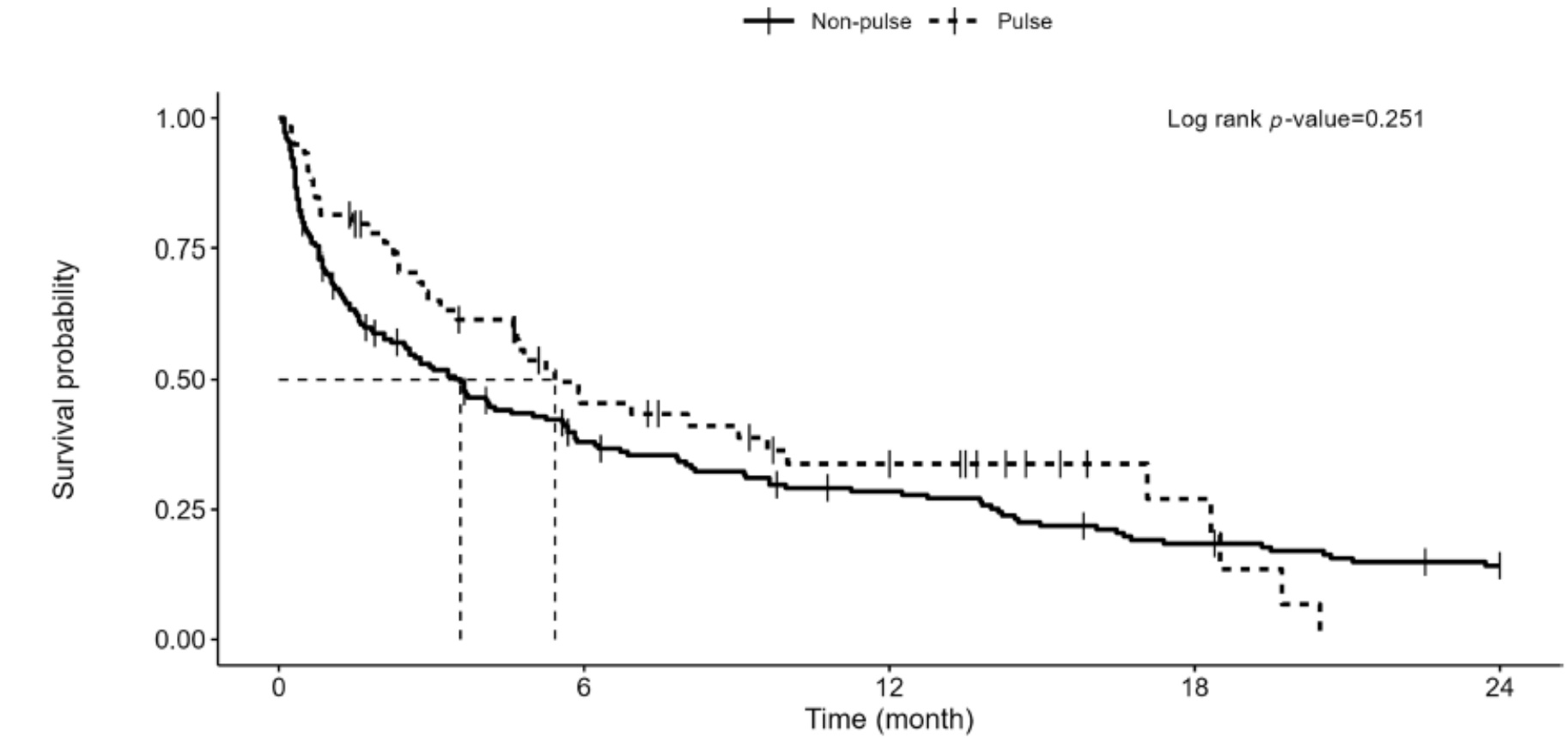
Kwonhyung Hyung[1] | Jong Hyuk Lee[2] | Joong-Yub Kim[1] | Sun Mi Choi[1] | Jimyung Park[1]

Retrospective study, January 2013 – December 2021
238 patients with AE-IPF with corticosteroids
Pulse regimen group (mPD of ≥ 250 mg/d or equivalent)
Non-pulse regimen group (mPD, 1mg/kg/d)
Survival outcomes : 3- and 12- month survival

