Repeat Prostate Biopsies Do Not Raise the Risk of Post-Prostatectomy Complications

Undergoing repeat biopsies during active surveillance (AS) for prostate cancer does not result in higher rates of erectile dysfunction (ED) or urinary incontinence (UI) within one, two, and three years after radical prostatectomy (RP). The study was published online ahead of print in Urologic Oncology.

Biopsies can cause local inflammation, prostatitis, edema, and hematoma that, in theory, might worsen functionality after RP. Clemens M. Rosenbaum, MD, and colleagues from University Hospital Hamburg-Appendix in Germany studied ED and UI rates for a cohort of 11,140 AS patients from their institution who had one or more biopsies prior to surgery.

Previous studies have examined functional outcomes within just one year of RP, so the team expanded the timeframe to within three years. During AS 86.9% of men had one biopsy, 8.4% had two, and 3.6% had three or more biopsies. Most patients (81.8%) had open retropubic RP and 18.2% had robotic-assisted laparoscopic RP (RALP) during 2007 to 2015. Men with three or more biopsies tended to be older (age 67 vs. 65 years), underwent RALP, and had bilateral nerve sparing.

Results showed that 45.9%, 57.9%, and 60.9% of men achieved potency at one, two, and three years after RP, respectively. Adjusted univariate and multivariate logistic regression analyses found no greater influence of repeat biopsy on ED rates at one, two, and three years compared with a single biopsy. UI rates followed the same trend: By one, two, and three years compared with a single biopsy.

Metastasis-Directed Treatment Improves Progression-Free Survival in Prostate Cancer

Nearly doubled survival time without androgen deprivation

Metastasis-directed therapy (MDT) for oligometastatic prostate cancer (PCa) improves progression-free survival (PFS) when compared to the use of active surveillance (AS) alone, according to Belgian investigators.

Their randomized, phase II study found that men given MDT had a median androgen deprivation therapy (ADT)-free survival of 21 months vs. 13 months for the AS group. Results of the STOMP (Surveillance or Metastasis-Directed Therapy for Oligometastatic Prostate Cancer Recurrence) trial, led by Piet Ost, MD, PhD, of Ghent University Hospital, were published online in the Journal of Clinical Oncology on 14 December 2017.
New Prostate Cancer Imaging Tracer Improves Detection

“Emerging agents for prostate imaging will dramatically improve the ability to determine the location of cancerous lesions,” stated Frederik Giesel, MD from Universität Heidelberg Germany. “This will allow the precise targeting of radiotherapy (RT).”

“One agent, 18F-PSMA-1007, has some characteristics that are different from other agents,” Dr. Giesel explained during his presentation of three different studies at the Radiological Society of North America (RSNA) 2017 Annual Meeting in Chicago.

“It has a longer shelf life than the others and minimal kidney clearance, so urinary excretion of it is minimal,” he said. “18F-PSMA-1007 is the first tracer that has a different elimination route, which I would say is an advantage.”

“But more important is the increased uptake in tumor tissue,” he stated. “Its tumor-to-background ratio makes the detection of small lymph node metastases easier than with other agents. We see advantages of diagnostic performance in this tracer,” he added.

In a 2017 study, Dr. Giesel and his colleagues demonstrated that 18F-PSMA-1007 has a 95% sensitivity for small lymph node metastases (Eur J Nucl Med Mol Imaging 44: 678-688, 2017). In a new study, Dr. Giesel’s team looked at the diagnostic potential of 18F-PSMA-1007. They analyzed biodistribution in the normal organs and tumors of seven men with a biochemical recurrence (BCR) of prostate cancer (PCa), and assessed lesion size. Men were injected with 18F-PSMA-1007 and underwent PET-CT scanning one hour and three hours after injection.

Local recurrence was detected in two men with PSA levels of 1.9 and 3.6 ng/mL, lymph node metastases was detected in two men with PSA levels of 0.16 and 2.0, and bone metastases was detected in one man with a PSA level of 3.8 ng/mL. In the other two patients, with PSA levels of 0.4 and 0.5 ng/mL, PET-positive findings were not observed.

Tracer uptake increased in all tumor lesions from one to three hours post-injection (increase in mean maximum standardized uptake value [SUV_max], 8.4 to 14.1). The 18F-PSMA-1007 tracer had high potential for non-invasive localization diagnostics in PCa patients with BCR, the researchers conclude.

