

Congress Review

Review of the European Association of Urology (EAU) Annual Meeting 2021

Location:	EAU Virtual meeting
Date:	8 th -12 th July 2021
Citation:	EMJ Urol. 2021;9[1]:12-24. Congress Review.

HILVERSUM the modern architectural city in Netherlands was the chosen location for the live studio that hosted the European Association of Urology (EAU) virtual congress on 8th-12th July 2021. The city is also known media city of the Netherlands, as it populated with headquarters of several broadcast studios, news stations, television, and newspaper companies. With its rich broadcasting history and influence, it is no wonder that it was scouted by the EAU central office to host this outstanding annual meeting.

The opening ceremony began with the Christopher Chapple, EAU Secretary General welcoming the attendees to the virtual event. The travel restrictions and social distancing due to the ongoing COVID-19 pandemic meant that the event could not be held in person as initially planned. However, with the adoption of modern technology in media the event, although long distance, was able to carry on as a hybrid event. The EAU was packed with education programmes, lectures,

poster presentations, and even a scavenger hunt competition. Chapple stated that there were over 6,000 delegates from 150 countries. There was a clear representation of the global urology collaboration in this event with several joint sessions with EAU and international societies: Korean Urological Association (KAU); Japanese Urological Association (JUA); Pakistan Association of Urological Surgeons (PAUS); Iranian Urological Association (IUA); Urological Society of India (USI); Arab Association of Urology (AAU); Société Internationale d'Urologie (SIU); Pan-African Urological Surgeons Association (PAUSA); Confederación Americana de Urología (CAU); Canadian Urological Association (CUA); Urological Society of Australia and New Zealand (USANZ); Russian Society of Urology (RSU); and Taiwan Urological Association (TUA).

Chapple thanked Arnulf Stenzl, University of Tübingen Medical Center, Germany, and Peter Albers, Universitätsklinikum Düsseldorf, Germany, as well as the overall



EAU central office for their hard work in developing the programme for this annual meeting. According to Stenzl, there were 1,268 selected abstracts out of 4,500 submissions, 65 sessions in total, with 43 poster sessions, and 22 video sessions. He shared that there would be a question-and-answer function that allowed the attendees to also participate in sessions ahead. "One of the things that we always do at our Welcoming Ceremony is to acknowledge the enormous contribution of colleagues to the field of urology, both eminent established colleagues as well as young urologists," said Chapple.

There were combinations of videos, put together by the EAU team, of the winners receiving their awards. The awards were for both EAU 2020, that did not take place, and EAU 2021. Manfred Wirth, former treasurer of the EAU, was the 2020 winner of the Willy Gregoir Medal for a significant contribution to the development of the urological specialty in Europe. Hendrik Van Poppel, EAU Adjunct Secretary General, responsible for Education, was the 2020 winner of the Frans Debruyne Lifetime Achievement Award. Jelle Barentsz, The Prostate MRI Reference Center, Nijmegen, the Netherlands, received the EAU Innovators in Urology Award. Mike Moran,

University of South Carolina, USA, received the EAU Ernest Desnos Prize for Medal for his remarkable contributions to urology history. Derya Tilki, Martini-Klinik, Hamburg, Germany, was awarded the 2020 EAU Crystal Matula Award, which is usually given to young European urologist, aged 40 or under, who have the potential to become future leaders in academic European urology. Véronique Phé, Pitié-Salpêtrière Hospital, Paris, France, received the 2021 EAU Crystal Matula Award. Alessandro Larcher, San Raffaele Hospital, Milan, Italy, received 2020 EAU Hans Marberger Award which is given to the best published European paper on minimally invasive surgery in urology. Andrea Gallioli, Fundació Puigvert hospital, Barcelona, Spain, was the 2021 EAU Hans Marberger Award winner. Daniël Osses, Erasmus University Medical Center, Rotterdam, the Netherlands, was the winner of the 2020 EAU Prostate Cancer Research Award. Wolfgang Fendler, University Hospital Essen, Germany received the 2021 EAU Prostate Cancer Research Award.

