



Clinical characteristics of patients simultaneously diagnosed with lung cancer and active pulmonary tuberculosis in countries where tuberculosis is moderately endemic

Yoshinori Uchida, Kenzo Soejima

Department of Respiratory Medicine, University of Yamanashi Hospital, Yamanashi, Japan

Correspondence to: Yoshinori Uchida, MD. Department of Respiratory Medicine, University of Yamanashi Hospital, Shimokato 1110, Chuo-shi, Yamanashi, 409-3898, Japan. Email: youchida@yamanashi.ac.jp.

Comment on: Lee HY, Kang HS, Kang JY, *et al.* Clinical characteristics and survival of patients concurrently diagnosed with lung cancer and active pulmonary tuberculosis. *Transl Cancer Res* 2022. doi: 10.21037/tcr-22-272.

Submitted Jul 17, 2022. Accepted for publication Aug 08, 2022.

doi: 10.21037/tcr-22-1904

View this article at: <https://dx.doi.org/10.21037/tcr-22-1904>

There have been many reports of pulmonary tuberculosis (TB) being a risk factor for the development of lung cancer. Yu *et al.* reported that TB is a risk factor for the development of lung cancer and that comorbidity with chronic obstructive pulmonary disease and other smoking-related cancers may further increase the risk of carcinogenesis (1). Qin *et al.* identified inhibition of immune cells and cytokines, and induction of reactive oxygen species, DNA damage, C-reactive protein, overexpression of cyclooxygenase 2 and aberrant expression of immune inhibitory receptors as mechanisms by which mycobacterium TB induces tumorigenesis (2).

Clinical and imaging features of patients with TB and TB complicated with lung cancer have been reported. Patients with lung cancer and pulmonary TB have a higher proportion of irritable cough but less night sweating than patients with pulmonary TB alone. Compared with the patients with TB alone, patients with pulmonary TB and lung cancer showed a higher proportion of lobulation sign, mass, nodular shadow, satellite lesion, small vacuole sign, vacuole sign, spicule sign and pleural indentation, but a lower proportion of cord-like shadow and cavitary lesions (3). However, there is still a lack of information regarding the clinical picture when active pulmonary TB and lung cancer are diagnosed at the same time. In the latest issue of *Translational Cancer Research*, Lee *et al.* assess the clinical characteristics of patients with active pulmonary TB at the time of initial diagnosis of lung cancer, a point that may be of interest to readers (4).

In general, the presence of active pulmonary TB causes delay of close examination and treatment of lung cancer. Previously reported that the presence of active pulmonary TB in highly endemic countries worsens treatment outcomes for patients with lung cancer (5). On the other hand, the significance of co-existence of pulmonary TB and lung cancer in low-endemic countries is unclear, as there are only few reports of pulmonary TB and lung cancer complications in low-endemic countries. Contrary to the previous report, the prognosis of lung cancer was rather improved in the present study. Lee *et al.* assessed that the reason for this was that when lung cancer and active pulmonary TB were diagnosed at the same time, patients were closely examined and aggressively treated. The presence of pulmonary TB may also affect lung cancer staging. The simultaneous presence of TB and lung cancer lesions may lead to overestimation of the staging of lung cancer, as it is difficult to distinguish between lung cancer and TB lesions. This might have improved the prognosis of lung cancer patients with active pulmonary TB.

There are still several concerns with this study. The first concern is that the target and the control groups were collected in different ways in this study. A retrospective chart review was performed between January 2009 and December 2017 based on the International Codes of Disease 10th edition Clinical Modification (ICD-10-CM) to identify patients in the target group, and the control group was established using the Catholic Medical Center (CMC) lung cancer registry, collecting cases from the

same hospitals. The CMC lung cancer registry has been continuously enrolling lung cancer patients confirmed by tissue biopsy since October 2014, and the data for this review appear to have been collected in August 2019. Although it was described in the text that lung cancer patients were collected at the same hospital during the same period, there is no detailed description of the CMC lung cancer registry, which began enrollment in October 2014, which raises suspicion of a discrepancy in the enrollment period.

The second concern is that although this study was conducted at a time when several molecular-targeted agents and immune-checkpoint inhibitors (ICIs) were already on the market, information regarding status of driver mutations, programmed death-ligand 1 (PD-L1) expression and usage of molecular-target agents and ICIs was limited, which might affect lung cancer prognosis. The use of molecular-targeted agents was only reported for epidermal growth factor receptor (EGFR), but not for anaplastic lymphoma kinase (ALK), c-ros oncogene 1 receptor tyrosine kinase (ROS1), B-Raf proto-oncogene, serine/threonine kinase (BRAF), etc. Some of them were already available during the study period and might affect the prognosis. As mentioned by the authors, the expression status of PD-L1 and the use of ICIs should be investigated in future comparisons between lung cancer complicated with active pulmonary TB and lung cancer uncomplicated with active pulmonary TB.

It is easy to accept that the lower body mass index (BMI) in patients with TB is due to the presence of chronic inflammation caused by TB in this study. However, it was not discussed in the paper why the prognosis of lung cancer is better despite the low BMI, and it should be clarified.

Hwang *et al.* reported that a history of TB is an independent risk factor for lung cancer in Korea (6). During the period of this study, Korea was a moderately endemic country for TB according to the World Health Organization definition. The prevalence and drug resistance of TB vary from region to region, and the available health care systems for TB vary from region to region. It should be noted that the results would be different if the study was conducted in a region where the level of endemicity and medical care system was different from South Korea. This study is interesting because it reveals the characteristics of patients diagnosed with active pulmonary TB and lung cancer at the same time in a high-income country with well-developed medical care, and in a moderately endemic area for TB. Close examination and aggressive treatment of

patients with lung cancer complicated by active pulmonary TB is recommended.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Translational Cancer Research*. The article did not undergo external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-1904/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Uchida Y, Soejima K. Clinical characteristics of patients simultaneously diagnosed with lung cancer and active pulmonary tuberculosis in countries where tuberculosis is moderately endemic. *Transl Cancer Res* 2022;11(8):2480-2482. doi: 10.21037/tcr-22-1904