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**Considerations in managing FDG PET-positive sarcoidosis with infliximab therapy** http://ow.ly/U0qUr

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# Haemoptysis: a frequent diagnostic challenge

*To the Editor:*

We read with interest the article by Abdulmalak *et al.* [1] recently published in the *European Respiratory Journal*. The authors reported the results of an observational, retrospective, 5-year, nationwide, multicentre study based on the medical information collected from a French database. The epidemiology of haemoptysis was evaluated through the hospital discharge diagnosis codes, focusing on incidence, aetiology, seasonal distribution, relapses and mortality in a 3-year follow-up analysis. The authors made a great effort to provide findings on the largest national cohort of hospitalised patients with haemoptysis (~15 000 per year) and update the current epidemiological understanding of this frequent symptom in high-income countries. However, some of the results described in the manuscript deserve a more detailed analysis and careful interpretation.

The authors found that cryptogenic or idiopathic haemoptysis, defined as haemoptysis without an established cause [2, 3], was the most frequent aetiology ranging from 48.9% in 2012 to 52% in 2008. Although the epidemiology of haemoptysis has changed in the last decades, these data are significantly different to those described in other European hospitalised cohorts. In two prospective series, idiopathic haemoptysis had an incidence range of 5.4–13% [2, 4], whilst three retrospective studies detected an

incidence of 6.3–33.7% [5–7]. Notably, another study in which the epidemiological retrospective design was based on discharge codes described a higher rate of idiopathic bleeds (42.2%) [8].

It is also worth noticing that a significant percentage of idiopathic haemoptysis reached a definite diagnosis during a recurrence. In both 2008 and 2009, about 10% of patients initially diagnosed with a cryptogenic or a respiratory infection-related haemoptysis were subsequently diagnosed with lung cancer in a follow-up period of 3 years. Of note, about half of these new cases of malignancies were diagnosed within only 2 months after the initial bleeding episodes. The only European study that prospectively assessed the course of inpatients with idiopathic haemoptysis described no lung cancer cases during a 4-year follow-up [2].

In our opinion, these findings may have two potential explanations: the lack of an accurate initial diagnostic workup and/or the questionable use of the administrative coding system to explore the epidemiology of a symptom. Cryptogenic haemoptysis was defined as an incident case without any database aetiologies coded as the main/associated/related diagnosis. Moreover, the same authors acknowledged that the haemoptysis code may have been used inappropriately, probably more often in cases requiring large amounts of care. The initial high percentage of idiopathic and infection-related haemoptysis subsequently diagnosed as lung cancer within only 2 months might be associated with a misleading approach related to a laboratory delay. Nevertheless, the discrepancy with other epidemiological reports confirms that the epidemiological approach adopted by Abdulmalak *et al.* [1] might have significantly biased the results. We deem that observational prospective or retrospective studies should include more information sources, including clinical files or hospital discharge letters.

Haemoptysis is a challenging symptom frequently involving life-threatening conditions, such as lung cancer. The aetiology of haemoptysis may sometimes be misled by an incomplete initial diagnosis: the diagnostic work-up should be as exhaustive as possible, particularly if malignancy risk factors are recognised [9]. Despite its clinical relevance, optimal diagnostic workup remains largely unclear. There is a lack of evidence-based guidelines regarding appropriate diagnostic management of patients with haemoptysis; the majority of the studies, mostly retrospective, show poor evidence on the best initial panel of tests [3–9]. This condition may lead to inaccurate diagnosis and to avoidable radiation exposure and invasive tests. Future prospective studies should clarify these issues, providing an essential diagnostic pathway according to the accuracy of the main tests (*i.e.* chest radiography, computed tomography and bronchoscopy), amount of bleeding, demographic and epidemiological data.

A prospective, Italian, multicentre trial (www.ClinicalTrials.gov identifier NCT02045394) is currently underway, focusing on the description of the epidemiology of haemoptysis in both in- and outpatients, and on the identification of an essential diagnostic algorithm.