In conclusion, the 36th Annual EAU Congress, had several remarkable sessions covering the

"One of the things that we always do at our welcoming ceremony, is to acknowledge the enormous contribution of colleagues to the field of urology, both eminent established colleagues as well as young urologists."

latest updates on important trial results and other breakthrough developments. Patients were also heavily involved this year, there were patient information sessions, patient poster sessions, and an androgen deprivation therapy educational programme. The EAU 2021 had an extensive coverage of the various aspects of the field of urology. ■



Low Testosterone and COVID Severity: Cause or Symptom?

INCREASED RISK of severe COVID-19 resulting in intensive care, intubation, and even death has been linked to lower levels of testosterone in males. A study carried out in Milan, Italy and presented at the EAU21 virtual congress on July 8th to 12th found that those with symptomatic COVID-19 who were found to have low testosterone were more likely to become severely ill and die from the disease.

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Andrea Salonia, a specialist in urology and Endocrinology at San Raffaele University Hospital compared levels of testosterone in 286 male patients with COVID-19 who attended the emergency department; the study included 305 healthy male volunteers. The threshold for low testosterone is deemed 9.2 (nmol/L) or below, 90% of the patients with COVID-19 had

testosterone below this level, compared to just 17% of the healthy volunteers. Furthermore, patients with mild symptoms tended to have slightly higher testosterone levels (3-4 nmol/L) than patients who were admitted to the ICU or died of the disease (0.7-1.0 nmol/L).

Salonia stated: "The relationship is clear; the lower the testosterone, the higher the severity of the condition, and the likelihood of death. I've never seen anything like it in my 25 years in the field."

As the team did not have access to data on the testosterone levels of patients prior to contracting COVID-19, the research does not reveal whether the low testosterone was a pre-existing condition or whether the virus itself induces the acute reduction in the hormone. Other research has indicated that the virus can reduce the number of Leydig cells, the cells responsible for producing testosterone. Furthermore, testosterone is understood to play a role in protecting males from disease. Salonia has called for further research following changing levels of hormones in patients over a longer period in order to answer these questions. ■



Urinary Incontinence Linked to Poor Mental Health Among Females

FEMALE urinary incontinence is a relatively common condition, especially among older females; however, there has been very little research into its effect on their mental health. For this reason, Margarida Manso and colleagues at the University Hospital Centre of São João, Porto, Portugal, analysed data from a population-based survey conducted by the Portuguese Health Ministry every 5 years, which asks respondents about various aspects relating to health and wellbeing. The principal results were presented at this year's 36th Annual EAU Congress, 8th-12th July 2021.

