Prostate Cancer Care Declined During the COVID-19 Pandemic

Access to medical care for men with prostate cancer (PCa) was sharply reduced last year during the COVID-19 pandemic, according to real-world data from Verana Health and the American Urological Association (AUA). The data was presented at the 2021 virtual American Society of Clinical Oncology (ASCO) Annual meeting.

A total of 267,691 men with PCa visited 158 US urology providers within the AUA’s Quality (AQUA) registry during 2019 and 2020. From March 2 to November 1, 2020 (week 10 to week 44) the magnitude of the decline and recovery in health care visits, including telehealth, varied by PCa risk category, with the steepest drops observed for low-risk PCa, Matthew R. Cooperberg, MD, MPH, of the University of California, San Francisco, and colleagues reported.

For the first 9 weeks of 2020, health care providers had 25.6 mean visits per day, similar to 2019. Visits declined from weeks 10 to 14 (early March to the first week of April) to 18.03 per day — a 31% drop compared with 2019. Visits recovered to 2019 levels by week 23 (early June 2020), then declined to 11.89 per day by week 44 — a 58% drop from the same period in 2019.

For low-risk PCa, average visits per day declined from 6.57 at week 10 to 4.49 at week 14, rebounded to a peak of 7.04, then declined again to a new low of 3.62 at week 44, Dr. Cooperberg’s team reported. Intermediate-risk PCa visits followed the same pattern, but were lower than low-risk PCa. High-risk PCa visits were almost halved, with a similar pattern of increase in March and April, then decline to a new low in week 44.

(Continued on page 5)

Is Abiraterone Plus ADT and Docetaxel a New Standard of Care for Metastatic Castration-Sensitive Prostate Cancer?

Adding abiraterone to the current standard of care (SOC) prolonged radiographic progression-free survival (rpPFS) vs. SOC alone in men with metastatic castration-sensitive prostate cancer (mCSPC), according to results of the phase 3 PEACE-1 trial presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting.

“In fact, the rpPFS results demonstrated a 2.5-year difference in favor of abiraterone plus SOC,” said Ka-rim Fizazi, MD, PhD, of Institut Gustave Roussy in Villejuif, France, when presenting the study at the meeting.

The phase 3 trial (ClinicalTrials.gov Identifier: NCT01957436) included 1,173 men with de novo mCSPC randomly assigned to the treatment arms below:

• SOC: androgen deprivation therapy (ADT) alone or ADT plus docetaxel
• SOC plus abiraterone (given with prednisone)

(Continued on page 3)

Genomic Landscape of PCa Differs by Ancestry but Frequency of Actionable Alterations is Similar

Rates of actionable genetic alterations were similar in prostate cancer (PCa) patients with African ancestry and those with European ancestry, according to results of a large-scale genomic analysis presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting.

These results were presented by Brandon A. Mahal, MD, of the University of Miami Sylvester Comprehensive Cancer Center. Dr. Mahal noted that men of African ancestry have a higher burden of PCa when compared with men of European ancestry. This may be a result of differences in socioeconomic factors, environmental exposures, and biologic or epigenetic phenomena.

“We sought to characterize the genomic landscape, comprehensive genomic profiling utilization, and treatment patterns based on genomic ancestry in an effort to better understand advanced PCa,” Dr. Mahal said.

He and his colleagues analyzed samples from 11,741 patients with advanced PCa who had undergone comprehensive genomic profiling (CGP) by Foundation Medicine as part of routine care.

Genomic ancestry was determined using a single nucleotide polymorphism-based approach, which revealed that 12% of men had African ancestry and 79% had European ancestry.

Patients with African ancestry had a median lower age at diagnosis compared with patients who had European ancestry — 64 years and 67 years, respectively. Only 4.2% of men with African
Inverse Stage Migration in Radical Prostatectomy — a Sustaining Phenomenon

**Objective:** To investigate temporal trends in prostate cancer (PCa) radical prostatectomy (RP) candidates.

**Materials and Methods:** Patients who underwent RP for PCa between January 2014 and December 2019 were identified from our institutional database. Trend analysis and logistic regression models assessed RP trends after stratification of PCa patients according to D’Amico classification and Gleason score (GS). Patients with neoadjuvant androgen deprivation (ADT) or radiotherapy (RT) prior to RP were excluded from the analysis.

**Results:** Overall, 528 PCa patients that underwent RP were identified. Temporal trend analysis revealed a significant decrease in low-risk PCa patients from 17% to 9% (estimated annual percentage change [EAPC] -14.6%, p < 0.05) and GS6 PCa patients from 30 to 14% (EAPC) -17.6%, p < 0.01). This remained significant even after multivariable adjustment [low-risk PCa: (Odds Ratio [OR]): 0.85, p < 0.05 and GS6 PCa: OR: 0.79, p < 0.001]. Furthermore, a trend toward a higher proportion of intermediate-risk PCa patients undergoing RP was noted.

