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Prostate cancer management shows major shifts in PSA era

By Laszlo Dosa

Lap RP and LHRH therapy are increasingly popular, while watchful waiting has declined

Orlando, FL—The management of localized prostate cancer has undergone a significant, dramatic shift in recent years. Both pure and robot-assisted laparoscopic prostatectomy appears to be a viable treatment option that is popular with patients; watchful waiting has declined, despite the stage migration seen in the PSA era; and hormonal therapy has become more widely used in low-risk patients, a source of controversy.

Dr. Sandler

These were among the trends in prostate cancer management discussed by experts at a session of the 2005 Multidisciplinary Prostate Cancer Symposium.

"The treatment each patient selects varies quite a bit by the age of the patient," said Howard M. Sandler, MD, professor of radiation oncology at the University of Michigan, Ann Arbor, re-viewed the session in an interview with *Urology Times*.^{Dr. Labrie}

Younger patients tend to have surgery because they suffer fewer side effects from the operation itself, while older patients are more likely to undergo radiation therapy—either external beam or brachytherapy. Traditional open radical prostatectomy seems to be the surgery of choice, although there is growing interest in the laparoscopic procedure.

Lap RP: Upsides, downsides "Recovery is much quicker so that patients have less time off work, they have fewer postoperative restrictions and less postoperative pain with the laparoscopic procedure, compared to conventional open prostatectomy," Dr. Sandler said of the increasing popularity of laparoscopy.

Dr. Kane

"But there are two downsides. One is that the operation itself takes longer, so patients are in the operating room longer. And second, the technique is potentially associated with a higher rate of impotence than open prostatectomy if excess cautery is used. Nevertheless, patients often prefer that minimally invasive surgical approach, and so it is a frequently used surgical procedure where robotic technology is available," Dr. Sandler said.

Hormonal therapy was discussed by endocrinologist Fernand Labrie, MD, PhD, a pioneer of that treatment modality for prostate cancer, who is head of the Oncology and Molecular Endocrinology Research Center at Laval University in Quebec City, Canada.

Hormonal castration is not always sufficient because 30% to 50% of the male hormones are left behind and continue stimulating prostate cancer. Recognition of that problem led Dr. Labrie to the discovery that adding antiandrogens enhances the effect of LHRH treatment. Randomized studies have shown the benefits of hormone blockade in prostate cancer and resulted in a one-third reduction of death from prostate cancer at 10 years, he said, referring to a meta-analysis by Prof. Richard Peto, FRS, using monotherapy or treatment limited to blockade of the secretion of testicular androgens.

"Even with combined androgen blockade, if you treat for 1 year and then stop, the cancer comes back right away, the PSA comes back right away as soon as you stop the treatment," Dr. Labrie noted. "If you treat for 5 years with a combination of castration (LHRH agonist or surgery) with a pure antiandrogen, it's about 50/50. So in half of the cases, the PSA remains undetectable, indicating that the cancer is probably cured. But if you want to go to 90%, you have to treat for 7 years. If you need to treat for that long period, it means that...short-term hormone therapy is not enough and if hormone therapy is used, it should be combined blockade of androgens. You need to treat for years."

Side effects a concern Many experts consider that data to be not definitive, and there is concern that the side effects of hormonal therapy are substantial, especially in older men. Dr. Sandler suggested that many prostate cancers would be better served by observation. In the same vein, Dr. Sandler said it is critical to identify those patients whose prostate cancer has been detected and need treatment, and those who have prostate cancer detected and can be monitored without undergoing treatment.

"Not everyone with a diagnosed prostate cancer needs aggressive treatment, and I hope that in the future we will be able to identify which patients need treatment and which ones do not need treatment," Dr. Sandler said. "I am optimistic that genetic tumor testing will provide an insight into those patients who have genetically aggressive tumors, versus those who have genetically benign tumors. I think it will be available in the near future."

"However, for the time being, there is no satisfactory means of identifying with certainty when cancer is no threat to the patient's life," said Dr. Labrie, "thus suggesting to be on the safe side and thus avoid metastases to the bones where possibility of cure is lost."

CaPSURE: Tracking PCa trends An important instrument for monitoring prostate cancer is CaPSURE, a national data registry at the University of California, San Francisco. It provides a snapshot of where prostate cancer treatment has been, where it is today, and even perhaps where it is heading in the future.

"As we look at trends over time, [CaPSURE] summarizes a remarkable stage and PSA migration in the PSA era," said Christopher Kane, MD, associate professor of urology at UCSF. "Today, patients presenting with a much lower PSA than in the early 1990s are more likely to have clinical stage T1 disease. As many as 50% of the patients currently have T1 disease. That's much greater than early in the PSA era. And patients presenting with advanced disease are much less common than early in the PSA era."

The CaPSURE database summarizes outcomes with 12,000 patients, managed by about 120 urologists in 31 urology practices across the country. Its survey of changes in therapy confirms Dr. Labrie's point that primary hormonal therapy has increased in use over the period of study of the PSA era. Radical prostatectomy remains a very common treatment for low- and intermediate-risk disease. External radiation therapy has become somewhat less common as a primary therapy. But an interesting trend noted by Dr. Kane is the growing popularity of combination therapies.

"The majority, as many as 80% of the high-risk patients, receiving external radiation therapy are getting neoadjuvant androgen deprivation," he said. "And even low-risk patients, among whom there is no good support for androgen deprivation, are getting androgen deprivation with radiation therapy. Brachytherapy, which has become a more common treatment, especially for low-risk patients, has significantly increased.

"And watchful waiting has decreased as a treatment. This in spite of the fact that we are seeing lower-risk disease, where we think that watchful waiting would be a good option for many of those patients."

The CaPSURE database reveals that the outlook for prostate cancer patients has improved over time. However, this new information brings up another question: Are low-risk patients being overtreated?

"It looks like many of them may do well with watchful waiting, and yet many of them are receiving treatment in the United States," Dr. Kane said. "Part of that is patient-driven, and part of it is that it is difficult for us to differentiate the low-risk patients destined to progress and the low-risk patients who would do well with watchful waiting. So we are still facing unanswered, controversial questions."

Dr. Sandler
Dr. Labrie
Dr. Kane

