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APRILE
8



OTTICA RESPIRO

VERONA 2017

CROWNE PLAZA

Effetti sistemici delle riacutizzazioni di BPCO



Enrico Clini

Conflicts of interest

Research / Conference funding

Medical Products Research (MI)

Consuntalships/Lecture fees

Linde (D), AstraZeneca, Menarini, Novartis

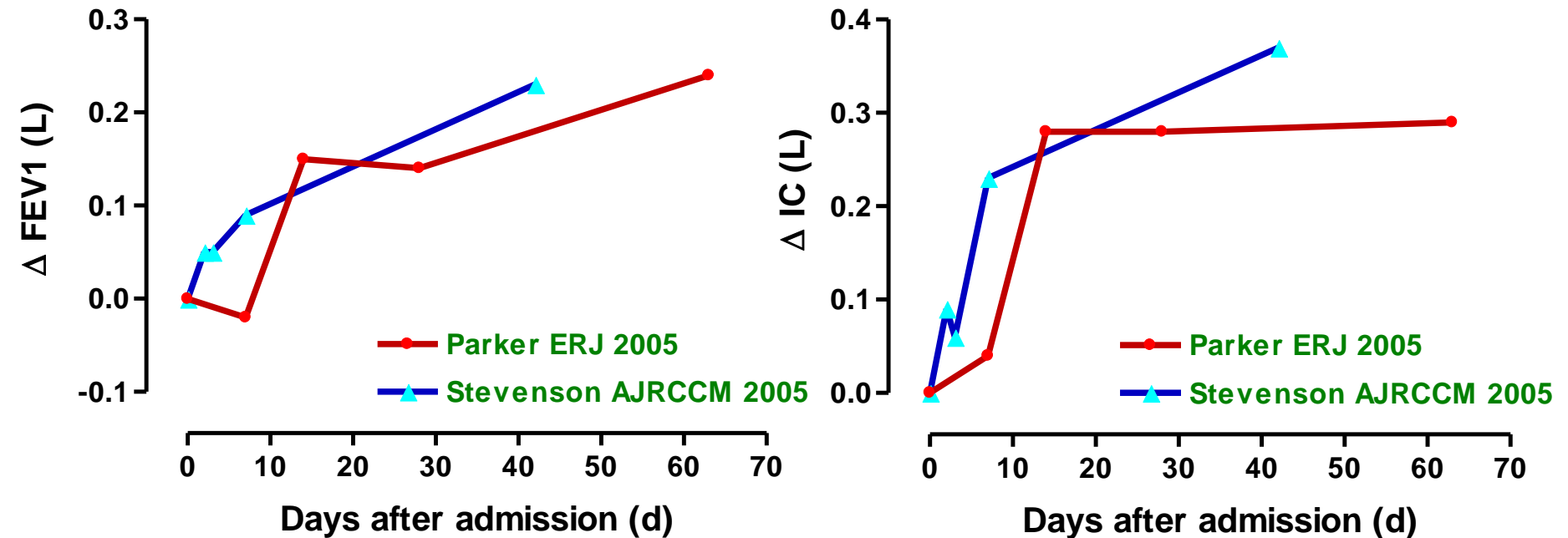
Outline

- Impact of AECOPD
- COPD and comorbidities (CMBs)
- AECOPD and acute CMBs
- Impact of CMBs during treatment for AECOPD

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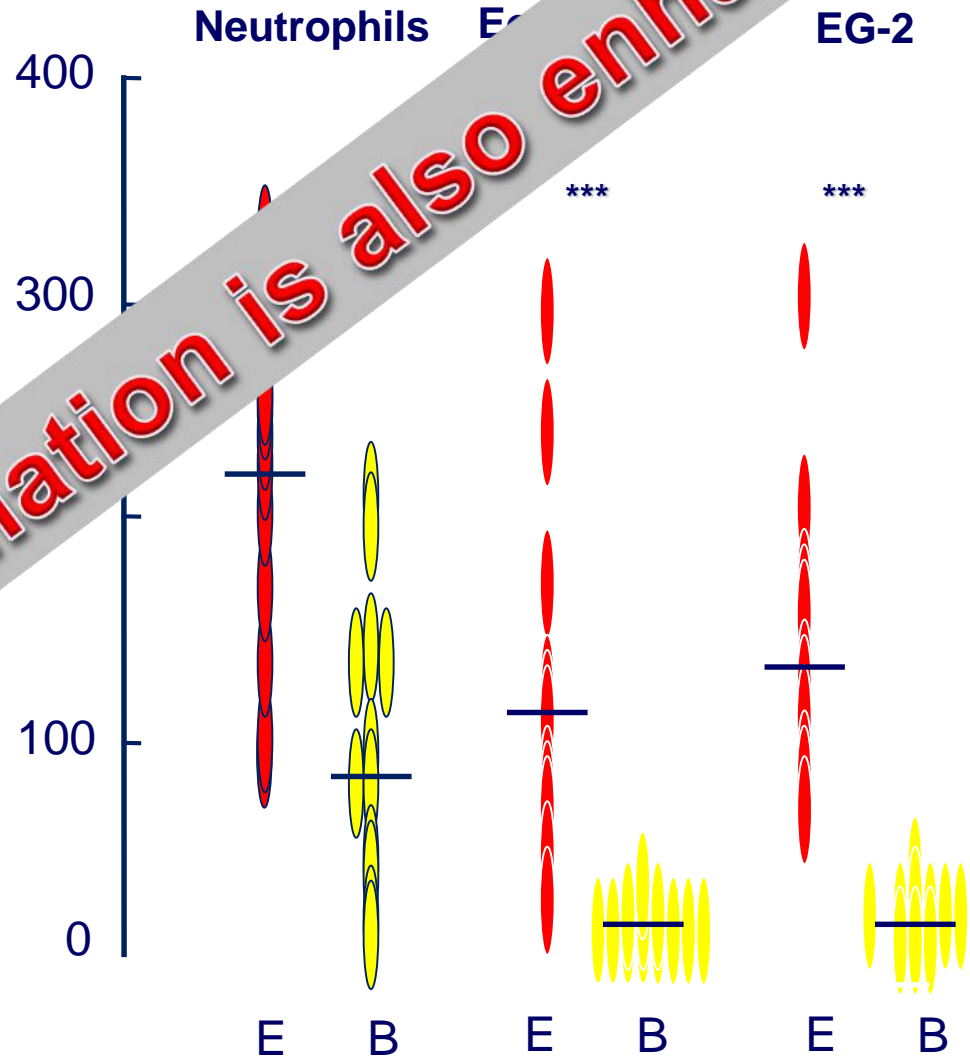
Exacerbations a complex problem