**Conclusion:** Our results confirm that inverse stage migration represents an ongoing phenomenon in a contemporary RP cohort in a European tertiary care PCa center. Our results demonstrate a significant decrease in the proportion of low-risk and GS6 PCa patients undergoing RP and a trend toward a higher proportion of intermediate-risk PCa patients undergoing RP. This indicates a more precise patient selection when it comes to selecting suitable candidates for definitive surgical treatment with RP.

Time Trends in Use of Radical Prostatectomy by Tumor Risk and Life Expectancy in a National Veterans Affairs Cohort
JAMA Netw Open. 4: e2112214, 2021

**Question:** How has the use of radical prostatectomy (RP) changed over time with respect to tumor risk and life expectancy (LE)?

**Findings:** In this cohort study of 5,736 men treated with RP at 8 Veterans Affairs (VA) hospitals from 2000 to 2017, the proportion of low-risk tumors decreased 44%, the proportion of intermediate-risk tumors increased 29% (with favorable intermediate-risk tumors decreasing 20% and unfavorable intermediate-risk tumors increasing 11%), and the proportion of high-risk tumors increased 15%. During this period, the proportion of men treated with RP with LE less than 10 years increased 9%.

**Main outcomes and measures:** Stratified linear and log-linear Poisson regressions were used to estimate time trends in the proportion of men treated with RP across American Urological Association tumor risk and PCCI (a validated predictor of LE based on age and comorbidities) subgroups.

**Results:** Among 5,736 men (mean [SD] age at surgery, 62 [6] years) treated with RP from 2000 to 2017, the proportion of low-risk tumors treated with RP decreased appears unchanged across tumor risk subgroups and increased overall.

**Design, setting, and participants:** This cohort study of 5,736 men treated with RP at 8 VA hospitals from January 2000, to December 2017, used a nationally representative, multicenter sample from the VA SEARCH (Shared Equal Access Regional Cancer Hospital) database. Statistical analysis was performed from June 2018 to August 2020.

(Continued on page 8)

Join us for the fifth webinar in our series, “What is Right for Me in My Prostate Cancer Treatment?” - a discussion on Genetics and Genomics, with Dr. Heather H. Cheng and Dr. Brittany Szymaniak. Thursday, July 29, 7:00 - 8:30pm Central. www.ustoo.org/mypcawebinar.
Doc Moyad’s What Works and What is Worthless Column – Also Known as “No Bogus Science” Column
“Will Lycopene and I Say Asparagus?!”
Mark A. Moyad, MD, MPH, University of Michigan Medical Center, Department of Urology

Editor’s Note: Us TOO invites certain physicians and other interested parties 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.

More than 20 years ago the medical literature, along with countless public educational sources, began to inundate us with the idea that lycopene from tomatoes might have the ability to prevent or fight prostate cancer (PCa).

I remember the actual week back in 1999 when arguably the most respectable publication on the subject was first published.1 I remember that week because I swear you could not find a single tomato at any grocery store. Not a single tomato or tomatoe, so I decided to call the whole grocery store visit thing off for a while (did you see how I threw that funny, but deferential Fred Astaire and Ginger Rogers song reference in?)

Yet, what I believe few people realized from that 1999 groundbreaking tomato and lycopene nexus publication was the actual conclusive unequivocal beautiful words of advice from the Harvard author in the final published manuscript itself. The advice was not to buy up all the tomatoes or pills, but rather wonderfully concluded by suggesting that all the positive anti-cancer data with tomatoes or tomato products “adds further support for current dietary recommendations to increase fruit and vegetable consumption.”

Wait!! What?!! Not to just eat raw or cooked tomatoes and pizza all day? No! This was the beauty of the author’s recommendation that, in my opinion, was and has been missed by so many for the last 20+ years. Today, research is still going back and forth on whether lycopene or tomatoes have special anti-cancer effects. Some new analyses say “no” and others say “yes” while others suggest “maybe.” Yet, if you would have followed the original advice from that historic publication there would still be no ambiguity today.

Eating more whole non-processed plant-based foods such as fruits and vegetables is part of an overall healthy dietary pattern.

