

Are the Diagnostic Criteria for Asthma–COPD Overlap Syndrome Appropriate in Biomass Smoke-induced Chronic Obstructive Pulmonary Disease?*



¿Son adecuados los criterios diagnósticos del fenotipo mixto EPOC-asma en la enfermedad pulmonar obstructiva crónica por humo de biomasa?

To the Editor,

Our scientific community agrees that some patients present overlapping features of chronic obstructive pulmonary disease (COPD) and asthma. The Spanish COPD guidelines (GesEPOC)¹ call this the mixed COPD–asthma phenotype, but it is known internationally as asthma–COPD overlap syndrome (ACOS). Its prevalence has not been well defined, and various studies report differences in sex and age.² Variations in the prevalence of ACOS are primarily due to discrepancies among the consensus-based diagnostic criteria.^{2,3} Indeed, in a Canadian study, prevalence ranged between 5% and 27% depending on the diagnostic criteria applied.⁴ According to clinical guidelines, significant criteria for establishing a diagnosis of ACOS include a previous diagnosis of asthma and, particularly, early onset of respiratory symptoms.^{1,2}

The studies cited above mainly focus on COPD caused by tobacco smoke. We know, however, that exposure to biomass smoke is a major cause of COPD, although the characteristics of this entity remain to be defined. Specifically, little information is available on the prevalence of ACOS in COPD caused by biomass smoke. In a study conducted by our group, we found a 21.3% prevalence of ACOS in patients with COPD caused by biomass smoke, compared to 5% in COPD caused by tobacco, but these differences may be related to an uneven gender distribution in study groups.⁵ In this study, we used modified GesEPOC criteria to diagnose ACOS; however, the retrospective nature of the study was a major limitation, and prevented us from systematically investigating all possible diagnostic criteria in each case. The diagnostic factor most frequently used was personal history of asthma, based primarily on onset of respiratory symptoms before the age of 40 years. However, this

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Usefulness of Biomarkers as Prognostic Factors of Mortality in Elderly Patients with Community-acquired Pneumonia*



Utilidad de los biomarcadores como factores pronósticos de mortalidad en los pacientes ancianos con neumonía adquirida en la comunidad

To the Editor,

We read with great interest the study of Calle et al.,¹ recently published in ARCHIVOS DE BRONCONEUMOLOGÍA, which analyzes the

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criterion may not be applicable to COPD caused by biomass smoke, since, unlike tobacco, exposure to this noxious substance typically begins in early childhood, a crucial stage in the development of the respiratory system. For this reason, early onset is a specific feature of COPD caused by biomass smoke, and does not constitute a reliable indicator of coexisting asthma in this population. ACOS, then, may have been overdiagnosed in our series, and we must question whether the usual diagnostic criteria are applicable in this COPD subtype.

We believe research should be undertaken to identify biomarkers that would allow ACOS to be reliably differentiated in populations with different risk factors for the disease. The clinical implications are obvious, because ACOS patients and particularly those with COPD caused by biomass smoke have typically been excluded from clinical studies, resulting in a scarcity of scientific evidence on which to base therapeutic decisions.

References

- Miravittles M, Soler-Cataluña JJ, Calle M, Molina J, Almagro P, Quintano JA, et al. Guía española de la EPOC (GesEPOC). Tratamiento farmacológico de la EPOC estable. Arch Bronconeumol. 2012;48:247–57.
- Diagnosis of diseases of chronic airflow limitation: Asthma, COPD and Asthma–COPD Overlap Syndrome (ACOS). Based on the Global Strategy for Asthma Management and Prevention and the Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (2014). Available from: <http://www.goldcopd.org/asthma-copd-overlap.html> [accessed 10.11.14].
- Soler-Cataluña JJ, Cosío B, Izquierdo JL, López-Campos JL, Marín JM, Agüero R, et al. Documento de consenso sobre el fenotipo mixto EPOC-asma en la EPOC. Arch Bronconeumol. 2012;48:331–7.
- Morogan A, Pinto LM, Tan WC, Li P, Aaron SD, Chapman KR, et al. Asthma COPD overlap syndrome (ACOS): what can we learn from the Can-COLD population? Available from: <http://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2014.189.1.MeetingAbstracts.A5937> [accessed 10.11.14].
- Golpe R, Sanjuán López P, Cano Jiménez E, Castro Añón O, Pérez de Llano LA. Distribución de fenotipos clínicos en pacientes con enfermedad pulmonar obstructiva crónica por humo de biomasa y por tabaco. Arch Bronconeumol. 2014;50:318–24.

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relationship between mortality and geriatric assessment parameters and standard clinical variables in very elderly patients with community-acquired pneumonia (CAP). The authors conclude their article by saying that age and other clinical, laboratory and geriatric assessment parameters, such as functional capacity, are useful for predicting mortality in the short term.

We have few points we would like to add to this report. In the last 10 years, the incidence of CAP seen in emergency departments in Spain has increased from 0.85% to 1.35% ($P < .001$).² In total, 51% of CAPs were recorded in patients aged 70 years and older, and clinical presentation and mortality were significantly worse in this population than in patients aged 15–69 years ($P < .001$).² These data have generated a growing awareness of the need for an accurate prognosis of mortality in elderly patients. Some biomarkers have proven useful as independent predictors of mortality in CAP patients,^{3,4} but reports of varying results in elderly individuals and other adults⁵ have raised questions about the usefulness of these biomarkers in patients of different ages.

