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Limited Resection vs. Radiation for Marginal Patients with Early Stage NSCLC

The standard of care for at least stage I and II NSCLC is surgery, sometimes followed by chemotherapy. We know, however, that not every patient who presents with early stage NSCLC is healthy enough to pursue surgery, whether due to general age-related or other illnesses, or due specifically to a low pulmonary reserves, usually from years of smoking. As our population ages and the median age of newly diagnosed lung cancer patients crosses 70, this is likely to become a bigger issue, but unfortunately we haven’t got a lot of information on the best way to treat sicker patients who are on the border of safety and feasibility for standard surgery for lung cancer. I’ve described in a prior post that there is some evidence that older patients may do as well with a limited, smaller resection (the different types of surgery described in another prior post). Otherwise, we know that many patients who are marginal for surgery are recommended to receive radiation instead. Perhaps not surprisingly, the survival results of patients with early stage NSCLC who receive radiation are not as favorable as the results with surgery, stage for stage.

While one explanation for this may be that surgery is just more effective in curing early stage lung cancer than radiation, there are some confounding issues. One is that it’s not uncommon for the patients who undergo surgery to be found to have involved lymph nodes or other findings at surgery that increase their stage. In contrast, patients who never undergo surgery may have those same lymph nodes or other findings but never be properly staged pathologically, so they would potentially be considered a stage I patient but really be a stage II or III if surgery had been done and could detect occult cancer involvement. Probably more important, though, is the fact that the vast majority of patients who receive radiation have been recommended to not receive surgery, presumably because they were felt to have too many competing risks and to not be healthy enough to pursue the rigors of surgery. Therefore, we’re really talking about two different populations of patients, one likely appreciably healthier than the other, so it shouldn’t be surprising that the excluded group does less well.

There are some novel radiation approaches that have been developed over the past several years that may serve as alternatives to surgery for some patients with early stage NSCLC, so it would be great to really know how advantageous surgery is vs. a non-surgical approach in marginal resection candidates. What would really answer the question is a randomized trial of borderline patients to receive either surgery or radiation. Well, dream on, because that’s not happening. At least in the US, it’s nearly impossible to imagine doctors and patients accepting a randomization to either surgery or non-surgery — it’s very difficult to do such randomizations in a system where people are used to having much more control.

In the absence of such a trial, perhaps the best we can get is a report such as the one recently published by Yendamuri and colleagues from the thoracic surgery and radiation oncology divisions at MD Anderson Cancer Center in Houston, TX (abstract here). Now, MD Anderson is a huge cancer center, and to their credit they review their large volume of prior clinical experience to glean useful information that couldn't be obtained almost anywhere else. In this report, they reviewed the survival of 160 patients with stage I NSCLC over the period from
1988 through 2005 who received either a limited resection or modern radiation therapy (RT) with “3-D conformal radiation”, basically a limited radiation approach with tight borders that allowed for high doses to be given to the cancer and minimal damage to surrounding tissues (basically a similar approach to limited surgery, but with RT). They ended up with 68 who received surgery and 92 who received radiation, and, as you would expect, the radiation group on average had a worse performance status, as well as a larger tumor size (2.8 vs. 2.2 cm) than the folks in the surgery group.

First, looking at all of the data for both groups, they found that older patients did less well than younger ones, those with larger tumors did less well than those with small tumors, women did significantly better than men, and those who had surgery lived significantly longer and were significantly more likely to go on without recurrence than patients who had surgery:

(Click image to enlarge)

While you might conclude that these findings clearly demonstrate that marginal patients do better with surgery, the investigators recognized that this was a retrospective review of patients who chose or were recommended for one approach or another. The patients getting RT had larger cancers and were much, much more likely to have a poor/marginal performance status than the patients who went to surgery. So the researchers matched similar pairs of patients with several variables identical within the pair. Looking only at stage IA patients (again, to keep as many variables controlled as possible), they matched for age, sex, tumor size, histology (squamous vs. non-squamous), and performance status. And when you compare patients with very similar characteristics to each other, there was no difference in outcomes between those receiving limited surgery and those who underwent radiation:
At the end of all of this, there were only 34 matched pairs, so even starting with an 18-year experience from the biggest cancer center in the US (world, too, I think), these results aren’t the definitive word. But they do suggest that when we compare apples to apples as best we can, you actually achieve similar results from limited surgery or good radiation in marginal candidates for surgery. This may be the best answer we’re going to get for a long while.

There have also been some interesting new developments in techniques for radiation, particularly for earlier stage patients, and I’ll cover some of that emerging work in upcoming posts.