Editorial

Analyzing competing risks in the treatment of lung cancer: a good start

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With the advent of low-dose computed tomography for lung cancer screening, it is expected that more lung cancers will be diagnosed at an earlier stage. Currently, the United States Preventive Services Task Force (USPSTF) recommends screening for patients aged 55–80 years with at least a 30 pack year history of smoking (1). The age cutoff of 80 years is due to the presumption of decreasing benefit of screening for older patients, yet recent data may call into question the sensibility of a firm age cutoff. As part of these recommendations, the USPSTF calls for shared decision making with a thorough discussion of the potential risks and benefits of screening. Similarly, shared decision making is essential for developing a treatment plan after lung cancer has been diagnosed. Shared decision making is one of the fundamental tenets of patient centered care, but it requires an understanding of the risks, benefits, and alternatives of a proposed treatment (2).

To that end, Eguchi and colleagues have made an important contribution to our understanding of the potential benefits and risks of surgery for the treatment of early stage lung cancer (Stage I) (3). In a competing risks analysis, they found that with increasing age, the risk of surgery increased and noncancer-specific causes of death after surgery became more significant. In patients ≥75 years of age, the 5-year lung cancer-specific cumulative incidence of death (CID) was 13% compared to 9% for the noncancer-specific CID. In contrast, patients <65 had a 5-year lung cancer-specific CID of 7.5% *vs.* only a 1.8% noncancer-specific CID. The 90 day mortality rate for patients ≥75 years was 2.2% compared to just 0.6% for patients <65 years. This is despite the fact that older patients were more likely to undergo sublobar resection. The 5-year overall survival for the younger age group was 85% *vs.* 64% for the older group.

The results have great relevance for clinicians who are challenged with treating an aging population. The majority of lung cancer patients in the United States are older than 65 and the median age at diagnosis is 70 (4). The study by Eguchi and colleagues helps to quantify the competing risks that patients face when confronted by the immediate danger of a known lung cancer *vs.* the slow, but inexorable risks of old age. Yet the study also illustrates that to some degree, clinicians and patients already balance competing risks. In the real world, multiple levels of patient selection exist. Primary care providers decide which patients should be offered lung cancer screening (5). A pulmonologist or other specialist may initially see a patient before referring the patient to a surgeon. The thoracic surgeon then makes a recommendation regarding surgery. The patient ultimately self-selects by deciding whether to undergo surgery.

In the United States, more than a quarter of patients with early stage lung cancer do not undergo resection (6). The excellent outcomes reported from Memorial Sloan Kettering likely reflect not just superb surgical technique, but patient selection. Surgery was likely not offered to many patients who were too ill to benefit from resection. In the study, older patients were also more likely to undergo sublobar resection despite the fact that sublobar resection was associated with a significantly higher 5-year lung cancer-specific CID (14% *vs.* 9.3%). Perhaps more tellingly,

sublobar resection was also associated with significantly higher 5-year noncancer-specific CID (8.3% *vs.* 4.1%). Patients who underwent sublobar resection were older, sicker, and more likely to die of a noncancerous cause within 5 years of surgery. With the increasing use of ablative therapies, such as stereotactic ablative radiotherapy, it is likely that more marginal surgical candidates who would have previously undergone sublobar resection will now opt for ablation.

The results from Eguchi and colleagues should also be interpreted within the context of the actuarial survival for age matched controls. An analysis of the United States population yields an expected 5-year overall survival of 80–84% for 75-year-olds in the general population (7). In the group of patients ≥75 years and older, the overall survival was 64%, but lung cancer-specific deaths accounted for over 30% of deaths within 5 years for that cohort. If lung cancer deaths were eliminated from the group, the overall 5-year survival might be expected to be closer to 75%, which is similar to the general, age-matched population. The data from the study also reinforces the importance of personalizing care. There were clearly many older patients who benefited from surgery for many years and there were also a few younger patients who succumbed to a noncancer-specific cause of death, thus not realizing the full benefit of their cancer therapy. As the authors demonstrate, a multitude of factors aside from age contribute to long term survival, including pulmonary function and cardiovascular disease. Thus, a more complete assessment of the patient contributes to a more accurate view of the competing risks.

The data about competing risks is important because it helps quantify the potential risks and benefits of surgical treatment of lung cancer and part of that is understanding the increasing likelihood for older and sicker patients that they may be cured of their lung cancer only to die of another cause within a few years. Although this information is necessary for shared decision making, it is not sufficient, because it tells only half the story. What is equally important to patients is the long term impact of treatment on quality of life (8). A common measure of the benefit of a treatment is the number of quality-adjusted life years gained by the intervention. Although the study by Eguchi *et al.* gives us more information about the impact of age on the potential life years gained, it does not speak to the quality of those years. Lung cancer patients begin treatment with compromised quality of life at baseline, reporting higher levels of distress, anxiety, fatigue, and breathlessness compared to other cancer patients. A growing body of literature demonstrates that lung cancer surgery can exacerbate these issues and cause long-term impairments in multiple domains of quality of life (9). Particularly for older patients, these quality of life issues are just as important as extending life. Yet, we have much less quality of life data because these endpoints remain less prioritized for funding and for publication. A competing risks analysis of quality of life in patients with early stage lung cancer is needed so that we can understand the quality of life for patients who undergo lung cancer surgery, those that undergo alternative treatments, and those who don't undergo any treatment. With a more complete understanding of all the risks, we can then move toward truly patient centered care.

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Footnote

Conflict of Interest: The author has no conflicts of interest to declare.

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