	Pulse regimen ($n = 59$)	Non-pulse regimen ($n = 179$)	p-value
Age, year	73 (68–79)	72 (67–77)	0.407
Sex, female	15 (25.4)	44 (24.6)	1.000
Body mass index, kg/m^2	23.4 ± 3.3	22.1 ± 3.5	0.013
History of cigarette smoking	42 (77.8)	114 (69.5)	0.320
Comorbidities			
Hypertension	27 (45.8)	52 (29.1)	0.027
Diabetes	16 (27.1)	53 (29.6)	0.841
Cardiovascular disease	16 (27.1)	50 (27.9)	1.000
Lung cancer	12 (20.3)	42 (23.5)	0.751
Use of antifibrotics	35 (59.3)	72 (40.2)	0.016
Pulmonary function test[a]			
FVC, L	2.3 (1.6–2.6)	2.0 (1.5–2.4)	0.291
FVC, % predicted	69.0 (55.0–77.5)	61.0 (50.0–74.0)	0.173
DLCO, ml/min/mm Hg	7.2 (5.9–9.7)	6.4 (5.2–8.6)	0.212
DLCO, % predicted	45.0 (38.0–57.0)	41.0 (34.0–54.0)	0.240
GAP stage			0.857
Stage 1	13 (24.5)	35 (21.3)	
Stage 2	27 (50.9)	90 (54.9)	
Stage 3	13 (24.5)	39 (23.8)	
Use of home oxygen	21 (35.6)	55 (30.9)	0.611

Respirology 2024;29:235–242

	Pulse regimen ($n = 59$)	Non-pulse regimen ($n = 179$)	p-value
Respiratory support			0.073
Low-flow oxygen	46 (78.0)	115 (64.2)	
High-flow oxygen or mechanical ventilation	13 (22.0)	64 (35.8)	
Laboratory finding			
White blood cell, $10^3/\mu L$	9.8 (8.3–12.3)	11.2 (9.0–14.4)	0.025
C-reactive protein, mg/dL	3.6 (1.2–7.6)	8.2 (3.0–17.2)	<0.001
PaO_2/FiO_2 ratio, mm Hg[a]	285.9 (160.9–362.5)	252.0 (177.9–328.6)	0.904
Quantitative CT analysis			
Emphysema, %	0.5 (0.2–2.2)	1.0 (0.3–3.0)	0.083
Reticulation, %	18.9 (11.3–30.1)	22.2 (12.7–30.8)	0.380
Ground glass opacity, %	19.7 (10.7–35.3)	16.1 (5.4–31.5)	0.192
Consolidation, %	2.0 (0.5–6.6)	6.0 (2.0–14.5)	<0.001
Honeycombing, %	1.8 (0.2–8.4)	3.2 (0.3–14.0)	0.080
Lung volume, mL	2756 (2260–3420)	2722 (2276–3205)	0.575
Steroid therapy			
Interval from admission to initiation of steroid therapy, day	0.0 (0.0–1.0)	0.0 (0.0–1.0)	0.522
Average daily steroid dose			
Day 1–3 dose, mg	500 (129–500)	50 (40–60)	<0.001
Dose per weight, mg/kg	6.4 (2.1–8.6)	0.9 (0.7–1.0)	<0.001
Day 4–7 dose, mg[b]	51 (30–173)	40 (30–55)	0.004
Dose per weight, mg/kg	0.8 (0.5–3.4)	0.7 (0.5–0.9)	0.014
Day 8–14 dose, mg[b]	27 (20–44)	25 (13–39)	0.026
Dose per weight, mg/kg	0.5 (0.3–0.8)	0.4 (0.2–0.6)	0.032
Death from any cause			
In-hospital mortality	11 (18.6)	65 (36.3)	0.018
3-month mortality	21 (35.6)	85 (47.5)	0.149
12-month mortality	35 (59.3)	125 (69.8)	0.183