Bronchial inflammation in COPD exacerbations

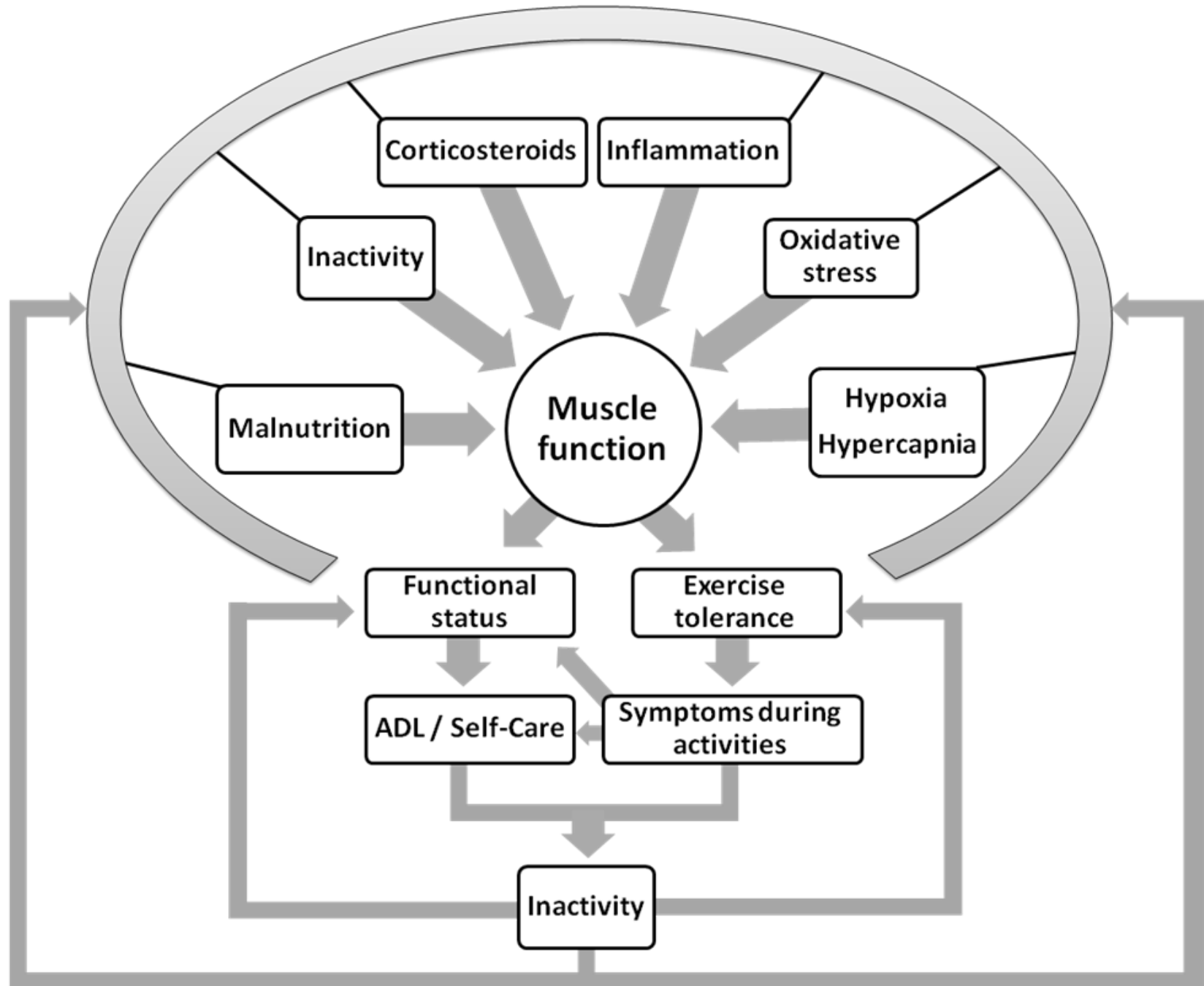
Increased
Neutrophils
and Eosinophils
in COPD
exacerbations

(Saetta 1994, 1995)



Systemic inflammation is also enhanced

Acute exacerbation



AECOPD – PATIENT PERSPECTIVE

Nr=125, age≥50 yrs, ≥2 AE in the previous year

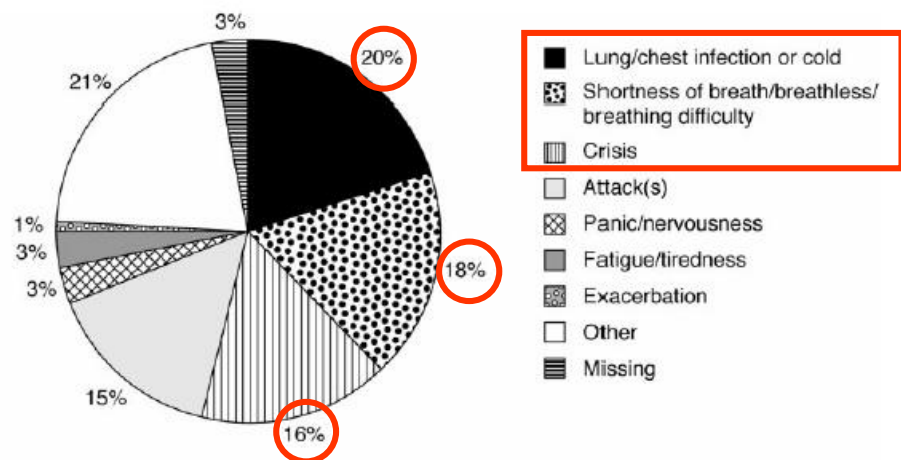


FIGURE 1. Variations on expressions used by more than one patient to describe a worsening of their condition (n = 125).

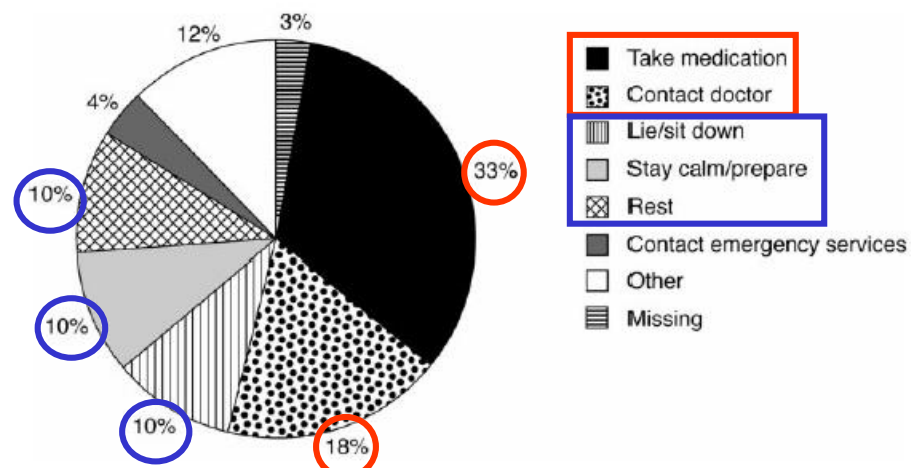


FIGURE 3. Patients' reported reactions at the onset of an exacerbation of COPD (n = 125).

AECOPD – PATIENT PERSPECTIVE

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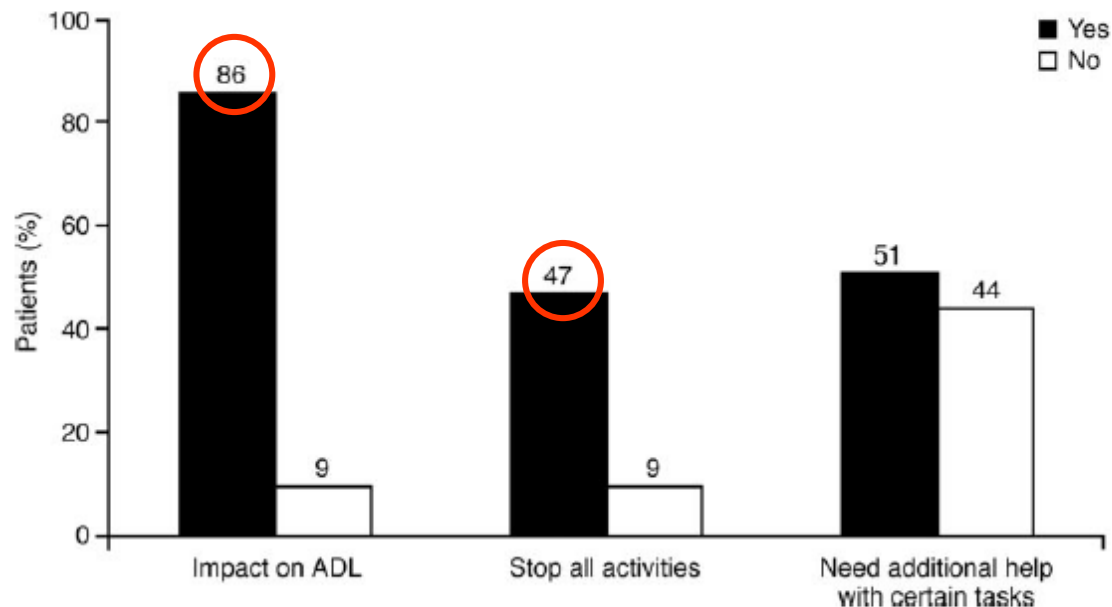
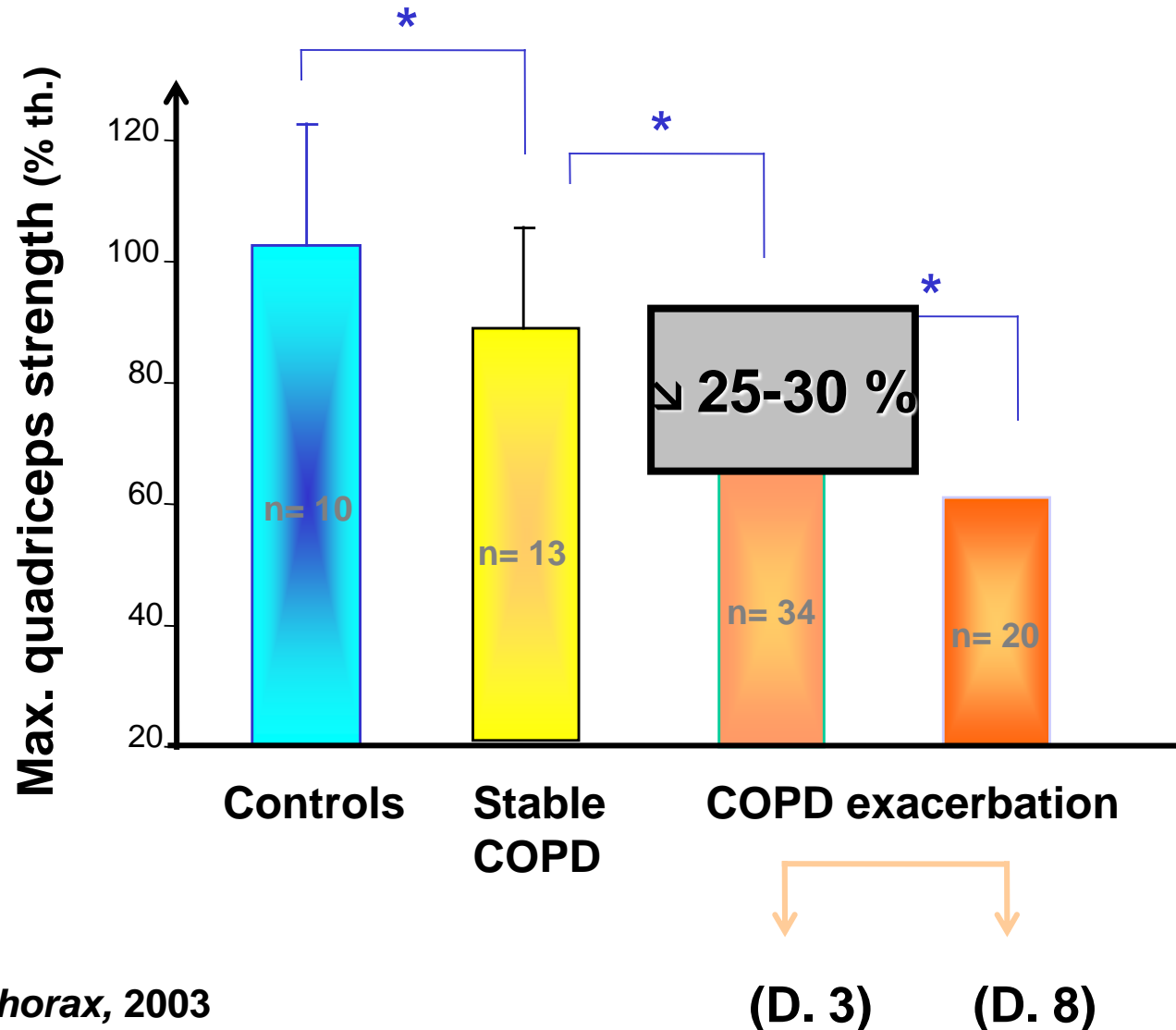


