Can Lung Cancer be Clinically Insignificant? The Case for “Overdiagnosis” and “Overtreatment” of Lung Cancer

For all too many people with lung cancer or caring for someone with it, the concept that lung cancer may not be threatening may seem sacrilegious. It is, after all, by far the leading cause of cancer deaths in the US in both men and women, far ahead of both breast cancer and prostate cancer in its fatality rate, though breast cancers and prostate cancers are more commonly diagnosed in women and men respectively. Yes, lung cancer is far more deadly than those two cancers, but both breast and prostate cancer are diagnosed in tens of thousands of people who aren’t truly threatened by it. The world has been slow to recognize that lung cancer can also sometimes be minimally threatening, but it’s worth discussing that possibility. And it shouldn’t lead us to minimize the danger of lung cancer any more than we should become complacent about handling deadly snakes just because there are some that are are perfectly safe. In the real world, a far greater proportion of lung cancers than snakes are deadly, but the main idea is that we should consider each based on individual characteristics. It is absolutely possible to “over-treat” a lung cancer.

This issue became newsworthy because of a new article in JAMA Internal Medicine that did a very complex calculated analysis (i.e., I didn’t understand it) of the lung cancers detected in the National Lung Screening Trial (NLST) and concluded that

18.5% of the lung cancers detected by chest CT screening and 22.5% of non-small cell lung cancers represented an “overdiagnosis” — a cancer that was detected but that would not be clinically relevant (as the numbers reflect, this is rarely a concern for small cell lung cancer). For bronchioloalveolar carcinoma (BAC), which is often indolent (and especially likely when detected as a solitary lesion), up to nearly 80% of these lesions were potentially overdiagnosed cancer.

As someone who sees the clinical behavior of hundreds of cases of lung cancer ever year, I’m here to tell you that this seems about right. This doesn’t mean that I don’t believe in CT screening for lung cancer: the NLST trial showed a 20% improvement in lung cancer-specific survival, which to me illustrates that screening for lung cancer is valuable. But it’s also worth knowing two things:

1) Not all lung cancers are life threatening.

2) There is a real risk of overtreating some lung cancers, causing more harm than benefit by treating it.

How might this happen? First, the truth is that very small lung nodules, especially nodules biopsied as showing BAC or designated in a new terminology as adenocarcinoma in situ (AIS), meaning that it’s a pre-cancerous lesion, pose an extremely minimal threat to survival over the next 5-10 years. It’s worth clarifying whether they are growing, whether they are growing at a meaningful rate (can you see a change over 6 months, or does it take 2 years for it to grow a millimeter in diameter?), and whether the threat of the cancer is a realistic concern relative to a
patient’s other medical problems. If I see a lesion grow from 8 to 14 mm in 6 months, that’s a lesion that should be resected. But I will tell you that there are many 78 year old patients with heart disease “saved” from a cancer growing from 8 to 9 mm over 18 months. That’s like saving someone from a box turtle approaching from two blocks away. And for the lung cancer, that involves a surgery in which the risk from anesthesia and the cancer itself probably exceeded the risk from the cancer over the next 5 years.

Though not relevant to screening, this also comes up in multifocal/advanced lung cancer. Most lung cancers progress at a rate that is a real threat, but a minority grow slowly enough that the risk and side effects of the treatment exceed the symptoms of the cancer over the foreseeable future. This is more likely for BACs, but other lung cancers can be quite indolent, and we get a hint of this when we see that a patient feels well and hasn’t had a real change in their cancer over scans done a few months apart.

My key point is that it’s important to tailor the treatment to the individual patient’s cancer. Even with lung cancer, we need to ensure that the treatment is appropriate for the disease, and there is a potential risk of overtreatment and not just undertreatment.

What do you think? Do you find this believable, or is it too hard to imagine such a thing as a non-threatening lung cancer?