Elderly patients with stage I-III non-small-cell lung cancer (NSCLC) constitute a peculiar patient population and need specific therapeutic approaches. Limited resections are an attractive alternative for elderly patients with resectable NSCLC because of the potential reduction in postoperative complications. Curative radiation therapy is an acceptable alternative for elderly patients who are unfit for or refuse surgery. Hypofractionated stereotactic body radiation therapy is of particular interest for this population because of its favorable tolerance.

The paper by Gridelli and colleagues nicely covers the landscape of local lung cancer management in the elderly, but it fails to define exactly "elderly" means. Under the scholarly words is the quiet assumption that somehow old people are different. The truth of the matter is that hale and hardy older people do just as well with standard treatments as their younger counterparts. Even some people with controlled comorbidities appear quite well, so performance status alone does not reveal the truth about treatment tolerance. We all know that out-of-control or marginal comorbidities make treatment in any age group a challenge.

Some clinicians have simplified this problem by counting the patient's medications, and once they surmount seven, declaring the person "comorbid." (Since it takes me an hour each month to sort my own multiple medications, I'm defeated by this method!) The problem with those over age 70, and more so in those over age 80, is that many who appear fit have too little reserve, which we have no way of knowing. Their pulmonary function tests and chemical profiles do not lie, but we can be misled by those that offer no complaints and seem fit as a fiddle.

On the other hand, just because someone is 80 does not mean that they cannot withstand aggressive treatment. Much depends on what superannuated folks expect and what we are willing to provide. Unlike those of us baby boomers in later middle age, many at 80 are wiser about risking morbidities and more fatalistic about disease. Those who take care of the old need to be more vigilant than usual—one cycle of chemotherapy may remove this last veil hiding all of the wrinkles and warts of old age that our sophisticated tests missed.

Regardless of what definition of elderly we agree upon, one must inform patients of the risks of aggressive treatment and the penalties of allowing nature to take its course. Too often the option of doing no intentional harm provides the unintended consequence of cancer left untreated.

Early-Stage Disease
Most suggest that surgery provides the "best option" for cure for patients with lung cancer. Thoracotomy and pneumonectomy are assaults that may seem to offer the best chance of cure for the very fit, but sometimes at a price, especially in the elderly. All operations have some associated mortality, which is regularly measured in the young and extrapolated to older populations. Gridelli and coauthors comment on video-assisted thoracic surgery (VATS) and its lesser morbidity. Wedge resections and segmentectomies are compromises used for patients with limited pulmonary function. These compromises seem rational when one sees the small differences in survival and balances those against the risks of operative mortality.

Data from surgical trials always represent patients selected for their apparent fitness to undergo surgery. Comparisons to groups that do not undergo surgery and seem matched in age or tumor factors are never lined up with comorbidities. Surgical techniques now include robotic arms that allow for smaller incisions and less morbidity, but all of these cases must be fit enough to undergo thoracotomy if something goes wrong.

At the International Association for the Study of Lung Cancer (IASLC) meeting in Barcelona this past July, the two hottest topics were dealing with target motion[1] and the medically inoperable patient.[2-4] In the latter setting, the issues of dose, target, and fractionation (dose/time) are each
different from that in classic use. Doses have been both precipitously[5] and cautiously escalated[4] with attention to targets that do not include elective nodes that markedly increase normal tissue exposure. When elective mediastinal irradiation is omitted—a prospective tactic used in the Michigan dose-escalation trial—esophagitis disappears,[6] and the higher doses appear to result in improved local control and survival. Although doses were escalated to over 100 Gy, pneumonitis of consequence (grade 3) was a rare event.[7] Following this lead and cautiously escalating the dose per fraction from 2.1 to 2.3 Gy but fixing total radiation treatment time to 7 weeks, survival and local control using doses of 80.5 Gy become competitive.[4] With impetus from early studies by Uematsu from Japan[8] and moved swiftly forward by Timmerman and McGarry,[9] very large dose per fraction (20 Gy) and remarkably short treatment periods (1 week to deliver 60 Gy) have been shown to produce impressive local control and very little acute morbidity. On a cautionary note, the follow-up for these studies is very short; the dose-escalation series have few patients followed for more than 36 months. These enormous fraction sizes—larger than those used with Gamma Knife ablations—may obliterate cancer, but may not differentiate from any normal tissues encompassed in the high-dose treatment volume. As a result, tubes (blood vessels, bronchi, and esophagi), wires (phrenic and recurrent laryngeal nerves and the spinal cord), and pumps may develop holes and dysfunction with longer follow-up. Nevertheless, radiation treatment may become a legitimate contender and alternative treatment for those who wish to avoid operative risk. Cryotherapy and radiofrequency ablation may also turn out to be treatment options that can be accomplished in one day.

Locally Advanced Disease

Nodal involvement implies that the tumor has a genetic package providing a capability of invasion, locomotion, evasion of the immune system, angiogenesis, and the ability to metastasize. Twentieth century radiation therapy was devoted to targeting nodal spread, but today we need to define the benefit vs the liability of treating nodes that are not overtly involved, understanding that nodal involvement predicts for systemic spread and brain metastasis. These axioms are true for elderly and young patients alike. The ability to tolerate chemotherapy may not be the same for both groups, but we have hard evidence that younger patients with poor performance status tolerate systemic multiagent therapy poorly.

The eagerly awaited and aggressively marketed targeted therapies have advantages: They seek a specific tumor-associated pathway and usually predict for less systemic toxicity. Until we have studies comparable to the head and neck trial clearly showing a benefit for cetuximab (Erbitux) and radiotherapy over radiotherapy alone,[10] we will need to embrace systemic agents with their attendant toxicities. Dr. Gridelli’s group has led us with findings suggesting that fewer drugs are better than more.

The challenge is to construct trials with single variables for relatively homogeneous patients. Trying to define homogeneity in an older population with perfectly good function on paper but that really has marginal bone marrow, renal, or hepatic functional reserves may be quite difficult. As to treatment tactics with combined-modality therapy, despite indications supporting the use of concurrent therapy, the benefit is quite small and the price may be substantial. A sequential approach may be more plausible, with either modality used first. Today, either modality alone seems too timid an approach. However, many patients in the older category might opt for timid, even after consequences are clearly outlined.

Palliation

The use of single-fraction radiotherapy is now an evidence-based strategy for bony metastasis, supported by three randomized trials from abroad and in the United States. An editorial on the subject seriously quipped that some clinicians practice remuneration-based rather than evidence-based medicine. While the data provide solid evidence for such treatment of bony metastasis including spinal cord compression, it also seems prudent to offer 8 to 10 Gy for many problems requiring urgent relief—hempoptysis and airway occlusion are examples that come to mind—rather than protracted futile treatment for the ventilator-bound or telemetry patient. In conclusion, once we carefully look at what might be best for older people, we acknowledge that there are too few trials that include this population, so stretching data from general population trials to this vulnerable group has hazards. Paternalistically deciding what's best without their input and their support network being informed may be equally wrong. As always, we can learn from our elders if we approach them appropriately and with a degree of humility about how little we know. We
should remember not only to do no harm, but also to honor our parents. Go forth and conduct some trials to provide some guidance! When there is evidence, we are likely better off to heed it than explain it away.

—Andrew T. Turrisi III, MD

Disclosures:
The author has no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.

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