Focal Therapy for Primary Localized Prostate Cancer Remains Investigational

Focal therapy for primary localized prostate cancer should remain investigational pending further study, according to a 2018 European Association of Urology (EAU) position paper.

“The method is promising, but the often multifocal nature of prostate cancer renders it not applicable for all prostate cancer,” Dr. Henk G. van der Poel from Netherlands Cancer Institute, Amsterdam, the Netherlands told Reuters Health by email.

Low PSA on Androgen Deprivation Therapy is Still Prognostic in New Treatment Era

A low PSA value continues to be a helpful prognostic marker in the setting of hormone-sensitive metastatic prostate cancer, even as standard treatment evolves. The finding comes from a retrospective analysis published online December 20, 2017, in the Journal of Clinical Oncology.

Among oncologists and urologists, it is well known that a PSA level ≤0.2 ng/mL in these men at seven months after the initiation of androgen deprivation therapy (ADT) portends a significantly longer survival than seen in men with PSA values above this cutoff point. But that insight comes from a study published more than 10 years ago - the Southwest Oncology Group 9346 trial (J Clin Oncol 24: 3984-3990, 2006). At that time, ADT alone was the mainstay of treatment. However, over time, treatment options change.

Now, thanks to findings from the more recent CHAARTED and STAMPEDE trials, many of these patients receive chemotherapy with docetaxel in addition to ADT, especially if they have high-volume metastatic disease. Both major trials showed significantly improved overall survival when chemotherapy was added to ADT in advanced prostate cancer.

But it has not been known in the current treatment era whether the PSA biomarker remained prognostic when docetaxel was added to ADT. So the CHAARTED investiga-
Effect of Starting Penile Rehabilitation with Sildenafil Immediately After Robot-Assisted Laparoscopic Radical Prostatectomy on Erectile Function Recovery: A Prospective Randomized Trial

Jo JK, Jeong SJ, Oh JJ, et al.

J Urology Article in Press

Purpose: It has not been clearly proven in real practice whether early rehabilitation with phosphodiesterase type five (PDE-5) inhibitors starting immediately after radical prostatectomy (RP) improves erectile function recovery more effectively compared with delayed treatment with the same regimen. We performed a prospective randomised trial to identify this.

Patients and Methods: Men with prostate cancer and pre-operative International Index of Erectile Function (IIEF)-5 score ≥17 were randomly assigned to regularly receive sildenafil (Viagra) 100mg twice a week for three months immediately after urethral catheter removal (early group) or only at three months after nerve-sparing robot-assisted laparoscopic RP (delayed group). The primary endpoint was full erectile function recovery rates (defined as IIEF-5 ≥17) over the 12 months.

Results: In the 120 randomised patients, the proportion of men achieving full recovery was significantly higher over the 12 months in the early group than in the delayed group (β: 0.356, p <0.001, generalized estimating equation). After 9 months following surgery, the proportion of patients achieving full recovery had steadily increased, resulting in 41.4% at 12 months in the early group, while patients in the delayed group had not shown further improvement, thus achieving full recovery only in 17.7% of men at 12 months. Only early sildenafil treatment (hazard ratio 2.943, p = 0.034) independently improved full recovery at 12 months.

Conclusions: Our trial provides clinical data to suggest that the earlier rehabilitation with PDE-5 inhibitors can contribute more to the recovery of erectile function after RP in the clinical setting.

Long-Term Antitumor Activity and Safety of Enzalutamide Monotherapy in Hormone Naïve Prostate Cancer: Three-Year Open Label Followup Results

Tombal B, Borre M, Ratheborg P, et al.

J Urol 199: 459-464, 2018

Purpose: A phase 2 study of enzalutamide (Xtandi) monotherapy in men with hormone naïve prostate cancer demonstrated high PSA response rates at 25 weeks, one year and two years of treatment with minimal effects on total body bone mineral density and favorable safety. In this followup analysis, we evaluated enzalutamide antitumor activity and safety at three years.

Materials and Methods: In a single arm analysis 67 patients with hormone naïve prostate cancer and noncastrate testosterone (230 ng/dL or greater) received enzalutamide 160 mg per day orally until disease progression or unacceptable toxicity. The primary end point was PSA response (280% decline from baseline).

