KESHO
Kenya Society of Haematology & Oncology

REPORT OF 1st KESHO
ANNUAL PROSTATE CANCER SYMPOSIUM

BY

KENYA SOCIETY OF HAEMATOLOGY AND ONCOLOGY (KESHO)

26 MARCH, 2O22

RAPPORTEURS:

Maria & Co

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EXECUTIVE SUMMARY:

The Kenya Society of Haematology and Oncology (KESHO) organized its first annual symposium on prostate cancer on 26th March 2022. The event was hybrid in nature, in-person as well as virtual. The event attracted over 280 virtual participants and 62 participants in person.

The talks covered diagnosis, screening, risk stratification, management of prostate cancer, the role of various treatment modalities, as well as case presentations. The event started early in the morning and was divided into four sessions, each one of them followed by a questions and answers session for participants to engage with all the speakers of that session. A sponsor presentation was part of the program in the end. The presenters and participants included mid-career professionals, students, residents, as well as veteran professors.

The event concluded with remarks from KESHO Chair Dr. Miriam Mutebi who thanked all the speakers and participants for sparing their day-long time to make the event a success.

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OPENING AND PROGRAM INTRODUCTION

The symposium was opened by KESHO Treasurer Dr. Mohammed Ezzi. The program comprised four sessions besides the introductory session, including Prof. Peter Ngugi's opening lecture. Dr. Ezzi welcomed the participants and introduced them to the program of the day-long event. He informed the audience that prostate cancer is the most common cancer in males in Kenya. Furthermore, it is cancer that has a lot of controversies starting with screening, diagnosis, and treatment for both early and metastatic cancers.

It is noted especially for prostate cancer that everyone has their right and wrong answers. Even in multidisciplinary tumor boards, professionals agree to disagree, and discussions can even take hours for simple questions and ways forward. He thanked all the speakers and participants and hoped that this event continues annually, or even biannually, with this one being the first one. He opened the symposium by inviting Prof Peter Ngugi for his talk on the epidemiology of prostate cancer.

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EPIDEMIOLOGY OF PROSTATE CANCER – KEY STATISTICS

BY DR PETER NGUGI

Prof Mungai is a Consultant Urologist and associate professor in the Department of Surgery at the University of Nairobi. He is the director of the East Africa Kidney Institute. Prof Mungai is the Editor-in-chief of the Kenya Urology Journal. He is a member of KAUS, BAUS, SIU, AUA.

He started his talk by humorously asking how someone can be prostateful (knowledgeful of the prostate) if we don't have a prostate; maybe we can ask those who have it. He reminded the audience that almost half of them (i.e., females) don't even have a prostate. He shared key statistics on the epidemiology of prostate cancer. There are about 1.5 million patients with prostate cancer, with 375,000 deaths each year, as reported by Simon Giona. Most statistics come from western countries because our diagnosis is still poor. As per World Health Organization (WHO, 2020), is the third most common cancer, lagging behind only the lung and colorectal cancers.

It was shared by the speaker that men of African origin have the highest incidence. Mortality rates differ significantly from incidence rates (the incidence is much higher than the mortality). The highest incidence is reported in the Caribbean, Sub-Saharan Africa, and Micronesia/Polynesia. Almost 50% of all the United Nations (UN) countries in the world have prostate as the commonest diagnosed malignancy.

It is interesting to note that Human Development Index (HDI) appears to have a relationship with the diagnosis of prostate cancer. Those with high HDI have a reported incidence of 37.5 per 100,000 people whereas those with low HDI have an incidence of 11.5 per 100,000 people. This does not mean that the incidence itself is low in the low-HDI countries. Rather, the diagnosis is poor, and we need to investigate why there is such a disparity in incidence correlated to HDI. This gap, however, is reduced for the mortality statistics compared to that of incidence. Those with high HDI report 8.1 deaths due to prostate cancer per 100,000 compared to 5.9 deaths per 100,000 in low-HDI countries. Again, the statistics could be lower due to issues with diagnosis and reporting.

The reported incidence is higher in Northern and Western Europe, the Caribbean, Australia/New Zealand, North America, and Southern Africa. The lowest incidence is found in Asia and North Africa, which, again could purely be a reporting issue. There is an under-reporting of prostate cancer in North Africa. The problem in those areas is due to lower PSA (prostate-specific antigen) testing. If we increase PSA testing, we will have more incidence of prostate cancer.

He showed the audience a bar graph being statistics on incidence and mortality in various regions of the world. Highlighting the Eastern African region, he noted that we are grouped with a lower incidence of prostate cancer. Prof said that it is hard for him to digest these statistics as a clinician because he usually sees more than twenty patients every week. These statistics resonate with the observation: lower the HDI, lower the incidence, and again that reflects poor reporting. If we look at the SEER database on the diagnosis of prostate cancer. In the early seventies, there was a lower incidence even in America itself and it went up in the mid-nineties and then reduced and stabilized after it. For mortality, it looks much different from what we have discussed previously. The highest is in the Caribbean with 75.8 per 100,000 people, followed by Sub-Saharan Africa with 22 and Micronesia/Polynesia with 18.8 per 100,000.

The Professor shared another bar graph with the audience showing the incidence and mortality cases per 100,000 of the population of various races in America. The mortality is not as high as shown in the other parts. He noted that mortality was steadily changing until 1987 when it reached its peak, and then reduced especially after 1991 due to interventions introduced. In the US, a diagnosis is no longer like a death sentence where it was 30 years ago. That is true, although, on our side. With age, the incidence increases until the mid-eighties and declines afterward due to people dying due to other causes.

If we look at GLOBOSCAN by WHO (2012), some areas like Africa are under-reporting. The incidence of prostate cancer in Africa is thought to be high, but that inference might divide the audience into thinking about whether it is high or not. If we see in other parts of the world, men of African origin do have a high incidence and mortality, as shown by Eichenemane et. al. from Abidjan, Ivory Coast. Surprisingly, Chu et. al. showed that incidence in African Americans is as much as forty times higher than that in Africans. Within Africa, we see higher rates of reporting in East Africa (10.7 – 38.1 per 100,000) compared to West Africa (4.7 – 19.8 per 100,000). Again, that is because of poor data collection and minimal PSA testing.

Commenting on the population pyramid, he noted that the mean age is moving upward in Kenya. Resultantly, we can expect the rate of prostate cancer incidence to go up compared to the past. Even now, the professor recalled that he sees more patients with prostate cancer than those in past. The literature also shows higher mortality due to prostate cancer in men compared to other cancers. The commonest age for prostate cancer is between 61 and 80 years. This data can help us recommend anyone above 60 undergo PSA testing. If we observe the statistics given in the literature, the bulk of our patients (about 80%) do have metastasized prostate cancer.

In conclusion, the professor apprised the fact that there has hardly been any change in prostate cancer presentation in Kenya in the last 20 years. He reminded the audience that the lower incidence and mortality are generally due to a lack of reporting, thereby stressing the need for PSA reporting. Dr. Ezzi thanked Prof Ngugi for his insightful talk. He handed the floor over to Dr. Sitna Ali for chairing the very first session of the symposium.

SESSION 1: PREVENTION, SCREENING, AND EARLY DIAGNOSIS

CHAIRED BY DR SITNA ALI

This first-morning session of the symposium included three oral presentations followed by questions and answers for all speakers of this session. She invited Dr. Francis Kiigu for a talk on the role of PSA in the screening, early detection, and monitoring of prostate cancer.

The session chair, Dr. Sitna Ali Mwanzi is a Consultant Medical Oncologist working at the Aga Khan University Hospital, Nairobi. She is the former Chair of the Kenya Society of Hematology and Oncology (KESHO) which is a professional organization whose aim is to reduce the cancer burden and mortality in Kenya through education, research, and advocacy initiatives.

ROLE OF PSA IN SCREENING, EARLY DETECTION & MONITORING OF PROSTATE CANCER

BY DR FRANCIS KIIGU

Dr. Kiigu is a Clinical Pathologist at The Nairobi Hospital. His main areas of interest in chemical pathology are biomarkers in oncology and diagnostic testing in non-communicable diseases. He is a member of the Kenya Association of Clinical Pathologists and the American Association of Clinical Chemistry.

He started his talk by introducing tumor markers which are a broad category of compounds or molecules. They can help us differentiate between malignant and benign strips in varying degrees. Most of them are in the blood, which makes sampling easier. It is quite a diverse group of molecules as we have enzymes (i.e., PSA), hormones (i.e., Human chorionic gonadotropin / HCG), proteins (i.e., β2-microglobulin), receptors (i.e., estrogen), etc. They can either be produced either by the tumor or by the host in presence of tumors. An ideal tumor marker should be sensitive; it should not be detectable in non-malignant or other physiological conditions (to avoid false positives). It should be highly specific i.e., it is detectable in only one tumor type.

Expanding on more characteristics of tumor markers, he added that it should provide a lead-time over clinical diagnosis. Its level should correlate with tumor burden. The procedure for estimation should be readily available and affordable. The specimen should be easily obtainable. If we look at the biology of PSA, most of it is a complex state (bound to protein inhibitors). It is important because the assays used for testing should be able to pick both bound and free PSA without any bias. The PSA testing started in the 1980s and there have been a lot of changes. The major change is the increase in analytical sensitivity (0.1 in 1980 to 0.001 ng/ml now). One of the challenges with assays is that they preferred detecting free PSA over the bound one. Thus, in cases where there will be a higher percentage of free PSA (in benign conditions), PSA will be overestimated.

Therefore, it was important to develop assays that have a similar preference for both free and complex PSA; these assays are called equimolar assays. There has been a standardization program to bridge the variations that come in testing from platform to platform. If you have assays that are traceable to WHO, they will be 20% underestimated from the assays traceable to hybritech standard. Thus, inter-assay variability still exists. For screening and early detection, a PSA level of more than 4 ng/ml is considered a widely accepted standard because we want to trade off sensitivity and specificity to balance false positives (too sensitive) and false negatives (too specific). This way, this screening test is not dichotomous, but it

will help reduce morbidity/mortality through early detection. However, increased detection may lead to over-treatment.

The speaker informed the audience of the limitations of PSA testing. The range for gray area is 4-10 ng/ml which can be either BPH (benign prostatic hyperplasia) or prostate cancer. The American Association of Family Physicians as well as the Canadian Task Force recommends against the PSA-testing for screening purposes. The American Urological Society and US Preventive Services Task Force allows PSA testing with some limitations, i.e., using it against a framework where an informed discussion is held for decision making, or for a certain group of individuals who are at high risk (e.g., Afro-Americans, or those with a family history of the prostate cancer). The frequency of the screening can either be single or serial. There has been no difference in terms of mortality/morbidity with either form, but there are other advantages for each of them. The routine interval for rescreening is two years, but this interval can be increased to four years for those with low PSA values in initial screening (less than 1 ng/ml).

Research studies have been performed to improve the diagnostic utility of PSA testing, especially for the gray area of 4-10 ng/ml. One such work is in the stratification of reference intervals for various age groups. There are no exact values or cut-offs, but age-specific free PSA levels can be stratified. Yet another way is to use the percent of free PSA. Interestingly, men with prostate cancer have less circulating free PSA (~10-30%) compared with men without cancer. Therefore, the percentage of free PSA has particular use in evaluating men who had a previous negative biopsy. Also, we can look at the kinetics of PSA (i.e., velocity or rate of change of PSA, or doubling time). These parameters can play an important role in prognostication in advanced or relapsed prostate cancer.

The speaker continued by explaining ways for improving the diagnostic utility of PSA testing. PSA density has also been used in such a way that PSAD > 0.15ng/ml2 is typically associated with an increased risk for prostate cancer. Likewise, patients with PSAD below 0.09 ng/ml2 are unlikely to harbor clinically significant prostate cancer. PSAD density can be determined by using PSA values and measuring prostatic volume through transrectal ultrasonography. Besides PSAD, there have been other combinations of PSA values or PSA scores, such as total PSA, free PSA, intact PSA, prostate health index (PHI), etc. The issue with the validation of cut-off values across different populations remains there.

Towards the end of his talk, Dr. Kiigu informed the audience of other uses of PSA, i.e., in stratification. PSA has been found to correlate with pathologic stages of tumor extension and metastases, cancer volume, and cancer grade. However, PSA by itself should not be used to decide whether a patient has prostate cancer confined to the organ. This is because there is a significant overlap in PSA among stages. Other modalities can be used to define such areas.