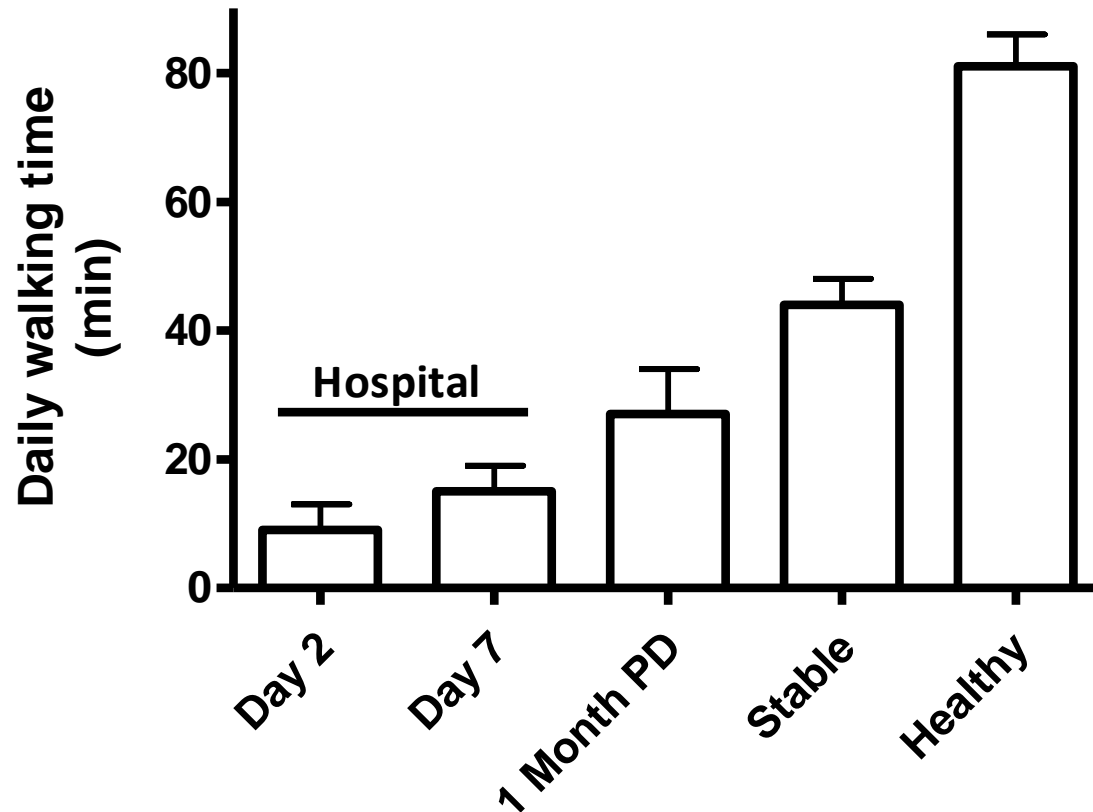
FIGURE 6. Impact of exacerbations of COPD on ADL. Data are expressed as a percentage of the whole patient population (n = 125).

Muscle function in severe COPD

During exacerbation



Physical inactivity during and after exacerbations



Burtin C, et al. ERJ 2011

Hana Müllerova, PhD; Diego J. Maselli, MD; Nicholas Locantore, PhD; Jørgen Vestbo, MD;

John R. Hurst, PhD; Jadwiga Wedzicha, MD; Per Bakke, MD, PhD; Alvar Agusti, MD, PhD;

Antonio Anzueto, MD for the ECLIPSE investigators

Parameter	<i>follow-up</i>		
	HR	HR (95% CI)	P Value
COPD hospitalization, prior 12 months	2.71	(2.24, 3.29)	<.001
SGRQ Total score (per 4 pt increase)	1.08	(1.06, 1.10)	<.001
FEV ₁ % predicted (per 5% drop)	1.12	(1.09, 1.16)	<.001
Age (per 10 year increment)	1.29	(1.13, 1.46)	<.001
Has emphysema (>5% by radiology)	1.56	(1.23, 1.97)	<.001
White blood cell count (per 1x10 ⁹ /L)	1.15	(1.07, 1.24)	<.001

Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease

J J Soler-Cataluña, M Á Martínez-García, P Román Sánchez, E Salcedo, M Navarro and R Ochoa

Thorax 2005;60:925-931; originally published online 29 Jul 2005;
doi:10.1136/thx.2005.040527

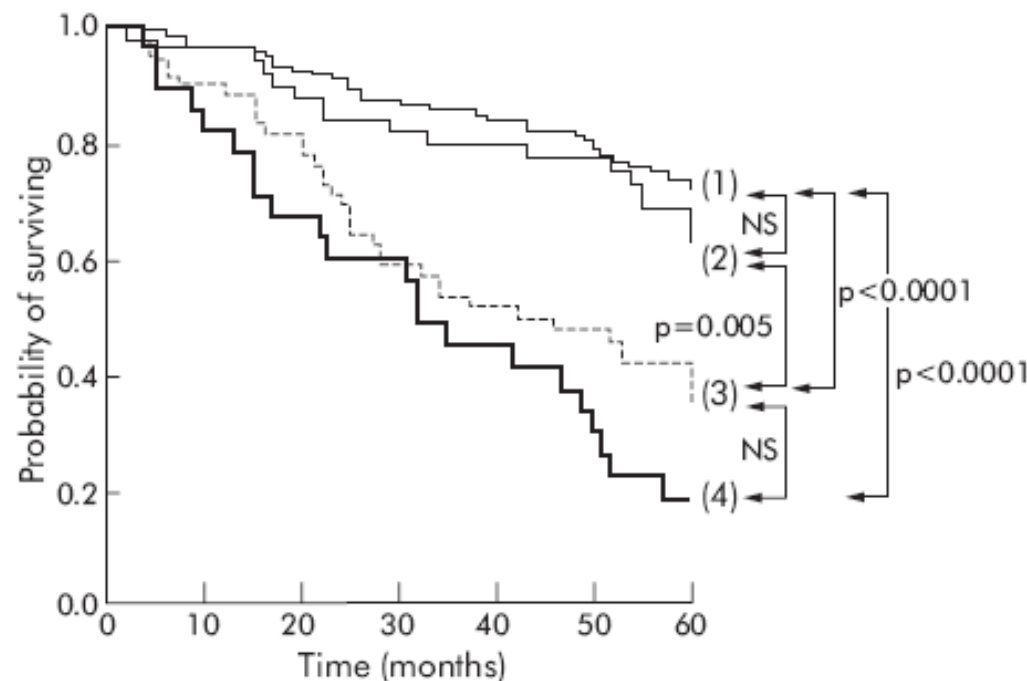


Figure 2 Kaplan-Meier survival curves by severity of exacerbations in patients with COPD: (1) no acute exacerbations of COPD; (2) patients with acute exacerbations of COPD requiring emergency service visits without admission; (3) patients with acute exacerbations of COPD requiring one hospital admission; (4) patients with readmissions.