“Everyone is excited. We are now able to identify PCa early and accurately,” said Andrei Iagaru, MD, from the Stanford University School of Medicine. He added, “These new radiopharmaceuticals will play important roles at all stages of PCa.”

Dr. Iagaru’s presentation highlighted performance of these new classes of agents by describing his experience with 68Ga-PSMA-11 and gastrin-releasing peptide receptor (GRPR) ligands for the imaging of PCa at initial diagnosis and BCR. 68Ga-PSMA-11 can be used for PCa imaging, but it has “a short half-life and production limitations,” said Dr. Giesel.

His group selected 18F-PSMA-1007 because of its high labeling yields, excellent tumor uptake, and non-urinary background clearance, which minimizes radiation exposure to other parts of the body. “This agent is much more precise, compared with others, for N (lymph node) and M (metastatic) staging, and opens a new field of radiology, where we also consider PET for an important part of patient stratification.”

Presented at the RSNA 2017 Annual Meeting; abstracts SSA16-06, SSA16-07, SPSh52D, and SPSh52B.

Medscape Medical News
4 December 2017

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Okay, if people really appreciated breaking news in medicine, the American Academy of Neurology (ANN) just put exercise in their clinical guidelines as arguably the only way to officially slow the progression to dementia, but where the HECK is the love and appreciation?
The one of the most dramatic and significant moments in my medical career just occurred, but all I heard were crickets (aka “silence!”) So, this is why my column is so darn important. If a drug or supplement was invented that was now recommended in clinical guidelines to reduce the risk of dementia in some of those at the highest risk of getting dementia/Alzheimer’s disease then it would make the cover of every darn newspaper and major media outlet. Yet, here the lack of attention is embarrassing.

And, how does this apply to cancer or prostate cancer? That is easy! Whether it is hormone therapy or other drugs, we focus on whether or not these things increase the risk of dementia. Despite lack of a proven cause and effect, let us just assume that prostate cancer patients are at increased risk of dementia not just because of age but because of hormone therapy. So, why should we not focus on a potential solution or how to prevent it? Individuals at higher risk of dementia are also commonly labeled with the term “Mild Cognitive Impairment” (MCI), which basically means the situation is not normal but it does not mean the person has dementia. It basically means that things are progressing toward dementia. Now, after countless hundreds of millions of dollars spent on research (actually billions) what does research have to show for it? What drug is recommended to stop MCI or slow its progression? None! What dietary supplement? None! What medical procedure? None! So, let me read you the new guidelines for the AAN: First, it says clinicians may choose not to offer prescription medications, but if offering, “they must first discuss lack of evidence.” And, then here comes the moment that should have changed all our lives! Are you ready for it? Here it is (capitalized by me for emphasis but still word for word): “CLINICANS SHOULD RECOMMEND REGULAR EXERCISE.” What the heck?! Take just one moment in your life to appreciate this because it is amazing! If this is not enough to get you off your glutus maximus to move more… well then, probably nothing else will do it! Several clinical trials have shown the ability to delay the progression of cognitive impairment and memory loss with exercise! WHERE THE HECK IS THE COMMEMERAL? Well, you just got a true commercial from Dr. Moyad and Us TOO, and remember it forever or especially the next time you do not want to go out for a walk, or get on a treadmill, or elliptical, or go swimming, or do tai chi or whatever! Now, I’ve got to go walk my dog and then go for a run because clinical guidelines now suggest that it really matters! How about that for a start to 2018?! Wow! And wow spelled backwards!

References:

Shorter but Higher Dose Radiation Course Cuts Risk of Prostate Cancer Returning

Delivering radiotherapy (RT) over a shorter time frame significantly reduced the chance of prostate cancer (PCa) returning in men with an intermediate-risk form of the disease, a study found. The approach failed to improve survival, however. Researchers argued that a survival benefit may occur only in a subset of patients in excellent health. They called for more research on the topic. The study was published in European Urology Focus.

Standard RT, called conformal RT (CRT), delivers daily doses over 40 to 45 treatment sessions. RT reduces cancer recurrence and can increase survival. CRT is the standard RT approach. RT can also be given at higher doses over 15 to 30 sessions. This approach, called hypofractionated RT (HRT), reduces cost and inconvenience. A research team at Brigham and Women’s Hospital decided to compare the effectiveness of both RT approaches.

They analyzed data from three large clinical trials covering 5,485 PCa patients, of whom 3,553 (65%) had intermediate-risk prostate cancer. Researchers found that HRT reduced the risk of recurrent cancer by 13% compared with standard CRT. There was a trend toward better overall survival in the HRT group, but this was not statistically significant.