You could also argue that the obsession with the tomato and lycopene was also misdirected for another related reason. There are numerous other lycopene sources that should also receive more love. According to USDA testing and other reputable sources there are many other foods with lycopene that are healthy, including: grapefruit (pink & red), red-fleshed papayas (one study showed more bioavailability vs. raw tomatoes), persimmons, mangos, passion flower fruit, jackfruit, apricots, guava, and fresh watermelon, which of course do not need to be heated (like tomatoes) to achieve better absorption of lycopene, and that was from a study back in 2003.2,3

Heck, we have also learned since 1999 that some types of bananas, carrots, oranges, grapes, and even asparagus contain some lycopene! What?! Yes, even the USDA found some lycopene in asparagus and, coincidentally as I am writing this column, right now it is asparagus season, my friends. I know what you are thinking! There is only a small amount of lycopene in asparagus and when I eat a tomato (or tomatoe) it does not make my urine smell “malodorous.” Yes, but 1 piece of asparagus is just 3 calories, so 10 pieces is just 30 calories! So, when you consider the small amounts of lycopene per tiny caloric contribution then it becomes an impressive source or ratio of lycopene-to-calories along with countless other nutrients. Look, to say I love tomatoes is an understatement. I adore them, but I do not hold them in higher esteem (or steam) than the other sources of lycopene. In my world, I often rearrange that original song and sing the (Continued on page 8)

Is Abiraterone Plus ADT and Docetaxel the New SOC for mCSPC?

(Continued from page 1)

there was no interaction between abiraterone and RT. Median follow-up was 36 months.

Abiraterone plus SOC significantly prolonged rPFS vs. SOC alone. Median rPFS was 4.5 and 2.2 years, respectively (hazard ratio [HR], 0.54; 95% confidence interval [CI], 0.46-0.64; P <0.0001). In men who received ADT plus docetaxel as the SOC, the addition of abiraterone prolonged rPFS. The median rPFS was 4.5 years with abiraterone and 2.0 years without it (HR, 0.50; 95% CI, 0.40-0.62; P <0.0001, a statistically significant difference).

Abiraterone also improved castration-resistant prostate cancer (CRPC)-free survival. In the overall population, the median CRPC-free survival was 3.8 years with abiraterone plus SOC and 1.5 years with SOC alone (HR, 0.40; 95% CI, 0.35-0.47; P <0.0001). In men who received ADT plus docetaxel as the SOC, the median CRPC-free survival was 3.2 years with abiraterone plus SOC and 1.4 years with SOC alone (HR, 0.38; 95% CI, 0.31-0.47; P <0.0001).

“Abiraterone resulted in a very clear and significant improvement of CRPC-free survival, with a 60% reduction in the risk of developing castration resistance or death in both the overall population and the ADT plus docetaxel population,” Dr. Fizazi said. The overall survival (OS) data are not yet mature.

Grade 3-5 liver toxicity and hypertension were more common in the abiraterone-SOC arm, but the frequencies of febrile neutropenia and neutropenia (very low white blood cell count) were similar to the SOC-alone arm.

“Adding abiraterone and prednisone to ADT plus docetaxel clearly improves rPFS in men with de novo metastatic prostate cancer (PCa),” Dr. Fizazi said.

He added that, although the OS data are maturing, “regardless of survival results, these data question whether we should deny men approximately 2.5 years without radiographic progression or death, or whether combining ADT plus docetaxel and abiraterone-prednisone should simply become the new SOC for men with de novo mCSPC.”

Reference

Cancer Therapy Advisor
10 June 2021
Bone-Protecting Agents (BPAs) Cut Fracture Risk in Metastatic Prostate Cancer
Those Receiving Enzalutamide With and Without Radium-223 Saw Benefits in Updated Safety Analysis

The use of bone-protecting agents (BPAs) substantially reduced the risk of fracture in men with castration-resistant prostate cancer (CRPC) and bone metastases who were being treated with enzalutamide with and without radium-223 (223Ra), according to an updated safety analysis of the EORTC 1333/PEACE III trial.

Among patients who did not receive zoledronic acid or denosumab, cumulative incidence of fracture was 37.1% in the combination arm and 15.6% in the enzalutamide-alone arm at 1 year vs. 2.7 and 2.6%, respectively, of men who took BPAs, reported Silke Gillessen, MD, of the Oncology Institute of Southern Switzerland.

“This safety analysis confirms the importance of giving a BPA when treating CRPC with bone metastases (mCRPC),” Gillessen said at a presentation at the virtual American Society of Clinical Oncology (ASCO) Annual meeting.

“Skeletal complications are common in men with advanced prostate cancer (PCa),” she added. “And they have an impact on the quality of life of our patients. These complications result from osteoporotic fractures and skeletal-related events (SRE), including pathologic bone fracture, spinal cord compression, orthopedic surgery, and palliative radiation, which occur due to bone metastases.”

To prevent skeletal complications, many guidelines recommend the use of BPAs such as zoledronic acid and denosumab in patients with CRPC and bone metastases.

The ongoing phase III EORTC 1333/PEACE III trial has a history that was complicated by results from the ERA 223 trial, which compared 223Ra plus abiraterone acetate vs. abiraterone acetate alone in men with chemotherapy-naive CRPC with bone metastases. The primary outcome of the trial was symptomatic SRE-free survival.

ERA 223 was prematurely unblinded in 2017 after significant increase in fracture rates and deaths was reported in the combination group. Sixty percent of men had not received a BPA at trial entry, and a post-hoc analysis showed that BPAs significantly decreased the rate of fractures in both study arms.