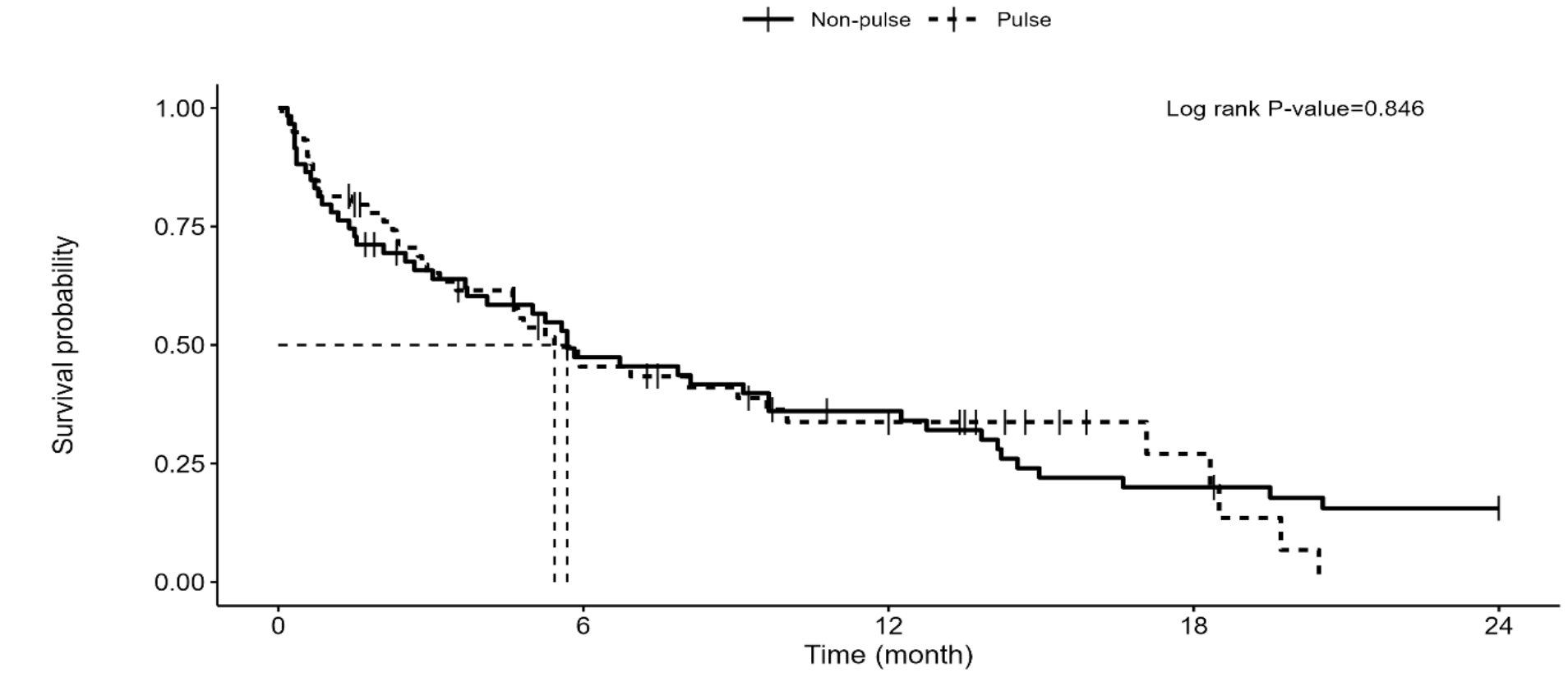


Number at risk

Non-pulse	179	61	43	27	19
Pulse	59	22	13	4	0

	Unadjusted HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value
3-month mortality				
Age, per 1 year	1.01 (0.98–1.03)	0.529	1.00 (0.98–1.03)	0.685
Male sex	0.92 (0.60–1.43)	0.715	0.83 (0.52–1.32)	0.429
Body mass index, per 1 kg/m^2	0.94 (0.89–0.99)	0.015	0.93 (0.88–0.99)	0.017
Lung cancer	1.75 (1.16–2.64)	0.008	1.93 (1.24–3.02)	0.004
Baseline use of antifibrotics	0.72 (0.49–1.06)	0.097	0.97 (0.64–1.47)	0.878
Requirement of high-flow oxygen or mechanical ventilation	2.09 (1.42–3.07)	<0.001	1.45 (0.93–2.26)	0.098
Extent of consolidation, per 1%	1.03 (1.01–1.04)	<0.001	1.02 (1.00–1.03)	0.027
Extent of ground glass opacity, per 1%	1.01 (1.00–1.02)	0.012	1.01 (1.00–1.03)	0.024
Steroid pulse regimen	0.64 (0.40–1.04)	0.072	0.82 (0.50–1.37)	0.456
12-month mortality				
Age, per 1 year	1.01 (0.99–1.03)	0.434	1.00 (0.98–1.03)	0.713
Male sex	1.09 (0.75–1.30)	0.650	1.03 (0.60–1.25)	0.877
Body mass index, per 1 kg/m^2	0.92 (0.89–0.97)	0.001	0.93 (0.89–0.98)	0.003
Lung cancer	1.59 (1.12–2.25)	0.009	1.68 (1.15–2.44)	0.007
Baseline use of antifibrotics	0.78 (0.57–1.08)	0.133	0.96 (0.69–1.35)	0.835
Requirement of high-flow oxygen or mechanical ventilation	1.83 (1.33–2.53)	<0.001	1.36 (0.95–1.97)	0.096
Extent of consolidation, per 1%	1.02 (1.01–1.04)	<0.001	1.02 (1.00–1.03)	0.014
Extent of ground glass opacity, per 1%	1.00 (1.00–1.02)	0.143	1.01 (1.00–1.02)	0.196
Steroid pulse regimen	0.75 (0.51–1.09)	0.130	0.89 (0.60–1.33)	0.580