Results: No patients discontinued treatment during year three. Of 42 patients with PSA assessments at three years, 38 (90.5%, 95% Confidence Interval [CI] 77.4-97.3%) maintained a PSA response. Of 26 patients with metastases at baseline, 17 (65.4%) had a complete or partial response as the best overall response during three years. In patients who completed the three-year visit, minimal mean changes from baseline were observed in total body bone mineral density (BMD) or BMD of the femoral neck (hip), trochanter (either of two knobs at the top of the femur), spine (L1-L4) or forearm (range -2.7% to -0.1%). At three years, total body fat had increased a mean of 16.5%, total lean body mass had decreased a mean of -6.5% and global health status had minimally decreased from baseline. Common adverse events were gynaecomastia (breast enlargement), fatigue, hot flush and nipple pain.

Conclusions: Enzalutamide antitumor activity was maintained in patients with hormone naïve prostate cancer at three years. Overall BMD, global health status and safety results were similar to those at two years.
Doc Moyad’s What Works & What is Worthless or “No Bogus Science” Column

“Get Your Flu and New Shingles Shot to Reduce the Risk of a Heart Attack & Stroke?”

Mark A. Moyad, MD, MPH, University of Michigan Medical Center, Department of Urology

Editor’s Note: Us TOO invites certain physicians and others to provide information and commentary for the Hot SHEET to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

Recently, I wrote in my Us TOO column about the importance of making sure that your adult vaccinations are up-to-date because they can provide ancillary and unadvertised benefits that are potentially incredible! I talked (preached) previously about some adult vaccinations that were being studied with cancer drugs in order to boost the response of the immune system. I also discussed the theory (that I fully support by the way) that by reducing chronic inflammation from an infection such as the flu or shingles you could reduce your risk of a heart attack or stroke.

Okay, fast forward about a year or so later and BAM! Moyad hits a grand slam baby! Researchers in Canada looked at 364 hospitalizations for a heart attack that occurred one year before or after a positive test result for influenza was reported. Researchers found that the risk of being admitted to the hospital for a heart attack was SIX time higher the week after a diagnosis of the flu compared to other times of the year. The risk was higher with increased age (greater than 65 years) but was also higher in younger male and female patients and it appeared higher for those that had never had a heart attack before and for those that were not vaccinated against the disease (but this was not the purpose of the study).

This research supports several other studies that demonstrate higher risk of cardiac events with respiratory infections. And, now that the new shingles vaccine is available known as “Shingrix,” you need to get that ASAP because there is a belief that shingles increases the risk of stroke and possibly heart attacks (which I agree with). It is easy to look at something like missing your adult vaccine as “no big deal.” People argue constantly about whether or not there are personal benefits to an adult vaccine. However, people miss the forest for the trees. Adult vaccines are heart healthy and it is the reason I get them. Also, the research on adult vaccines providing additional immune surveillance benefits against cancer are preliminary but are incredibly fascinating.

The number one killer of prostate cancer patients is cardiovascular disease (CVD) in many circles of the world. But what if there was another cheap way to reduce the risk of this major killer? Well, it seems that now there is, and I think it is worth a SHOT. (Did you see what I did there? Threw in an intended pun … shot and vaccine … man how does Moyad INJECT this kind of humor in his column? Ah, I did it again!).

References:

Physician Trust Tied to PSA Testing

The level of trust a man has in his physician is “strongly associated” with the decision of whether to undergo PSA screening, according to a new study of US attitudes and behaviors presented at the Genitourinary Cancers Symposium (GUCS) 2018. Interestingly, a man’s degree of trust in cancer information found on the Internet was not significantly associated with getting the test, when multiple variables were considered.

“If you trust your physician a lot, you are more likely to discuss PSA screening as well as receive it,” said Zachary Klaassen, MD, a urologist at the University of Toronto, Ontario, Canada. Dr. Klaassen is a member of the famed urology group in Toronto, which is led by active surveillance pioneer and PSA screening champion Lawrence Klotz, MD. They see patients at the Princess Margaret Hospital.

“The PSA test triggers a lot of feelings in men,” said Dr. Klaassen. “I have a colleague who says that PSA stands for ‘prostate- or patient-specific anxiety.’

“We wanted to assess factors that may lead patients to get PSA screening or not,” he continued. They especially wanted to address the variable of physician trust because shared decision making is becoming “more and more important.” To do so, the team had to use US data. “Physician trust is not in many databases,” Dr. Klaassen explained.