Another area where PSA testing can be used is treatment management. It has been used well to predict response to therapy or to detect disease recurrence following therapy. In radiotherapy, the levels of PSA will fall but not to the undetectable range because prostate tissue is not ablated fully. After Radical prostatectomy, however, serum PSA should decrease and remain at undetectable levels. Following an androgen suppression therapy, failure to achieve a PSA nadir of <4.0 ng/mL seven months after initiation of therapy is associated with a very poor prognosis.

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EARLY DIAGNOSIS OF PROSTATE CANCER: WHY, HOW, AND WHEN?

DR DK KIMANI

Dr. Kimani is a Consultant Urologist at Kenyatta National Hospital in Kenya, and an Honorary Lecturer in the Department of Surgery at the University of Nairobi. He has a keen interest in Prostate Care and Kidney Transplantation. He is a Member of SSK, KAUS, SIU, and AUA.

Dr. Kimani started his talk by highlighting a noteworthy feature of prostate cancer progression. There can be two groups of people; one where the disease is slow-growing and has organ-confined tumors, and the other where there are highly aggressive carcinomas associated with metastatic spread, thereby inducing significant morbidity and mortality. There are two main tools for screening prostate cancer. One is PSA as discussed already, and the other one is digital rectal examination (DRE); PSA performs better than DRE. Although DRE is cheap (no equipment cost) and easy to use, it has low sensitivity, especially in individuals whose PSA is less than 3 ng/ml. You go for a biopsy if you have an elevated PSA or abnormal DRE.

If we look at the history of PSA testing, FDA approved PSA in 1986 to monitor disease progression. In 1994 TPSA plus DRE was approved for screening. However, in 2012 the US Preventive Services Task Force (USPSTF) determined there was a "very low probability of preventing a death from prostate cancer in the long term" and recommended against routine use of the test. Since then, PSA screening rates and prostate cancer incidence rates in the United States have declined significantly. Therefore, we can see a reversal of the previous gains. Resultantly, USPSTF has reviewed its guidelines.

There are benefits as well as harms of screening, as we have seen its impact on incidence and mortality. There are risks associated with over-diagnosis, PSA false positive, prostate biopsy, risks of treatments as well as anxiety when a high PSA level is detected. If we look at the SEER database, it is obvious that PSA screening leads to stage migration, a better percentage of organ confinement, a smaller number of patients with regionally advanced disease, and fewer metastasized patients. There is, however, a lead time bias because the disease would be detected way before any symptoms appear. Thus, the survival time would seem to be high with screening introduced.

There have been two important randomized control trial (RCT) studies for assessing the effectiveness of screening. One is by Prostate, Lung, Colorectal, and Ovarian (PLCO) in the US and the other is The European Randomized study of Screening for Prostate Cancer (ERSPC). PLCO did an annual PSA screening program with a mandatory DRE. A biopsy threshold of 4 ng/ml was set. The compliance with screening was very good (88%) but compliance with biopsy was less (32%). In the European study ERSPC, DRE was optional, and the screening interval was 2-4 years. The biopsy threshold was 2.5-4 ng/ml and the compliance with biopsy was good too (80-90%). The compliance with screening was 82%. Both of the studies had contamination.

If we look at mortalities in the two studies, PLCO showed higher mortality in the screened group compared to the control group. The inverse was observed in the ERSPC study, where the benefit of screening was observed. However, various flaws were identified in the PLCO study, and it was deemed not suitable for inclusion in the meta-analysis, as pointed out by Shoag et. al. (2016). Therefore, we can't make conclusions on mortality related to screening. On the other hand, the European study had a very big group studied (162,389 men aged 55-69 years –one of the largest RCTs globally) and it was longer in duration (~16 years).

It was shown that better screening improves mortality due to prostate cancer. It was noted that the longer you follow up with the patient, the more the benefit of screening is. The number needed to screen (NNS) for preventing one death due to prostate cancer was reduced with a longer follow-up duration, i.e., 570 for 16 years, versus 742 for 13 years follow up. The main problem with the screening is the differences in the speeds at which one develops cancer that can potentially lead to death. Some people would have faster progression to that death-causing cancers, whereas the others will have very slow or non-progressive speed. If we focus on the latter group in screening, we end up treating them for something that would never lead to any mortality. To address this issue, the group in Austria has reported age-dependent PSA cut-offs which can help prevent overdiagnosis, and thereby reduce overtreatment.

On the other side, the false positives can be due to several factors, i.e., prostate diseases like prostatitis, obesity, sexual function, assay method, and recent surgical therapy by the patient. Resultantly, there can be a psychological burden, biopsy-related complications, risks of therapy (i.e., incontinence, erectile dysfunction, osteoporosis, etc.) as well as a financial burden. For addressing this issue, we can use other parameters besides just the PSA to determine the need for biopsy. He thanked Dr. Kiigu for discussing those parameters like PHI, PSA density, PSA kinetics, etc. He added one more parameter to the list, which is prostate 4Kscore, a non-invasive test that looks for four prostate-specific biomarkers.

The speaker informed the audience about the benefits and limitations of using 4Kscore. It is helpful for patients whom we are following up with or those needing re-biopsy. It reduces overtreatment and unnecessary biopsies and allows physicians to make better treatment decisions for their patients. It is not recommended for those less than 40 years or more than 80 years old. Also, those who had DRE within the last 96 hours or those with a previous cancer diagnosis are excluded.

If the PSA level is rising even with a negative biopsy, you can do a multi-parametric MRI, as recommended by the European Association of Urology (EAU). He shared the results of the PROMIS trial which showed that mp-MRI-targeted biopsy had greater sensitivity than transrectal ultrasound (TRUS)-guided biopsy (87% vs. 60%) and a higher negative predictive value (NPV (72% vs. 65%) for detecting significant prostate cancer. Thereby, the general recommendation is to do MRI before the biopsy. For addressing the issue of overtreatment, two strategies are recommended. One is to increase the uptake of active surveillance in low-risk diseases. The second is to adopt more stringent criteria for biopsy than just looking at PSA.

Dr. Kimani apprised the audience of the changes in the guidelines. There should be an individualized risk-adapted strategy for the early detection of prostate cancer. And that too should be for well-informed men of at least 10-15 years of life expectancy. The issues of overdiagnosis and overtreatment remain there, so a careful identification of patients is necessary, in terms of the benefits and harms associated. The USPSTF issued a revised recommendation in 2018 with a grade of “C” for PSA-based prostate cancer screening for men 55 to 69 years of age. They recommend shared decision-making for men 55 to 69 years of age and do not recommend screening for men 70 years of age and older.

The USPSTF notes that the increased use of active surveillance (observation with selective delayed treatment) for low-risk prostate cancer has reduced the risks associated with screening. The American Cancer Society (2016) recommends that men with at least a 10-year life expectancy should have an opportunity to make an informed decision with their health care provider about prostate cancer screening beginning at 50 years of age for average-risk men and before 50 years of age for groups at higher risk. Likewise, the American Urological Association (AUA) recommends shared decision-making about screening for men 55 to 69 years of age. Based on the ERSPC, they suggest that a 2-year screening interval

would preserve the benefits and reduce harms from screening. The Europeans have similar guidelines with slight variations.

He reminded the audience of doing an MRI before any repeat biopsy, after a negative biopsy even with high PSA levels, abnormal DRE, or any other indication. He concluded his talk by presenting some local guidelines, which are more like the American guidelines. We start screening at 40 years and stop at 70 years unless there is a life expectancy of more than 10 years. Also, we do both PSA and DRE as DRE doesn't harm. The rescreening interval depends on the initial PSA level. An MRI and a referral to a Urologist are recommended before the biopsy.

CASE PRESENTATION - EARLY PROSTATE CANCER

BY DR DANIEL NGUNYI

Dr. Ngunyi is a resident of urology at the University of Nairobi. He is currently in his 5th year of the master's program. His supervisor is Dr. DK Kimani.

The patient is 73 years old, initially managed at Kajiado Level V, and was referred to UOPC in December 2021. He is a known hypertensive patient, who presented with lower urinary tract symptoms (LUTS) since July 2021. His presentation was mixed voiding and storage LUTS of moderate severity (16/35). He was dissatisfied with his symptoms. The patient had no urge incontinence, nocturnal enuresis, or hematuria. He was presented with no back pain, bone pain, or lower limb weakness. There was no family history of prostate, breast, or ovarian cancer. He was put on combination therapy from August 2021 to January 2022. No symptom improvement was observed and was thus referred to our facility.

His examination at our facility showed a fair general condition, with poorly controlled blood pressure (181/94). Abdominal examination was normal, but DRE had benign features (40cc firm prostate, symmetrical, non-nodular prostate, palpable median sulcus, and free rectal mucosa). In July 2021, a KUB ultrasound diagnosed BPH features. The upper tract was normal, and the bladder had a well distended thick wall. Post Void Residual (PVR) was not accessed. The prostate size was measured as 45cc with no report of lesions. The PSA level measured in November was quite high (38 ng/ml). The patient then underwent a finger-guided prostate biopsy. The patient was diagnosed with adenocarcinoma of Gleason's 4+4 (ISUP Grade Group 4). The burden was estimated as 3 out of 12 cores involving 25% of needle core tissue. There was no lymphovascular invasion, perineural invasion, periprostatic fat, or seminal vesicle invasion.

Following the biopsy, he was referred to our facility for further management. At our center, mp-MRI was performed. There was a t2-weighted hypointense nodule in (33 x 37mm) right central gland. The tumor was localized in the prostate and seminal vesicles were clear. A bone scan was performed about 10 days after the MRI and no skeletal Mets were found. So currently, the patient has high-risk localized prostate cancer. The patient is counseled for radical prostatectomy by explaining the pros, cons, and alternatives. The cardiology has given clearance for surgery. MDT discussion is due, after which surgery will be performed.

SESSION 2: DIAGNOSTIC TOOLS IN PROSTATE CANCER

CHAIRS: DR. MUSILA MUTALA AND DR. CHARLES WAHOME

The second session in the morning was comprised of three presentations. Dr. Wahome introduced the first speaker Dr. Yogeswaran Carnjini and invited her to the talk.

The session chair Dr. T Musila Mutala is a Consultant Radiologist, Cancer Imaging Specialist, and Lecturer at the Department of Diagnostic Imaging and Radiation Medicine, University of Nairobi. He is a graduate of Medicine and Surgery from the University of Nairobi and achieved a Master of Medicine in Radiology from the University of Nairobi and a Master's in Oncologic Imaging from the University of Pisa, Italy.

The co-chair Dr. Wahome is the Chief Consultant Pathologist at Pathologists Lancet Kenya. Dr. Wahome has been working with the Lancet Group of Laboratories in Kenya since 2016, and his area of pathology specialization is anatomical pathology with a focus on histopathology and cytopathology. He is a member of the Kenya Association of Clinical Pathologists (KACP) and the East African Division of the International Academy of Pathology (EADIAP).

HOW SHOULD A PROSTATE BIOPSY BE PERFORMED? FINGER BIOPSY, TRUS GUIDED BIOPSIES, GRID BIOPSIES

BY DR YOGESWARAN CARNJINI

Dr. Carnjini is a Consultant Urological Surgeon based in Nairobi. She has a keen interest in the minimally invasive treatment of urological cancers. Dr. Carnjini is keen to improve prostate cancer diagnosis and research in Sub-Saharan Africa.

She started her talk by presenting a history of prostate biopsy. It has been there since the very start of the twentieth century and the very first biopsy was performed in 1926 by Young. The technique was an open perineal biopsy. The very first finger-guided transrectal biopsy was performed in 1937. The evolution continued with the development of the TRUS probe in the 1980s, leading to TRUS-guided biopsies becoming a standard. The evolutions mainly occurred because of an awkward anatomical position of the prostate. Its proximity to feces and urine increases the risk for sepsis. However, improvements in imaging allow for the identification of significant lesions. There has been great difficulty in precisely targeting significant lesions leading to the evolution.

Moving on, she discussed the indications for biopsy. Anyone undergoing a biopsy should be fit for radical treatment. The metastatic prostate patient should be fit to undergo chemotherapy or other second-line therapies. As per current guidelines, anyone having PIRADS >= 3 on mpMRI Prostate should have a biopsy. Anyone with persistently raised PSA and with a palpable malignant lesion should also undergo a biopsy. Likewise, one having a normal PSA but with a palpable malignant lesion is also a candidate for biopsy. Anyone with persistently raised PSA and PSA Density with PIRADS <=2, or where MRI is unavailable should also undergo biopsy.