Overall survival of propensity score-matched groups



Number at risk

Non-pulse	59	25	18	10	7
Pulse	59	22	13	4	0

Respirology. 2024;29:235–242

Corticosteroid therapy for treating acute exacerbation of interstitial lung diseases: a systematic review

Narat Srivali ,[1] Federica De Giacomi,[2] Teng Moua,[3] Jay H Ryu[3]

Cohort studies 7
Case Control studies 2
Total participants: 18,509

Results Analysis of nine studies (total n=18 509) revealed differential treatment effects based on the ILD subtype. In non-idiopathic pulmonary fibrosis (IPF) ILD, high-dose corticosteroid therapy (>1.0 mg/kg prednisolone) demonstrated improved survival (adjusted HR 0.221, 95% CI 0.102 to 0.480, p<0.001) and reduced 90-day mortality. Early tapering of high-dose corticosteroids (>10% reduction within 2 weeks) reduced in-hospital mortality (adjusted HR 0.37, 95% CI 0.14 to 0.99). Higher cumulative doses in the first 30 days (5185±2414 mg/month vs 3133±1990 mg/month) were associated with lower recurrence rates (adjusted HR 0.61, 95% CI 0.41 to 0.90, p=0.02). In IPF patients, however, high-dose therapy showed inconsistent benefits, with some studies reporting increased mortality risk (OR 1.075, 95% CI 1.044 to 1.107, p<0.001).