But it is in the Health Information National Trends Survey (HINTS), a survey of people living in the US. So the team performed a cross-sectional study using data from 2011 to 2014. The primary exposure was degree of trust in cancer information from a participant’s physician. The secondary exposure was the same thing, but for cancer information obtained from the Internet. The primary outcome was patient-reported receipt of PSA screening.

There were 5,069 eligible men in HINTS. Trust in their doctors was “a lot” in 3,606 (71.1%) men and “some” in 1,186 (23.4%) men. Only small fractions trusted a little” (N=219, 4.3%; ) or “not at all” (N=58, 1.1%; ). About half of the total group was PSA screened (52.4%; N=2,655). The degree of trust in cancer information from the physician was strongly associated with the likelihood of being screened. Among the men who reported “a lot” of trust, 54.9% underwent screening, as did 48.6% of the “some” trust group, 38.4% of the “little” trust group, and 27.6% of the “not at all” trust group (trend P <0.0001).

Sumanta K. Pal, MD, urologic oncologist at City of Hope Cancer Center in Duarte California, and an American Society of Clinical Oncology expert, suggested the findings make sense. “It’s somewhat implicit: the more a patient trusts a physician, the greater the likelihood that they will follow recommendations, which may include PSA screening,” Dr. Pal told Medscape Medical News. The relationship between physician trust and the presence of PSA screening (or not) “should probably go hand in hand,” he added.

However, Cara Litvin, MD, an internist at the Medical University of South Carolina in Charleston, found the results hard to interpret without (Continued on page 8)
Obese Men May Have Higher Risk for Biochemical Recurrence Following Radical Prostatectomy

Among men with prostate cancer (PCA) who underwent radical prostatectomy (RP), those who were obese had a higher risk of biochemical recurrence (BCR), according to data presented at the American Association for Cancer Research (AACR) Special Conference on Obesity and Cancer. BCR was defined as two consecutive PSA levels ≥ 0.2 ng/mL after RP, which is indicative of recurrent PCA.

“Obesity and metabolic syndrome have become increasingly widespread in our society,” said Arash Samiei, MD, a basic scientist and clinical researcher in the Department of Urology at the Allegheny Health Network in Pittsburgh, PA. “PCA is the most common cancer in men, and up to 30% will develop recurrence after RP. We investigated the association between obesity and metabolic syndrome with the oncologic outcome post-RP.”

Previous studies linking high body mass index (BMI) and metabolic syndrome to increased risk of post-RP recurrence showed mixed results. To build upon previous research, Dr. Samiei and colleagues performed a large study with long-term follow-up to conduct a more comprehensive analysis.

Researchers conducted a retrospective study of all RPs (1,100 surgeries) performed by two surgeons at Allegheny General Hospital between 2003 and 2013. They analyzed Gleason score; pathologic stage; preoperative PSA; BCR time; surgical margin status; and metabolic factors, such as fasting glucose, triglycerides, cholesterol levels (including high-density lipoprotein [HDL]), preoperative BMI, and blood pressure. Men were categorized as having low-, intermediate-, or high-risk PCAs based on pathologic staging and grading of the disease. Metabolic syndrome positivity was determined using the World Health Organization (WHO) classification, where at least three of the following five factors are simultaneously present in an individual: insulin resistance or type 2 diabetes, obesity, high total cholesterol or low HDL (good cholesterol) levels, high triglycerides, and hypertension.

The mean age of the men at diagnosis was 60 years, and the mean follow-up time was 48 months. Among the men studied, 34% were obese as defined by BMI, and 19% had metabolic syndrome.

Study results showed a higher percentage of obese men in the high-risk group (41.2%) vs. obese men in the low- and intermediate-risk groups (32%). Additionally, BCR was higher in men with BMI ≥30 (32.4%) compared to those with BMI <30 (16.9%). Men with metabolic syndrome had more than a fourfold increased risk of BCR compared to those without metabolic syndrome.

“Our study indicates that PCA patients who are obese or have metabolic syndrome undergoing RP may have a higher chance for recurrence of the disease, and these individuals should have more focused follow-up care,” said Dr. Samiei. “By preventing metabolic syndrome, men with PCA may have a higher chance of a favorable oncologic outcome post-RP.”

Dr. Samiei noted that future work is needed in large, multicenter prospective studies.

Focal Therapy (Continued from page 1)

To date, there has been insufficient long-term follow-up regarding toxicity and cancer progression after focal therapy, as well as the toxicity of secondary treatments and retreatments after focal therapy. Given these considerations, the panel concludes that “focal therapy should be considered an investigational modality only.”