“Our results provide evidence for clinicians to consider CRT vs. CRT as a preferred RT method in men with intermediate-risk prostate cancer and at low risk of other complications,” stated Dr. Trevor Royce, a radiation oncologist at Brigham and Women’s Hospital and the first author of the study.

However, the HRT-treated patients were at higher risk of side effects — 42% more likely to have acute gastrointestinal toxicity, and 18% more likely to have genital or urinary-organ complications.

“Late bladder and urethral toxicities were noted to be higher in the HRT as compared to CRT group, which necessitates carefully choosing men who are not at risk for sustaining a late bladder or urethral side effect,” said Dr. Anthony D’Amico, chief of Genitourinary Radiation Oncology at Brigham and Women’s Hospital.

“More studies are needed to determine the benefits vs. toxicities of CRT as a treatment for high-risk prostate cancer,” the team said.

Prostate Cancer News Today
8 December 2017
NCCN Favorable Intermediate-Risk Prostate Cancer Patients: Is Active Surveillance Appropriate?


J Urol, Epub 26 December 2017; Article in Press

Purpose: To compare pathology and biochemical outcomes after radical prostatectomy (RP) in favorable intermediate-risk (IR) patients who fulfilled current NCCN active surveillance (AS) criteria to outcomes in men who met more traditional criteria for AS.

Materials and Methods: Our IRB (Institutional Review Board)-approved prostate cancer database was queried for men meeting NCCN criteria for very low (T1c, Grade Group I, ≤3/12 cores, ≤50% core volume, and PSA density <0.15), low (T1-T2a, Grade Group 1, PSA <10), or favorable intermediate (major pattern grade 3, percentage of positive biopsy cores <50%, and one IR factor [T2b/c, Grade Group II, or PSA 10-20]) risk. IR patients not meeting favorable criteria were labeled as unfavorable IR. Favorable IR (FIR) patients were compared to lower-risk (LR) (very low- and low-risk patients) and unfavorable IR (UIR) patients to identify differences in rates of adverse pathologic findings at RP (Gleason score Grade Group III-V, non-organ confined disease, or nodal involvement). The groups were compared on time to biochemical recurrence using Cox regression.

Results: 3,686 men underwent RP between 1/1/04 and 12/31/15; 1,454, 250, and 1,362 men fulfilled criteria for LR, FIR and UIR groups, respectively. The rate of adverse pathological findings for FIR (27.4%) was significantly higher than that for LR (14.8%, p <0.001) and significantly lower than for UIR (48.5%, p <0.001). Time to biochemical recurrence differed significantly over risk groups (p <0.001).

Conclusions: Relative to LR patients, FIR patients represent a distinct group and care should be taken in selecting these patients for AS and in monitoring them once in AS programs.
Enzalutamide Safe in Seizure-Prone Prostate Cancer Patients

(Continued from page 1)

established efficacy profile, suggests that enzalutamide can benefit men with seizure risk factors, who should be closely monitored throughout treatment duration to ensure continued benefit and safety,” they added.

Jim Hu, MD, MPH, of New York Presbyterian/Weill Cornell Medicine in New York, who wasn’t involved in the study, noted that the results contrast with those of a prior study, but they do suggest “enzalutamide does not predispose to seizure. This demonstrates that enzalutamide may be safely used in men with metastatic prostate cancer who have risk factors for seizure.”

UPWARD was initiated after requests for additional safety information from the FDA and the European Medicines Agency. Although enzalutamide is known to prolong survival in men with mCRPC, phase I and II studies reported seizures in 3 of 140 (2%) enzalutamide-treated patients at doses greater than 360 mg/day.

Controlled clinical trials such as AFFIRM, PREVAIL, TERRAIN, and STRIVE have shown that only 0.5% of men treated with enzalutamide 160 mg daily experienced a seizure. However, men with a history of seizure or risk factors were excluded from these trials, the researchers noted.

For UPWARD, they evaluated 423 patients at 73 sites in 20 countries, all of whom had at least one risk factor for seizure, including drugs to lower seizure threshold (57.2%); history of brain injury (26.5%); and history of cerebrovascular accident or transient ischemic attack (22.2%).

All men received oral enzalutamide at a dose of 160 mg/day for an initial four-month treatment period, and were given the option to extend treatment for one year.