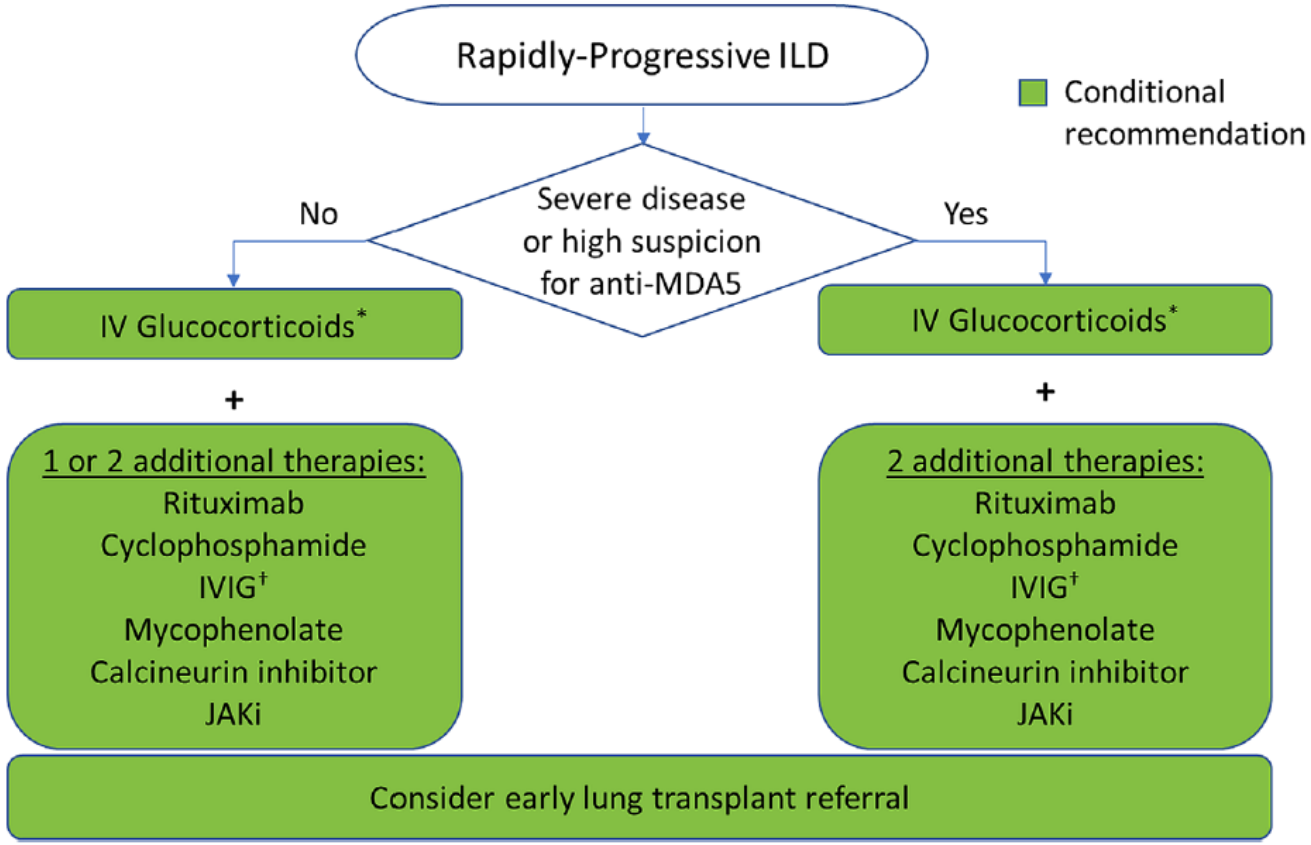
4 studies: all ILD subtypes
5 studies: only IPF

Various definition of exacerbation
Definition of high dose steroid with variations in dosage

Conclusion This review emphasises the potential benefits of individualised treatment approaches for AE-ILD but highlights the need for caution in making definitive recommendations. Although high-dose corticosteroids may show promise, particularly in non-IPF cases, the current evidence is inconsistent, and the lack of robust supporting literature makes it difficult to draw firm conclusions. Further research through randomised controlled trials is necessary to refine and optimise therapeutic strategies for AE-ILD.

Thorax 2025;80:140–149

2023 American College of Rheumatology (ACR)/American College of Chest Physicians (CHEST) Guideline for the Treatment of Interstitial Lung Disease in People with Systemic Autoimmune Rheumatic Diseases



Recommendations for management of SARD with RP-ILD

For people with SARD and RP-ILD, we conditionally recommend pulse intravenous methylprednisolone as first-line RP-ILD treatment.

Intravenous pulse methylprednisolone is recommended as first-line RP-ILD treatment because of rapid onset of action. Usual practice is to use intravenous glucocorticoids followed by high-dose oral prednisone. Glucocorticoids are typically administered with other immunosuppressive agents. RP-ILD in SSc is rare and may have an overlap syndrome or MCTD. Generally, we strongly recommend against use of glucocorticoids in SSc, but in the rare occurrence of RP-ILD in a person with SSc, there was no Panel consensus on whether to recommend glucocorticoids. Therapy may be warranted given the life-threatening nature of RP-ILD, despite the potential risk for SRC with glucocorticoids. We suggest an individualized approach in rare instances of RP-ILD in SSc.