“Focal therapy for prostate cancer is extremely interesting, but further study, including the risk of (longer-term) recurrences, is needed,” Dr. van der Poel said.

Dr. Ryan P. Werntz from the University of Chicago, who recently reviewed focal therapy treatment options for prostate cancer, stated “AS and more minimally invasive treatments, such as focal therapy, in theory aim to minimize treatment-related side effects while maintaining therapeutic efficacy. We have good data now to support AS in men with very low-risk cancers (as defined by National Comprehensive Cancer Network), but in general low volume Gleason 3+3 disease.”

“In my mind, focal therapy really is for men with a clinically significant (Gleason 3+4, debatably 4+3) MRI visible solitary lesions (maybe 2) who want to avoid radical therapy (radical prostatectomy, radiation) to minimize treatment-related side effects,” he said. “Multiple energy platforms and phase 1 and 2 trials have been performed, as mentioned in this review, with mixed short-term oncologic results.

“There are no cancer-specific survival data,” Dr. Werntz said. “In the low-risk (main AS) cohorts that are being treated in these studies, 15-20 years are needed to adequately determine if the treatment impacts either metastasis-free or cancer-specific survival.”

“Surveillance is still required after focal therapy and is difficult to do,” he added. “There are no defined PSA guidelines to hint at a cancer recurrence. Patients who wish to pursue this treatment option should do so only in the setting of a clinical trial,” Dr. Werntz agreed.

Reuters Health 2 February 2018

New Resources Address Anxiety, Depression and Prostate Cancer

Many men who are diagnosed with prostate cancer, or are managing the disease, experience some level of anxiety and/or depression. Caregivers may also be affected. The psychosocial challenges surrounding treatment choices and side effect management can have a negative impact on the prostate cancer journey. Anxiety and depression aren’t always effectively treated, in part because the symptoms may not be recognized.

We encourage you to visit the new Us TOO web page for information on recognizing and managing anxiety, depression and prostate cancer.

www.ustoo.org/anxiety-and-depression
Pelvic lymph node dissection (PLND) for men with prostate cancer (PCa) may be one of the most intriguing and debated topics in urologic oncology. Nowadays, three relevant discussions may be highlighted from the available literature: diagnostic effectiveness, morbidity, and therapeutic effectiveness. PLND is the most accurate staging procedure for nodal assessment in PCa. It outperforms any imaging approach, and is superior to CT scan, PET/CT scan, and diffusion-weighted MRI in both sensitivity and specificity. Furthermore, the extent of PLND is highly associated with its diagnostic accuracy; a more extended PLND provides a more accurate assessment of lymph node invasion with a higher rate of nodal metastases, whereas a limited PLND is associated with a high rate of false-negative findings. PLND extension is also associated with worse intraoperative and postoperative outcomes, which translates into increased operative time, intraoperative complications, bleeding, hospital stay, and risk of lymphocele. As such, the better diagnostic accuracy of extended PLND has to be balanced with its higher morbidity. Extended PLND should be avoided when the harms are expected to exceed the possible benefits. Predictive models assessing the risk of lymph node metastasis represent the best available tool to facilitate decision-making. The therapeutic benefits of PLND and its extent during radical prostatectomy (RP) remain unproven: the majority of the studies comparing different extents of PLND are affected by high risk of bias, providing low quality of evidence. However, two important factors must be considered. First, PLND may be curative for selected men with limited nodal involvement (pN1) that is entirely removed at the time of surgery (i.e., direct effect). A recent retrospective study showed that a considerable subset of men with low-volume lymph node metastasis remained disease free 10 years after RP and bilateral extended PLND without additional therapy. Second, PLND may represent a stratification tool for identification of men who benefit from adjuvant treatments, which may improve survival outcomes (i.e., indirect effect).

As an example, a recent retrospective analysis identified specific categories of men with pN1 disease who benefited from combined adjuvant radiotherapy and hormonal therapy. Thus, more comprehensive and accurate nodal staging via extended PLND may indirectly improve the prognosis for selected men with pN1 disease. However, the potential benefit of extended PLND observed in retrospective studies should always be balanced by the so-called “Will Rogers phenomenon.” When more extensive lymphadenectomy is performed, the rate of pN1 disease increases. An increased number of harvested lymph nodes improves the prognosis of all groups since the pN0 group (unknown lymph node status before RP) becomes less contaminated with cases harboring micrometastases, and the pN1 group is enriched with those with a low metastatic tumor burden.