Further, she discussed the complications of biopsy and the importance of counseling. Vasovagal syncope is very common (10% reported in the literature but it could be more than that). TRUS- and TP-biopsies are essentially similar in terms of risks, except for the infection risk, favoring the latter. Other common

complications are bleeding (rectal, urinal, seminal), and infections (prostatitis, UTIs – urinary tract infections, etc.).

She discussed the features of various techniques for prostate biopsy in clinical practice. The very ancient method of biopsy is the finger-guided transrectal biopsy which is still being used although it is not a standard of care. An advanced methodology is a TRUS-guided biopsy, where ultrasound is used. Another one is Local Anesthetic Transperineal Prostate Biopsy (LATP) which is known for its reduced risk of sepsis (which is 1% TRUS vs 0.1% for Transperineal/LATP). Recently, Koome (2017) studied the risk of UTIs which was found to be 15.2% for finger-guided biopsies. LATP got a higher sensitivity to cancer detection (86% vs 73%) because of its ability to access the anterior and apex of the prostate.

Another advanced technique the speaker discussed is Transperineal Template Guided Saturation Biopsy of Prostate. Depending on the size of the prostate, you need to take more than 20 cores (i.e., even 60 cores for a 60cc prostate). The rate for detection of prostate cancer is improved up to 38%. The limitations include the use of a general anesthetic and a higher rate of urinary retention (10%).

For TRUS biopsy, you need to do some pre-procedure preparations. This includes informed consent (explaining the procedure, risks, and complications). I would always check for the use of any anticoagulants and stop them all except junior aspirin (up to 75 mg). I would also do a urine dipstick on the day of the procedure, and I would cancel if there is any indication of a UTI, treat for it and then rebook for the biopsy. I always give them analgesia, i.e., paracetamol, 30 minutes before the procedure. Also, I will give antibiotic prophylaxis if you are doing TRUS. The use of rectal povidone has also been shown to reduce infections.

For set up, you must have the probe (ideally a prostate probe with a minimum of an 8-MHz transducer, and ideally tri-planar although bi-planar can work too). You would need an angled needle guide with a side-fire, a biopsy gun, a long spinal needle for local anesthesia, and 10mls of 1% lignocaine, specimen pots, swabs, gloves, and jelly. You start by positioning the patient in a left lateral position. You should be knowledgeful about ultrasound anatomy and how to guide the probe. You do a TRUS scan to identify the size of the prostate. Following that, you would give the anesthetic, which could be a local anesthetic jelly. You do your systematic and targeted biopsies.

For a systematic biopsy, you should take a minimum of 12 cores, 6 on each side, starting the sample from the base to the apex in the peripheral zones. For the targeted biopsy, you target the suspicious areas that you see on the pre-biopsy MRI. You can either do it cognitively or do US-MR fusion. The speaker showed a YouTube video of a performance of a TRUS biopsy to the audience. She, then, informed the audience of post-procedure recovery. As vasovagal syncope is common, ask your patient to lie flat, and rise slowly. Give them about 30 minutes, check the blood pressure, and make sure they can void before you discharge them. I tend to give them three days of antibiotic prophylaxis, as guided by your local guidelines.

Moving on to the procedure for LATP, the speaker highlighted that the pre-procedure preparation is almost the same as TRUS, except for the use of antibiotic prophylaxis. You use it for covering the skin flora because you are not traversing the rectum in LATP. Another difference would be of the probe which is only bi-planar here, and you use a Precision Point kit where you have a bracket that fits on the probe, a sliding device with a needle which you push in, and this is what guides where your biopsy goes. Another key aspect is to use a local anesthetic as this procedure is extremely painful.

The positioning is different from that in TRUS, as you use lithotomy position here. You can use a chair designed for this purpose. You start with a TRUS scan and give them some local anesthetic initially before infiltrating the entire needle tract from perineal skin to prostate apex. After this infiltration, you give them a good couple of minutes before fixation of the precision point needle guide. Again, you will perform systematic and targeted biopsies just like TRUS. The difference would be better access to the anterior part of the prostate which you can't do from the back. The post-procedure recovery is like that in TRUS, except that the patient is not lying down; just make them sit for some time to manage vasovagal syncope.

The speaker moved on to the next technique which was Transperineal Template Guided Saturation Biopsy (TTSB) of the Prostate. It involves the use of quite a bulky device, essentially like what is used in brachytherapy. The grid can sample the entire prostate, as you need a minimum of 20 cores, and may need even more depending on the size of the prostate. The limitations include a requirement for general anesthesia, and you can't perform it for prostate volume more than 60cc. That's because you cannot adequately sample due to interference of pubic bone interference. The risk for urinary retention is up to 10%.

She concluded her talk by showing the audience a video of the performance of TTSB. Dr. Wahome thanked her for such an informative and visual talk.

PATHOLOGY REPORTING: SLIDES, GLEASON SCORING, GRADE GROUP SCORING, ROLE OF MOLECULAR TESTS IN PROSTATE CANCER

BY DR TOM NYABOGA, AND DR ANDERSON MUTUIRI

Dr. Nyaboga is a Medical Doctor and Anatomical Pathologist with a ten-year of experience in general Surgical Pathology, Cytopathology, and Molecular Pathology. His special interest areas include Uropathology, Gynecologic Pathology, and Cytopathology. Currently, he is stationed at the Nairobi Hospital Laboratory as a resident Consultant Pathologist.

The other co-speaker of the presentation was Dr. Anderson Mutuiri who is an anatomical pathologist and Assistant Professor of Pathology at the Aga Khan University Medical College. His areas of practice are autopsy pathology, histopathology, and cytopathology, with expertise in medical kidney biopsy interpretation. He is a member of the Kenya Association of Clinical Pathologists and the East African Division of the International Academy of Pathology.

Dr. Nyaboga started his talk by appreciating the efforts of biopsy surgeons. Introducing the audience to the Gleason grading system, he appreciated the contribution of Donald Floyd Gleason who introduced this system in 1966. There were other classification systems but Gleason's system was a major departure from prior classifications. Gleason used prostate cancer histologic architectural pattern, rather than cytology, for assigning the grade. The classification was developed using biopsies, transurethral resections, and RPs from 270 patients. The number rose to 1032 patients later and it was found that the grading system can also help predict cancer-related mortality. Since then, the Gleason grading system has received worldwide acceptance.

The speaker showed the audience the original five patterns based on the data of 1032 patients.

- Pattern 1. Well-differentiated uniform single glands, closely packed in masses with relatively circumscribed boundaries.
- Pattern 2. Well-differentiated, but more variable single glands slightly spaced apart, boundaries of tumor less well circumscribed.
- Pattern 3. Moderately differentiated glands; may range from small to large, growing in spaced-out infiltrative patterns, maybe papillary or cribriform.
- Pattern 4. Raggedly infiltrating, fused-glandular tumor, frequently with pale cells, may resemble hypernephroma of the kidney.
- Pattern 5. Anaplastic carcinoma with minimal glandular differentiation, diffusely infiltrating prostatic stroma.

He informed the participants that the definition of the pattern 5 category is still very much similar even after 60 years today. Patterns 1-4 have undergone a lot of changes in definitions. He displayed the original diagram used for the illustration of the grading system by Gleason. Gleason noted that, in most cases, more than one histological pattern was present. He designated the predominant pattern as the primary pattern and the subordinate pattern as the secondary pattern. You get the Gleason score by combining the two. If only one pattern was present then this was considered both the primary and secondary pattern, so it was doubled for analytical purposes. The grading was undertaken at low power magnification (x40–100).

Since the introduction of the Gleason system, there have been numerous changes in clinical and pathologic practices relating to prostate cancer. In the original publications by Gleason, patterns 1 and 2, comprised more than 30% of cases, but we are no longer reporting them on biopsy, and they are rarely diagnosed on radical prostatectomy. Pattern 1 was either benign or just mimickers. It was realized that the original Gleason system was not serving us in terms of histopathology in the modern era. To address these issues, the International Society of Urological Pathology (ISUP) first revised the grading system in 2005, and subsequently in 2014.

In this presentation, the speaker chose the 2005 version as we don't have validating data for a lot of changes made in 2014. In the revised grading system of 2005, pattern 1 is rarely, if ever, diagnosed. The reporting in the modern era starts from pattern 3 and a minimum Gleason score of six on a scale of 2-10. The overtreatment comes from the gray area of a Gleason score between 2 and 6. Numerous studies have confirmed the prognostic value of Gleason grading. The Gleason system has been classified as a category 1 prognostic factor by the College of American Pathologists (CAP). In separate reports, Gleason grading has been correlated with biochemical failure, the development of distant metastases, survival following radiotherapy or with deferred treatment, progression-free survival, and overall survival.

The speaker highlighted the problems with the current Gleason System. First, it is a floating grading system as the scores of 2-5 are currently no longer assigned. Certain patterns that Gleason defined as a score of 6 are now graded as 7. Mostly, nowadays patients are dumped into three categories: low, intermediate, and high risk (with a 3-tier grouping of 6,7,8-10). There is a lot of confusion as a score of 6 is in the middle of the scale (2-10) is the lowest level of the disease.

Because of those problems, there was a proposal for a new Grading System. The Grade Group system came from a team at the John Hopkins Hospital. It was first validated in a large multi-institutional study based on an analysis of more than 20,000 prostate cancer cases treated with radical prostatectomy and more than 5,000 cases treated by radiation therapy. The system was presented at the 2014 ISUP meeting

and was accepted both by participating pathologists as well as urologists, oncologists, and radiation therapists. The nomenclature is now accepted by several bodies like AJCC, CAP, WHO, ISUP, and GUPS.

The speaker shared the grade groups with the participants:

- Grade Group 1 (Gleason score ≤6) – Only individual discrete well-formed glands
- Grade Group 2 (Gleason score 3+4=7) – Predominantly well-formed glands with a lesser component of poorly-formed/fused/cribriform glands
- Grade Group 3 (Gleason score 4+3=7) – Predominantly poorly formed/fused/cribriform glands with a lesser component of well-formed glands
- Grade Group 4 (Gleason score 8)
    - Only poorly formed/fused/cribriform glands (4+4) or
    - Predominantly well-formed glands with a lesser component lacking glands (3+5) or
    - Predominantly lacking glands with a lesser component of well-formed glands (5+3)
- Grade Group 5 (Gleason scores 9-10) – Lacks gland formation (or with necrosis) with or w/o poorly-formed/fused/cribriform glands

Moving on, he showed various pathology images to the audience. Furthermore, he discussed the five-year biochemical recurrence-free progression probabilities for radical prostatectomy. The values for Grade Groups 1-5 were 96%, 88%, 63%, 48%, and 26%. As all of these are very well differentiated, showing 5 distinct categories but people still dump them into 3 categories (low, intermediate, or high). As a result of significant differences in criteria and reporting compared to Gleason's original grading system, the authors have regarded the newly proposed grade groups as a new grading system. The speaker regarded this as a very controversial statement because it is a direct derivation from the Gleason pattern.

The speaker highlighted the benefits of the new system. One of the benefits is a more accurate grade stratification than the current Gleason system. Further, the grading system is simple (only 5 grades) as opposed to multiple possible scores depending on various Gleason pattern combinations. The lowest grade is 1 as opposed to the current practice of a Gleason score of 6. It has the potential to reduce the overtreatment of indolent prostate cancer.

The speaker concluded his talk by proposing the application of the new system in surgical pathology reporting. It will be good to report the new grading system, in conjunction with the Gleason system (as shown below), until it becomes widely accepted and practiced:

- Gleason score 3+3=6 (Grade Group 1)
- Gleason score 3+4=7 (Grade Group 2)
- Gleason score 4+3=7 (Grade Group 3)
- Gleason score [4+4, 3+5 ,5+3] = 8 (Grade Group 4)
- Gleason score 9-10 (Grade Group 5)

The second part of the lecture was by Dr. Mutuiri. He presented a bird's eye view of the role of molecular testing in prostate cancer. He divided the biomolecules into three categories: risk assessment biomarkers, prognostic biomarkers (in localized prostate cancer), and predictive biomarkers. The risk assessment biomarkers help you decide if a biopsy is needed, whether initially or for re-biopsy. The serum markers include PHI, 4Kscore, and Stockholm 3 Model (S3M). The first two were discussed previously by other speakers and Dr. Mutuiri discussed the last one. S3M combines the serum biomarkers (PSA and its

derivatives) with the clinical parameters (age, family history, previous biopsy, and DRE) and genetic polymorphisms (232 single-nucleotide polymorphism / SNPs) to give an estimate of risk and determine if a biopsy is needed.

