

Longitudinal stability of blood eosinophil count strata in the COPD COSYCONET cohort

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Introduction

It has been increasingly recognized that the numbers of blood eosinophils (eos) might be an important biomarker in patients with COPD to identify patients at risk for exacerbations and for treatment to inhaled corticosteroid (ICS) treatment or anti-interleukin-5 therapy.¹⁻³ However, data about the stability of blood eos counts over time are rare. We used data from the multicenter COSYCONET study to analyze the variability of eos by strata over a period of 18 months.⁴

Methods

The German COPD and Systemic Consequences-Comorbidities Network (COSYCONET) cohort study is a multicenter, longitudinal, prospective, observational study, into which 2,741 patients with the diagnosis of COPD were recruited between 2010 and 2013 in 31 study centers throughout Germany.⁴ Eos were collected in a number of centers as part of routine clinical assessments. To determine the longitudinal stability of their counts, we included all patients in whom a differential blood cell count was available at the study visits V1–V3 (baseline, 6 months, 18 months). These 334 patients were more prone to exacerbations and were more likely to have an ICS-containing treatment regimen than the remaining part of the COSYCONET population (Table 1).

First, we determined the absolute number and proportion of patients, who exhibited eos of <150 cells/μL (rated as non-eosinophilic), 150–299 cells/μL (intermediate), and ≥300 cells/μL (eosinophilic) at visit 1. Next, we analyzed the longitudinal stability of the three strata from visit 1 to visit 2, and from visit 2 to visit 3. Finally, we displayed the results in analogy to the stability analysis performed by Hurst for the susceptibility to exacerbations.⁵

Results

At visit 1, 165 patients (50%) were non-eosinophilic, 121 (36%) intermediate, and 48 (14%) eosinophilic. The overall distribution remained fairly stable over time (visit 2: 43%, 40%, 18%, respectively; visit 3: 46%, 40%, 14%, respectively). The changes between strata over consecutive visits and the resulting distributions are shown in Figure 1. Putting the data from the three visits together, 26% of patients

Table 1 Baseline data from 334 patients in whom a differential blood cell blood count was available at visits VI–V3 as compared to 2,407 patients without differential blood cell count available at all time points VI–V3

	Current study population	Residual COSYCONET population	P-value ^a
n	334	2,407	NA
Age, years	64.37±8.33	65.15±8.66	0.12
Male, %	63.2	58.5	0.1
BMI, kg/m ²	27.49±5.41	26.97±5.38	0.1
FEV ₁ , % predicted	55.5±17.97	57.11±21.63	0.2
FEV ₁ , l	1.66±0.64	1.67±0.73	0.77
No of exacerbations previous year	1.85±4.57	1.21±2.24	<0.001
6-MWD, min	429±98.42	418.95±109.83	0.09
BODE	2.1±1.88	2.27±2.01	0.16
SGRQ	43.09±19.69	42.63±20.03	0.69
ICS-containing treatment, %	57.8	63.9	0.03
History of asthma, %	20.1	18.4	0.45

Notes: Data are displayed as mean ± SD. ^at-test was calculated for continuous variables, Fisher's exact test was calculated for dichotomous variables.

Abbreviations: NA, not applicable; BMI, body mass index; FEV₁, forced expiratory volume in 1 second; 6-MWD, 6-minute walking distance; BODE, score based on body mass index, obstruction, dyspnea, Exercise capacity; SGRQ, St George's Respiratory Questionnaire; ICS, inhaled corticosteroid.

were persistently non-eosinophilic (<150 eos/μL), which implies that 74% exhibited ≥150 eos/μL at least at one occasion. Conversely, 28% exhibited ≥300 eos/μL at least once within 18 months, but only 5% of patients were persistently eosinophilic (≥300 eos/μL) at all three study visits. Excluding patients whose status regarding corticosteroid treatment (on/off) changed from one visit to another (n=63) did not change the results significantly (data not shown).

Discussion

The main findings of this analysis are (1) that 26% of COPD patients in the study cohort were persistently non-eosinophilic, (2) 5% were persistently eosinophilic, and (3) 28% exhibited ≥300 eos/μL at least once in three observations over a period of 18 months.

Few longitudinal studies evaluated the robustness of eos strata in COPD before.^{6,7} Oshagbemi et al found the stability of counts higher in patients showing <340 eos/μL compared to patients showing ≥340 eos/μL.⁶ Using a lower cut-off level of 2%, Singh et al observed that the majority of patients showed variations around a value of 2%.⁷ When defining three different strata in absolute

eos numbers, we observed that among those that were robust over time the non-eosinophilic stratum (<150 eos/μL) was the most frequent one. Still it comprised only about one quarter of the population, while the majority of patients were in the intermediate or high eosinophilic group at least at one occasion. More than one quarter of the population exhibited ≥300 eos/μL at least once in three visits.