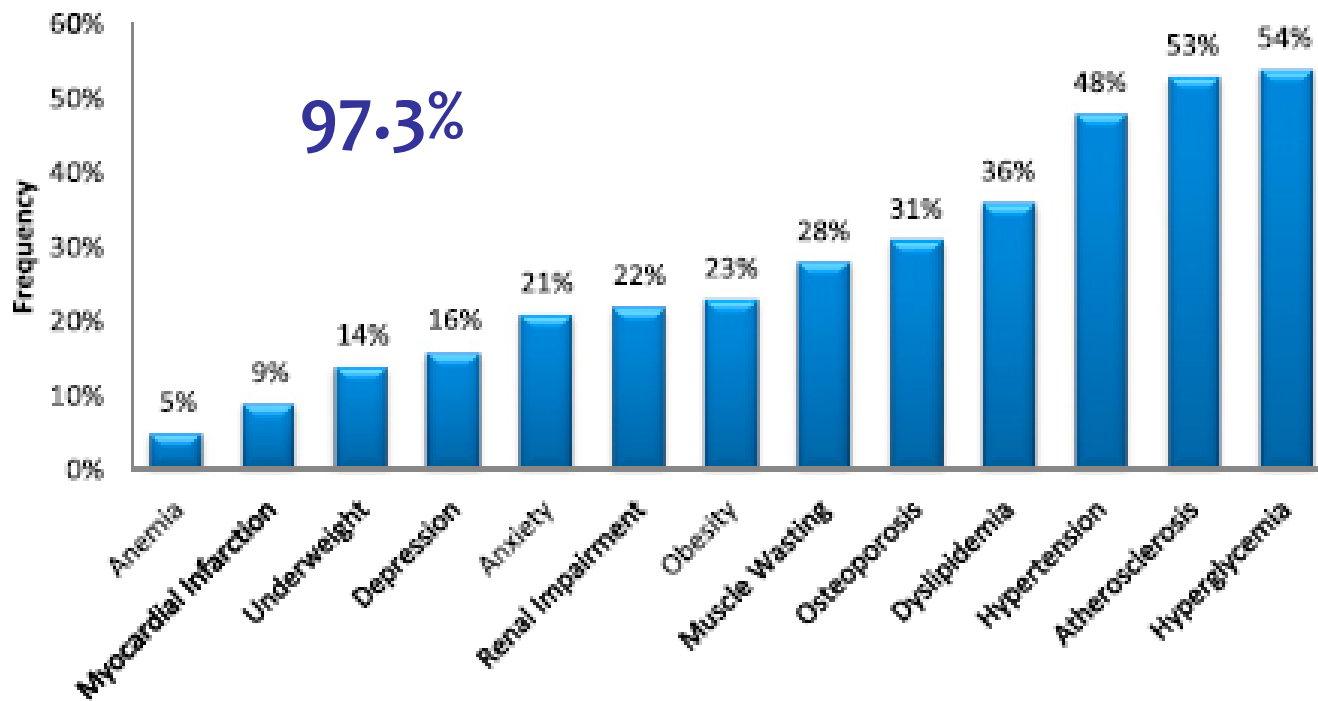
Management of Exacerbations

Key Points

- An exacerbation of COPD is an acute worsening of respiratory symptoms that results in additional therapy.
- Exacerbations can be precipitated by several factors. The most common causes are respiratory tract infections.
- The goal for treatment of exacerbations is to minimize the negative impact of the current exacerbation and to prevent subsequent events.
- Short-acting inhaled beta₂-agonists, with or without short-acting anticholinergics, are recommended as the initial bronchodilators to treat an acute exacerbation.
- Maintenance therapy with long-acting bronchodilators should be initiated as soon as possible before hospital discharge.
- Systemic corticosteroids improve lung function (FEV₁), oxygenation and shorten recovery time and hospitalization duration.
- Antibiotics, when indicated, shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration.
- Methylxanthines are not recommended due to side effects.
- Non-invasive mechanical ventilation should be the first mode of ventilation used to treat acute respiratory failure.

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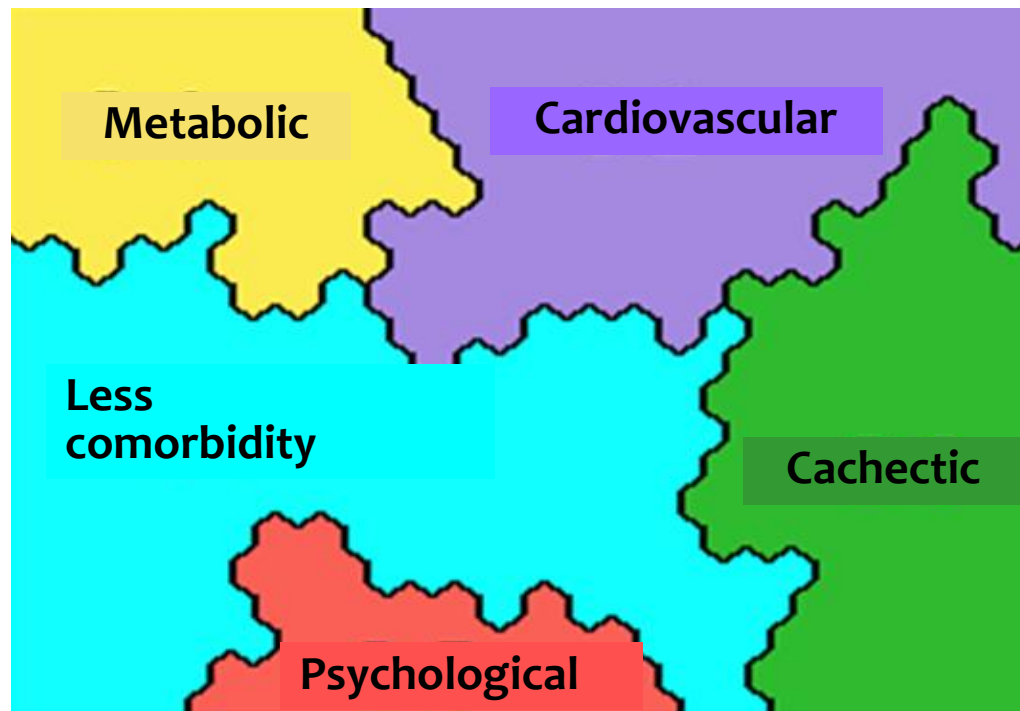
<div><div><div></div><div></div><div></div><div></div></div><div>< 20%</div><div>20-40%</div><div>40-60%</div><div>>60%</div></div>		% RENAL IMPAIRMENT	% ANEMIA	% HYPERTENSION	% OBESITY	% UNDERWEIGHT	% MUSCLE WASTING	% HYPERGLYCEMIA	% DYSLIPIDEMIA	% OSTEOPOROSIS	% ANXIETY	% DEPRESSION	% ATHEROSCLEROSIS	% MYOCARDIAL INFARCTION
RENAL IMPAIRMENT (n= 47)			6	49	9	32	45	43	36	38	13	11	47	11
ANEMIA (n= 11)		27		45	36	9	18	64	18	36	18	18	73	0
HYPERTENSION (n= 103)		22	5		27	12	23	58	35	26	20	16	62	12
OBESITY (n= 50)		8	8	56		0	0	72	42	18	12	18	72	4
UNDERWEIGHT (n= 30)		50	3	40	0		93	37	27	57	21	4	17	3
MUSCLE WASTING (n= 60)		35	3	40	0	47		42	22	55	33	14	29	9
HYPERGLYCEMIA (n= 116)		17	6	52	31	10	22		41	29	22	20	55	12
DYSLIPIDEMIA (n= 77)		22	3	47	27	10	17	62		20	14	18	63	11
OSTEOPOROSIS (n= 66)		27	6	41	14	26	50	52	23		29	23	49	13
ANXIETY (n= 43)		14	5	47	14	14	44	58	26	42		40	46	12
DEPRESSION (n= 33)		15	6	49	27	3	24	67	42	42	52		70	19
ATHEROSCLEROSIS (n= 106)		20	8	57	31	5	15	57	43	28	17	21		14
MYOCARDIAL INFARCTION (n= 19)		26	0	63	11	5	26	68	42	42	29	35	75	