Based on these results, the independent data monitoring committee of the EORTC 1333/PEACE III trial—which has a primary endpoint of radiographic progression-free survival in men with asymptomatic or mildly symptomatic metastatic CRPC—mandated the use of BPAs in study participants.

The trial as amended requires the use of a BPA at least 6 weeks before the injection of 223Ra. Before this requirement was mandatory, however, 45% of men randomized into the trial had not received a BPA. After the mandate, this proportion fell to 2.9%. At 21 months, men who did not take a BPA in the combination arm and the enzalutamide-alone arm had a cumulative incidence of fracture of 52.0 and 21.9% vs. just 4.3 and 2.6%, respectively, for men using BPAs.

“Our updated safety analysis confirms that the risk is well controlled in both arms when a BPA is administered,” Gillessen noted.

“It was good to see that the fracture rate in the 223Ra arm did in fact improve,” observed ASCO discussant Lisa Horvath, PhD, MBBS, of Sydney Cancer Center in Australia. “But what I found most impressive was the efficacy of BPAs in the standard-of-care enzalutamide arm.”

Horvath pointed out that the analysis was not a randomized comparison, contained small numbers, and has yet to report on toxicity and quality of life. “But it does prove the point we should be using these agents more frequently.”

Presented at virtual 2021 Annual ASCO meeting; abstract 5002.

MedPage Today 8 June 2021

Genomic Landscape of PCa Differs by Ancestry (Continued from page 1)
Perioperative treatment to preserve nerve function did not significantly improve erectile function (EF) after surgery for prostate cancer (PCa), a randomized, placebo-controlled study showed.

Six months after radical prostatectomy (RP), men treated with erythropoietin (EPO) or placebo had similar scores on a validated scale of EF. In fact, the median score favored the placebo group (19 vs. 14). Investigators also found no significant difference between groups at 3, 9, and 12 months. Adjustment for nerve-sparing surgery, which was associated with recovery of EF, had minimal effect on analyses of primary and secondary endpoints.

The EPO group had significantly higher hemoglobin levels during treatment, consistent with use of EPO, reported Hiten D. Patel, MD, of Johns Hopkins School of Medicine in Baltimore, and co-authors online in The Journal of Urology.

"Unfortunately, the ERECT trial did not confirm an independent benefit for EPO as suggested by retrospective data and highlights the need for high-quality, randomized, placebo-controlled trials prior to widespread implementation of these types of adjuncts," the authors said. "It is possible the lack of efficacy could be due to the target population destined to do relatively well regardless of interventions beyond RP technique."

"Cases where complete nerve sparing cannot be achieved or men with some degree of erectile dysfunction (ED) prefer RP may be future populations of interest and better approximate preclinical models, which had more significant cavernous nerve injury," the researchers continued.

Despite technical advances in surgery for PCa, ED remains a common adverse effect and a barrier for men who are candidates for RP, according to the authors of an accompanying editorial. The ERECT trial added to a list of adjunctive therapies evaluated (unsuccesfully) to preserve and enhance cavernous nerve restoration, but the search should continue.

"The study failed to show a benefit of EPO on EF but may have been limited by small sample size (number of patients) and confounders, including both patient and technical factors," wrote Poone S. Shoureshi, MD, and Mark Garzotto, MD, both of Oregon Health & Science University in Portland, OR.

"Peripheral nerve regeneration and neuroprotection are critical areas of research with the potential to change clinical management of post-RP patients ... Ultimately, it is through progress in these and other areas of research that surgeons will be able to reduce the morbidity and improve patient acceptance of RP," the editorialists said. Though a common complication of RP, postoperative ED tends to decline over time. In the randomized PROTECT trial, the incidence of ED decreased from 67% at baseline to 21% at 36 months. However, a substantial proportion of men have long-term ED of varying degrees of severity. "ED after RP results from surgical injury to erection-producing nerves. The advent and adoption of nerve-sparing RP substantially improved EF outcomes, but no additional intervention has demonstrated ability to alter the natural history of postoperative ED," the authors noted.

Phosphodiesterase-5 (PDE-5) inhibitors aid in EF recovery, but placebo-controlled trials showed no permanent benefit.

"Recovery rates for EF have flattened in the past decade despite advancements in surgical and postsurgical care," the team stated.

EPO is expressed in the central and peripheral nervous systems, and receptors have been identified in human penile tissue and neurovascular bundles. Studies involving a preclinical model of cavernous nerve injury showed that EPO improved erection recovery, suggesting a neurotrophic effect. Additionally, retrospective clinical data showed sustained improvement in the International Index of Erectile Function (IIEF) in men who received subcutaneous (SQ) injections of EPO prior to RP.

(Continued on page 8).