Even though our data may not be fully representative for the entire COSYCONET cohort (eg, higher exacerbation rate, higher percentage of patients on any ICS-containing regimen) and some groups at visit 3 included a small number of patients (making the results somewhat preliminary), they help to assess the stability of the eos signal, which will potentially be used in the future to come to treatment decisions.

Conclusion

Our analysis demonstrates that in COPD non-eosinophilia in blood is more robust over time than eosinophilia defined as count ≥300 eos/μL. These observations might be helpful for the design of studies that address the question, whether rational and effective treatment decisions should better refer to persistent or to occasional eosinophilia.

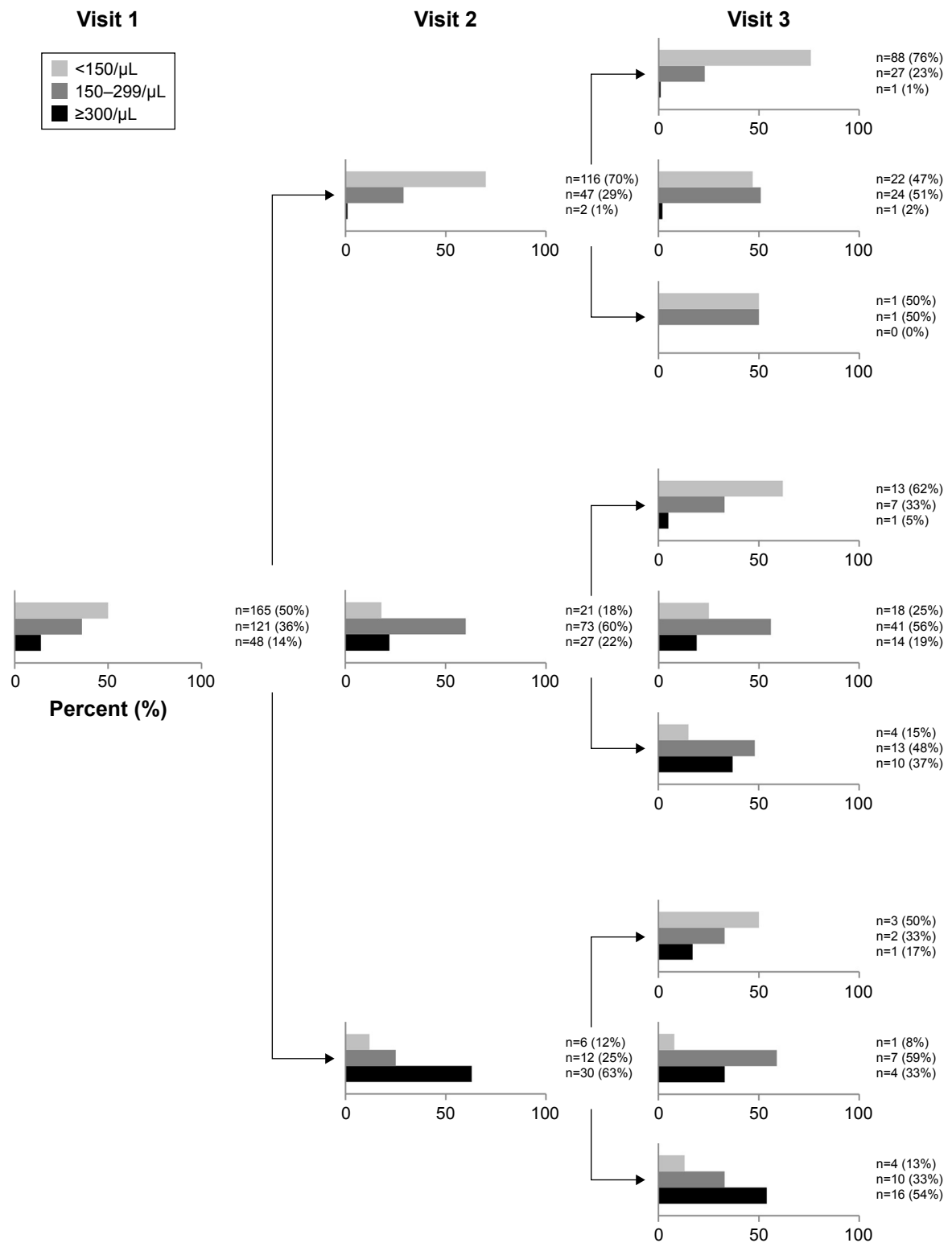


Figure 1 Absolute number and proportion of patients according to blood eos count at visits 1, 2, and 3.

Note: The proportions of participants at visit one are sequentially subdivided according to their eos blood count at visit 2, and the proportions of patients at visit 2 are sequentially subdivided according to their eos blood count at visit 3.

Abbreviation: eos, eosinophil.

Disclosure

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