Arthritis and rheumatology 2024; 76: 1182-1200

Trial	Type	Intervention	Outcome	Result
EXAFIP[10]	RCT, double-blinded, multi-centre	Cyclophosphamide (600 mg/m^2) days 0, 15, 30, 60 (+uromitexan for prophylaxis) ($n = 60$) Control: Placebo ($n = 59$) Background: methylprednisolone 10 mg/kg/d × 3 days	Primary: 3-month all-cause mortality	All-cause mortality was not statistically different between the treatment and placebo arms (45% vs. 31%, $p = 0.10$)
Thrombomodulin alfa for AE-IPF[9]	RCT, double-blinded, multi-centre	Thrombomodulin alfa (380 U/kg/d × 14 days) ($n = 40$) Control: Placebo ($n = 37$) Background: methylprednisolone 500–1000 mg/d × 3 days, followed by prednisolone 0.5–1 mg/kg/d × 4 days	Primary: 90-day survival	90-day survival was not statistically different between treatment and placebo arms (72.5% vs. 89.2%, $p = 0.0863$)
STRIVE-IPF[11] ClinicalTrials.gov Identifier: NCT04996303	RCT, multi-centre	Therapeutic plasma exchange days 1, 2, 3, 5, 6, 9, 11, 13, 15. Rituximab 1 g, days 6 and 15. IVIG 0.5 g/kg days 16–19 (planned $n = 34$) Control: Placebo (planned $n = 17$) Background: Prednisone 60 mg PO × 1 day, then 20 mg PO days 2–19 except days 6 and 15 (methylprednisolone 100 mg given as premedication for RTX) and 8 days of empiric antibiotics	Primary: 6-month survival Secondary: supplemental oxygen requirements at rest, 6MWD, adverse events	Ongoing
Pulse Steroid in AE-IPF Admitted in ER ClinicalTrials.gov Identifier: NCT04996303	Open-label RCT	Pulse steroid for 3 days with methylprednisolone 10 mg/kg (~500–1000 mg) daily followed by background steroid therapy Control: Background steroid therapy Background: methylprednisolone 1 mg/kg × 7 days, then 0.5 mg/kg × 7 days, then 0.25 mg/kg ×7 days Estimated enrolment of 200 patients with 1:1 randomization to treatment vs. control arms	Primary: 3-month mortality rate Secondary: Inflammatory markers, radiographic improvement, and PFT at discharge or 12 weeks after first visit for AE	Pending

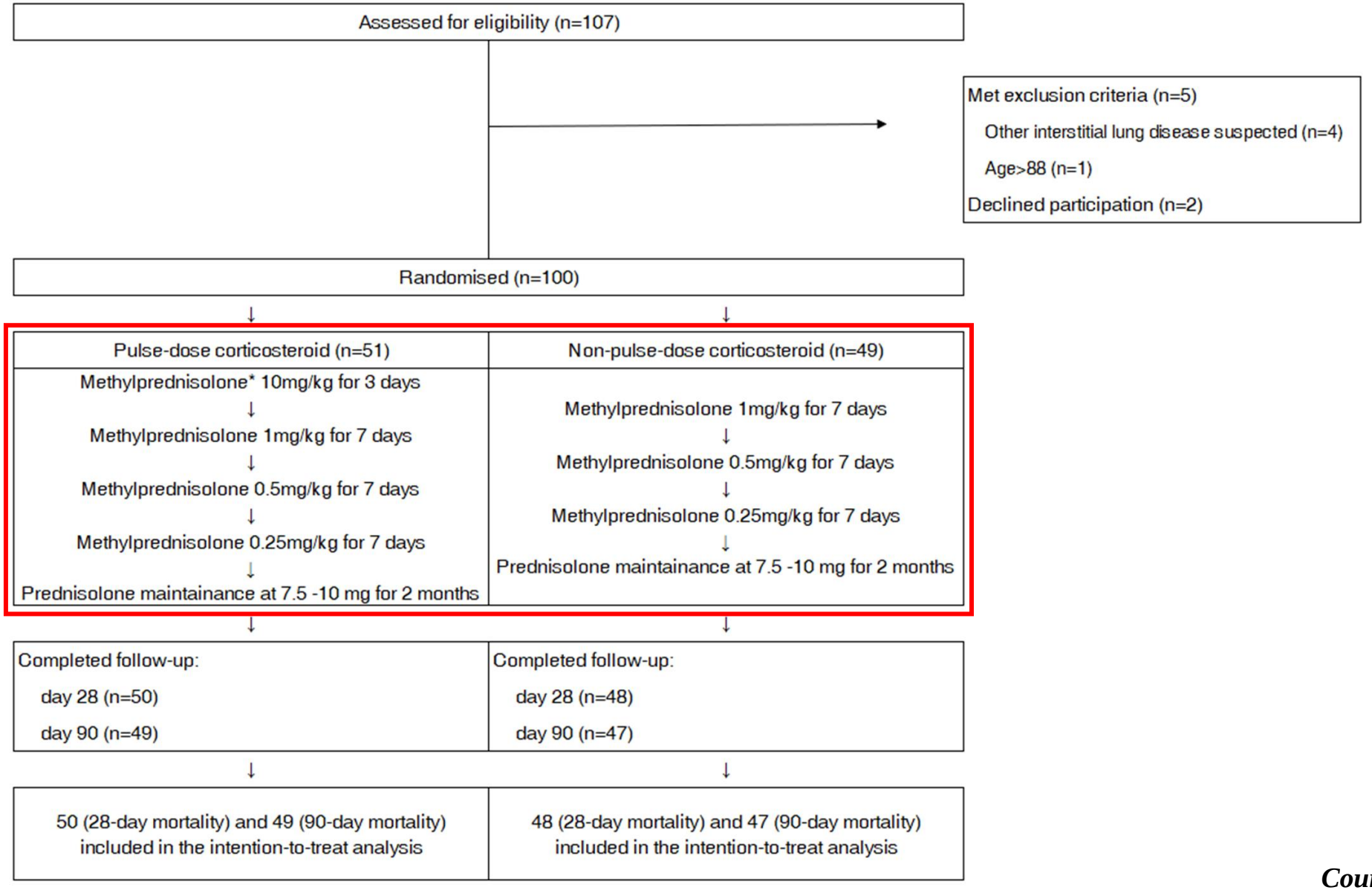
Efficacy of pulse versus non-pulse high dose corticosteroid therapy in acute exacerbation of idiopathic pulmonary fibrosis: an open-label randomised controlled trial

