Salvage radiotherapy may be of benefit to more men with a prostate cancer recurrence after radical prostatectomy than commonly believed, according to a study published in *JAMA* (2004;291:1325–1332). Researchers found that even some men with aggressive disease responded to treatment under certain circumstances.

Although previous studies of salvage radiotherapy have had mixed results, principal investigator Kevin Slawin, MD, said his findings “confirm a notion that’s already been out there.”

“What’s novel and important is that even men who had a short prostate-specific antigen (PSA) doubling time or aggressive high-grade disease, even a large number of those men are curable,” said Slawin, a Professor of Urology at Baylor College of Medicine. “Standard belief was that those men were destined to progress, and radiation couldn’t be of help.”

Mack Roach III, MD, Professor of Radiation Oncology, Medical Oncology, and Urology at the University of California, San Francisco, agreed that the benefits of salvage radiotherapy for high-grade prostate cancer are not widely appreciated.

“Some people think if you have a high-grade tumor there’s no point,” said Roach, who was not involved in the study. “I’ve had patients who’ve done very well with treatment despite having high-grade tumors.”

Slawin and his colleagues conducted a retrospective review of 501 men who had undergone salvage radiotherapy after radical prostatectomy, searching for clinical characteristics that might help predict which men were more likely to respond to the radiation treatments. Not unexpectedly, they found that men with lower preradiation PSA levels (below 2.0 ng/mL) and low Gleason scores (between 4 and 6) were most likely to respond to the salvage radiotherapy.

But even some men with more aggressive disease responded to the treatments, as long as they were given early in the course of the recurrence, before PSA levels had reached 2.0 ng/mL.

“The better results when [radiation] is given early aren’t widely known yet,” said Slawin.
Involvement of surgical margins of the prostatectomy specimen also appeared to be an important factor in the success of the salvage radiation. Men with positive margins were more likely to respond to radiotherapy, even if they also had high-grade disease. That’s because in such men, rising PSA levels are likely caused by residual cancer in the pelvis, Slawin and colleagues wrote; in men with negative surgical margins, rising PSA is more likely to be caused by metastatic disease.

Roach cautioned, though, that clear surgical margins alone shouldn’t be used to disqualify someone from salvage radiotherapy.

“Whether a margin is positive or negative can depend a lot on who’s looking at the margins,” he said, suggesting that some pathologists may sample the prostatectomy specimen’s margins more completely than others. “I wouldn’t want people to reach the conclusion that if a patient doesn’t have positive margins, he won’t benefit from treatment.”

Slawin said his findings suggest that a greater proportion of men who have a recurrence initially have localized disease. Based on the calculated four-year probability (45%), he estimated that 52% of patients with rising PSA levels after surgery fall into this category.

Yet most patients who receive secondary treatment after radical prostatectomy are given hormonal therapy, which is not curative, he wrote. Fewer than half receive salvage radiotherapy.

“I think currently not enough men are being offered this therapy,” Slawin said. “It seems that more men are good candidates.”

The study could give physicians and patients a more reliable estimate of what to expect, based on clinical parameters, if they’re considering the treatment, he added.

Roach said the study also gives researchers a framework to design future trials in hopes of further improving outcomes for men in this situation.

TREATMENT OF DCIS VARIATES WIDELY

Treatment of ductal carcinoma in situ (DCIS) varies widely across the United States, according to a study in the *Journal of the National Cancer Institute* (2004;96:443–448) that examined treatment trends between 1992 and 1999. Nancy Baxter, MD, PhD, and colleagues from the University of Minnesota, reported that substantial numbers of women might be getting overly aggressive treatment or potentially inadequate treatment for this earliest stage of breast cancer.

She and her colleagues analyzed treatment data from 25,206 DCIS patients from the National Cancer Institute’s Surveillance, Epidemiology, and End Results database. The discrepancies they found point to a need for greater consensus on how best to manage the disease, said Baxter, who is Assistant Professor of Colon and Rectal Surgery and Surgical Oncology at the University of Minnesota.

“The problem is there’s such variation in terms of the disease,” Baxter said.

Although DCIS is by definition not invasive, it can nonetheless manifest as a very large lesion or as multicentric tumors in different quadrants of the breast. Women with large or multicentric tumors may require mastectomy, while most with small lesions are candidates for breast-conserving surgery. DCIS has the potential to progress to invasive breast cancer, but there is currently no good way to predict which women face this risk and which do not.

Still, treatment has evolved in recent years. Baxter and colleagues found that rates of mastectomy for DCIS decreased from 43% in 1992 to 28% in 1999. Thirty percent of women treated by mastectomy in 1999 were also getting axillary dissection, a procedure rarely indicated for DCIS treatment, Baxter said.
More worrisome, though, was the number of women who did not receive radiation after lumpectomy, Baxter said. Radiation has been shown to reduce the risk of recurrence in women with DCIS, yet over the course of the study, about half the women treated with lumpectomy did not receive subsequent radiation (55% in 1992; 46% in 1999).

About 33% of women with comedo histology did not receive radiation after lumpectomy in 1999, even though, Baxter said, “most people can agree that women with adverse risk factors should have radiation.”

Baxter and colleagues reported substantial geographic variation in rates of radiation after lumpectomy, ranging from about 39% in San Francisco to 74% in Hawaii, and suggested that “... selection of patients for breast-conserving therapy without radiation therapy cannot be explained solely on the basis of unmeasured tumor characteristics.”

Such variations in treatment don’t necessarily mean that bad practice is rampant, said Monica Morrow, MD, who wrote an editorial accompanying the study.

“When you see wide variation in practice, it means there is not a single right answer, and patient and physician preferences come into play,” said Morrow, Professor of Surgical Oncology at Northwestern University’s Feinberg School of Medicine. “Local physician leaders do have an impact on issues where there’s not a clear-cut answer.”

Because of the nature of DCIS, mastectomy may be the only treatment option for some women. In other cases, risk-averse women may choose mastectomy over lumpectomy.

For some women, the magnitude of benefit from radiation may not be worth its side effects. Studies that examine women’s perceptions about their treatment experience could help doctors understand some of the existing treatment discrepancies, Morrow said.

“What we need to be concerned about is, are women being offered the appropriate treatment option,” she added. “We need to help women understand that their treatment is geared to the prevention of a life-threatening disease, invasive breast cancer. Women with DCIS think their risk of dying is the same as that of a woman with invasive breast cancer, but it’s not.”

Baxter agreed that educating patients about DCIS is difficult. Ten-year survival of DCIS is estimated at close to 98%, but many patients miss that message.

“When you tell someone they have DCIS, even though you try to explain it, you see the fear in their eyes,” Baxter said. “We need to find better ways of communicating about the disease and the excellent prognosis.”

Getting a second opinion on treatment may also be helpful for some patients, Baxter said.

“We have a high rate of variation in care,” she said. “As professionals, we need to admit that and empower patients to get a second opinion about treatment. I think people perceive that as threatening their doctor, but if someone wants a second opinion, it’s better for them to get it than to have lingering doubts about their treatment.”

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