**PCa Care Declined During the COVID-19 Pandemic**

(Continued from page 1)

same temporal trend. Mean visits per day declined from 9.68 at week 10 to 7.36 at week 14, rebounded to a peak of 10.04, then declined to 5.65 at week 44. High-risk prostate cancer visits showed less fluctuation but were still down by nearly a third, according to the investigators. Mean visits per day declined from 6.31 at week 10 to 5.24 at week 13, rebounded to a peak of 6.45, then dropped to 4.31 at week 41.

"For urologists and genitourinary cancer patients, early detection and treatment are critical to successful outcomes," David F. Penson, MD, MPH, chair of the AUA Science and Quality Council, stated in a news release.

"Thanks to our collaboration with Verana Health, we now understand better the changes in care due to the COVID-19 pandemic that we can study to gauge the long-term impact of delayed diagnoses and treatments for PCa."

"The most surprising finding was the depth of the second decline in PCa visits in October to early November after the initial drop in March and the recovery in June," stated Dr. Cooperberg.

"Clearly as a country we have struggled to restore access to cancer care to pre-pandemic levels, even more so in the latter half of 2020 than in the first half," he said. "We have multiple guidelines, developed in the past year, to help decide which man’s cancer care can and cannot be safely deferred, but based largely on expert opinion. It will take time and attention to measure the impact of COVID-related delays on outcomes.

"Telehealth access needs to be uniform," he added. "Telehealth is very likely here to stay, and the regulatory reforms enacted in early 2020 to enable this — for example, suspension of interstate practice prohibitions and re-interpretations of HIPAA — will hopefully be permanent."

Dr. Cooperberg noted that urologists can join AQUA, which now offers free standard membership, and contribute their data. "AQUA yields insights into the successes and challenges facing the specialty as a whole."

Presented at the 2021 ASCO Annual meeting; Poster 5061.

Cancer Therapy Advisor
8 June 2021
Radiologists in front of a computer monitor evaluate the radiotherapy (RT) treatment area using a treatment planning system. The use of artificial intelligence (AI) in creating RT plans for prostate cancer (PCa) appeared to be a success, according to a blinded, head-to-head study. Overall, radiation oncologists considered the vast majority (89/100) of machine learning (ML)-generated plans clinically acceptable for treatment, reported Thomas Purdie, PhD, and colleagues at Princess Margaret Cancer Centre in Toronto. This finding was stable across both the simulation phase (92%) and the deployment phase (86%) of the study.

Moreover, in a head-to-head comparison of radiation treatment plans generated by an ML algorithm or humans, 72% of the ML-generated plans were selected over human-generated plans, “indicating the potential for ML to even surpass human performance owing to increased consistency whereby the ML plan amalgamates a consensus of experts as opposed to a single expert,” they wrote in a research letter published in Nature Medicine.

However, when radiation oncologists were faced with actually putting patients on these treatment plans, the number of ML plans selected for treatment was significantly reduced (83% in the simulation phase vs. 61% in the deployment phase).

“Once you put ML-generated treatments in the hands of people who are relying upon them to make real clinical decisions about their patients, that preference towards ML may drop,” said Purdie in a press release.

“There can be a disconnect between what’s happening in a lab type of setting and a clinical one.”

While machine learning “holds great promise for healthcare delivery, its impact has been mostly tested in simulated environments that can’t be replicated in real-world clinical practice,” noted Purdie and colleagues. Therefore, in this study, they wanted to prospectively deploy and test an algorithm for therapeutic RT planning for PCa patients.

The study involved 2 phases. The first was a retrospective simulation phase in which previously delivered RT plans were compared with ML-generated plans in 50 men by 7 radiation oncologists under blinded review. In the second prospective deployment phase, 9 radiation oncologists compared ML and human-generated radiation treatment plans for 50 patients under blinded review. The selected plan — ML or human — was used for treatment following all standard clinical quality controls.

“RT planning using ML reduced the median time needed for the entire planning process by 60%,” Purdie and team noted. Overall, the radiation oncologists selected the RT plan that was “quantitatively superior based on compliance with clinical guidelines” in 85 and 72% of cases in the simulation vs. deployment phases, respectively.

“Preference towards ML or human-generated RT plans was attributed at the individual level based on the perceived origin (ML or human) of the selected RT plan, when it was quantitatively inferior based on consensus review,” the authors wrote. For example, they noted that most of the observed preference for human-generated treatment plans was accounted for by 2 of the 9 treating radiation oncologists.

The study demonstrates “that fully automated, ML-generated therapeutics are realizable in a clinical environment,” Purdie and colleagues wrote. “Prospective deployment studies validating the impact of ML on real-world clinical settings are necessary to quantify the value of these methods, and to drive acceptance for routine use in patient care.”