Hyesoo Kim1, Hyejin Jang1, Eun Young Kim2, Se Hyun Kwak2, Eunhye Lee2, Ji Soo Choi2, Min Kwang Byun3, Chi Young Kim3, I Seul Yu4, Chang Youl Lee5, Chang Hoon Han6, Seon Cheol Park,6 Jae Ho Chung7, Ji Eun Park8, Ji Won Park8, Song Yee Kim9, A La Woo9, G Raghu10, Sang Ha Kim4*, Moo Suk Park9*

- ✓ **This trial was a multi-centre, open-labeled, investigator-initiated, randomised controlled clinical trial conducted across eight university hospitals in South Korea between July 2021 to April 2024.**
- ✓ **The primary outcome was 28-day and 90-day all-cause mortality.**

Courtesy of 1st author and Park MS
Confidential
Prepared in submission

Figure 1. Enrollment, randomisation, and follow-up.



*Note that an equivalent dose of prednisolone could be used in place of methylprednisolone throughout the study.

Table 2. Primary and secondary outcomes.

	Pulse-dose corticosteroid	Non-pulse-dose corticosteroid	Between-group difference (95% CI)	P-value
Primary outcome				
Mortality at day 28	5/50 (10.0%)	7/48 (14.6%)	-4.6% (-17.6 to 8.4)	0.637
Mortality at day 90	12/49 (24.5%)	14/47 (29.8%)	-5.3% (-23.1 to 12.5)	0.723
Secondary outcome				
Mortality or lung transplantation at day 28	6/50 (12.0%)	12/48 (25.0%)	-13.0% (-28.2 to 2.2)	0.161
Mortality or lung transplantation at day 90	20/49 (40.8%)	23/47 (48.9%)	-8.1% (-29.4 to 10.8)	0.552
Admission to intensive care unit during hospitalization	6/51 (11.8%)	12/49 (24.5%)	-12.7% (-28.2 to 2.2)	0.163
ECMO support during hospitalization	3/51 (5.9%)	5/49 (10.2%)	-4.3% (-15.3 to 6.4)	0.669
Mechanical ventilation support during hospitalization	5/51 (9.8%)	12/49 (24.5%)	-14.7% (-29.8 to 0.2)	0.091
Median hospital stay before first discharge, days	24.3 [29.1]	31.7 [39.0]	-7.5 (-21.2 to 6.25)	0.283

Data are n/N (%), mean [SD], and risk difference (95% CI).

CI, confidence interval; ECMO, extracorporeal membrane oxygenation.

Summary

❖ **AE-ILD**

Not uncommon and poor prognosis irrespective of ILD subtypes

Exploration of pathogenesis

Development of universal definition and diagnostic criteria

❖ **High dose corticosteroid in AE-ILD**

Still weak evidence of efficacy based on current literatures

Non-IPF: improvement of clinical outcomes

IPF: inconsistent data

non-pulse high dose therapy, early tappering in clinical practice

경청해주셔서 감사합니다

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