Table 1
Capacity of Biomarkers for Predicting Death in Community-acquired Pneumonia in the Emergency Department.

	Concentrations in Group A		Concentrations in Group B		30-day mortality after admission	
	Mean±SD		Mean±SD		ROC-AUC (95% CI)	
	P-value ^a		P-value ^a		P-value ^b	
	Survived (75)	Died (4)	Survived (58)	Died (9)	Group A	Group B
MR-proADM (nmol/l)	1.18±0.88 P=.006	461±3.66	1.57±0.94 P=.001	5.09±4.58	0.909 (0.806–1) P=.006	0.858 (0.722–0.993) P=.001
PCT (ng/ml)	3.06±1.33 P=.047	6.48±19.80 P=.005	0.75±1.64 P=.049	6.13±5.75 P=.005	0.794 (0.697–0.891)	0.790 (0.581–1)
CRP (mg/l)	76.32±45.20 P=.177	101.50±43.30	82.89±46.15 P=.296	95±41.82	0.706 (0.449–0.964) P=.167	0.606 (0.391–0.822) P=.309

Group A: 79 patients aged 15–74 years.

Group B: 67 patients ≥75 years.

CI, confidence interval; CRP, C-reactive protein; MR-proADM, mid-regional proadrenomedullin; PCT, procalcitonin; ROC-AUC, receiver operating characteristic–area under the curve; SD, standard deviation.

^a Comparison of means between groups 2×2 (Student's *t* test and Mann–Whitney *U* test), as applicable.^b P-value: indicates the risk of a type I error in rejecting the null hypothesis that AUC–ROC=0.5.

These results motivated our group to retrospectively analyze the databases of some of our studies^{3,4} in order to determine diagnostic factors for predicting mortality in the short term among CAP patients aged 75 years or older, or younger than 75, who were admitted to our hospital between November 2011 and July 2012. A total of 146 patients were included. Two subgroups were formed: group A (15–74 years: 79 cases, 54.1%) and group B (≥75 years: 67 cases, 45.9%). Some results are shown in Table 1. Despite the limitations of a small sample size and the retrospective, single-center nature of the analysis, we found mid-regional proadrenomedullin (MR-proADM) to be the most useful biomarker for predicting short-term mortality (intra-hospital and up to 30 days post-admission) in both group A and group B, and the one with the largest area under the receiver operating curve (AUC–ROC). Similarly, albeit to a lesser extent, procalcitonin levels significantly predicted differences in survival in both age groups and differences in mean numbers of survivors and non-survivors. No significant differences were observed between mean concentrations of C-reactive protein (non-survivors vs survivors) and the AUC–ROC curves are of little use, particularly in group B.

While awaiting the findings of a prospective study specifically designed to determine the utility of procalcitonin and, more importantly, MR-proADM for predicting mortality in elderly patients, initial determinations of these biomarkers in emergency departments could orient the prognosis of elderly patients with CAP. These patients often have a more deceptive and unclear clinical presentation, limited functional status and a high comorbidity burden. Although the role, utility and effectiveness of each biomarker will have to be defined, we believe they will be of use in determining the prognosis and care of elderly patients with CAP, and for making decisions on admission and the most appropriate destination of these fragile individuals.

Conflict of interests

None declared.

References

1. Calle A, Márquez MA, Arellano M, Pérez LM, Pi-Figueras M, Miralles R. Valoración geriátrica y factores pronósticos de mortalidad en muy ancianos con neumonía extrahospitalaria. Arch Bronconeumol. 2014;50:429–34.
2. Martínez Ortiz de Zárate M, González del Castillo J, Julián-Jiménez A, Piñera Salmerón P, Llopis Roca F, Guardiola Tey JM, et al. Estudio INFURG-SEMES: Epidemiología de las Infecciones en los Servicios de Urgencias Hospitalarias y evolución en la última década. Emergencias. 2013;25:368–78.
3. Julián-Jiménez A, Timón-Zapata J, Laserna-Mendieta EJ, Sicilia-Bravo I, Palomo-de los Reyes MJ, Cabezas-Martínez A, et al. Poder diagnóstico y pronóstico de los biomarcadores para mejorar el manejo de la neumonía adquirida en la comunidad en los servicios de urgencias. Enferm Infecc Microbiol Clin. 2014;32:225–35.
4. Julián-Jiménez A, Parejo Míguez R, Cuenca Boy R, Palomo de los Reyes MJ, Laín Terés N, Lozano Ancín A. Intervenciones para mejorar el manejo de la neumonía adquirida en la comunidad desde el servicio de urgencias. Emergencias. 2013;25:379–92.
5. Julián-Jiménez A, Candel-González FJ, González del Castillo J. Utilidad de los biomarcadores de inflamación e infección en los servicios de urgencias. Enferm Infecc Microbiol Clin. 2014;32:177–90.

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