Another type of risk assessment marker is urinary markers. These markers measure the expression of messenger RNA in urine post-DRE. These are also used in combination with clinical parameters to come up with a score to help determine if the patient has clinically prostate cancer. He showed the audience an algorithm for diagnosis (not screening) of prostate cancer. Interestingly, the algorithm suggests that you can do a biopsy if you don't find any of these markers. This brings us to think, what is the utility of these markers then? The suggested use is to use these biomarkers either together with MRI or as a standalone alternative to come up with a score. If the score is high, you go for a biopsy.

The speaker shared an ISUP report where they came up with prognostic biomarkers, the second category of molecular biomarkers. These markers estimate the overall likelihood of an adverse clinical outcome, regardless of the specific therapeutic setting. In English, these are essentially risk stratifiers. The two suitable immune-histochemistry tests are the Ki67 index and loss of PTEN. Another prognostic biomarker is the mRNA-based genomic signature. A high Ki67 (more than 15%) predicts mortality and the presence of non-organ confined disease in a subsequent radical prostatectomy. Ki67 index has issues with standardization as there is gray area for 5-15% as 5% is low, and 15% is high. Similarly, loss of PTEN expression is associated with a risk of upgradation to a higher grade subsequent radical prostatectomy or biochemical recurrence.

The ISUP recommends that both biomarkers are potentially useful in Grade Group 1 (and/or Grade Group 2) to determine eligibility for active surveillance. However, this is just one factor among several to keep in mind while suggesting that the patient should seek definitive treatment. The mRNA-based genomic signatures provide additional information regarding progression risk in active surveillance and post-radical prostatectomy settings. The issue again is heterogeneity in needle biopsy samples.

The three main tests, as included in the current NCCN guidelines, are Oncotype Dx Genomic Health, Polaris Myriad Genetics, and Decipher Genome Dx Biosciences. These are all propriety tests where you send the sample to the lab, and they give you results in the form of a score. The fundamental principle is that they look for the messenger RNA expression and the clinical utility varies between the tests. Oncotype Dx is used for needle biopsy samples and gives a likelihood of freedom from Dominant 4 or a high Gleason score, and/or non-confined disease. The Decipher is used in post-surgery cases, and recent development also allows needle biopsy samples. It gives a probability of metastasis after 5 years of prostatectomy or 3 years after PSA recurrence.

Explaining the third category of molecular biomarkers, the predictive biomarkers, the speaker said that these can estimate the chances of response to a specific therapy. However, it is usually not possible to distinguish predictive biomarkers from prognostic biomarkers unless you are comparing two different therapies in patients with or without the biomarker. The predictive biomarkers have largely been studied for metastatic disease. The two predictive biomarkers are germline (or somatic) testing for DNA repair deficiency and androgen receptor-related markers. The two main DNA repair deficiency pathways that we have some application in prostate cancer are homologous recombination defects (HRD) and the DNA mismatch repair / MMP. HRD includes BRCA1/2, ATM, PALB2, and CHEK2. The testing can be recommended when you have to choose treatment options, enroll in a clinical trial, or for management of cancer risk in the patient and their family.

The speaker concluded his talk by presenting scenarios where either germline or somatic testing should be performed. NCCN recommends germline testing for prostate cancer in scenarios:

- By prostate cancer stage or risk group: Metastatic, very high-risk localized
- By family history and/or ancestry
    - 1st, 2nd, or 3rd degree relative with:
    - ≤50y: breast, colorectal, endometrial Ca.
    - Any age: Male breast Ca, ovarian Ca, exocrine pancreatic Ca, metastatic, regional, very-high risk, high-risk prostate
    - ≥1 brother/father with prostate cancer ≤60y
    - ≥2 1st, 2nd or 3rd-degree relatives with breast or prostate ca
    - ≥3 1st, 2nd or 3rd-degree relatives with Lynch syndrome-related Ca, especially if <50y
    - Known history of familial cancer risk mutation
    - Ashkenazi Jewish ancestry
- Breast cancer

Moreover, you can consider the germline testing if there is intermediate-risk prostate cancer with intraductal/cribriform histology, or a prior personal history of pancreatic, colorectal, gastric, melanoma, upper urothelial Ca, GBM, biliary and small intestine Ca. On the other hand, Somatic tumor DNA testing should be offered to all patients with metastatic disease. It should ideally be performed on the metastatic tissue but that may not be possible. Alternatively, plasma circulating tumor DNA, or the primary tumor tissue can be used. The testing includes the two DNA repair deficiencies mentioned earlier. He shared a list of various biomarkers that we should look for in somatic testing.

The co-chair of this session, Dr. Musila Mutala thanked the speaker for a wonderful talk. He invited the speaker for the third talk of this session, Dr. Alfred Odhiambo who is also his teacher.

PROSTATE CANCER IMAGING: CONVENTIONAL IMAGING VS NEW GENERATION IMAGING

BY DR ALFRED ODHIAMBO

Dr. Odhiambo is the Chief radiologist at The Nairobi Hospital. He is also a Lecturer at the University of Nairobi. He is an active member of the Prostate Cancer Kenya Chapter.

Before his talk, he made the room dark, as he is a radiologist and knows how to improve the contrast of his slides. He started by highlighting the importance of imaging in cancer care. Out of the seven interventions in cancer care (Prevention, Screening, Diagnosis, Staging, Treatment, Treatment response, Monitoring / Follow-up), 5 need imaging for sure, leaving just the prevention and treatment itself. He chose the specific roles of imaging in the diagnosis of prostate cancer and locoregional staging and imaging for metastatic disease for this talk. He said he would include conventional diagnostic tools that are standard of care, as well as the new generation imaging. (NGI).

He shared with the audience the tools of the trade for locoregional prostate cancer staging. These included Transabdominal Sonography, Transrectal Ultrasound, Multiparametric Transrectal Ultrasound, Ultrasound with AI, Micro-ultrasound, and Multiparametric Magnetic Resonance Imaging (mp-MRI). He showed the participants various ultrasonic images with different US techniques. The accuracy of the first two techniques is under question because of the lower sizes of prostate detected these days, thanks to

PSA. It was thought that maybe the human eye is not able to pick up small lesions, so AI-based software was developed. The new kid on the block is micro-ultrasound which has an accuracy comparable to MR.

Moving on, the speaker shared the research featuring mp-MRI. Four level-1A papers emphasize the role of MR before the biopsy. Technologically, we had PROMIS, PRECISION, and the latest MRI-FAST. It is important because involves ordinary equipment of 1.5 Tesla and a regular radiologist, not a sub-specialist. He showed the images obtained with mp-MRI in which the seminal vesicles are visible and the prostate is visible from the base to the apex very well delineated. A series of studies in the late 1980s established that prostate cancer is characterized by low T2 signal intensity replacing the normally high T2 signal intensity in the glandular peripheral zone. However, today the buzzword is mp-MRI.

He said that MRI has advanced recently in such a way that not only we can look at tissue water content (T2), but also, we can look at how tightly cells are packed (diffusion-weighted imaging or DWI), how blood flows into and out of tissues (dynamic contrast-enhanced/perfusion MRI) at the chemical makeup of tissue (spectroscopy). Hence, we get anatomy (T2), biology (DWI), as well as vascularity (dynamic contrast-enhanced MRI). The information that we get with T2 weighted imaging is the best depiction of the prostate's zonal anatomy and capsule. However, it lacks requisite accuracy so additional functional techniques improve both sensitivity and specificity.

What is important about DWI is that it is a powerful clinical tool allowing apparent diffusion coefficient (ADC) maps to be calculated, enabling qualitative and quantitative assessment of prostate cancer aggressiveness. Cancer shows a lower ADC value than normal prostate tissue. Furthermore, ADC values correlate with Gleason scores. In 1954, we could feel or palpate a hard lump, but now since 2014, we can see it with DWI.

Another important modality is contrast enhancement. Hara et al have shown that DCE-MRI can detect clinically important prostate cancer in 93% of cases. In patients with previous negative TRUS-guided biopsy sessions and rising PSA levels, DCE-MRI plays an important role in lesion detection. Likewise, Magnetic resonance spectroscopic imaging (MRSI) can show the lower levels of citrate and higher levels of choline in prostate cancer compared with benign tissue.

Bridging all the concepts presented above, the speaker highlighted the need for a modality of one language that can connect all the modalities. Pi-RADS (Prostate Imaging-Reporting and Data System) was the solution initially introduced in 2012. The latest version is 2.1 which was introduced in 2019 by Baris Turkbey, a Turkish guy.

The speaker then informed the participants of some challenges with mp-MRI. He shared an example where in the region of the posteromedial base-to-mid gland, the peripheral zone may be misinterpreted as suspicious for peripheral zone tumor on basis of inspection of the two images alone, as shared in a study by Rosenkrantz and Taneja, featuring ten such pitfalls. Likewise, in the New Orleans study of 2014, mpMRI failed to identify 16% of men with high-grade cancer (Gleason score ≥7). It was a prospective study of 1044 men with an elevated PSA.

He gave a summary of the merits of mp-MRI of the prostate:

- It aids the detection of clinically significant prostate cancer with high sensitivity and specificity.

- It reduces the number of indolent low-grade tumors, thereby reducing overdiagnosis and overtreatment.
- A high negative predictive value (NPV) helps identify who to biopsy.
- The mp-MRI combined with ultrasound dictates how to biopsy.
- At least 4 papers provide Level 1a evidence of its place before biopsy for the locoregional staging of prostate cancer.

In past, mp-MRI was investigational and is now an established modality, but it is going to be integral to care in near future.

The speaker then moved on to discuss other modalities i.e., bone scan and PET. He read a statement from a research article:

> "Recently, a multidisciplinary panel of international experts convened at the European Association of Nuclear Medicine (EANM) Focus 1 meeting produced a comprehensive series of statements on prostate cancer imaging and therapy with radiopharmaceuticals. Notably, bone scintigraphy and CT have never been recommended for the majority of patients by experts despite the fact that these methods are still largely included in most clinical guidelines." – verbatim from Minozzi et. al. (2018)

Dr. Odhiambo discussed the challenges with a bone scan and PSMA-PET for their role in imaging metastatic prostate cancer. He recommended starting with CT instead for metastatic workup so that involvement of lymph nodes can be diagnosed. However, there is difficulty with CT scan validation, either at initial diagnosis or for recurrence. In a single >10-year-old review manuscript, the overall sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of LN metastases detection with CT were 16, 100, 85, and 100%, respectively.

He showed the audience a CT image sliced from the middle of the lungs to find out where the tumor deposit is. It was noted that a CT scan could not detect any tumor. But with the addition of molecular imaging, the big red spot in the breastbone could be seen. This is molecular imaging detection of malignancy that is invisible on what would be considered other standard of care imaging modalities.

The speaker then moved on to teach the basics of radioactivity and nuclear medicine. He discussed the phenomenon of alpha-, beta-, and position-emission based on basic nuclear principles. He expounded on ways to improve the detectability of certain lesions that is not possible otherwise, including PSMA-PET, whole-body MRI (WB-MRI), and a merger of bone scan and CT. He summarized his talk by presenting some ideas. Modern PET/CT has a high overall sensitivity, whereas WB-MRI has high specificity. They are therefore complementary techniques, hence the interest in PET/MRI. The future is certainly in the combination of imaging techniques. A recent EORTC consensus proposed clinical trials that use modern imaging methods to evaluate the benefits of metastasis-directed therapies.

He concluded his talk by giving the take-home message:

- For locoregional staging its mpMRI and Micro ultrasound – not in competition but in combination.
- For metastatic workup, the Standard of Care needs to give way to New Generation Imaging best in multimodal application.

SESSION 3: MANAGEMENT OF EARLY PROSTATE CANCER

CHAIRS: DR CATHERINE NYONGESA AND DR ANDREW ODHIAMBO

This was the first session after the morning break of 15 minutes. Dr. Catherine Nyongesa moderated the session and invited Prof Ngugi for his talk on risk stratification for prostate cancer.

The chair of this session, Dr. Catherine Nyongesa Watta is a Clinical Oncologist at Texas Cancer Centre Nairobi and Kenyatta National Hospital, with over 10 years of experience in Oncology conducting inpatient and outpatient management of cancer patients. She has a bachelor's degree in Medicine and Surgery (University of Nairobi), a Master of Medicine in Radiation Oncology (University of the Witwatersrand, South Africa), and a Fellowship (FC Rad Onc) in Radiation Oncology from the College of Radiation Oncologists of South Africa. Among the key organizations, she has been a member of the American Society of Clinical Oncology (ASCO), Health Professions Council of South Africa, and International Gynecologic Cancer Society.