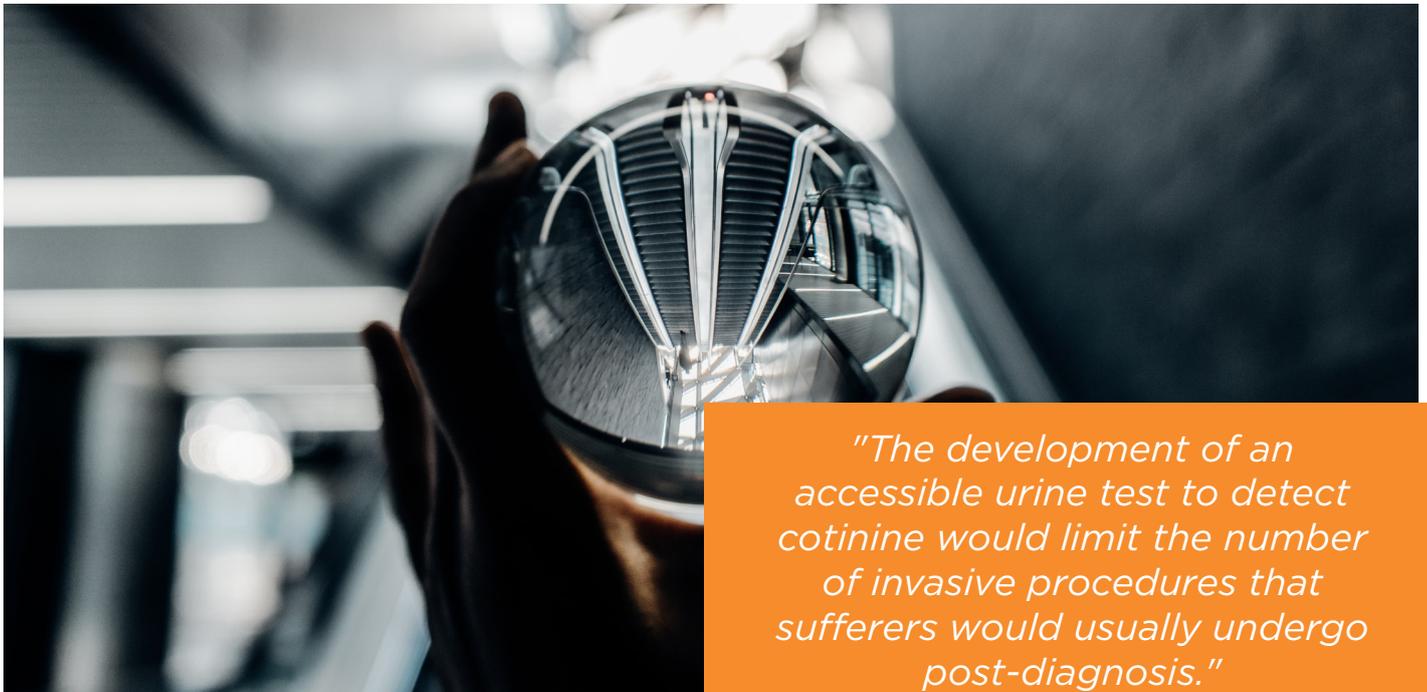
Manso and collaborators investigated the responses of approximately 10,000 females aged ≥ 18 years, comparing addictive behaviours (e.g., smoking and alcohol consumption), the dimensions of mental health disease, the prevalence of depression diagnosis, and the use of mental health consultations between women who did and did not report urinary incontinence.

Overall, around 10% of females reported having urinary incontinence, rising to 40% for females aged over 75 years. Individuals who reported

incontinence were 66% more likely to be diagnosed with depression and saw their doctor more frequently for mental health-related issues. In addition, females with incontinence were 65% more likely to classify their health status as 'bad', reported greater difficulty concentrating, and had more feelings of guilt and lower self-worth relative to those without the disorder. Interestingly, no substantial differences in smoking or alcohol consumption between the two groups were observed.

Manso highlighted the wider relevance of the research findings: "We believe the conversation between patients and their urologists needs to change. Clinicians should be asking patients about their mental health when discussing treatments, because treating their physical challenges could help with the psychological cost of the condition." Manso added: "Personally, I will be emphasising this more with my patients and trying to understand better the mental burden of living with incontinence." Going forward, the team behind this study are imploring healthcare practitioners to ask women with incontinence about their mental health and to offer potential treatments. ■

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Could Nicotine By-Product Predict Cancer Return?

PROMISING new evidence has emerged suggesting that cotinine, a by-product of nicotine, can be used as a biomarker to detect the recurrence of bladder cancer. This information was presented by researchers at the virtual 2021 EAU Congress, who found that those with high levels of cotinine present in their urine were four times more likely to experience a return of bladder cancer. The development of an accessible urine test to detect cotinine would limit the number of invasive procedures that sufferers would usually undergo post-diagnosis.

Bladder cancer is one of the most common forms of the disease, particularly in the older generation. Although it is widely known that smoking increases the risk of developing this type of cancer, this study is the first of its kind. Cotinine is a chemical that is produced by the body when nicotine is metabolised, and is usually used as a marker of tobacco smoke exposure.