Overall, four out of 366 evaluable patients (1.1%) had at least one confirmed seizure within four months of starting enzalutamide. Seizures were considered enzalutamide-related in three of the four patients. In addition, three patients (0.8%) had a seizure in the four-month period after the study ended.

All 423 patients were included in the safety analysis. The majority (84.4%) experienced at least one treatment-emergent adverse event (AE), 33.3% had at least one serious treatment-emergent adverse event, and 6.9% had at least one drug-related serious adverse event.

A total of 66 patients (15.6%) permanently discontinued treatment as a result of a drug-related AE, and three of these patients had a seizure, the researchers reported.

During the four-month study period, or within 30 days of the treatment ending, there were 38 deaths (9%), four of which were considered possibly drug-related. One patient died of cerebral hemorrhage, one of mCRPC, one experienced sudden cardiac death, and another had general deterioration. No seizure-related deaths were reported.

“Study limitations included that it was not a randomized trial, and that predisposing risk factors for seizure such as a history of seizure or of brain arteriovenous malformations were underrepresented,” the researchers said.

“The risk profile presented and an established efficacy profile, suggests that enzalutamide can benefit patients with seizure risk factors, who should be closely monitored throughout treatment to ensure continued benefit and safety,” they concluded.

MedPage Today
11 December 2017

Contemporary Incidence & Outcomes of Prostate Cancer Lymph Node Metastases


J Urol, Epub 26 December 2017; Article in Press

Purpose: The incidence of localized prostate cancer (PCa) has declined with shifts in PCa screening. While recent population-based studies show a stable incidence of loco-regional PCa, this categorized organ-confined, extra-prostatic and lymph node positive disease together. The contemporary incidence of PCa with pelvic lymph node metastases (PLNM) however, remains unknown.

Methods: We used Surveillance, Epidemiology and End Results (SEER) from 2004 to 2014 to identify men diagnosed with PCa. We analyzed trends in age-standardized PCa incidence by stage. The impact of extent of disease on mortality was assessed by adjusted-Cox proportional hazard analysis.

Results: During the study period, the annual incidence of non-metastatic PCa declined from 5119.1 per million to 2931.9 per million (Incidence Ratio [IR]: 0.57, 95% confidence interval [CI]: 0.56-0.58, p <0.01), while PLNM increased from 54.1 per million to 79.5 per million (IR: 1.47, 95% CI: 1.33-1.62, p <0.01). The incidence of distant metastases in men aged 75 years and over nadiere in 2011 vs. 2004 (IR: 0.81, 95% CI: 0.74-0.90, p <0.01), and increased in 2012 (IR: 1.13, 95% CI: 1.02-1.24, p <0.05) vs. 2011. Risk of cancer-specific mortality was significantly increased in men diagnosed with PLNM (hazard ratio [HR]: 4.5, 95% CI: 4.2-4.9, p <0.01) and distant metastases (HR: 21.9, 95%CI: 21.2-22.7, p <0.01) vs. non-metastatic disease.

Conclusions: The incidence of PLNM is increasing, coincident with a decline in detection of localized disease. Whether this portends an increase in the burden of advanced disease or simply reflects diminished lead-time remains unclear. However, this should be monitored closely, as the increase in N1 disease reflects an increase in incurable PCa at diagnosis.
New research shows that prostate cancer (PCa) mortality risk is lower after radical prostatectomy (RP) compared with radiotherapy (RT), but the difference in risk is much smaller than found in previous studies. In fact, among men with high-risk cancer, no significant difference in risk exists between the treatments.

In a population-based Swedish study of 41,503 men with PCa, investigators found that RT was associated with a 35% higher risk of PCa mortality compared with RP among men with low- and intermediate-risk PCa and 14% higher for patients with high-risk PCa, in fully adjusted analyses. In period analyses with full adjustment, the difference in PCa risk decreased to 24% among men with low- and intermediate-risk cancer, and the difference in risk among men with high-risk cancer decreased to 3%, a non-significant difference between the treatment groups.

The investigators defined risk categories according to National Comprehensive Cancer Network (NCCN) criteria. The absolute difference in risk of death within 10 years was less than 1% across all Cancer of the Prostate Risk Assessment (CAPRA) risk categories, David Robinson, MD, of Ryhov Hospital in Jönköping, Sweden, and colleagues reported online in European Urology.

Compared with previous studies, the difference in PCa death risk between RP and RT “was much smaller than in previous studies and very small in absolute terms,” the authors concluded. As a result, they noted, the choice between the treatments should be guided by the risk of side effects and patient preference instead of PCa mortality risk.