The co-chair Dr. Andrew is a board-certified Medical Oncologist. He is a member of ASCO, ESMO, KESHO, and AORTIC. Fellow of the Royal College of Physicians of Edinburgh as well as East Central & Southern College of Physicians. His key interests are GI & HPB Malignancies, Lung Cancer, Breast Cancer, Lymphoma, Newer therapies i.e Immunotherapy & Targeted therapy.

PROSTATE CANCER RISK STRATIFICATION

BY DR PETER NGUGI

This was the second talk by Dr. Peter Ngugi in this symposium. Dr. Peter started his talk by introducing the topic which was risk stratification for prostate cancer patients. He informed the audience that a lot of work has been defined and we have guidelines for classification. Yet, we should have our stratification locally because our treatments differ significantly from what is offered elsewhere. Stratification is conducted after the stage of biopsy and staging (T1-2, N0 or NX, M0 or MX). It includes defining the severity or aggressiveness of the disease to help make appropriate decisions.

You start with the staging, followed by pathological staging, and metastasis. When you stratify the risk, we have various classifications. We employ the risk profile as used by NCCN, an American organization. We have very low risk, low risk, intermediate-risk, and high-risk classifications here. These classifications are not based on a single parameter and rather have multiple indicators including PSA level and Gleason score, etc. among them.

Following a prostate cancer diagnosis, patients are faced with a multitude of care options, the advisability of which is influenced by patient factors and by cancer severity or aggressiveness. The risk stratification provides the ability to categorize patients based on cancer aggressiveness which is invaluable for facilitating care decisions. It is important to make sure that it is a shared decision which is only possible when the patient is well-informed and does not leave the decision mainly to the doctor.

Dr. Ngugi recommended that the clinicians should not perform abdominopelvic CT or routine bone scans in the staging of asymptomatic very low- or low-risk localized prostate cancer patients. Active surveillance should be recommended as the best and preferable available care option for very low-risk patients.

Clinicians may offer definitive treatment (i.e., radical prostatectomy or radiotherapy) to select low-risk patients who may have a high probability of progression on active surveillance. ADT should not be added along with radiotherapy for low-risk patients except for reducing the size of the prostate for brachytherapy. Such patients should be informed of newer treatments and inadequate evidence for their use in this group. We should recommend observation or watchful waiting for men with a life expectancy ≤5 years with low-risk localized prostate cancer. Among most low-risk patients, tissue-based genomic biomarkers are not necessary.

He shared the expert opinion of considering staging unfavorable for intermediate-risk localized prostate cancer patients with cross-sectional imaging (CT or MRI) and bone scan. A stronger recommendation (with level A evidence) is that radical prostatectomy or radiotherapy plus ADT should be recommended as standard treatment options for patients with intermediate-risk localized prostate cancer. Likewise, a moderate recommendation (with evidence level B) is to inform patients that favorable intermediate-risk prostate cancer can be treated with radiation alone, but that the evidence basis is less robust than for combining radiotherapy with ADT.

He further added that in select patients with intermediate-risk localized prostate cancer, clinicians may consider other treatment options such as cryosurgery. Active surveillance may be offered to select patients with favorable intermediate-risk localized prostate cancer; however, patients should be informed that this comes with a higher risk of developing metastases compared to definitive treatment. Similarly, we should recommend observation or watchful waiting for men with a life expectancy ≤5 years with intermediate-risk localized prostate cancer. The patients who are considering focal therapy or HIFU should be informed that these interventions are not standard care options because comparative outcome evidence is lacking.

Moving on, it was recommended by the speaker that the high-risk localized prostate cancer patients should be staged with cross-sectional imaging (CT or MRI) and bone scans. A stronger recommendation is that radical prostatectomy or radiotherapy plus ADT are recommended as standard treatment options for patients with such patients. Active surveillance should NOT be recommended, and watchful waiting should only be considered in asymptomatic men with limited life expectancy (≤5 years). Cryosurgery, focal therapy, and HIFU treatments are not recommended, and primary ADT should not be recommended for patients with high-risk localized prostate cancer unless the patient has both limited life expectancy and local symptoms.

You may consider referral for genetic counseling for patients (and their families) with high-risk localized prostate cancer and a strong family history of specific cancers (e.g., breast, ovarian, pancreatic, other gastrointestinal tumors, lymphoma). We should not treat localized prostate cancer patients who have elected to undergo radical prostatectomy with neoadjuvant ADT or other systemic therapy outside of clinical trials. The relevant patients should be informed that older men experience higher rates of permanent erectile dysfunction and urinary incontinence after prostatectomy compared to younger men. Pelvic lymphadenectomy can be considered for any such patients undergoing radical prostatectomy and is recommended for those with unfavorable intermediate-risk or high-risk diseases.

The speaker further added that patients should be counseled regarding the common complications of lymphadenectomy, including lymphocele development and its treatment. The localized prostate cancer patients with unfavorable intermediate-risk or high-risk prostate cancer should be informed about the

benefits and risks related to the potential option of adjuvant radiotherapy when locally extensive prostate cancer is found at prostatectomy.

The clinical principle is that a single modality should be offered (external beam radiotherapy or brachytherapy) for patients who elect radiotherapy for low-risk localized prostate cancer. For intermediate-risk patients, however, combining the two modalities is also an option. There is a stronger recommendation with level A evidence that we should offer 24-36 months of ADT as an adjunct to either external beam radiotherapy alone or external beam radiotherapy combined with brachytherapy to patients electing radiotherapy for high-risk localized prostate cancer. Alternative recommendation (evidence level B) is to inform such patients that the use of ADT with radiation increases the likelihood and severity of adverse treatment-related events on sexual function in most men and can cause other systemic side effects.

The speaker concluded ed his talk by highlighting the importance of a local system of stratification as it affects the treatment options suitable for the patient. He informed the audience that the Cambridge prostate cancer group has come up with its stratification system and is no longer using NCCN. We also need local stratification based on local disease behavior so that we can treat them appropriately.

RADICAL PROSTATECTOMY

BY DR. SNK WAWERU

Dr. Waweru is a Consulting Urologist at the Nairobi Hospital and Mater Hospital among others. He is formerly the chair of the Department of Surgery at the Mater Hospital. His interests are in prostatic cancer and urolithiasis.

He initiated his talk by defining radical prostatectomy (RP). It is a surgical procedure for localized prostate cancer to remove the prostate together with the seminal vesicles, and occasionally the lymph nodes close by. The history of RP goes back to 1905 when the first RP was performed by Hugh- H. Young, which was a perineal one with attended bleeding, sepsis, and other complications. Terrence Millins did the very first retropubic RP in 1947, but this was a patient of chronic prostatitis and not cancer. Patrick Walsh revolutionized the process of RP which previously was a bloody operation with a lot of morbidities. He studied the dorsal complex of veins; a lot of bleeding was coming from there.

He further added that Patrick Walsh collaborated with Pieter Donker to demonstrate a nerve-sparing procedure for RP. Moving on, Schuessler did the very first laparoscopic RP. Likewise, Binder and Kramer did the very first Robot-Assisted Laparoscopic Prostatectomy (RALP) in 2000. Locally, here in Kenya, Prof Mungai has many firsts in urology, so he did the first one to do RP. The speaker recalled doing two cases with him in 2005. Many more urologists are now empowered to do this.

The speaker continued to explain the gold standard for anatomical RP as originally described by Walsh and Donker in 1982. One has to understand the crucial anatomy, including the dorsal vein complex if you want to do a meaningful prostatectomy without much bleeding. We need to understand the Pelvic plexus, cavernous nerves, and Pelvic fascia. Also, we need to know the position of the external Sphincter in relation to the venous urethra. As a surgeon, you want to have Trifecta's ideal of oncological success. You want to look at the functional success of the patient in terms of adequate continence and potency.

He informed the participants that the RP procedure itself is not simple. Yet, you must do technical refinements. He shared various techniques to help us do better in RP. The first one is the nerve-sparing technique. There is a hammock of nerves on the pelvic floor. He taught the audience the basic anatomy of nerves in relation to other organs nearby. If you want to have a potent patient after dissection, it is important to understand the anatomy well. We want to do minimal traction. We do not use any thermal agents around the nerves. We need to know the correct planes and perform a meticulous dissection.

Moving on, he explained the basics of the Veil of Aphrodite technique. He reminded the audience that Aphrodite was known as the Greek goddess of love, lust, beauty, pleasure, and passion. The veil is an area of the cavernosal nerve from the postereo-lateral to the anterolateral surface of the prostate like a curtain. Prostatic fascia is incised anteriorly to enter the intra-fascial plane, thereby sparing the nerve. He shared with the audience the outcomes of a successful application of this technique, as published by Kaul et. al. (2005), where the potency was achieved in 96% of the men 1 year after the procedure. Positive surgical margins were observed in 4.6%, whereas continence was present in 97% of individuals.

The speaker continued further to explain the continence technique. The technique first described by Rocco et. al. can help preserve the lateral prostatic fascia and urethral length. He shared with the audience the technological advancement in robot-assisted RP (RARP) and other techniques. He shared that vesicourethral anastomotic stenosis (VUAS) is one of the major complications that could occur after the surgery. He described his own way of doing it, through a ‘canoe-shaped transection at apex rather than transverse; it gives extra diameter. It should give good bladder neck reconstruction and you get a tension-free anastomosis as a result.

The procedure of RP resembles the elections where you are trying to balance a lot of things. Showing a cartoon from 2013, he told the audience to note that we are balancing the regional fair and national interest in elections. Similarly, in RP, you are trying to balance continence, oncological control, and potency (also known as the “Trifecta” ideal). Persistence is the key to making things easier for you.

He shared a profile of the patients that he usually sees. Most of our patients have early cancer diagnoses and are younger patients. Our emphasis is on functional outcome and oncological control. The patients prefer minimally invasive surgery. For patient preparation, the speaker shared that he performs 12 core TRUS guided biopsy which is laterally directed. They get staging done by Pelvic MRI & radionuclide bone scanning (RNB). A cardiac evaluation is performed. Bowel expression is also done for preparation. He shared a case study like what was discussed in the morning session and said that a nerve-sparing RP can be performed in this case of adenocarcinoma.

He continued to explain his practice by sharing the details of the anesthesia that they perform. Hypotension is induced to reduce blood loss and get a relatively bloodless operative field. Informed consent is then obtained, and the patient is given certain medications. The catheter is kept for 21 days, which they are trying to reduce. They performed the procedure for 32 patients between 2009 and 2016. The patients were followed up for 5 years for biochemical recurrence. The patients were aged between 48 and 71 years. The PSA ranged from 4.84 to 94.3 ng/ml where more than 50% had PSA of more than 20 ng/ml. The mean Gleason score was 7. The upgrading occurred in 36% of patients. The biochemical recurrence occurred in 25% of the patients and 1 patient died in 5 years (3% mortality).

Towards the end of his talk, he shared the challenges faced in Kenya for the management of prostate cancer. Late presentation and diagnostic backup are the main issues. The patients prefer minimally

invasive treatment options. We lack resources for robot-assisted procedures. We also need to build surgical capacity and expertise. Medical tourism is another key issue in Kenya, where quite a few people opt to go to other countries for treatment.

THE ROLE OF HYPOFRACTIONATION

BY DR. ANGELA WAWERU

Dr. Angela is a Consultant Clinical Oncologist. She is the Section Head of Radiation Oncology in the Department of Hematology-Oncology at the Aga Khan University Hospital, Nairobi. Her areas of interest include gynecological, head, and neck cancers.

She appreciated Prof Ngugi for appreciating the role of radiotherapy in the management of prostate cancer. She started her talk by introducing the concept of fractionation. The concept was established about 50 years ago as the best way of obtaining a differential effect between the tumor and normal tissues around it. It is the process of dividing the total dose of radiation into smaller multiple fractions. By doing so, we maximize the destruction of malignant cells whilst allowing for normal cells to repair themselves. The biggest disadvantage is the logistic and economic burden on the patient & public health systems. The patient usually does not want to undergo a long course of radiotherapy spanning over multiple weeks and prefers a one-off surgery over it. However, radiotherapy is advantageous in certain cases.