Clusters of Comorbidities Based on Validated Objective Measurements and Systemic Inflammation in Patients with Chronic Obstructive Pulmonary Disease

Lowie E. G. W. Vanfleteren^{1,2}, Martijn A. Spruit¹, Miriam Groenen¹, Svetlana Gaffron³, Vanessa P. M. van Empel^{1,4}, Piet L. B. Bruijnzeel⁵, Erica P. A. Rutten¹, Jos Op 't Roodt⁶, Emiel F. M. Wouters^{1,2}, and Frits M. E. Franssen^{1,2}

¹Program Development Centre, CIRO+, Centre of Expertise for Chronic Organ Failure, Horn, The Netherlands; ²Department of Respiratory Medicine, ⁴Department of Cardiology, and ⁶Department of Internal Medicine, Maastricht University Medical Centre (MUMC+), Maastricht, The Netherlands; ³Analytics, Viscovery Software GmbH, Vienna, Austria; and ⁵Clinical Respiratory and Inflammation, AstraZeneca, Mölndal, Sweden

Vanfleteren et al, AJRCCM 2013; 187; 728-735



COPD and Comorbidities

Key Points

- COPD often coexists with other diseases (comorbidities) that may significantly impact patient outcome.
- The presence of comorbidities should not alter COPD treatment and comorbidities should be treated per usual standards regardless of the presence of COPD.
- When COPD is part of a multi-morbidity care plan, attention should be directed to ensure simplicity of treatment and minimize polypharmacy.

AE HISTORY

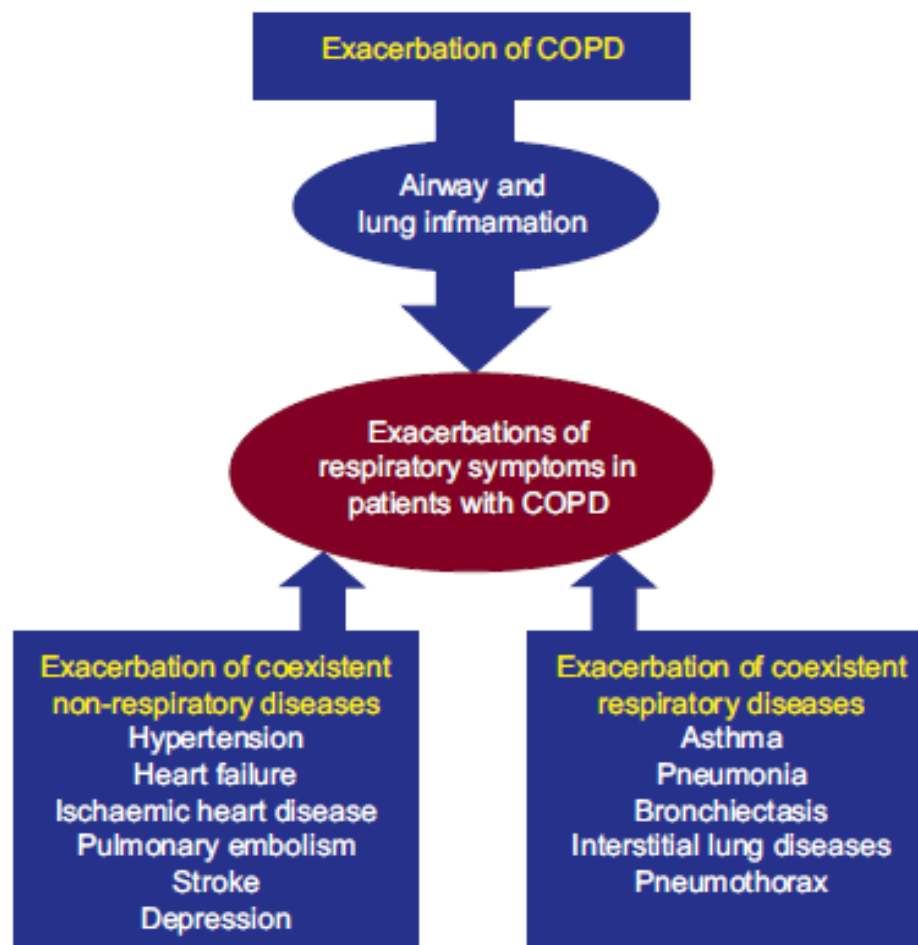
- Consider **non-respiratory causes** for AE of COPD

Mechanisms of respiratory symptoms in exacerbations of airway inflammation in COPD

Roca M, Verduri A, Corbetta L, Clini E, Fabbri LM, Beghè B

Eur J Clin Invest 2013; doi:10.1111/eci.12064

Exacerbation of respiratory symptoms in COPD patients may not be exacerbations of COPD



Beghe B, Verduri A, Roca M and Fabbri LM. Eur Respir J 2013, April 1; 41: 993-5
Roca M, Verduri A, Clini EM, Fabbri LM and Beghè B. Eur J Clin Invest, Feb 11, 2013

Exacerbation-like respiratory symptoms in individuals without chronic obstructive pulmonary disease: results from a population-based study

W C Tan,¹ J Bourbeau,² P Hernandez,³ K R Chapman,⁴ R Cowie,⁵ J M FitzGerald,⁶ D D Marciniuk,⁷ F Maltais,⁸ A S Buist,⁹ D E O'Donnell,¹⁰ D D Sin,¹ S D Aaron,¹¹
for the CanCOLD Collaborative Research Group

Thorax 2014;**0**:1–9. doi:10.1136/thoraxjnl-2013-205048

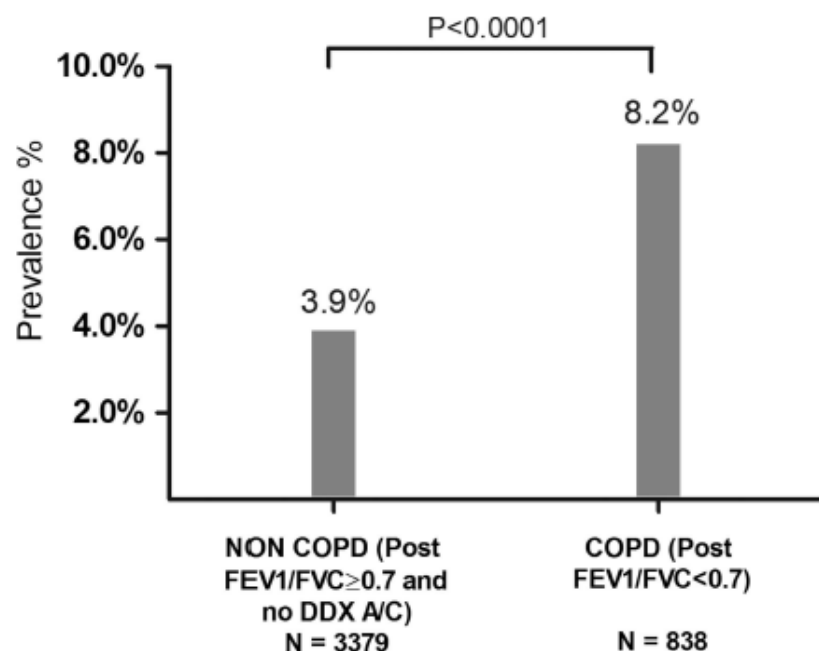


Figure 1 Frequency distribution of proportion of people in non-COPD and COPD groups with exacerbation in the past 1 year (DDX A/C: self-reported doctor's diagnosis of asthma/emphysema/chronic bronchitis/COPD).