The current poor quality of evidence indicates the need for robust and adequately powered clinical trials with appropriate controls, stan-
Routine Office Urine Culture Before Prostate Biopsy is Unnecessary

In a single center study, asymptomatic bacteriuria (bacteria in the urine) resolved before prostate biopsy, without additional treatment. Pre-biopsy bacteriuria does not appear to increase the risk for infectious complications following prostate needle biopsy (PNB), a new study suggests. “Routine office urine culture in the asymptomatic male prior to PNB is unnecessary,” Jay D. Raman, MD, of Pennsylvania State University and colleagues concluded in *International Urology and Nephrology* (Vol. 50, pp. 21-24, 2018). Of 150 men who had urine cultures 14 days before PNB, just six (4%) had asymptomatic bacteriuria of >10,000 colony forming units (CFU) per mL. Two men were infected with Escherichia coli of >100,000 CFU/mL; one with Klebsiella of >100,000 CFU/mL; one with E. coli of 10,000 CFU/mL and two with mixed flora of >10,000 CFU/mL. None of the infected men developed asymptomatic bacteriuria after receiving antibiotics. Repeat urine cultures immediately before biopsy yielded an overall mean bacterial count of 55 CFU/mL. The six men with pre-biopsy infection each had <100 CFU/mL, indicating their infections had resolved. Post-biopsy infection developed in four men (2.7%), including two with sepsis and two with confirmed urinary tract infections. Quinolone (ciprofloxacin)-resistant E. coli was responsible for all cases. Post-biopsy infection did not develop in any of the six patients who had a positive office urine culture two weeks prior to biopsy.

The American Urological Association recommends fluoroquinolones for antibiotic prophylaxis prior to biopsy. “This class of antibiotic has great efficacy in urine and prostate tissue, with broad coverage of both gram-negative and prostate needle biopsy (PNB), a new study suggests. “Routine office urine culture in the asymptomatic male prior to PNB is unnecessary,” Jay D. Raman, MD, of Pennsylvania State University and colleagues concluded in *International Urology and Nephrology* (Vol. 50, pp. 21-24, 2018). Of 150 men who had urine cultures 14 days before PNB, just six (4%) had asymptomatic bacteriuria of >10,000 colony forming units (CFU) per mL. Two men were infected with Escherichia coli of >100,000 CFU/mL; one with Klebsiella of >100,000 CFU/mL; one with E. coli of 10,000 CFU/mL and two with mixed flora of >10,000 CFU/mL. None of the infected men received dedicated treatment, per the study protocol. All men then received usual antibiotic prophylaxis, including 500 mg ciprofloxacin the night before and the morning of the biopsy. Repeat urine cultures immediately before biopsy yielded an overall mean bacterial count of 55 CFU/mL. The six men with pre-biopsy infection each had <100 CFU/mL, indicating their infections had resolved. Post-biopsy infection developed in four men (2.7%), including two with sepsis and two with confirmed urinary tract infections. Quinolone (ciprofloxacin)-resistant E.

Low PSA on ADT Is Still Prognostic in New Treatment Era (Continued from page 1)

tors performed a retrospective "landmark survival analysis" at seven months using the database from their trial. They conclude that “PSA ≤0.2 ng/dL at seven months is prognostic for longer overall survival with ADT for metastatic hormone-sensitive prostate cancer irrespective of docetaxel administration.” For clinicians, the new findings provide both “optimism at the bedside and perhaps also guidance on how close to follow patients,” said investigators Lauren Harshman, MD, and Christopher Sweeney, MD, from the Dana-Farber Cancer Institute in Boston, MA. The suggestion here is that for clinicians working with men whose PSA levels are below the cutoff point, there is positive news to share, while for men with PSA levels above that cutoff point, there is possible guidance for closer monitoring.

In the study, 719 of the original 790 patients were eligible for the new subanalysis; 358 were treated with ADT plus docetaxel and 361 with ADT alone. The team used the three prognostic classifiers identified from the earlier SWOG 9346 trial: PSA ≤0.2 ng/dL, >0.2 to 4.0 ng/dL, and >4.0 ng/dL. The median follow-up was 23.1 months. Across all patients, median overall survival was significantly longer if the PSA at seven months reached ≤0.2 ng/dL vs. survival seen with levels >4.0 ng/dL (median survival, 60.4 months vs. 22.2 months, respectively; P<0.001). On multivariable analysis, a seven-month PSA level ≤0.2 ng/dL and low-volume disease were prognostic of longer overall survival (all P<0.01).