Expanding on the topic, the speaker informed the audience that the standard fractionation includes 1.8-2 Gy per fraction, five days a week, typically over 5-8 weeks depending on the disease site. For prostate, we usually do 78 Gy in 39 fractions, over 8 weeks. With technological advances, we can now better spare the normal tissues. This raises the question of whether we need the fractionation at all? There have been altered fractionation schemes introduced. Besides hypofractionation, the topic of today's talk, two other fractionation schemes are hyper-fractionation and accelerated fractionation. In hyper-fractionation, the dose per fraction is reduced and overall treatment time is maintained, by delivering multiple fractions in a day. In accelerated fractionation, the overall treatment time is reduced. A combination of these two techniques is also used, especially in lung cancers.

Hypofractionation is well-established for breast cancers and is getting introduced for prostate cancers as well. The dose per fraction is increased in this protocol. For prostate, we give 3 Gy instead of 2 Gy, once a day, but the total duration comes down. The total dose may seem to be lower than regular fractionation. However, that's not the case. Due to the concept of 'biologically effective dose', a higher dose per fraction given over a shorter period, you achieve a similar or better effect in terms of efficacy. Commenting on the evolution of hypofractionation, the speaker said that it was considered a primitive treatment till mid 20th century and was used in a palliative setting usually. As radiobiology became better understood & technology got advanced, the utility of hypofractionation increased. It is now known as efficient (or even better) as standard fractionation in breast cancer and prostate cancer.

Recalling her training, the speaker informed the audience that radiobiology was one of the most difficult topics for us. However, to understand the basics of radiotherapy and fractionation, we need to have a how-know of it, mainly the alpha/beta ratio. As we know that response to radiotherapy depends on some inherent characteristics of the organ treated, primarily alpha/beta ratio. It is a reliable estimate of radiation response. The alpha constraint looks at the damage with a single dose whereas the beta constraint measures multiple sublethal damages. These constraints vary between different tissues and

tumors. Something called the linear-quadratic ratio best describes the radiation response in terms of the alpha/beta ratio.

Traditionally in radiotherapy, we say that all tumors have a high alpha/beta ratio (10) and normal surrounding tissues have a low ratio. What we know after in-vitro and in-vivo research is that some tumors (breast and prostate) have a lower alpha/beta ratio. Breast cancer has an alpha/beta ratio of 3, and prostate cancer have an even lower ratio of 1.5. For non-radiation oncology professionals, what this simply means is that we require different treatment strategies i.e., hypofractionation. A lower ratio of alpha/beta means that the tumor is more responsive to changes in the dose per fraction. For a higher dose per fraction, these tumors have a bigger therapeutic index.

The speaker gave a quick recap of the fractionation. The standard fractionation is 2Gy per fraction, five days per week, and typically for 25- 30 days. In hypofractionation, the dose is more than 2Gy per fraction, five days a week, typically for 10-15 days. We get a clinical advantage in tumors with a low alpha/beta ratio. It is thus most utilized in breast cancer with increasing use in prostate cancer. There are two forms of hypofractionation in prostate cancer. There is moderate hypofractionation, which is typically given in 20 fractions, so it is 4 weeks instead of the typical 8 weeks. Also, there is ultra-hypofractionation, where treatment ranges from 5-to 7 fractions.

Through several studies, the role of hypofractionation is established in prostate cancer. Our focus is on the CHHiP trial (Conventional versus hypo-fractionated high dose intensity-modulated radiotherapy for prostate cancer). It is a randomized phase 3 non-inferiority trial with a big enrollment of around 3000 men. About 71 centers were participating, mainly from the UK. The standard fractionation was 74Gy in 37 fractions, whereas the hypo-fractionated treatments included 60Gy in 20 fractions as well as 57Gy in 19 fractions. The primary endpoint was defined as time to biochemical or clinical failure.

The 60Gy/20fx arm was non-inferior to the standard fractionation. The failure-free survival for the standard arm was 88.3%, whereas it was 90.6% for the 60/20 arm, and 85% for the 57/19 arm. It is interesting to note that the same result is achieved with hypofractionation but with half of the cost. In overall survival also, no significant differences were observed in the three arms. For radiation oncologists, it is important to consider if there is any harm to the normal tissues in terms of toxicities. The acute GI toxicities were picked sooner with hypofractionation, but these were the same as those in the standard arm at 18 weeks. For the GU side effects, there was no difference between the three arms.

The speaker continued to describe the new frontier that is ultra-hypofractionation. In intermediate and high-risk diseases, new research has suggested that a combination of external beam therapy and brachytherapy is advantageous to external beam therapy alone. However, stereotactic body radiotherapy (SBRT) may replace brachytherapy. It is delivering the image-guided high-dose radiotherapy with tumor ablative intent. Typical doses are 15-20Gy per day, in 1-3 days/week and it usually does not exceed 5 fractions. Sites with increased SBRT utility include lung, liver, spine, pancreas, kidney, and prostate. Although not all of them have a low alpha/beta ratio, a precise delivery coupled with hypofractionation benefits them all. There have been prospective trials that have demonstrated efficacy and acceptable acute toxicities. However, the late toxicities remain a concern.

The speaker explained that if the hypofractionation is done well, the late effects can be avoided too. It is now included in the NCCN guidelines as an external beam radiotherapy option. In summary, Hypofractionation is the delivery of a larger dose per fraction over a shorter treatment time. Its utility is

increasing as radiobiology is better understood. It has clear practical and economic advantages to the patient as well as the healthcare systems.

THE ROLE OF BRACHYTHERAPY IN PROSTATE CANCER MANAGEMENT

DR. NJOKI NJIRAINI

Dr. Njoki is a Consultant Clinical Oncologist based at the Cancer Treatment Centre in The Nairobi Hospital. She has been a key in instituting multidisciplinary meetings, problem-oriented research in the department, and streamlining patient care within the oncology clinics in the public and private sectors.

She started her talk by explaining how they still get a flux of patients in radiotherapy despite surgery being the first option for most of the patients. Those who are not fit for surgery due to age or something else automatically get selected for radiotherapy. Brachytherapy either attracts those patients who do not want several weeks of external beam radiotherapy or those for whom it can be used as an add-on.

The history of brachytherapy dates back to 1910 when the radium was put itself in the urethra. In 1930, radioactive gold was injected into the prostate. It was the year 1970 when radioactive material was used in the form of seeds for implantation into the prostate. It happened at Memorial Sloan Cancer Center where iodine seeds were used by Whitmer et. al. In 1983, it become even better with the advent of ultrasound as you can localize the prostate and figure out where the seeds are going.

Referring to the previous talk, she reminded the audience that we exploit the lower alpha/beta ratio of the prostate to make the duration of treatment shorter through brachytherapy. We try to be more conformal despite its proximity to the bladder and rectum. We want to increase the dose to the prostate and reduce the dose to the organs at risk. Then we have late reacting tissue that is more sensitive to dose per fraction. High doses to the prostate can only be given if either it can be moved away from the rectum or the dose can be made more conformal.

Expanding on the topic, she said that we have two types of brachytherapy. We have either a low dose rate or a high dose rate of brachytherapy. For low dose rate brachytherapy, which is between 0.4-2 Gy per hour, we leave the seeds or sources within the patient permanently. Whereas in the high dose rate of brachytherapy, which is usually more than 12 Gy per hour, the patient has to come to our clinic to get the seeds for a shorter time and they are removed then. The high dose rate form of brachytherapy has a lucrative advantage in that the same iridium sources that we use for prostate can be used for other sites as well.

Now, the types of those seeds are different. There are classic LDR (low dose rate) seeds versus ultra LDR seeds. The classic LDR seeds included Radon-222 and Au-198. We don't use a lot of classic seeds; the gold seeds are more common in the US. We use the ultra LDR sources here, which include Palladium-103 (also commonly used in the US), Iodine-125, and Cesium-131 (it is not that common). The ultra LDR seeds have a longer half-life. Palladium-103 has mean photon energy of 22 keV and a half-life of about 17 days. By using them, you will give a dose to the patient of about 125 Gy.

If we look at Iodine-125, which is used more commonly, it has a half-life of 59 days with a mean energy of 28 keV. For radiation oncologists, it is very lucrative to us as the distance with which this radiation travel is much shorter, thereby we can protect the bladder and rectum. In the case of Iodine, the dose will be 145 Gy. Gold seeds would have higher energy (412 keV) and lack that advantage. Likewise, Radon-222 seeds give photons of 1.2 MeV, so the distance they travel will be longer. The dose to the rectum and bladder will be much higher.

Moving on, she shared the details of seeds used in brachytherapy. Their shape is usually like a capsule whose typical length is 4.5 mm, and diameter is 0.8 mm. The core is made of titanium and the actual radioactive material is sealed within it. This provides some sort of protection in the handling of the seeds by the surgeon and radiation oncologist using them. The dose prescription that we usually give is to the volume of the prostate. So, we calculate the volume first with the help of the imaging team. With ultrasound, we confirm if this is the same extent of volume that we are expecting. The dose to 90% of this volume is 100%, or the 100% of the volume is receiving 95% of the prescribed dose. For the rectum, we limit the dose to 2cc to be less than the prescribed dose.

In general, we are battling between achieving the target dose and reducing the rectum and bladder. These constraints are fed into the planning system that we use. Another aspect is that 150% of your dose must cover the gross tumor volume, so it must cover the prostate. The advantage of low-dose brachytherapy is that you don't spend that much time in the hospital (usually just a night). Further, it is less invasive than prostatectomy. She said that the RP procedure resembles taking a big chuck (like a small chicken) out of the patient.

Another advantage of LDR is that you don't have to undergo repeated treatments; the risk to normal tissues (rectum, bladder, urethra) is lower, and the erectile function is well-preserved due to low doses. The disadvantage is that it is not widely available (only in Nairobi Hospital). The urinary side effects may last longer than those expected with regular radiotherapy, and even last up to six months. As anesthesia is required, the patient needs to be fit for anesthetics. Now, as you have a radioactive implant in you, you can't have sexual intercourse (in the next 2 months) or take a baby in your lap (at least 2 weeks). The cost is about 850,000 in Kenya.

The speaker then moved on to sharing the details of HDR (high dose rate) brachytherapy. The patient is inserted with catheters which sometimes remain there for a few hours. The seeds are placed in the periphery so that you can protect the urethra in the center. The advantage is that it is a shorter course of treatment in comparison to regular radiotherapy. However, you need to be in the hospital for about a week. You should be able to lie flat so that catheters can be inserted. The side effects include bladder and bowel complications; erectile dysfunction may occur in the longer term.

She explained the inclusion criteria, i.e., who can get the brachytherapy done. One factor is life expectancy, and it should be more than 5 years. We need to look at co-morbidities; what is his functional status; what kind of support he has at home. The prostate volume should be less than 60cc, although there are centers that do up to 100cc. If the patient had a previous transurethral resection of the prostate (TURP) in the last six months (some people limit it to 3 months), you can't do brachytherapy. For patients with a narrow pubic arc, it may interfere with accessing the anterior aspect of the prostate and brachytherapy may not be possible.

Before the implant, you admit the patient and get the anesthetic review. You have to fast them for 6 hours before the procedure. You prepare the perineum; get them shaved and cleaned. The anti-coagulants and anti-inflammatories are stopped because of the risk of bleeding. She continued to explain the implant procedure by saying that you get general (or spinal) anesthesia. The patient is positioned in a lithotomy position and catheterized. The patient is inserted with an ultrasound probe in the rectum to get the prostate volume, which is correlated with the 2-D images. Real-time planning is done depending on the volume of the prostate. The seeds are prepared and loaded into the patient through catheters. For 40 seeds, we don't do 40 passes into the prostate, rather we use stranded seeds where we can 3, 4, or even 5 in one track. She added that we must confirm where the seeds are sitting at least one-month post-implant. This is done through a dosimetry CT scan, and we will map out the seeds. If there are any missing seeds, a chest x-ray is recommended.

The advantage of brachytherapy is that we reduce the toxicity of the bladder and rectum. There are, however, other toxicities present. One such issue is urinary toxicity. The catheter usually remains there for 24 hours post-procedure. Patients can have urinary frequency and urge incontinence can occur. These problems usually go away within 6 months, but after a year it is completely settled. The rectal toxicity manifest as bleeding, which is usually self-limited within 12 months. Patients who experience erectile dysfunction do very well with sildenafil.