Maher Abdessater and Raghid El Khoury from the Notre Dame de Secours University Hospital focused their study on low-risk, non-invasive bladder cancer, in which sufferers undergo surgery to remove cancerous tissue of the bladder lining. Following surgery, no additional treatment is required, and patients are monitored

through regular cystoscopies. The study involved 135 patients who were undergoing these regular checks over a period of 18 months, received no additional treatments and had no urinary conditions likely to compromise the results.

Results showed that 80 of the patients had cotinine levels of 550 ng/ml, which were consistent with heavy smoking. 75% of these patients experienced a return of their cancer, whilst only 18% of moderate smokers developed bladder cancer again. Abdessater explained: "One of the major advantages of using cotinine is that it can be detected using a simple urine test, which is a cheaper and less invasive alternative to cystoscopy." Cotinine detection is also a useful technique to identify where patients are not accurately disclosing their smoking habits.

Those involved in this study are currently seeking out other hospitals around the globe who may be interested in co-operating to expand this research to a wider range of patients. Arnulf Stenzl of the University of Tübingen Medical Center and Secretary-General Adjunct of the EAU stated: "We now need to test this in a larger trial, and also look at more precise indications of smoking levels and the type of cigarettes involved." ■

MRI Screening and Targeted Biopsies to Halve Overdiagnosis of Prostate Cancer

SUBSTITUTING traditional prostate biopsies with MRI and targeted biopsies, in a Swedish study, has halved overdiagnoses and reduced both unnecessary biopsy and identification of low-risk tumours. This new method is just as effective in detecting clinically significant tumours, and is of great interest when it is considered 1.4 million males develop prostate cancer globally and at least 375,000 die as a result of the disease.

Adding to the existing literature, which demonstrates organised screening can reduce risk of prostate-cancer death due to earlier detection, one of the researchers, Tobias Nordström stated, “Our results from a large, randomised study show that modern methods for prostate cancer screening maintain the benefits of screening, while decreasing the harms substantially.” Labelled the STHLM3MRI study, conducted between 2018 and 2021, the participant cohort included 12,750 males subject to a prostate specific antigen (PSA) blood sample analysis and Stockholm3 test analysing protein and genetic markers for predictive risk of prostate cancer. Elevated scores in these tests stratified the participants for randomly selected traditional biopsy or MRI to detect prostate cancer, with biopsy conducted strictly on tumours identified by MRI in this second group.

The current PSA test and traditional biopsies result in frequent unnecessary invasive procedure and diagnoses, the strength and necessity of this

new method can be seen through its specificity; “refined screening methods are required to reduce overdiagnosis and overtreatment of low-risk tumours, and prevent unnecessary biopsies and biopsy-related side-effects,” was the statement made by Martin Eklund, another associated investigator. Further successes to carry forward can be observed in the large sample size and randomised design of study, the next steps in research were mentioned as nationwide screening efforts at early cancer detection.

Nordström concluded, “We will soon present the second of the two main reports from the STHLM3MRI trial where we assess the role of a novel blood test as adjunct to MRI in prostate cancer screening. The future of prostate cancer diagnostics probably includes both improved blood-tests and MRI.” With the take home message, “We will finally be able to show that men can also reduce their risk of malignant cancer through nationwide prostate-cancer screening that utilises modern methods.” Hendrik Van Poppel, Adjunct Secretary General at EAU, showed his support for the research, “It is exciting to see breakthroughs such as this in the field of early detection of prostate cancer” and highlighted, “the EAU is working hard to ensure that early detection of prostate cancer is adopted across the whole of Europe.” ■

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Testosterone Therapy Linked to Reduced Heart Attack and Stroke Risk

RECENT evidence has surged linking testosterone therapy to a significantly lowered risk of heart attacks and strokes in males with a deficiency of the hormone. The 10-year study included over 800 people from Germany and Qatar displaying abnormally low levels of testosterone. Males involved in the study were at an increased risk of both heart attacks and strokes due to family history and diabetes profiling and were encouraged to make lifestyle changes to improve their cardiovascular health.