“When it comes to new technologies and devices, I think there is a general distribution of uptake and acceptance, with some early adopters, some who are more skeptical but convincing, and then the late or reluctant adopters,” said Neha Vapiwala, MD, of Perelman School of Medicine at the University of Pennsylvania, who was not involved in the study.

“There is also something to be said for some of the nuances that simply can’t be captured with machine learning, such as the body of one’s professional experience and history with a specific tumor type, or a particular kind of clinical case,” she told MedPage Today. “You might follow the typical guidelines, and a treatment plan may look ‘perfect,’ but perhaps you’ve observed outcomes with patients in that particular scenario that you incorporate in your decision making and that may favor a non-automated approach.”

Vapiwala also noted that, while machine learning as described in this study is not yet broadly available, there are certain elements that are more prevalent in today’s clinical practice and appear to be more readily adopted, such as auto-contouring of structures on simulation CT images that are used for dose modeling.

MedPage Today
16 June 2021

No Need to Raise Salvage Radiation Dose After RP
Conventional-Dose Salvage Radiation (RT) is Sufficient for Men with Early Biochemical Progression After Prostatectomy

The phase 3 SAKK 09/10 trial recruited 350 men with biochemical progression (BP) after radical prostatectomy (RP) and randomly assigned them 64 Gy or 70 Gy of RT to the prostate bed without hormonal therapy. The primary endpoint was freedom from biochemical progression (FFBP). The median age at randomization was 67, and the median PSA level was 0.3 ng/ml.

As reported online in European Urology, after a median follow-up of 6.2 years, the median FFBP was 8.2 and 7.6 years in the 64 and 70 Gy arms (hazard ratio, 1.14). Six-year FFBP rates were 62% and 61%, respectively. No significant between-group differences were observed in progression-free survival, time to hormonal treatment, or overall survival.

However, late grade 2 and 3 genitourinary toxicity occurred in 21 and 7.9% and 26 and 4% of men in the 64 and 70 Gy arms. Further, late grade 2 and 3 gastrointestinal toxicity was seen in 7.3 and 4.2% and 20 and 2.3% of those in the 64 and 70 Gy arms. The authors conclude “Conventional-dose SRT to the prostate is sufficient in men with early BP of PCa after RP.”

Reuters Health
June 25, 2021
Purpose: Adjuvant compared with early salvage radiation therapy (sRT) following radical prostatectomy (RP) has not been shown to reduce progression-free survival in randomized controlled trials. However, these trials might have missed a benefit in men with adverse pathology at RP given that these men were under-represented and immortal time bias might have been present; herein, we investigate this possibility.

Methods: We evaluated the impact of adjuvant RT (aRT) vs. early sRT on all-cause mortality (ACM) risk in men with adverse pathology defined as positive pelvic lymph nodes (pN1) or Gleason score 8-10 prostate cancer (PC) and disease extending beyond the prostate (pT3/4). We used a treatment propensity score to minimize potential treatment selection bias when estimating the causal effect of aRT vs. early sRT on ACM risk and a sensitivity analysis to assess the impact that varying definitions of adverse pathology had on ACM risk adjusting for age at RP, PC prognostic factors, site, and the time-dependent use of post-RP androgen deprivation therapy (ADT).

Results: After a median follow-up (interquartile range) of 8.16 (6.00-12.10) years, of the 26,118 men in the study cohort, 2,104 (8.06%) died, of which 539 (25.62%) were from PC. After excluding men with a persistent PSA, aRT compared with early sRT was associated with a significantly lower ACM risk among men with adverse pathology at RP when men with pN1 PC were excluded (0.33 [0.13-0.85]; P = 0.02) or included (0.66 [0.44-0.99]; P = 0.04).

Conclusion: Adjuvant radiation therapy should be considered in men with pN1 or Gleason score 8 to 10 and pT3/4 PC given the possibility that a significant reduction in ACM risk exists.

Quantitative Total Bone Imaging in Prostate Cancer: Novel Technology, and a Promising Biomarker

Response evaluation of bony metastases in patients with metastatic prostate cancer (PCa) remains challenging. Bone scintigraphy detects osteoblastic activity in PCa but has inherent limitations such as inability to define changes within existing lesions, as well as non-specific uptake in areas of bone degeneration. Further, treatment response in individual lesions can be heterogeneous and difficult to characterize.

Incorporation of image-derived metrics and their application as a potential biomarker in PCa is an area of growing interest. In the early days of radiographic biomarker development, bone scan index (BSI) was proposed as a semi-quantitative measure of the percentage of the adult skeleton involved by tumor.

In 2010, SUVmax, a measure of tumor glycolytic rate was identified as a predictor of survival in advanced PCa.

Quantitative total bone imaging (QTBI) is a novel method of analyzing changes in functional metrics such as SUVmax, SUVtotal, and SUVmean on [18F] sodium fluoride (NaF) positron emission tomography (PET/CT) scans, that allows characterization of treatment-related changes of individual lesions besides quantification of overall disease. This automated technology has previously demonstrated a correlation between progression-free survival (PFS) with the total functional burden after 3 cycles of hormonal or chemotherapy in men with metastatic castration-resistant prostate cancer (mCRPC).