The speaker shared one example of a patient whom they managed recently. He was aged 68 years old with not so well-controlled hypertension. He had a urinary frequency since last year. His PSA was 24 ng/ml as measured in January of this year. The MRI showed a 36 g prostate with a PIRADS-V lesion on the left. He had an intact capsule with no invasion of the seminal vesicle and no adenopathy. He had a biopsy and 5 out of 12 cores showed a Gleason 4+4, 60% involvement with perineural invasion and lymphovascular invasion. As per our clinical assessment, he was at high risk. We sent him for PSMA-PET, which showed localized disease within the prostate with no adenopathy or metastasis noted.

She added that the case was discussed in the tumor board by our colleagues and was classified as localized high-risk prostate cancer. The discussion resulted in offering him a combined modality treatment which was brachytherapy followed by external beam radiotherapy and hormonal therapy. During the procedure, his prostate was sized at 33cc. The procedure was performed, and post-op care was provided. She concluded her talk by presenting a summary of brachytherapy, and its case selection, and highlighted the importance of reporting the outcomes.

ROLE OF HORMONE THERAPY IN EARLY PROSTATE CANCER

BY DR. ANGELA MCLIGEYO

Dr. McLigeyo is a Medical Oncologist and a Lecturer at Kenyatta University. Her core skills are in clinical decision-making in internal medicine and oncology, conducting training, streamlining medical education, and conducting research. She is a member of KESHO, ESMO, and ASCO.

She introduced the contents of her talk which included observation, active surveillance, and ADT. In observation, you look at the signs and symptoms that a patient has. The application is mainly the low-risk patients with low life expectancy and comorbidities. The intention is to transition the patient to palliative treatment when needed. Active surveillance is needed when patients are looking for a transition to curative intent when cancer progresses. It is important to look at the patient's disease risk and life

expectancy. The advantage is that about half to 70% of the patients can avoid active treatment for up to 10 years. It is important to tell the patient that the delay in treatment when they are under active surveillance does not impact the cure rate.

The speaker informed the participants that the very low and low-risk groups with an expected survival of more than 10 years are candidates for active surveillance. Likewise, a very selective group among intermediate-risk patients can be put under active surveillance. What entails active surveillance is a PSA testing every six months, DRE at least once a year, a repeat biopsy, and mp-MRI annually. The frequency can be increased if needed. For considering the transition to treatment, a lot of factors play their role. Grade progression is one of the main factors. Likewise, a rise in PSA level or patient's anxiety may necessitate conversion to treatment.

The role of ADT becomes important when the patient has undergone radiotherapy or RP. Prostate cancer is really an androgenic disease. Testosterone production is regulated by luteinizing hormone (LH) and luteinizing hormone-releasing hormone (LHRH). Hypothalamus releases LHRH, which stimulates the release of LH from the pituitary gland. LH acts on specific cells in the testes to produce the majority of testosterone. Most of the remaining androgens are produced by the adrenal glands. Androgens are taken up by prostate cells, where they either bind to the androgen receptor (AR) directly or are converted to dihydrotestosterone (DHT) which binds to AR with a higher affinity.

Therefore, LHRH agonists and antagonists are really the keys to the medical management of early prostate cancer. There is data supporting the use of ADT as neoadjuvant/concurrent/adjuvant in unfavorable intermediate risk, high or very high-risk patients. There is no survival benefit in the early stage, low risk, on a non-curative pathway. When a patient is on ADT, their testosterone levels should be monitored 12 weeks after 1st dose of LHRH therapy or upon an increase in PSA.

She presented an interesting question to the audience: in early prostate cancer, where you are treating curatively with two treatments that have been discussed, can you use bilateral orchiectomy to achieve ADT? We know that it does work. However, from the literature, the only reason to do orchiectomy is in the setting of biochemical recurrence as salvage. As we know that hormonal therapy can cause cardiovascular issues, diabetes, and lipidemia, so if the patients have those complications, orchiectomy might be safer than medical castration.

Likewise, medical castration has been proven to be beneficial both in overall and disease-specific survival (TROG 960, DFCI 950961, RTOG 9408). A question comes up what is the optimal duration for ADT? For patients with an unfavorable intermediate-risk, 4-6 months of ADT is optimal in conjunction with EBRT. For high risk or very high risk, they are given ADT for a longer duration, usually between 2 to 3 years. For salvage ADT, do start it early or late? Although there is controversy on what is termed as early or late, usually earlier is better.

The speaker concluded her talk by discussing the last question is the use of ADT. Is it Intermittent or the continuous salvage ADT that should be used? She favored the former as there is evidence showing that intermittent is not inferior to continuous with respect to survival and better quality of life is reported for intermittent ADT.

SESSION 4: MANAGEMENT OF METASTATIC AND RECURRENT PROSTATE CANCER

CHAIR: PROF ALICE MUSIBI

This was the very first session after the lunch break. The session chair, Prof Alice Musibi is Professor and a Medical Oncologist. She currently serves as the Head of the Haemato-Oncology Unit at the Kenyatta National Hospital, Cancer Treatment Centre – TNH and is the Lead Oncologist at Kenyatta National Hospital in Othaya. She has vast experience in the clinical care of patients within the National and International Practice Guidelines and actively participates in the different institutional multidisciplinary tumor boards. She undertakes teaching and dissertation supervision of Medicine postgraduate students at the Aga Khan University, and Medical Oncology Fellows at the University of Nairobi.

She thanked the participants to bear with the symposium after lunch. She opted for a co-chair as a rescue in case she fall asleep, and invited the first presenter for a case presentation.

CASE PRESENTATION – LOCALLY ADVANCED OR METASTATIC DISEASE

BY DR JOSEPH ABUODHA

Dr. Abuodha is a physician and currently a fellow in Medical Oncology at the Aga Khan University Hospital. He has a keen interest in research for health in oncology and building capacity for medical research in larger Eastern Africa.

He started his talk by sharing the details of the case that was being presented. It was a case of an Asian male born in 1934 who spent most of his life in Kenya with occasional trips to India. He has remained engaged in various business activities and is currently retired from active work. He is widowed as his wife died 10 years ago. He has 3 children, 2 daughters, and a son, all in their late 30s. He had comorbidities including dyslipidemia and systemic arterial hypertension for quite a while. He developed coronary artery disease for which he has coronary artery bypass surgery in 2003. He has been on medications for managing his comorbidities. He had intermittent admissions for upper GI bleeding but has remained relatively well in general.

He had follow-ups with his cardiologist and had regular PSA testing. In 2013, when he was 79 but fit, his PSA was 12.58 ng/ml. A review of his records showed that it was 8.25 in 2012, and 2.91 in 2009. He did not have any symptoms and his DRE at that time showed a smooth non-nodular prostate gland. He had his prostate ultrasound done and his prostate volume was 14.1 ml. His post-void residual was 58.5ml. At that time, his raised PSA level was thought to be due to benign prostatic hyperplasia (BPH) and he was

started on α1 blockers. His PSA decreased for some time but 2 years after starting therapy, he experienced a peak in his PSA level (27.33 ng/ml) in 2015. He went for a subsequent workup. This time, he was presented with LUTS – urinary incontinence, and incomplete voiding. Repeat PSA (with a month gap) showed a level of 19.64 ng/ml.

The repeat ultrasound showed a huge difference in prostate volume from the previous finding (31 ml compared to 14.1 ml). The post-void residual volume was significant (332.1 ml). He underwent TURP and got diagnosed with prostate cancer, adenocarcinoma of Gleason score 5+4 with 90% of prostate tissue involved by tumor. It was quite a high-risk adenocarcinoma. The bone scan showed the bone involvement with increased tracer uptake in multiple areas. He was started with ADT at that time (2015) with 3 months of LHRH agonist therapy alone. The follow-up included bone scans, clinical examination, and PSA-testing. Bone metastasis was negative in 2016 and 2018 bone scans. Clinically he had reduced symptoms of LUTS and remained in good health. His PSA reached a nadir of 0.057 ng/ml in 2016. However, in 2019 we see a spike in his PSA level (17.86 ng/ml).

It was kind of a biochemical recurrence that needed to be evaluated further. A bone scan done at that time showed increased tracer uptake seen in the proximal diaphysis of the right humerus. With CT, we noted degenerative changes in the imaged spine. After confirming progressive disease, a clinical decision was to be made. He was considered castrate-resistant due to the rise in PSA level while on ADT previously. He had a low volume metastatic prostate cancer with a single bone lesion on the humerus and no visceral disease. The treatment options were radical prostate treatment with SBRT to a single bone lesion, or systemic treatment with intensification therapy. He commenced on ABIRATERONE 1000mg once daily, with daily prednisone 10mg and Zolendronic acid added.

After 3 months of treatment (in Feb 2020), he developed right-sided lower abdominal pain, with no significant physical examination findings. He underwent CT where an ill-defined lesion was found in the L2 vertebral body. Furthermore, several sclerotic bone lesions were seen in the iliac bones and right proximal femur. He was continued with the same therapy with a recommendation of a bone scan after 6 months. In the subsequent bone scan, he had Increased tracer uptake in the proximal diaphysis of the right humerus again seen with increased size and intensity. There was an Increased focal tracer uptake in the T4, T8, T10, L1 vertebrae, tenth rib posteriorly, both iliac bones, and the trochanteric region of the right femur. These all findings were suggestive of skeletal metastases.

Through shared decision-making, he was continued on Abiraterone + Prednisone but Zolendronic acid was replaced with Denosumab. He was given analgesia and the pain was not severe to warrant immediate radiation therapy. There was a consistent rise in PSA level observed. The family was bent on continuing Abiraterone. Thus, he was switched from Abiron© to Zytiga© in Aug 2020. There was a persistent rise in PSA to 93 in Oct2020. The therapy was switched to Enzalutamide 120mg once daily. ADT was continued but Denosumab was given. After 3 months (in Jan 2021), he developed worsening back pain and was evaluated with an MRI spine. He has heterogeneously enhancing lesions in various vertebrae of the thoracic, lumbar, and sacral spine. He received radiotherapy treatment of 20Gy in 5 fractions to C5-T3 and 30Gy in 10 fractions to L4-S4. His PSA was slightly decreased (to 78 ng/ml) but rose to 111 ng/ml in Jul 2021 (10 months of Enzalutamide).

At this time, a PSMA-PET was performed and had massive bone involvement but there was no visceral disease. This was progressively metastatic prostate cancer with bone involvement and also with an uptake in the prostate bed. He was 84 years old at this time. One of the possible options was systemic

chemotherapy with Docetaxel, which the patient declined. The second option was Leutichium177 PSMA radionuclide therapy due to the predominantly osseous disease. The patient preferred this option, traveled to South Africa, and had the first session of 177Lu done on 1-Mar-2022. He returned to Kenya a week later Returned to Kenya but had several toxicities (fatigue, dry mouth, and eyes, poor feeding) requiring hospitalization. The PSA on his return was 196ng/ml (9Mar2022). He underwent 5 days of hospitalization and stabilization.

The speaker saw him in the clinic on 24Mar2022. He looks and feels better, with persistent dryness of mouth and eyes, and normal blood counts. The PSA was 19 ng/ml this time.

THERANOSTICS IN PROSTATE CANCER

BY DR SAMUEL NGUKU

Dr. Nguku is a consultant in radiology and nuclear medicine at Aga Khan University Hospital Nairobi. He was integral in setting up the first PET CT service in Kenya at the Aga Khan University Hospital in Nairobi. He has a great passion for improving cancer imaging in the country and integrating molecular imaging in the management of cancer patients.

The speaker started his talk by presenting an outline that included basic principles, uses, and prospects of theranostics or radioligand therapy. He stated that thera(g)nostics is a combination of diagnostics and therapy using radiopharmaceuticals. The ‘g’ here is mostly used by Europeans to emphasize the fact that the diagnosis is used to guide the treatment.

He, then, moved on to give some basics of nuclear medicine. It is the use of radionuclides/radioisotopes for imaging and therapy. Unstable radionuclides are used which mostly decay through gamma emission (and a few of them through beta emission) which are then detected either through a gamma camera or a PET scanner. You can either use a radioisotope alone or bound with a career molecule (radiopharmaceutical). Theranostics, or radioligand therapy, has been around since the 1940s with RAI. Just like nuclear medicine, we use a radionuclide alone (e.g I-131) but at a higher dose or radionuclide bound to a ligand (e.g I-131 MIBG, Lu-177-PSMA). Technically, we replace gamma emitter radionuclide (diagnostics) with alpha or Beta emitter (therapy).

