Letter to the Director

A Novel Figure and Algorithm for the GOLD-ABE Classification: Additional Comments

To the Director,

Miravitlles et al. propose in their recent editorial a new figure and algorithm for the GOLD-ABE assessment tool.[1] They rightly point out that the ABE classification is actually made up of four groups, because patients in group E with blood eosinophilia should be started early on triple therapy (LABA/LAMA/ICS). One of the authors also proposed another modification of the ABE classification that adds a third dimension to said classification.[2] The authors' proposal characterizes B and E patients as B+ and E+ if they have cardiovascular disease (CVD) or increased cardiovascular risk (CVR). They suggest that this scheme could serve as a basis for earlier treatment of some patients with triple therapy and mention two potential benefits: a reduction in the decline of lung function, and a possible benefit in mortality, which could be partially mediated by a reduction in cardiovascular events. In fact, both benefits could be related, since there may be an association between lung function and CVD.[3] Adoption of this modified scheme to guide therapy should be preceded by appropriate studies, and a first step should be to assess whether this modified classification improves prediction of future risk compared to the current GOLD scheme.

Neither the current GOLD-ABE nor the latest GOLD-ABCD classifications (2017 and later) used lung function to decide initial drug treatment, unlike previous GOLD-2011 recommendations or current GesEPOC algorithms.[4] In a previous study, we found that a three-dimensional modification of the GOLD-2017-ABCD scheme, similar to that proposed by Kostikas et al.,[2] but using lung function instead of CVD/CVR, increased its ability to predict future risk.[5] We performed a post hoc analysis of the data from said study with the objectives of (A) verifying whether the classifications proposed by Kostikas et al.[3] (GOLD-ABE-3D) and Miravitlles et al. (GOLD-ABE-Eos)[1] increase the capacity of predicting future mortality risk over current GOLD-ABE classification and (B) determine how another three-dimensional modification of GOLD-ABE, using lung function to establish the third dimension of the scheme (GOLD-ABE-function), compares with the other classifications.

The patients were classified according to the four schemes. For GOLD-ABE-3D, patients from the B and E groups were classified as B+ and E+ if any of the following diseases had been diagnosed on the index date: chronic heart failure, ischaemic heart disease, peripheral vascular disease, cerebrovascular disease or atrial fibrillation. For GOLD-ABE-Eos, patients from the E group were classified as E-1 (non-eosinophilic) or E-2 (eosinophilic), following the methodology of a previous study.[6] For GOLD-ABE-function, patients from the A, B and E groups were classified into subgroups -1 or -2 according to whether their FEV_1% was $\geq 50\%$ (−1) or <50% (−2). The outcome

variable was all-cause mortality. The ability of the classifications to predict outcome was compared using receiver-operating characteristics curves. The areas under the curves (AUCs) were compared according to DeLong et al.[7]

A total of 954 patients were studied, of whom 169 died after a mean follow-up of 51.8 ± 29.2 months. Eosinophils counts were not available for all participants, so only 920 patients could be classified according to GOLD-ABE-Eos. The AUCs were: GOLD-ABE: 0.676 (95% CI: 0.645–0.705); GOLD-ABE-Eos: 0.657 (95% CI: 0.625–0.687), GOLD-ABE-3D: 0.689 (95% CI: 0.659–0.718); GOLD-ABE-function: 0.695 (95% CI: 0.664–0.724). AUCs for GOLD-ABE-3D and GOLD-ABE-function were significantly higher than for GOLD-ABE ($p < 0.001$ and $p = 0.02$, respectively). There were no significant differences between GOLD-ABE-3D and GOLD-ABE-function ($p = 0.54$), nor between GOLD-ABE-Eos and GOLD-ABE ($p = 0.83$).

These results indicate that the proposed GOLD-ABE classification[1] can be refined to better predict mortality risk, including either CVD/CVR or lung function. This is a relevant finding to design future studies that evaluate early triple therapy, with the aim of improving survival. A three-dimensional classification that uses lung function instead of CVD increases the prediction of mortality similarly to that of Kostikas et al.[2] A possible link between lung function and CVR might explain this finding. The diagnosis of CVD is challenging in COPD patients, since the symptoms of both diseases overlap, whereas lung function measurement is a simple and indispensable evaluation in COPD. Therefore, modifying the ABE algorithm proposed by Miravitlles et al.[1] by adding lung function could be considered when designing future clinical trials on early implementation of triple therapy.

Conflict of Interests

The authors state that they have no conflict of interests.

References

1. Miravitlles M, Kostikas K, Bizymi N, Tzanakis N. A novel figure and algorithm for the Gold ABE classification. Arch Bronconeumol. 2023, http://dx.doi.org/10.1016/j.arbres.2023.06.001. S0300-2896(23)00177-1.
2. Kostikas K, Gogali A, Hillas G. Cardiovascular disease and COPD: adding a third dimension to the ABE GOLD 2023 COPD classification. Am J Respir Crit Care Med. 2023;208:502–4, http://dx.doi.org/10.1164/rccm.202304-0691LE.
3. Buch P, Friberg J, Scharling H, Lange P, Prescott E. Reduced lung function and risk of atrial fibrillation in the Copenhagen City Heart Study. Eur Respir J. 2003;21:1012–6.
4. Miravitlles M, Calle M, Molina J, Almagro P, Gómez JT, Trigueros JA, et al. Spanish COPD guidelines (GesEPOC) 2021: updated pharmacological treatment of stable COPD. Arch Bronconeumol. 2022;58:69–81.
5. Golpe R, Figueira-Gonçalves JM, Amado CA, Martín-Audera P, Esteban C, García-Talavera I, et al. A new, three-dimensional approach to the GOLD COPD assessment tool. Respir Med Res. 2022;81:100879, http://dx.doi.org/10.1016/j.resmer.2021.100879.
6. Golpe R, Figueira-Gonçalves JM, Esteban C, Amado-Diago CA, Aramburu A, García-Talavera I, et al. Relationship between the GesEPOC 2021 classification of risk

levels and phenotypes and the incidence of adverse events. Arch Bronconeumol. 2022;58:451–3.

7. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988;44:837–45.

Rafael Golpe [a,*], Juan Marco Figueira-Gonçalves [b,c], Cristóbal Esteban [d,e], Carlos A. Amado [f,g], David Dacal-Rivas [a], Iria Veiga [a]

[a] *Servicio de Neumología, Hospital Universitario Lucus Augusti, Lugo, Spain*
[b] *Servicio de Neumología y Cirugía Torácica, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain*
[c] *University Institute of Tropical Diseases and Public Health of the Canary Islands, University of La Laguna, Santa Cruz de Tenerife, Spain*
[d] *Servicio de Neumología, Hospital Galdakao-Usansolo, Bizkaia, Spain*
[e] *Red de Investigación en Servicios de Salud en Enfermedades Crónicas (REDISSEC), Hospital Galdakao-Usansolo, Bizkaia, Spain*
[f] *Servicio de Neumología, Hospital Universitario Marqués de Valdecilla, Santander, Spain*
[g] *Universidad de Cantabria, Instituto de Investigación Sanitaria de Cantabria IDIVAL, Spain*

[*] Corresponding author.
E-mail addresses: rafagolpe@gmail.com, rafael.golpe.gomez@sergas.es (R. Golpe).