In a recent publication in the Journal of Clinical Oncology (Vol. 38, pp. 3662-3671, 2021), Kyriakopoulos, et al. evaluated spatial temporal changes using QTBI in 23 mCRPC patients initiating enzalutamide. Imaging using NaF PET/CT was performed at baseline (PET1), 13 weeks (PET2) and at the time of PSA, radiographic or clinical progression, or at 2 years without progression (PET3).

The authors hypothesized that disease progression may be a result of increase in disease burden in some non-responding, but not all lesions. A biomarker study enumerating circulating tumor cells (CTCs) was also conducted.

The primary study endpoint was the proportion of men with at least one responding bone lesion at the time of PET3. The secondary end-point was SUVhetero, which is a measure of the variance of mean SUV of an individual lesion, assessed at the time of the primary endpoint.

SUV metrics decreased from baseline to PET2 and then increased at PET3. There was a significant correlation between PSA progression and changes in SUVhetero from PET1 to PET3. All evaluable men were noted to have at least 1 responding bone lesion on PET3, while demonstrating an admix of new, stable, responding, and progressing lesions.

This regarding response heterogeneity in individual osseous lesions in mCRPC. The strength of this automated technology lies in its ability to break down treatment response at the level of individual lesions. It also highlights the role of early radiographic response metrics as a potential biomarker of early resistance.

Future trials should explore the role of radiographic response adaptive treatment strategies, incorporating the use of radioablation for oligoresistant lesions, as suggested by the authors. It will also be interesting to study the correlation of SUV metrics with long-term survival within larger trials of mCRPC.
The ERECT Trial: EPO No Help for ED Following RP (Continued from page 5)

The ERECT trial progressed clinical evaluation of EPO in ED to the phase II setting. Of 63 men with localized PCs enrolled, 56 were randomly assigned to receive SQ injections of EPO or placebo. Blinded treatment was administered the day before, the day of, and the day after RP. The primary endpoint was an improved IIEF score from baseline to 6 months. The 56 men had a median age of about 55, and 50 underwent robot-assisted RP. Two experienced surgeons rated each procedure for nerve sparing, and both groups had a total score of 9 (very good or excellent). The median baseline IIEF score was 12. After 6 months of follow-up, the scores did not differ significantly between the 2 groups (P=0.50).

Time Trends in RP (Continued from page 2)

from 51 to 7% (difference, −44%; 95% CI, −50 to −38%). The proportion of intermediate-risk tumors treated with RP increased from 30 to 59% (difference, 29%; 95% CI, 23-35%), with unfavorable intermediate-risk tumors increasing from 30 to 41% (difference, 11%; 95% CI, 4-18%) and favorable intermediate-risk tumors decreasing from 61 to 41% (difference, −20%; 95% CI, −24 to −15%). The proportion of high-risk tumors treated with RP increased from 18 to 33% (difference, 15%; 95% CI, 9-21%). Among men treated with RP, the proportion with the highest PCCI scores of 10 or more (i.e., LE <10 years) increased from 4 to 13% (difference, 9%; 95% CI, 4-14%). Within each tumor risk subgroup, no significant difference in the rate of tumors treated with RP over time was found across PCCI subgroups. Conclusions and relevance: In this study, the use of RP shifted from low-risk and favorable intermediate-risk to higher-risk PCs. However, its use among men with limited LE appears unchanged across tumor risk subgroups and increased overall.

Check Out the Us TOO Advanced Prostate Cancer Brochure at: www.ustoo.org/AdvancedBrochure

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QUESTION FROM PROSTATE CANCER SURVIVOR:
What kind of lubricant can I use with the vacuum device and what if my wife likes other kinds of lubricants during sex?

RESPONSE FROM DR. JEFFREY ALBAUGH:
Thank you for your question. It is most important that you only use water based/soluble lubricants with the vacuum device itself so as not to create problems with the device. Do not use Vaseline or oil-based lubricants with the vacuum device. You can get these types of water-soluble lubricants in any pharmacy near the condoms and they vary greatly in price. They typically come in a bottle or tube and most pharmacies have their own less expensive version of a water-soluble/water-based lubricant.

Lubricant is used several times throughout the process with the vacuum device. It is used on the penis and inside the vacuum device before putting the penis into the device. It is also used to apply the ring on the loading cone and under the ring on the device so the ring will glide off the device onto the penis. After sex, lubricant is reapplied to the penis to reduce friction to get the constriction ring off the penis. It is applied to the penis before stretching the ring around the penis to remove it off the lubricated penis. If your partner likes other lubricants such as silicone lubricants or coconut oil, these lubricants can be used after finishing with the vacuum device, during sex.