Also, achieving a seven-month PSA level ≤0.2 ng/dL was more likely with docetaxel, low-volume disease, prior local therapy, and lower baseline PSA levels (all P≤0.01). The addition of docetaxel increased the likelihood of achieving a PSA level ≤0.2 ng/dL at seven months (45.3% vs. 28.8% of men receiving ADT alone). However, the patients who had the best median overall survival in the study (72.8 months) were those receiving ADT alone who achieved a seven-month PSA level ≤0.2 ng/dL (these men were also more likely to have low-volume disease, at 56.7%). Drs. Harshman and Sweeney pointed out that the timing of docetaxel was variable in the study. Notably, they also observed that “getting docetaxel around the time of ADT initiation increased the chances of achieving this good prognostic feature, and there was evidence patients may have been more likely to achieve this endpoint, the closer the docetaxel was given to the ADT start.” However, the pair cautioned clinicians not to make too much of the new findings in terms of making upfront treatment decisions. “While intriguing, given the study’s retrospective nature, clinicians should not make treatment decisions based on the PSA level at seven months (e.g., defer adding docetaxel based on the seven-month PSA level),” they said.

“Our results are prompting many questions about whether these patients would benefit from therapy intensification prior to PSA or radiologic progression with newer androgen-receptor targeted agents,” they said. These newer agents include abiraterone acetate (Zytiga) and enzalutamide (Xtandi). All study authors have financial ties to industry, including to Sanofi (maker of docetaxel) and other companies with drug treatments for prostate cancer.

Medscape Medical News 23 January 2018

Check out information on 16 prostate cancer topics and add your post to the Us TOO Prostate Cancer Online Support & Discussion Community on Inspire at: www.inspire.com/groups/us-too-prostate-cancer/
Doctor Chodak’s Bottom Line


Editor’s Note: Us TOO has invited certain physicians and others to provide information and commentary for the Hot SHEET to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

P1, “Focal Therapy...” Is focal therapy a reasonable option for treating localized prostate cancer (PCa)? A number of approaches are being used by different investigators, but so far, no randomized studies are being conducted to evaluate this approach and no survival data are available. As a group in Europe has pointed out, there is insufficient valid data to prove it is equivalent to whole gland therapy. Given the current lack of information, is it ethical for any clinician to even offer the therapy without being part of a properly designed randomized protocol? Unless that is occurring, the information obtained cannot prove this approach is appropriate.

The Bottom Line: Focal therapy of localized PCa is an interesting concept but it is unethical to offer to men unless it is part of a properly designed prospective trial.

P1, “Did They Die of...” Each year, the American Cancer Society puts out an estimate of the incidence and death rates from different cancers and the changes are viewed over time. These statistics are often used to plan policy and identify health needs. In some cases, these statistics are used to evaluate the effects of PCa screening or not screening or changes in management. It is important to recognize that we do not have in place a way of validating the accuracy of these statistics. There is no central review process taking place of the cause(s) of death assigned on all death certificates. Over the years, some studies have reported the accuracy by reviewing health records death certificates. A study by Liffeler, et al. did such a review in Norway and found that the inaccuracy rate is about 20%. US statistics have found higher accuracy but it may still be inaccurate 5-10% of the time. This points out the need to be careful as PCa mortality rates are viewed each year since the changed recommendation about screening was made in 2012. It is possible that small changes may be due to the accuracy of reporting rather than actual changes in the incidence of deaths due to PCa.

The Bottom Line: Care is needed in comparing PCa cancer mortality rates since the policy changed regarding screening for this disease.

P1, “Low PSA on ADT...” Can a PSA level of 0.2 ng/mL or lower at seven months after ADT be a predictor of long-term survival? That is the finding of a prospective randomized trial comparing ADT alone to ADT plus docetaxel by Harshman, et al. Improved survival was seen in the men getting ADT alone as well as those getting combination therapy. In both situations, the survival rate was significantly greater in the men whose PSA dropped to that level. This could be important for future trials, if an early marker could be used as a surrogate for long-term survival because it would permit more rapid assessment of therapies.

The Bottom Line: Data from a randomized trial suggests that a PSA level of 0.2 ng/mL or lower after seven months of ADT could be a possible surrogate predictor of long-term survival, but more assessment is still needed.