Of the 412 people who opted for testosterone therapy, 16 died, but none suffered a heart attack or stroke. The remaining 393 individuals who opted for no treatment saw 74 deaths, 70 people suffering a heart attack, and 59 a stroke. Testosterone therapy reduced the risk of both heart attacks and strokes in males under 55 by 25% and reduced this risk in over 60s by 15%. Males on testosterone therapy also saw an overall improvement in their health including weight loss and lowered blood pressure.

Although significant improvements were seen following testosterone therapy, scientists have emphasised that this treatment should not be seen as a 'silver bullet' and can only be used in patients matching given criteria. Omar Aboumarzouk from Hamad Medical Corporation revealed "Testosterone can be seriously harmful if taken by men with normal levels, or who function perfectly well with reduced levels of the hormone." Aboumarzouk went on to explain the advantages of normalising testosterone levels in deficient males, which has been seen to improve the beneficial effects of actions taken to improve their health.

This non-randomised study saw positive outcomes, however those involved were at medium-risk of a heart attack or stroke, and those receiving testosterone therapy were slightly younger than those who went untreated. Although these factors present limitations, a new trial is currently progressing involving 6,000 participants, which will allow solid conclusions to be drawn as to the benefits of hormone therapy in men with low testosterone. ■

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Virtual Reality Setting of Icelandic Landscape Could Reduce Pain During Uncomfortable Cystoscopy Procedure

BLADDER cancer diagnosis and treatment requires patients to undergo an uncomfortable and painful cystoscopy procedure. A new study carried out at Wrocław Medical University, Poland, presented at the EAU annual meeting on 11th July 2021, showed that a virtual reality (VR) goggles and headphones could alleviate pain in patients undergoing this medical imaging procedure.

Rigid cystoscopy involves the insertion of a rigid telescope into the bladder via the urethra and is an effective method used in the diagnosis and treatment of bladder cancer. However due to the painful and unpleasantness of this procedure, some patients opt out by avoiding a follow-up and this could lead to the progression and further irreversible development of bladder cancer. Rigid cystoscopy can be carried out under local anaesthesia. General and spinal anaesthesia could also be used; however, these approaches may lead to further risk of complications. Technology advancements, such as VR technology, used in different aspects of medicine have proven to be an important tool in improving patients experiences and overall patient outcomes.

Wojciech Krajewski and his team selected 103 patients undergoing rigid cystoscopy with just

local, intraurethral anaesthesia, with a mean age of 66 years. The participants, either first time diagnosis or requiring a follow up, were randomly selected to undergo classic cystoscopy or the procedure with VR goggles and headphones displaying an image of the Skógafoss waterfall, Iceland. The patients completed a questionnaire on anxiety and depression prior to the procedure. The researchers measured blood pressure, oxygen saturation, and heart rate during the cystoscopy and a measurement score called FLACC that's involves observing face, legs, consolability, and cry was also utilised. Following the procedure, patients rated the pain perception and nausea. The pain scores were lower in the VR group compared to the score, however, the VR group experienced higher levels of nausea and vertigo. Increased blood pressure and heart rates was noted in all patients but was lower in the VR group. The findings were the same in male, female, in both first and follow-up cystoscopies.

Krajewski said that “patients reported less pain, and this was also reflected in our observations of their experience. VR is certainly an option for pain reduction in cystoscopies and we are looking into whether it will have the same effect in other medical interventions such as lithotripsy to break down kidney stones or prostate biopsy.” ■

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Patients Classed as Being Obese Have a Higher Survival Rate of Advanced Prostate Cancer

A new study presented at the EAU annual meeting on the 11th July 2021 says that patients classed as being obese could survive a metastatic castration resistant prostate cancer. A metastatic castration resistant prostate cancer is an advanced form of prostate cancer whereby the disease no longer responds to treatments that lower the levels of the testosterone hormones.