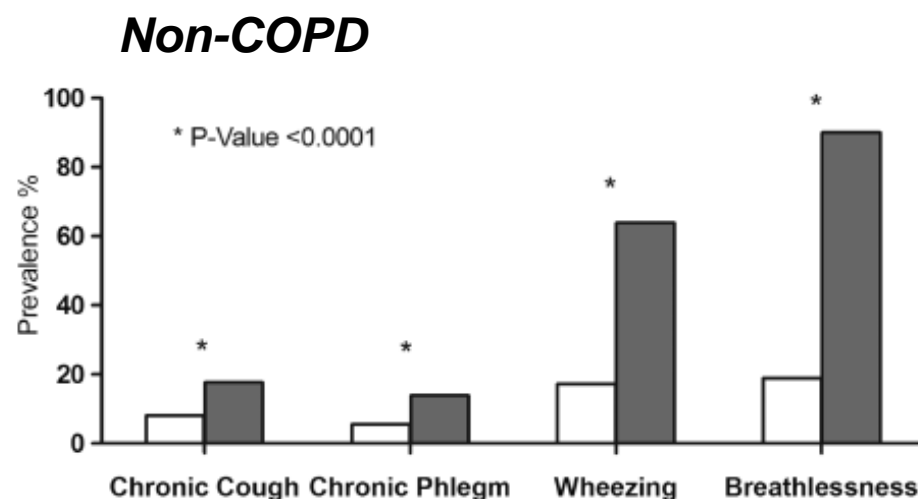


Figure 2 Frequency of chronic respiratory symptoms in 3379 subjects without COPD with and without exacerbation in the past 1 year. Non COPD=subgroup with post-bronchodilator FEV₁/FVC < 0.7 and no self-reported doctor's diagnosis of asthma/emphysema/chronic bronchitis/COPD. Open columns=no exacerbation in the past 1 year; closed columns=exacerbation in the past 1 year.

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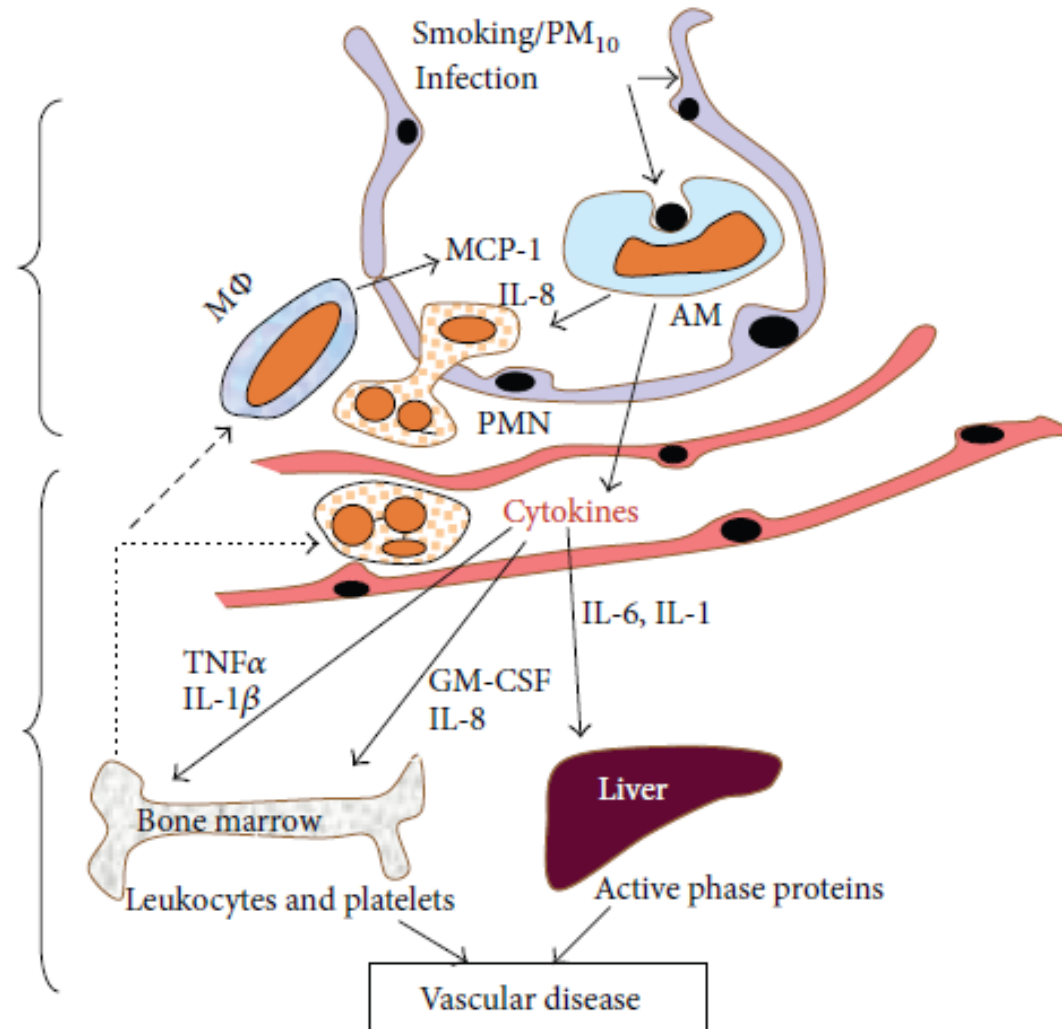
Effect of lung-induced systemic inflammation

Local inflammation:

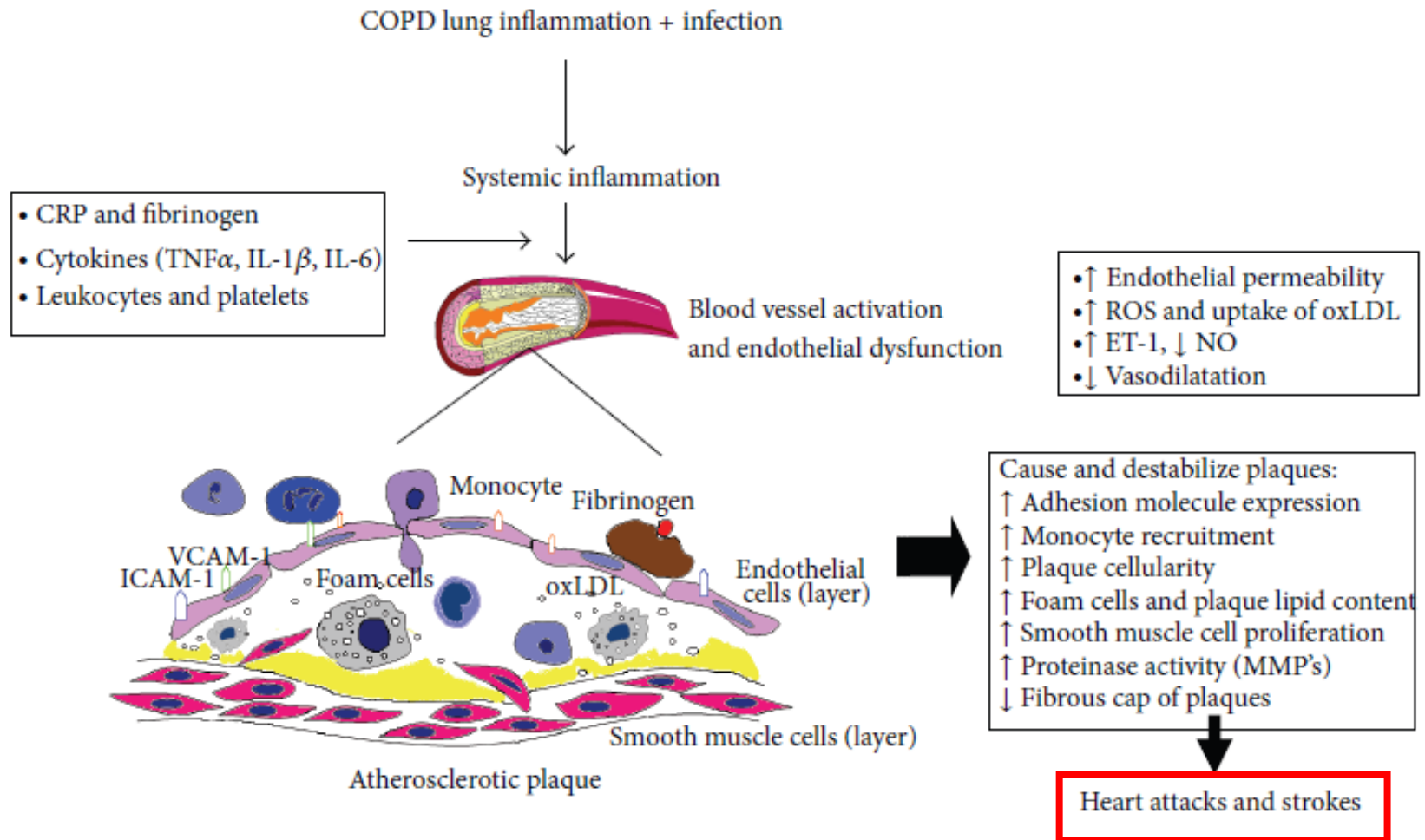
- Loss of lung function
- COPD exacerbations

