RE: Time to Smoke First Morning Cigarette (TTFC) and Lung Cancer in a Case-Control Study

In the recently published article “Time to Smoke First Morning Cigarette (TTFC) and Lung Cancer in a Case-Control Study” by Gu et al. (1), the authors demonstrate that a shorter TTFC leads to an increase in lung cancer risk for smokers. Summarizing two larger case-control studies, they determined the risk of developing lung cancer (LC) to be 2.45 times (95% confidence interval [CI] = 1.18 to 5.09) greater in strongly addicted smokers who smoke immediately after getting up than in smokers not consuming tobacco in the morning. They conclude that TTFC is a novel and substantial determinant of lung cancer, easily obtained and therefore useful in both clinical and research in addition to the well-established pack-year.

However, regarding TTFC as a risk factor in LC, which is also addressed by the Fagerström test for nicotine dependency (2), is contrary to the common paradigm of the association between smoking quantity and lung cancer: “nicotine is addictive, but tar content is harmful.” Based on two extensive systematic reviews of the complex relationship between smoking and LC comprising 287 studies from the 1900s (3,4), Lee et al. argued inter alia that LC risk is associated with higher tar content and to shorter cigarette butt lengths. Moreover, the risk of LC was 23% lower in lower-tar than in higher-tar smokers, even when adjusting for smoking behavior measures.

Therefore, I would like to add a possible explanation of the observed risk increase to the discussion. The authors report having applied logistic regression adjusted for a number of variables related to smoking behavior, such as smoking intensity, duration, pack-years, quitting, and age at smoking initiation. However, they did not adjust for any quantity related to the content of the carcinogenic substances in the inhaled smoke. Because cigarette tar and nicotine yields are highly and linearly correlated (5,6), it is likely that those more strongly addicted tend to smoke more harmful cigarettes. As a consequence, the observed association of TTFC to lung cancer risk may be spurious and caused by insufficient quantification of tar exposure by measures of smoking behavior. This can be substantial, since the plasma nicotine concentration in fresh blood samples increases with the nicotine and the tar yield of the smoked tobacco blend, but decreases with the number of cigarettes smoked per day (6).

Given this relationship and regarding the observations presented by Gu et al. (1), from another point of view, one may become aware of the undeniable deficit when reducing the quantification of smoking-related harm to smoking behavior. TTFC should rather be viewed as a surrogate measure of disregarded tar exposure than as a complementary risk-related factor.

Taking this into account, one may conclude that it is of greater advantage to incorporate tar exposure into the calculation of pack-years instead of incorporating TTFC in risk stratification. One can easily obtain this by asking, “What is your favorite tobacco blend?”

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References


Note

The author has no conflict of interest to declare.

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