P2, “Long-Term Antitumor...” Will Enzalutamide become a better choice for managing hormone naïve PCa than castration? One reason to ask this question is because the long-term side effects of castration are well known and include a decline in bone mineral density (BMD). Tombal, et al. are now reporting on the three-year findings in a small group of men managed with this drug and so far they are not seeing much change in the BMD. Of course, only a prospective randomized trial comparing safety and efficacy can determine if this drug can be substituted for castration.

The Bottom Line: After three years, enzalutamide is showing promise in avoiding changes in BMD, but only a randomized study can determine if this drug can be used in place of castration.

P2, “Effect of Starting...” Recovering erectile function (EF) remains a major concern for men undergoing radical prostatectomy (RP). Various approaches have been suggested to increase the likelihood erections will return, but results from randomized studies using PDE-5 inhibitors have only just now been reported. Jo, et al. randomized 120 men to sildenafil (Viagra) immediately after urinary catheter removal or delayed until three months post-RP. They found a significantly greater IIEF recovery in the men receiving immediate treatment. This is a very encouraging finding, although it will be important to carefully review their data since they judged complete recovery as having an IIEF score greater than 16. It is possible that some bias could have been introduced by using this criteria, given that some men may have had a much higher IIEF score before RP. The maximum value is 25, so a drop from 25 to 17 is very significant. What is really needed is a comparison of the absolute change in IIEF scores determined for the men achieving benefit.

The Bottom Line: Early use of a PDE-5 inhibitor may aid in men achieving full EF recovery after RP.

P4, “Obese Men May...” Is obesity a risk factor for post-RP biochemical recurrence (BCR)? Samiel, et al. retrospectively reviewed 10-year outcomes of men undergoing RP at a single hospital during a ten-year period. Results showed that men categorized as obese by BMI or with metabolic syndrome were more likely to develop post-RP BCR than non-obese men. As the authors acknowledge, this is an observational study and a prospective study is needed to validate their findings. Furthermore, it is unclear whether this higher BCR rate would translate into a higher mortality rate.

The Bottom Line: It appears from this study that obese men and those with metabolic syndrome MAY have a greater risk for post-RP BCR. However, prospectively collected data are needed to validate the accuracy of this observation. Validation is required before a different follow-up protocol can be recommended vs. the protocol used for the general population of men treated by RP.
The Role of Lymph Node Dissection (Continued from page 5)

dardized definitions of surgical templates, standard protocols for pathologic workup, and adequate duration of follow-up to determine the therapeutic effectiveness of PLND. Results from two ongoing prospective studies (NCT01812902 and NCT01555086) are currently awaited. However, when evaluating a randomized controlled trial in this field, three factors – patient selection, PLND procedure, and pathologic examination – must be considered.

Patient Selection: Risk assessment is a fundamental step in study design, and populations with higher risks of lymph node disease should be investigated. For example, PLND is unlikely to have a significant effect on patients with low-risk PCs. Therefore, accurate patient selection is mandatory.

PLND Procedure: The definition and extent of PLND represent other important factors to be considered. Although extended PLND has shown superior diagnostic accuracy compared with limited PLND, it is unlikely to detect all positive lymph nodes. Furthermore, several surgeon-related factors may have an important influence on the final results. As an example, in the SEAL/Association of Urogenital Oncology (AOU) AP 55/09 trial, rates of pN1 disease observed in the extended and limited groups were 15% and 12%, respectively. These findings suggest a surgeon-related bias toward more meticulous PLND in the limited PLND group. Therefore, predefined templates should be well defined in any ongoing and future studies.

Pathologic Examination: Pathologic evaluation of pelvic lymph nodes remains controversial, with a lack of consensus on specimen processing and node identification. There is evidence that

surgeons and pathologists may influence the number of lymph nodes removed and the number of positive nodes retrieved. Therefore, standard operating procedures for pathologic workup should be predefined in any studies.

Conclusion

PLND remains the most accurate and reliable approach for detecting the presence of lymph node metastases in prostate cancer. PLND and its extent are associated with less favorable intraoperative and perioperative outcomes, whereas a direct therapeutic effect is still not evident from the available literature. The current poor quality of evidence indicates the need for robust and adequately powered clinical trials. Meanwhile, because of its recognized staging benefits, extended PLND should be undertaken whenever it is indicated in selected men at high risk for lymph node invasion.