Systemic inflammation

- Strokes
- Acute MIs

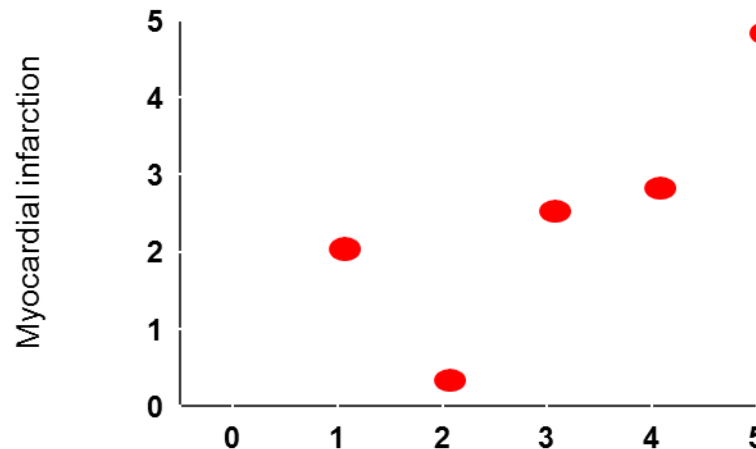


AECOPDs destabilize atheromasic plaques

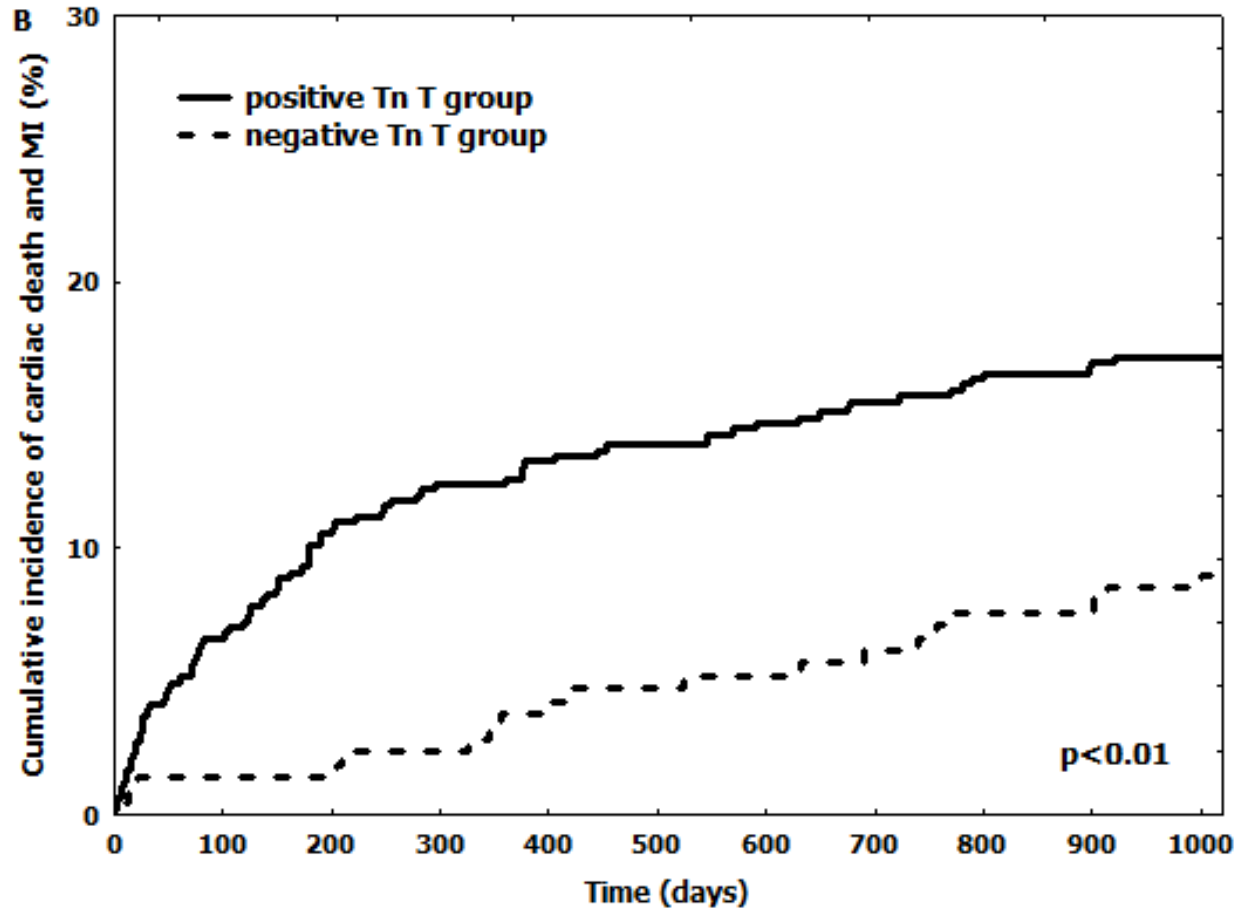


Risk of MI following AECOPD

IRRs for MI event on days 1 to 5		
	1 – 5 days	
Type of exacerbation	IRR (95% CI)	<i>P</i> value
Antibiotics	1.14 (0.7-1.8)	0.57
Steroids	1.55 (0.9-2.8)	0.15
Antibiotics + steroids	2.27(1.1-4.7)	0.03



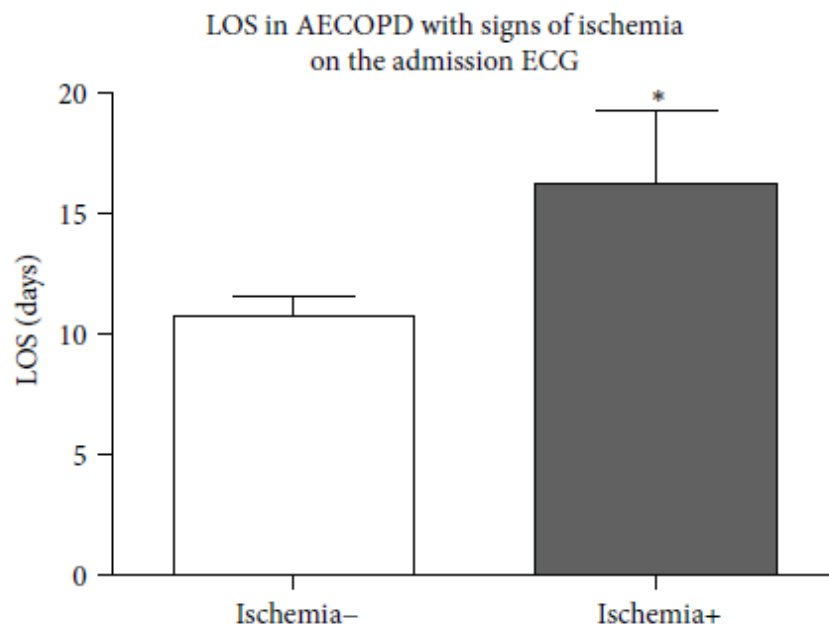
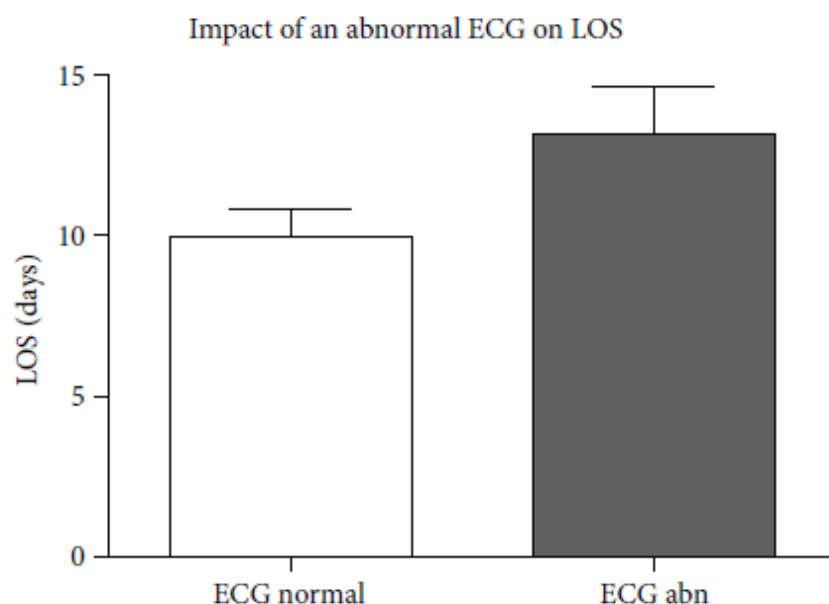
Relationship between Troponin Elevation and adverse events in patients with AECOPD