Watch Dr. Albaugh’s presentation on sexual health and intimacy from the Prostate Cancer Pathways for Patients and Caregivers event recorded at NorthShore University HealthSystem in Skokie, IL on November 3, 2018 at https://www.youtube.com/watch?v=Hiq0dDEb1l0&t=4483s.

Read previous issues of Between the Sheets at www.ustoo.org/BTS.

Do you have a question about sexual health or intimacy? If so, we invite you to send it to Us TOO. We’ll select questions to feature in future Between the Sheets columns.

Please email your question to: ustooBTS@ustoo.org

Or mail your letter to:
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Limiting Prostate Cancer’s Fuel
By Janet Farrar Worthington

Just when it seems like the picture of diet and prostate cancer is finally coming into focus, PCF-funded scientist Nicole Simone, M.D., a radiation oncologist at Thomas Jefferson University, has added a new dimension. It may not be just a question of the good foods you do eat, and the bad foods you don’t eat, it also appears to matter, very strongly, how much you eat at all.

Simone’s research in prostate cancer and also in breast cancer suggests that restricting calories has many anti-cancer effects in the body — including, in mice, decreasing the likelihood of metastasis. It lowers inflammation, changes the gut microbiome, may decrease the side effects of systemic therapy, and generally seems to slow down cancer. In effect, caloric restriction gives cancer a “brown-out,” limiting its energy.

Simone’s laboratory has been investigating caloric restriction for several years. In mouse models of hormone-sensitive breast cancer, Simone found that simply restricting the mice’s daily caloric intake made a big difference. It not only altered cell metabolism and made cancer cells more vulnerable to radiation and chemotherapy, it also decreased metastasis and increased overall survival.

“In several models of hormone-sensitive prostate cancer, we found the same,” she says. “We were able to decrease tumor growth, decrease metastasis, and increase survival.” Then Simone’s lab tested caloric restriction in mice with castrate-resistant prostate cancer (CRPC), cancer that is no longer controlled by androgen deprivation therapy (ADT). Again, caloric restriction affected how tumors responded to radiation. Simone says, “We wanted to take it a step further, and use that preliminary data as a launching pad to see what would happen in patients with prostate cancer if we put them on a caloric restriction diet.”

Eating 25 percent less: In a pilot study, 20 patients — men diagnosed with localized prostate cancer who were scheduled to have a prostatectomy — underwent caloric restriction for 21 days. Simone individually tailored each man’s daily calorie total, based on what he had reported eating for several days ahead of time. “We figured out their average caloric intake and then decreased that by 25 percent.” Simone’s team also gave the men some dietary guidelines, encouraging (but not requiring) an anti-inflammatory diet with less refined sugar and processed food, and more fruits, vegetables, and complex carbohydrates. “The men were able to stick to the diets really nicely,” she says. “They did increase their anti-inflammatory foods! They also lost an average of 12 pounds each.”

Could just three weeks of restricted-calorie, anti-inflammatory diet make a difference? Yes, in several ways, including: a decrease in systemic inflammation, changes in the gut microbiome, less inflammation in the gut wall, and less inflammation in the tumor.

Ultimately, Simone believes, caloric restriction can play an important role for men in all stages of prostate cancer — but to make it even more effective will also require precision nutrition, based on precision oncology. “Prostate cancer can metabolize through the glucose pathway, or through lipid pathways,” says Simone. Understanding which pathway really appeals to a particular cancer — some prefer sugar, some really go for fat — “can tell us how your cancer is driving its own energy.”

One of the biggest challenges with chemotherapy, ADT, or even radiation therapy, is resistance to treatment: the cancer evolves to minimize the damage of attempts to kill it. “Diet can almost be a more powerful tool,” says Simone. “Cancers get smarter; a drug will work well for a while, then all of a sudden, cancer will figure out a way around it. The power of restricting food is that it provides less energy for the cancer to use up.”

Note: Caloric restriction is done under careful supervision by medical professionals. It is strongly recommended that you talk with your doctor before making changes to your diet.
Us TOO is proud to offer our 2021 webinar series, What is Right for Me in My Prostate Cancer Treatment? This series of educational and interactive webinars will bring people together virtually and safely to access empowering, decision-making information and personal connections in a time of social distancing.

The fifth, and final, webinar in this series is a discussion on the topic of Genetics and Genomics. Genetics and genomics technology is changing rapidly and there are a growing number of options available to help guide treatment decisions. Join us as we discuss the latest developments in this exciting area.

Genetics and Genomics
Presented by Us TOO International
Thursday, July 29
7:00 - 8:30pm Central

Featuring:
Dr. Heather H. Cheng
Director, Prostate Cancer Genetics Clinic
Seattle Cancer Care Alliance

Dr. Brittany Szymaniak
Genetic Counselor, Urology Department
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