Future studies, based on a more accurate epidemiological design, could better describe the causes of haemoptysis and contribute to fill the gaps concerning the diagnosis and management of this symptom.

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**Haemoptysis is a frequent symptom, and the definition of aetiologies and a diagnostic pathway are often challenging** http://ow.ly/U0f2X

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*From the authors:*

We appreciate and agree with the comments of M. Mondoni and colleagues, that the results of the ongoing prospective Italian multicentre trial (www.ClinicalTrial.gov identifier NCT02045394) will be of considerable interest for the management of haemoptysis, a frequent and severe symptom, especially since there is no clear consensus concerning aetiology and treatment. Interestingly, beyond determining the prevalence of diseases that may present with haemoptysis, their epidemiological results will be analysed according to the severity of the symptom. More importantly, their trial will hopefully make it possible to analyse the sensitivity and specificity of complementary tests, such as chest radiography, chest computed tomography (CT) and bronchoscopy alone and in combination in the diagnosis of different causes of haemoptysis.

We acknowledged that our observational retrospective study had some limitations and possible bias due to the way data was collected, that is to say through hospital discharge diagnosis codes [1]. However, the national administrative database (PMSI/medicalisation of information system programme) has gathered national administrative health data in France from every french public and private teaching and nonteaching healthcare facility since 1997. Each hospital's budget depends on the medical activity, as described by a specific computer program, which compiled discharge abstracts related to all admissions since 2008. The fact that these national data are necessary to allocate hospital budgets has considerably encouraged improvements in data quality in terms of accuracy and exhaustiveness, and the results obtained in our study are consequently different from those in the publication of Boulay *et al.* [2], where data were collected between 1994 and 1997. In France, diagnoses identified during hospital stays have been coded according to the 10th edition of the International Classification of Diseases (ICD-10) since 1998. In ICD-10, there is a single specific code for haemoptysis (ICD-10 code R042). Therefore, and importantly, we are confident that the symptom was not over- or misreported in our study.

Our database did not allow us to collect data from out-patients, who may only have presented mild haemoptysis. There is therefore a possible risk that we over-selected moderate and severe haemoptysis and missed some cases of mild haemoptysis [3]. Physicians may also have underreported mild haemoptysis in patients with a previously known diagnosis of lung cancer when the patient was hospitalised with this symptom, but not due to it. The aetiology of haemoptysis may have been reported with a delay, and we believe this is particularly the case for lung cancer. Indeed, because it may take some time to gather results from other complementary examinations or pathology reports, the patient may have been discharged from the initial hospitalisation without a diagnosis of lung cancer, even though the physician suspected the disease. To report lung cancer in the PMSI, it is necessary to have definite pathological confirmation of the diagnosis. However, we were aware of this possible bias and considered that lung cancer was the aetiology of the initial haemoptysis episode when it was diagnosed within 2 months of the initial haemoptysis. We therefore discussed the hypothesis that lung cancer developed in 4% of patients with initial cryptogenic haemoptysis during the 3 years of follow-up [1]. This hypothesis is in accordance with previously published studies [4].

Despite these unavoidable biases and possible inaccuracies due to the coding system, we believe that our 5-year study provided unequivocal and important data regarding the 10 million patients who are hospitalised yearly in France, among whom 15 000 (0.2%) were admitted for haemoptysis or have haemoptysis as a complication of their hospital stay [1]. We provided important information regarding prognosis and follow-up. We showed that the frequency of recurrence was relatively low, since 84% of patients with initial haemoptysis had no recurrence within the 3 years of follow-up. Moreover, even though it was explored in small prospective studies, we found substantial mortality rates during the initial stay as expected [5] but, more interestingly, during the follow-up as well. Indeed, the 3-year in-hospital mortality rate, excluding lung cancers, was high at 20%. Even if death may have been more closely related