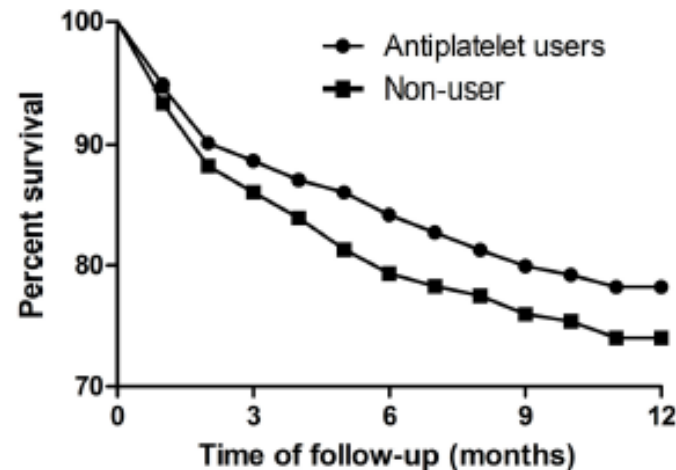
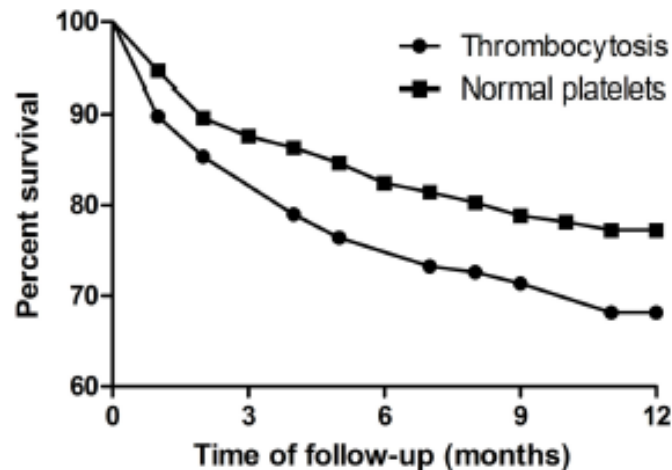
Acute Exacerbation of Chronic Obstructive Pulmonary Disease: Cardiovascular Links

Cheryl R. Laratta^{1,2} and Stephan van Eeden^{2,3}

Hindawi Publishing Corporation
BioMed Research International
Volume 2014, Article ID 528789, 18 pages



Thrombocytosis is associated with increased short and long term mortality after exacerbation of COPD: a role for antiplatelet therapy?



Thrombocytosis is an accessible, independent predictor of short term and 1-year mortality in AECOPD, and **antiplatelet therapy** may be associated with a survival benefit

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Acute exacerbations in patients with COPD: predictors of need for mechanical ventilation

M. Vitacca, E. Clini, R. Porta, K. Foglio, N. Ambrosino

Eur Respir J., 1996, 9, 1487-1493.

Table 1. – Demographic, nutritional data and APACHE score at admission

	Failure Group (n=14)	Success Group (n=25)	p-value
Sex M/F	12/2	20/5	
Age yrs	61±9 (38-73)	64±6 (38-82)	NS
Weight kg	53±12 (33-83)	67±16 (39-123)	<0.01
NPI*	46±22 (20-74)	24±8 (13-38)	<0.001
Albumin g·dL ⁻¹	3.8±0.35 (2.6-4.1)	4.1±0.4 (3.5-4.6)	
TSF mm	9±5 (4-20)	22±11 (13-31)	
Transferrin mg·dL ⁻¹	168±31 (126-206)	194±29 (153-280)	
Anergy %	95	69	
IBW* %	86±21 (47-110)	109±31 (77-170)	<0.01
APACHE II*	20±7 (15-29)	12±3 (10-22)	<0.001

Determinants of Noninvasive Ventilation Outcomes during an Episode of Acute Hypercapnic Respiratory Failure in Chronic Obstructive Pulmonary Disease: The Effects of Comorbidities and Causes of Respiratory Failure

Angela Maria Grazia Pacilli,¹ Ilaria Valentini,¹ Paolo Carbonara,¹ Antonio Marchetti,¹ and Stefano Nava^{1,2}

Hindawi Publishing Corporation
BioMed Research International
Volume 2014, Article ID 976783, 9 pages

TABLE 4: Multivariate analysis. OR = odds ratio. Probability of NIV success increases by 5.6 times for every 1 g/dL increase in albumin serum level, while presence of pneumonia decreases the success probability by 61.8%.

	OR	95% CI		P-value
		Inf	Sup	
Gender	0.566	0.243	1.318	0.187
Age	0.969	0.917	1.023	0.255
SAPS score	0.962	0.921	1.006	0.090
Albumin (g/dL)	5.617	2.242	14.078	0.000
Charlson index	0.938	0.717	1.227	0.639
Pneumonia	0.382	0.161	0.902	0.028
Renal disease	0.760	0.251	2.302	0.628

The most important determinants of NIV failure are the presence of **pneumonia** and the level of serum albumin (**nutritional status**)

Raffaele Scala
Sandra Bartolucci
Mario Naldi
Marcello Rossi
Mark W. Elliott

Co-morbidity and acute decompensations of COPD requiring non-invasive positive-pressure ventilation

n= 120

AECOPD undergoing NIV

Table 3 Distribution of chronic and acute non-respiratory co-morbidities (NRC) (n=120)

	Chronic NRC	Acute NRC
Cardiovascular	10 (8.3%)	34 (28.3%)
Non-cardiovascular	14 (11.6%)	16 (13.3%)
Gastrointestinal	7	6
Neurological	3	11
Metabolic	5	8
Oncological	5	–
Renal	0	6
Haematological	–	3

40%



Raffaele Scala
Sandra Bartolucci
Mario Naldi
Marcello Rossi
Mark W. Elliott

Co-morbidity and acute decompensations of COPD requiring non-invasive positive-pressure ventilation

Variables associated with NIV failure

Variable	Univariate analysis	Multivariate analysis		
	<i>p</i>	Adjusted OR	95% CI	<i>p</i>
ADL	<0.001	—	—	—
APACHE III score	<0.001	—	—	—
Acute NRC	0.001 ^a	8.344	2.082–33.445	0.003
Kelly-Matthay score	0.001	—	—	—
FEV ₁ predicted	0.004 ^a	0.877	0.804–0.956	0.003
pH 2-h NIPPV	0.013	—	—	—
Pneumonia	0.016	—	—	—
CPE (cause of AHRF)	0.029	—	—	—
Chronic NRC	0.043	—	—	—
PaO ₂ /FIO ₂ 2-h NIPPV	0.045	—	—	—

^a Variables selected to be entered in multivariate analysis

Variables associated with 6-month mortality

Variable	Univariate analysis	Multivariate analysis		
	<i>p</i>	Adjusted OR	95% CI	<i>p</i>
ADL	<0.001 ^a	0.060	0.020–0.182	<0.001
Non-cardiovascular chronic NRC	0.005 ^a	11.090	2.445–50.299	0.002
Acute NRC more than 1	0.007 ^a	6.304	1.030–38.593	0.046
HMV	0.008	—	—	—
FEV ₁ predicted	0.018	—	—	—
APACHE III score	0.022	—	—	—
BMI	0.032	—	—	—
Kelly-Matthay score	0.033	—	—	—

^a Variables selected to be entered in multivariate analysis

Conclusions

- AECOPD is a common and complex condition along the course of the disease.
- CMBs are very frequent in the COPD population and may refer to symptom-presentation at AE onset
- The presence of acute CMBs following AECOPD increase short- and long-term risk
- Attention should be reserved to **assess, monitor, and treat extrapulmonary decompensation** during AECOPD