The investigators cited results from the first randomized clinical trial comparing RT, RP, and active monitoring showing no significant difference in PCa mortality risk after 10 years of follow-up. However, in that study, which was published in the New England Journal of Medicine, there were only four PCa deaths after RT and five after RP. A previous systematic review and meta-analysis published in European Urology found that PCa patients who underwent RT had a significant two-fold higher risk of PCa mortality than those who underwent RP in adjusted analyses.

The authors noted that limitations of their study included incomplete data, misclassification of bone metastases, and subpar RT in the early calendar time. “To address this issue, we used period analysis, an analytical approach that increases the influence of data from more recent calendar time. Period analysis is arguably the best analysis to inform current treatment decisions.” (Continued on page 8)

Metastasis-Directed Treatment Improves PFS (Continued from page 1)

For example, more men in the AS arm had Gleason 6, low clinical disease stage and unknown lymph node status than the MDT arm, which meant that patients in the MDT arm had more advanced disease at diagnosis. “This suggests,” Philips and his colleagues wrote, “that the observed effect of MDT in STOMP may in fact be an underestimation.”

Philips and his colleagues also wrote that while forestalling systemic therapy is an attractive way of avoiding nasty adverse effects, the combination of MDT and immediate ADT “also warrants additional investigation,” considering that the immediate use of ADT can improve overall survival compared to delayed therapy.

“While great progress has been made in managing PCa, questions remain, particularly concerning the management of oligometastatic cancer,” Philips and his colleagues concluded. “The STOMP trial represents an important advance in this pursuit and provides a strong argument for continued investigation of the role of MDT for managing oligometastatic PCa.”
P1, “Enzalutamide Safe…” Enzalutamide has been an important addition to the treatment options for men with advanced prostate cancer (PCa) with a very low-risk profile. However, seizures have been one concern, with a reported incidence of approximately 3%. Accordingly, some physicians have been reluctant to prescribe the drug to men with risk factors for seizures. The new study conducted by the company looked specifically at the incidence of seizures in a group of men with potential risk factors for seizures. Fortunately, the incidence was less than 2% in this group of men when they were given a 160 mg/day dosage. This means that it is reasonable to offer the drug to men with risk factor for seizures, provided the men are carefully evaluated and closely monitored.

The Bottom Line: The risk of seizures in men receiving the lower dose of enzalutamide is still very low and therefore the drug is not contraindicated in these men.

P1, “Repeat Prostate…” One of the requirements for men on active surveillance (AS) is that they undergo repeat prostate biopsy depending on the protocol being used. In addition to the discomfort, there is a recognized risk of infection, bleeding and inflammation, which might impact on the development of impotence and/or incontinence of men who eventually undergo radical prostatectomy. The study by Rosenbaum and co-workers should alleviate some of that concern. They analyzed a large cohort of men who had been on AS but eventually underwent prostatectomy and found that the impotence and incontinence rates were not significantly different at three years whether they had undergone one, two, or three or more biopsies. One limitation is that it is not clearly stated whether an objective quality of life questionnaire was used prior to AS and then periodically throughout the study to make this comparison.

The Bottom Line: Repeat biopsies for men on AS does not appear to increase the risk for impotence or incontinence if they just undergo radical prostatectomy.

P1, “Metastasis-Directed…” Doctors have long debated the potential merits of treating metastatic PCa with either surgical removal or focal radiation (RT) to metastatic sites (MDT) in addition to androgen deprivation therapy (ADT). The merits of this approach have not been proven by a randomized study, but a new phase II study by Ost, et al. provides some interesting findings. A small group of men that developed fewer than four metastatic sites after failing primary therapy were progressively enrolled. The group was randomized to receive delayed ADT or focal treatment (surgery or RT) to the metastatic sites. The end point was time to ADT administration. The study showed an eight-month increase in time to endpoint in the group receiving focal treatment to the metastatic sites. We have several questions that need answers. First, why the authors enroll only men with fewer than four metastatic sites? Why did they choose that number? Wouldn’t MDT apply for men with a fewer or greater number of sites? Second, while delaying ADT spares patients from side effects, early ADT offers a survival benefit and delays metastatic events. Lastly, before MDT can be recommended, a significant survival benefit must be shown. For now, this approach should only be done as part of a properly designed randomized trial.

The Bottom Line: MDT therapy may have a role in managing men developing metastatic disease after local therapy but much more information must be obtained from a randomized trial before this approach should be recommended.

