

## Comment from the authors: the tests combination in patients with lung cancer and malignant pleural effusion

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Diagnostic yield of pleural thoracentesis in case of suspected malignant pleural effusion (MPE) varies according to the histological type of the primary tumor (1,2), to the local extent of the disease (involvement of both visceral and parietal pleura) (3) and of course to the expertise (4). In patients with non-small cell lung cancer (NSCLC) and MPE, the evidence of malignant cells in the pleura is critical as their presence directly means that the patient presents with metastatic disease, and therefore he will be treated accordingly despite the fact that there is no evidence of other metastatic sites (5). In the case of absence of malignant cells in fluid cytology the best way to confirm or rule out diagnosis is to "go and look inside", by thoracoscopy, a minimally invasive and safe technique, performed either by a pulmonologist or a thoracic surgeon (6). Furthermore, in the era of personalization of the therapeutic options, the need for large tissue samples provides important information on molecular factors that are actually in use to treat those patients, but also new factors may be discovered in the near future and used if stocking tissue samples (bio-banking) (4). Considering this, thoracoscopy is the examination of choice for all patients with lung cancer and MPE.

However, all centers do not dispose thoracoscopy as an option in their settings as this procedure requires expertise (7). Therefore, the idea behind our study (8) was what do if no thoracoscopy, although in our center we dispose this technique. More specifically, we would like to know whether the combination of all non-invasive tests, including chest computed tomography (CCT), positron emission tomography (PET), together with pleural cytology, help in diagnosing patients with MPE from lung cancer (8). Indeed, our study has limitations as it is a retrospective one. For instance, about half of the patients benefited of PET and the mismatch between fluid cytology, CCT and PET, may lead to a likely underpowered statistical analysis (8). Yet, at the metastatic stage of the disease PET is not systematically recommended (5).

Some important points in our study are that our population was homogenous (only lung cancer patients with MPE), coming from a single center (9). These two facts prevent from suffering of significant inclusion biases either from studying an heterogenous population (many different primary carcinomas) and/or many different centers with variations in the yield of the different examinations tested, such as pleural cytology, CCT and PET. In our study (8), taking the yield of pleural fluid cytology separately and compared to the current bibliography, our yield was of the higher in this patient population, and it was enhanced after thoracoscopy, a method that systematically may not be used, yet even in case of surgically treated peripheral NSCLC, positive pleural lavage may totally change the treatment strategy as it is a factor of poor survival (10,11). We agree that the results of CCT may be lower than the reported in the literature regarding MPE in general (9), and

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despite the fact of lung cancer patients, we believe that an important issue is the systematically use of thin sections to better look inside the pleura, and even though it is hard to detect specific features because of the partial volume effect and the growth of pleural nodules within fibrous tissues and exudates (12). PET in NSCLC (5) indeed has to be used only in case of possible radical surgery to detect distant metastasis, and our study (8) confirms the poor utility of PET in this patient population (7), and of course this is also true in patients with malignant pleural mesothelioma (13). When we tried to correlate these non-invasive techniques, no relation was found (8). Yet, their combination increased the yield up to 90%, and this is a novel information, although in our study we had a high proportion of adenocarcinomas (7).

But the most important message of our study, is that we may improve the diagnostic yield by the combination of all these non-invasive techniques, still a good number of patients, if not all, will necessitate thoracoscopic biopsy for diagnostic purposes, but also for "molecular staging".

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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