Younger, not better: No influence of age on lung cancer stage at diagnosis in South Africa

Lung cancer is the leading cause of cancer mortality worldwide, and has its peak incidence in the 7th and 8th decade of life. However, about 2 - 5% of all lung cancer cases occur in younger patients.[1-3] While what constitutes a 'younger' patient with lung cancer is not clearly defined in the literature, most studies define it as patients below 40 to 50 years in age. This subgroup of patients is currently a hot area of research interest for many reasons.

Firstly, from the human perspective, lung cancer among younger patients affects breadwinners and parents – in short, individuals in their socioeconomic prime. Their illness has major consequences for families, the wider community and the economy. Secondly, the biology of lung cancer in these patients may be different compared with their older counterparts. Younger patients generally have a much lower cumulative temporal exposure to the traditional carcinogens known to be associated with lung cancer, such as smoking and pollution. Molecular studies show that younger patients with lung cancer are more likely to have tumour genomic activating mutations in epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (*ALK*) and human epidermal growth factor receptor 2 (*HER2*) genes.[4-6] The potential for the use of driver gene specific drug therapy in this group of patients has important implications for prognosis and survival. It has also been suggested that the histological subtypes of lung cancer may be differently represented among younger v. older age groups. And lastly, there is a perception that cancer diagnosis in younger patients may be delayed because of a strong bias towards the consideration of other aetiologies (usually of an infective nature). The high prevalence of late-stage disease at presentation among younger patients has been reported in several studies, which have shown almost half of younger patients have metastatic disease at diagnosis.[7-9] A recent study[10] from Europe reported that 82% of younger patients had stage IIB/IV disease at diagnosis. These findings have obvious implications for survival; we can imagine that such proportions might be even higher in low-resource countries where infections such as tuberculosis (TB) and HIV are prevalent, where empirical treatment for TB is common, and where poor access to radiological and histological investigations is likely to be the norm.

In this issue of the *AJTCCM*, Mhlana and Koegelenberg[11] from the Division of Pulmonology at the University of Stellenbosch and Tygerberg Hospital report a retrospective comparison between patients younger and older than 45 years with lung cancer over a five-year period (June 2012 to December 2017). Of the total cohort of lung cancer patients, 4.8% were in the younger age group. Adenocarcinoma was the predominant histological subtype among non-small-cell lung cancer (NSCLC) in both groups, and there was no difference in the proportion of patients in either group presenting with advanced disease (stage IIIB to IV). Differences in gender, smoking status and mutational analysis (if available) were not presented.

Regardless of age group, these data make for sobering reading: overall, 93% of patients referred to the hospital with lung cancer already had advanced disease. In the 48 younger patients with NSCLC, only a single patient presented with early-state disease, and was treated with curative intent. As targeted therapy for NSCLC is unavailable in the public sector, further interrogation of the biology of these tumours is largely irrelevant. Sadly, this problem is not improving over time: a study from the same centre between 2008 and 2009 reported advanced disease in 89% of patients with NSCLC,[12] while an older report from 1987 at Groote Schuur Hospital in Cape Town also reported that 89% of patients with NSCLC were inoperable.[13] These findings emphasise the cumulative consequences of poor access to healthcare, incorrect diagnosis and delayed referral on lung cancer outcomes in South African patients, which as this study by Mhlana and Koegelenberg[11] shows, affect both younger and older patients indiscriminately.

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1. Gadgeel SM, Ramalingam S, Cummings G, et al. Lung cancer in patients <50 years of age: The experience of an academic multidisciplinary program. Chest 1999;115(5):1232-1236. https://doi.org/10.1378/chest.115.5.1232
2. Kuo CW, Chen YM, Chao JY, Tsai CM, Perng RP. Non-small cell lung cancer in very young and very old patients. Chest 2000;117(2):354-357. https://doi.org/10.1378/chest.117.2.354
3. Liu NS, Spitz MR, Kemp BL, et al. Adenocarcinoma of the lung in young patients: The M. D. Anderson experience. Cancer 2000;88(8):1837-1841. https://doi.org/10.1002/(sici)1097-0142(20000415)88:8%3C1837::aid-cncr12%3E3.0.co;2-e
4. Hou H, Zhu H, Zhao H, et al. Comprehensive molecular characterisation of young Chinese patients with lung adenocarcinoma identified a distinctive genetic profile. Oncologist 2018;23(9):1008-1015. https://doi.org/10.1634/theoncologist.2017-0629
5. Pan X, Lv T, Zhang F, Fan H, Liu H, Song Y. Frequent genomic alterations and better prognosis among young patients with non-small-cell lung cancer aged 40 years or younger. Clin Transl Oncol 2018;20(9):1168-1174. https://doi.org/10.1007/s12094-018-1838-z
6. Sacher AG, Dahlberg SE, Heng J, et al. Association between younger age and targetable genomic alterations and prognosis in non-small-cell lung cancer. JAMA Oncol 2016;2(3):313-320. https://doi.org/10.1001/jamaoncol.2015.4482
7. Liu B, Quan X, Xu C, et al. Lung cancer in young adults aged 35 years or younger: A full-scale analysis and review. J Cancer 2019;10(15):3553-3559. https://doi.org/10.7150/jca.27490
8. Rich AL, Khakwani A, Free CM, et al. Non-small cell lung cancer in young adults: Presentation and survival in the English National Lung Cancer Audit. QJM 2015;108(11):891-897. https://doi.org/10.1093/qjmed/hcv052
9. Subramanian J, Morgensztern D, Goodgame B, et al. Distinctive characteristics of non-small cell lung cancer (NSCLC) in the young: A surveillance, epidemiology, and end results (SEER) analysis. J Thoracic Oncol 2010;5(1):23-28. https://doi.org/10.1097/JTO.0b013e3181c41e8d
10. Bigay-Game L, Bota S, Greillier L, et al. Characteristics of lung cancer in patients younger than 40 years: A prospective multicenter analysis in France. Oncology 2018;95(6):337-343. https://doi.org/10.1159/000489784
11. Mhlana NA, Koegelenberg CFN. The impact of age of presentation on lung cancer staging. Afr J Thoracic Crit Care Med 2020;26(2):29-31. https://doi.org/10.7196/AJTCCM.2020.v26i2.045
12. Koegelenberg CF, Aubeelack K, Nanguzgambo AB, et al. Adenocarcinoma the most common cell type in patients presenting with primary lung cancer in the Western Cape. S Afr Med J 2011;101(5):321. https://doi.org/10.7196/samj.4554\
13. Willcox PA, O'Brien JA, Abratt RP. Lung cancer at Groote Schuur Hospital – a local perspective. S Afr Med J 1990;78(12):716-720.