P2, “New Prostate Cancer…” Until recently, bone scan and CAT scan imaging have been the standard of care for identifying metastatic disease in men with PCa. Both suffer, however, from poor sensitivity at PSA levels below 10 ng/mL. Early detection of metastases has presented a challenge in newly diagnosed patients and for those with a rising PSA after local therapy. In recent years, studies using PET scans using different radioactive reagents have been able to identify disease outside the prostate when PSA levels are lower. The current challenge is to decide which of the reagents work best in terms of sensitivity, stability of the reagent, cost and side effects. The presentation by Iagaru, et al. found good results using 18F-PSMA-1007, which has several advantages over other agents. The use of PET scanning is resulting in a paradigm shift in managing this disease. Although more studies are needed, it appears very likely that 18F-PSMA-1007 PET will replace bone and CAT scans for all patients. Currently, bone scan and CAT scan testing has been abandoned for newly diagnosed cases when the PSA is under 10 or 20 ng/mL, even though we know that some of these men, particularly those with high-grade disease, harbor metastases at the time they get their local therapy. It also will have great value in designing future studies of men with a rising PSA after local therapy.

The Bottom Line: PET scans will become the new norm to evaluate disease outside the prostate with the best agent to use yet to be determined.

P3, “Shorter but Higher…” To hypofractionate RT or not is the question. A meta-analysis by Royce and co-workers attempts to address this question. They critically assessed a large number of reports and extracted data from three randomized studies. They found a 13% reduced risk of recurrence in the men getting hypofractionated RT, but there was no difference in overall survival. Importantly, side effects were significantly higher. Acute gastrointestinal toxicity was 42% higher and late grade 2 or higher gastrointestinal toxicity was 18% higher in the hypofractionation group. The authors conclude that, “Treatment with a shorter course of radiation and higher doses over fewer days may be the preferred approach in appropriately selected patients with localized prostate cancer, reducing treatment time and cost to the patient, and increasing patient convenience and (Continued on page 8)
**RT vs. RP**

(Continued from page 6)

Other limitations included lack of data on PSA density and total cancer extent in biopsies in millimeters, both factors of which influence outcome.

Dr. Robinson’s team identified study patients using the National Prostate Cancer Register of Sweden. Of the 41,503 men, 26,449 underwent RP and 15,054 underwent RT. RT recipients were older than those who underwent RP (mean 67 vs. 63.1 years), and they had higher T stage, Gleason grade group, PSA level, and proportion of biopsies with cancer.

The Bottom Line: Without data from randomized trials, it is not possible to truly tell patients whether surgery or radiation offers better survival in men with localized prostate cancer.

**Repeat Biopsies**

(Continued from page 1)

after RP, 87.9%, 90.9%, and 91.6% of all men, respectively, had achieved continence, regardless of biopsies. “The growing acceptance of AS has led to a relevant number of patients who will require RP after multiple [biopsies]. Those patients can be counseled that repeat [biopsies] do not seem to result in worse functional outcomes,” Dr. Rosenbaum and colleagues stated.

Prior studies showed inconsistent results on the number of biopsies and ED risk, so the current study offers some assurance.

**Doctor Chodak’s Bottom Line**

(Continued from page 7)

access to treatment.” I strongly disagree with this conclusion for several reasons. First, the PCa morbidity is significantly higher. Second, there is no evidence this approach improves survival. Third, only one of the three studies combined the RT with ADT, which is known to improve survival in men with intermediate-risk disease. Without stratifying patients by disease risk in their findings, it is possible that the significance of the differences they reported may be lost.

The Bottom Line: It remains unclear whether hypofractionation is either as effective or as safe as standard radiation and additional well-done studies are needed.

P6, “Smaller Difference in...”

Which is better for men with PCa, surgery or RT? The debate continues, in part, because of the paucity of well-designed studies. Aside from a well-designed randomized study, a new population-based assessment by Robinson et al. of men in Sweden, found less than a 1% difference in survival. They used a method called period analysis to balance the effects of changes in RT given over time. Regardless of the methods used, this analysis, like previous uncontrolled studies, CANNOT provide us with a valid comparison of these two treatments. One must ask then, why they continue to be published given all the intrinsic biases that occur? Do they improve the ability to counsel patients? Not really. In my view, they can help with the design of the studies needed to answer the question. Unfortunately, time and money limitations continue to impede conducting the studies necessary to find the answer. Until they are done, patients need a balanced presentation of the reported odds of good and bad results.