

signs and bronchiectasis predominated in CVID. In line with their findings, in our cohort with proven granulomatous disease, the majority of HRCTs demonstrated macronodular lung involvement (eight out of 11 patients). The two patients with micronodular involvement showed a randomly distributed pattern, which also differs to the characteristic perilymphatic distribution in sarcoidosis, as already shown by BOUVRY *et al.* [1]. Moreover, some patients presented with predominant coarse reticular lines or ground-glass lesions. It is intriguing to speculate whether the difference in CD4/CD8 ratio reflects different forms or stages of pulmonary inflammation in CVID, which may correlate to certain computed tomography morphology. This has been previously described in sarcoidosis, where lower CD4/CD8 ratios and increased neutrophils correlated with progressive, fibrotic disease and the need for steroid treatment [3–5]. In our small CVID cohort, lung function and computed tomography findings were mostly stable during follow-up, suggesting that a high CD4/CD8 ratio in granulomatous CVID is associated with a mild and nonprogressive ILD (table 1). Only two patients showed a deterioration of lung function parameters. Interestingly, both of these patients showed rather low CD4/CD8 ratios in comparison to the total study population (2.0 and 3.8).

In conclusion, in addition to the report by BOUVRY *et al.* [1], we found that in a subgroup of CVID patients with histologically confirmed granuloma formation, BAL cytology resembles sarcoidosis. All patients presented with high BAL lymphocytosis, high CD4/CD8 ratio and the majority with nodular lung disease on computed tomography. Thus, differences in BAL cytology and computed tomography morphology most likely reflect heterogeneity in CVID-associated granulomatous and interstitial lung disease. Our preliminary data suggest a rather favourable prognosis of ILD in this subgroup of CVID with high CD4/CD8 ratio in the BAL. Some of these findings may potentially guide management and predict outcome of these patients, but larger studies are needed to determine diagnostic and prognostic value of specific markers during detailed characterisation of interstitial lung disease in this heterogeneous disease.



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Bronchoalveolar lavage cytology resembles sarcoidosis in a subgroup of granulomatous chronic variable immunodeficiency <http://ow.ly/pU6Pl>

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References

- 1 Bouvry D, Mouthon L, Brillet PY, *et al.* Granulomatosis-associated common variable immunodeficiency disorder: a case–control study *versus* sarcoidosis. *Eur Respir J* 2013; 41: 115–122.
- 2 Al-Herz W, Bousfiha A, Casanova JL, *et al.* Primary immunodeficiency diseases: an update on the classification from the international union of immunological societies expert committee for primary immunodeficiency. *Front Immunol* 2011; 8: 54.
- 3 Prasse A, Katic C, Germann M, *et al.* Phenotyping sarcoidosis from a pulmonary perspective. *Am J Respir Crit Care Med* 2007; 177: 330–336.
- 4 Ziegenhagen MW, Rothe ME, Schlaak M, *et al.* Bronchoalveolar and serological parameters reflecting the severity of sarcoidosis. *Eur Respir J* 2003; 21: 407–413.
- 5 Kollert F, Geck B, Suchy R, *et al.* The impact of gas exchange measurement during exercise in pulmonary sarcoidosis. *Respir Med* 2010; 105: 122–129.

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From the authors:

We would like to thank F. Kollert and co-workers for their interest in our article [1] and their accurate analysis and comments.

Our study was designed to compare interstitial lung disease (ILD) in granulomatosis-associated common variable immunodeficiency disorder (CVID) (ILD/CVID/granulomatous disease) with pulmonary sarcoidosis.

We found that lung manifestations in ILD/CVID/granulomatous disease were different from those in pulmonary sarcoidosis patients, taking into account their clinical history, physical examination, computed tomography (CT) imaging and bronchoalveolar lavage (BAL).

Regarding CT imaging, the features in the cohort of F. Kollert and co-workers are in accordance with ours. Most frequently, chest CT showed different findings from pulmonary sarcoidosis with nodular involvement (seven out of 11 patients in Kollert's cohort and 16 out of 20 in ours) and random distribution of micronodules when present. Other studies have previously suggested these findings [2–4].

The BAL differential count was lymphocytic in both our cohort and F. Kollert's cohort. However, the CD4/CD8 ratio was lower in our cohort. There is no clear explanation for this difference. The only evident difference stemmed from the design of the studies; ours was multicentric and that of F. Kollert and co-workers was monocentric. It is possible that the associated presence of some degree of CVID-linked lymphoid infiltration might have led to a high level of CD8 T-cells and, thus, a low CD4/CD8 ratio in BAL. Indeed, in two of our five patients with CD4/CD8 counts <1 who underwent a pathological analysis of the lung, one had granulomas and the other had lymphoid interstitial pneumonia. Thus, it could be argued that the BAL CD4/CD8 ratio depends on the proportion of granulomas and lymphoid lesions.

The prognostic value of the CD4/CD8 ratio in sarcoidosis has been discussed and seems to be insignificant. The CD4/CD8 ratio is increased in most patients, but can be normal and even decreased [5]. In the series of F. Kollert and co-workers, although the evolution was available in only nine patients, the prognostic significance of the BAL CD4/CD8 ratio is interesting. In our patients, poor prognosis was mainly linked to complications of CVID (*i.e.* infection and lymphoproliferation) and not to the lung granulomatous process, which was perhaps due to the treatments given. Consequently, we could not find any relationship between the CD4/CD8 ratio and the evolution of ILD.

In conclusion, we agree with F. Kollert and co-workers that there is heterogeneity in ILD/CVID/granulomatous disease, especially in the lung, that is linked to pathological substratum. This probably explains why the BAL CD4/CD8 ratio is variable. The prognostic value of the CD4/CD8 ratio observed by F. Kollert and co-workers was not shown in our study. This fact is challenging and further studies are needed that could help therapeutic management.



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ILDs in granulomatosis associated CVID are heterogeneous with variable proportions of granulomas and lymphoid lesions <http://ow.ly/rjkt>

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References

- 1 Bouvry D, Mouthon L, Brillet P-Y, *et al.* Granulomatosis-associated common variable immunodeficiency disorder: a case-control study versus sarcoidosis. *Eur Respir J* 2013; 41: 115–122.
- 2 Park JE, Beal I, Dilworth JP, *et al.* The HRCT appearances of granulomatous pulmonary disease in common variable immune deficiency. *Eur J Radiol* 2005; 54: 359–364.
- 3 Torigian DA, LaRosa DF, Levinson AI, *et al.* Granulomatous-lymphocytic interstitial lung disease associated with common variable immunodeficiency: CT findings. *J Thorac Imaging* 2008; 23: 162–169.
- 4 Vultaggio A, Matucci A, Parronchi P, *et al.* Association between “sarcoidosis-like” disease and common variable immunodeficiency (CVI): a new CVI variant showing an activation of the immune system. *Sarcoidosis Vasc Diffuse Lung Dis* 2007; 24: 127–133.
- 5 Kantrow SP, Meyer KC, Kidd P, *et al.* The CD4/CD8 ratio in BAL fluid is highly variable in sarcoidosis. *Eur Respir J* 1997; 10: 2716–2721.