The speaker said that you can see what you treat, and you can treat what you see, in theranostics. This makes it close to personalized therapy. He continued to explain PSMA and its role in theranostics. He referred the audience to read the results of trials TheraP and the Vision. He shared the local aspects with the audience. We do have PSMA PET for diagnosis. We do have therapy rooms and expertise. The hurdles include availability and importation issues. We have had trouble with clearance by authorities due to radioactive material. And of course, the cost is a challenge always.

He summarized his talk by saying that there is an established benefit of Lu-177 PSMA therapy in mCRPC and it just received FDA approval (on 24 March 2022). It has a potential role in early metastatic disease. Alpha emitters (e.g Ac-225 PSMA) are even better and we hope they would come to our home soon.

ROLE OF NOVEL ADT AND TARGETED TREATMENTS

BY DR ANDREW ODHIAMBO

Dr. Andrew is a board-certified Medical Oncologist. He is a member of ASCO, ESMO, KESHO, and AORTIC. Fellow of the Royal College of Physicians of Edinburgh as well as East Central & Southern College of Physicians. His key interests are GI & HPB Malignancies, Lung Cancer, Breast Cancer, Lymphoma, Newer therapies i.e Immunotherapy & Targeted therapy.

He started his talk by showing a landscape of what is available for prostate cancer therapy. We can see that many new molecules are coming in place. He then shared another illustration to show the mechanisms of action of antiandrogens. There exist various mechanisms of action, starting from suppression of testosterone production, competitive binding to androgen receptors, co-activator recruitment, and so on up to the DNA level. Referring to NCCN, he appreciated that for systematic treatment for the castration-sensitive disease, we have a lot of options to choose from, and all of them are combined with ADT.

Moving on, the speaker showed the audience a timeline of the trials that occurred since the era of ADT started in 1941. It mainly started in 2013 when we see something, especially for metastatic castrate-resistant patients. Before 2013, there were not many options for this group of patients. He shared the details of trials for each of the drugs (Abiraterone, Enzalutamide, Apalutamide) to inform the audience on how to choose the right drug.

He said that we need to consider the cardiovascular risk profile (Glucose, Fat, Lipid, Fluid retention, Hypokalemia) to help make a decision. We need to consider if they can be co-administered with steroids. Remember, we have the risk of falls, fractures & seizures in the patients. The cost and availability of original drugs also impact the decision to choose the prescription.

The landscape is changing very fast. The 5-minute consultation for the right drug has now changed to a 2-hours long discussion. For the resistant group, there is still an unmet need. These patients progress very quickly and they have very shorter survival. We are transitioning towards precision Oncology. It will be interesting to see what the future holds for us, especially in triple therapy. Maybe we should think of de-escalation trials. Can we challenge the standard of care and try to walk backward? Otherwise, we might be in a situation where we would have eight drugs all at once for one patient.

ROLE OF CHEMOTHERAPY

BY PROF NAO ABINYA

Prof. Abinya is a Consultant Medical Oncologist at the Nairobi Hospital Cancer Centre. His research interests are in malignant hematology and breast cancer, which he has published widely in peer-reviewed journals. He also has a keen interest in molecular oncology. He founded KESHO, of which he was the first Chair, and is still its Patron.

The Prof appreciated the talk in the evening as he only has to summarize what has been said earlier. Most people start with data from the US, but he shared the Kenyan statistics. Prostate cancer is the most common one in men, just like the American statistics where one out of every nine men may develop prostate cancer. He emphasized the use of Gleason scoring. He asked the audience to ponder on the

question if we need to biopsy metastasis. The answer is yes. Although imaging is good, you need other biological entities that may be used. The tissues are needed, sometimes.

He emphasized that hereditary genetic testing is important for certain individuals:

- Those diagnosed with prostate cancer with a Gleason ≥ 7.
- Those diagnosed with cancer that has spread outside the prostate
- Those diagnosed with metastatic prostate cancer
- Those with a close blood relative (mother, father, brother, sister) that has been diagnosed with ovarian cancer or breast cancer under the age of 50; or pancreatic cancer, prostate cancer or Lynch syndrome.
- Those who have BRCA1 and /or BRCA2 mutations found on tumor profiling.

He informed the audience that an early disease is usually left to surgeons but when it is spread out, chemotherapy plays its role. We can define it loosely to imply the application of all forms of medicines to treat cancer. This way, it includes Cytotoxic agents, hormonal therapies, targeted therapies, and immunotherapy in various forms. However, strictly speaking, chemotherapy is the use of cytotoxic agents to treat cancer. These are Alkylating agents, Antimetabolites, Topoisomerase 1 and 2 interactive agents, Mitotic spindle poisons, compounds, and miscellaneous cytotoxics.

The speaker said that the chemotherapy space has been evolving in metastatic prostate cancer. Since 2014, there is evidence that bringing docetaxel upfront has a survival benefit when added to ADT compared to ADT alone for patients who have high volume metastatic disease. Chemotherapy provides a life-saving impact earlier in the disease and is not just a last resort treatment. Docetaxel in combination with ADT is established for the treatment of high-volume metastatic prostate cancer in combination with ADT. Docetaxel is well established as first-line chemotherapy in metastatic, castrate-resistant prostate cancer for patients who can tolerate chemotherapy.

He added that Cabazitaxel is established as second-line chemotherapy for metastatic CRPC who have previously been treated with a docetaxel-containing regimen. PARP Inhibition in CRPC patients with DNA repair mutations is beneficial. Immune checkpoint inhibitors are showing some activity. Some of the few responders can show sustained response over long durations.

He ended his talk by thanking all the previous speakers for making his job easier and by appreciating the sponsors of the event.

SUPPORTIVE CARE FOR PROSTATE CANCER PATIENTS

BY DR ESTHER NAFULA

Dr Nafula is a Palliative Care & Pain Management Specialist based at the Kenyatta National Hospital where she heads the Pain & Palliative Care Unit. She is a tutor at Oxford Brookes University and a member of the International Cancer Institute (ICI) faculty.

She started her talk by appreciating the father of palliative care (another name for supportive care), Prof Balfour M. Mount who is still teaching at McGill University in Canada. The term ‘palliative care’ was coined

in 1973 by him when he was working with patients with prostate cancer. The word 'palliative' comes from the Latin word 'palliare' which means to cover or to cloak.

She added that it is an approach that improves the quality of life of patients and their families who are facing challenges associated with life-threatening illnesses whether physical, social, or spiritual. The success of treatment is defined by control of symptoms, and alleviation of suffering rather than curing the disease. In the current model of palliative care, we look at integrating palliative from diagnosis when the curative interventions are not working. It includes end-of-the-life care as well as anticipatory grief support to the family in case of death and post-death bereavement support to the family.

The patients who are under treatment, their problems start with the treatment. The side effects include urinary problems, erectile dysfunction, and pain, not only physical but also psychological. In palliative care, we manage the symptoms that they have. We give them psychological support through counseling. We provide them with spiritual and social support, like writing a will, declaring a child, etc.

The speaker shared the benefits of palliative care. It improves management at all phases of the disease. It allows for better decision making at the end of life, and potentially reduces hospital admissions.

In terms of physical problems, the patients are presented with pain, urinary symptoms, bowel problems, and anorexia/cachexia. There is a multitude of psychological problems that they face including discouragement, feelings of isolation at home, despair, dependence on others, anxiety, and fears, as well as concerns about a recurrence of the disease.

She concluded her talk by saying that palliative care is teamwork and is interdisciplinary in nature that ensures the best care by considering the patient and family as the unit of care. Everyone has a role to play in supporting the patient and their family.

SEXUAL HEALTH CARE SUPPORT

BY DR YOGESWARAN CARNJINI

This was the second talk by Dr Carnjini in this symposium. You can find her biography in the above pages. She started by explaining that besides erectile dysfunction (ED), there are multiple other issues with sexual health, i.e., decreased libido, anejaculation, changes in orgasm, and changes in penile length. These issues occur due to the prostate cancer itself as well as due to the treatments used for it.

There are no reports that the Cancer itself causes ED. But it can cause ED if it is associated with LUTS. Moreover, the psychological impact of a diagnosis of cancer definitely plays its role in the onset of sexual health issues. With radical prostatectomy, ED can be caused by injury to the neurovascular bundle. The recovery for ED can take up to 2 years. Is also related to a lack of nocturnal and early morning tumescence leading to fibrosis. Post RP, penile rehabilitation has been adopted for patients to help with improving ED.

Moving on, she said that with radiotherapy, ED is onset in 20-80% of patients post-radiation. It occurs in 14-35% of patients after brachytherapy. However, It usually develops later, up to 6 years after treatment. The pathophysiology effect on the neurovascular bundle is not clearly understood. In hormonal treatment, LHRH Agonist/Antagonist or anti-androgen therapy blocks the production or effect of

testosterone. However, some patients still maintain this. The reasons for individual differences are not clearly identified.

Further, she educated the audience on possible treatments for erectile dysfunction. These include the use of PDE5 inhibitors and intracavernosal injections. The patients prefer oral drugs, due to fear of injections and inconvenience. There are vacuum erection devices that are shown to be effective in 80% of the cases and are more effective if used immediately after surgery. However, there is no large-scale randomized study backing their use. There are Combination therapies as well, i.e., Oral and intracavernosal, OR Oral and Vacuum Pump. Some other options include penile prosthesis and testosterone replacement therapy (TRT). Although we don't find any good evidence to suggest that TRT increases prostate cancer risk. But many clinicians are very cautious in using this in patients with prostate cancer. You should do a risk-benefit assessment and make a shared decision with the patient.

She concluded her talk by hinting at some other promising treatments for ED, including Low-intensity Shock Wave Therapy, intracavernosal injection of Bone Marrow. However, these are still under clinical studies.

FUTURE DIRECTIONS: PROSTATE CANCER IN 2022 (GLOBAL AND LOCAL RESEARCH AREAS)

BY DR GLADWELL KIARIE

Dr. Kiarie is a Medical Oncologist. She currently runs a private practice at The Nairobi Hospital and also reviews patients at other leading hospitals. She was one of the founding members of the Oncology Unit at the Aga Khan University Hospital and was also part of the team that set up the first Kenyatta National Hospital Tumor Board in 2007.

She started her talk by appreciating all the speakers for their insights. She said that she is glad and thankful that she is not a man. The incidence of metastatic prostate cancer seems to have increased in all races and age groups over the past decade. Current prostate cancer management includes radical prostatectomy, pelvic lymphadenectomy (PLDN), external-beam radiotherapy (EBRT), brachytherapy, proton beam therapy (PBT), cryosurgery, hormonal therapy, chemotherapy, and dietary strategies.

She referred to the trials that have been and are being conducted for improving the management of prostate cancer and appreciated the efforts of researchers. The trials she discussed included HORRAD, STAMPEDE, CHAARTED, LATITUDE, etc. She added that the SABR-COMET trial supported the use of concurrent MDT and systemic therapy. Patients with 1–5 metastatic lesions and a controlled primary tumor can receive standard-of-care treatment with or without SBRT to all oligometastatic sites. Systemic therapy and MDT (Metastatic Directed Therapy), as well as treatment of the prostate, should be incorporated into the treatment of oligometastatic patients. However, the optimal ADT duration and sequencing of systemic and local therapy remains unknown.

The speaker further added that the isolated pelvic nodal disease is a unique scenario within the array of oligometastatic disease states, regionally metastatic disease signifies an early intermediate point on the spectrum between locally confined and diffusely metastatic disease. Salvage Treatment of Oligo-recurrent Nodal Prostate Cancer Metastases (STORM) 6 months of ADT along with MDT, and are subsequently randomized to pelvic RT.

Moving on, she highlighted the recently approved agents for prostate cancer management. She expanded on the research in gene therapy for prostate cancer and said that we can understand the development of prostate cancer through it. Through gene therapy, we can identify men at high risk who might benefit from screening or from chemoprevention clinical trials, which use drugs to try to keep them from getting cancer. In those already diagnosed with prostate cancer, tests for certain gene changes can give a better idea of how likely the cancer is to grow and spread, which might influence treatment options.

Further, she highlighted her concern for the prostate cancer by emphasizing on the prevention of prostate cancer. She shared with the audience that the researchers continue to look for foods (or substances in them) that can help lower prostate cancer risk. Scientists have found some substances in tomatoes (lycopenes) and soybeans (isoflavones) that might help prevent some prostate cancers.

She concluded her talk by hinting at areas of research that can be targeted locally. These include DRE correlation with PSAs, Characteristics of African prostate cancer, response to therapy, quality of life trials, and toxicity Trials including those on sexual function. She recalled that the screening of prostate cancer with DRE was quite horrible in older days, but the situation is much better now.