There is evidence in a few cancers of a survival superiority in patients with high BMI, despite the fact that obesity is linked to an increased risk of death from several cancers and other chronic diseases, this occurrence is known as the obesity paradox. The investigation was carried out by researchers from San Raffaele University, Milan, Italy, and Mount Sinai Hospital, New York, USA,

who followed 1,577 patients diagnosed with the advanced cancer over a period of 3 years. The aim of the study was to assess whether the obesity paradox phenomenon applied to patients diagnosed with metastatic castration resistant prostate cancer. The researchers observed the survival rates of patients, with an average age and BMI of 69 years and 28 respectively, who took part in three different clinical trials.

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The results revealed the higher BMI had a protective factor of 29% higher overall survival probability and 35% cancer-specific survival probability. Over the period of 36 months, up to 30% of patients classed as obese survived compared to 20% of individual who were considered overweight and of normal weight. Overall, patients that are classified as obese, having a BMI of over 30, had a higher survival rate of 10%.

Nicola Fossati, a urologist at San Raffaele University, Milan, Italy, stated that, "this obesity paradox has been seen in some other cancers, possibly due to the relationship between tissue fat and cancer genomes, and more research is needed in this area. It's also possible that improved survival may be due to the interaction of chemotherapy with other drugs. Obese patients in this older age group tend to be taking medication for other conditions and we do not fully understand how these medicines interconnect. ■



Using Old Drugs for Kidney and Bladder Cancer Treatment



ABSENCE of treatment for reoccurring kidney cancer is a vital gap in cancer research that needs to be urgently addressed. Unfortunately, there is a high risk of kidney cancer returning in patients even after undergoing surgery. An exciting Phase III trial, however, showed that an old drug, pembro, which is used to treat other cancers including late-stage kidney cancer, could reduce the risk of kidney cancer returning if used earlier.

The trial took place across 20 countries and involved approximately 1,000 patients with kidney cancer who had undergone surgery. Patients were either given pembro, usually reserved for late-stage kidney cancer, or a placebo. After 2 years, the scientists evaluated the results and found that patients taking pembro reduced their risk of cancer developing again by a third compared to patients on placebo. Promisingly, the side effects from pembro were like other cancer drugs on the market.

Thomas Powles, co-investigator of the trial, from Barts Cancer Institute at Queen Mary University of London, UK, concluded, "There are signs as well that the drug may improve survival rates, but we can't be sure of that for another few years. We're hopeful that this trial, when complete, will provide a strong case for this

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drug to be approved for use by the medicines regulator." The next steps for this study involve evaluating the results from the ongoing follow-up with patients after 5 years to determine the efficacy of pembro on survival rates.

Further to this research, Powles also shared findings from another trial that took a similar novel approach of using an existing cancer drug for advanced bladder cancer. The DANUBE study involved using darvalumab typically used for lung cancer for late-stage bladder cancer instead. Overall, however, the study showed this drug did not increase survival compared to standard treatment. Nonetheless, for patients unable to take chemotherapy drug cisplatin, this could provide an alternative treatment and further research is warranted. The promising results suggest that one day, scientists may be able to approve the use of existing cancer drugs for kidney and bladder cancer treatment. ■

Promising New Treatment for Late-Stage Metastatic Prostate Cancer

PROSTATE cancer (PCa) is the leading cause of cancer-related deaths in males, with one patient dying every 45 minutes. Cancer can go undetected for several years and can be very difficult to treat once the tumour metastases. Metastatic castration resistant PCa is currently incurable and life-threatening. Therefore, there is a desperate need to improve therapeutics and develop novel drug targets. A recent Phase III trial orchestrated by Johann de Bono from the Institute of Cancer Research, London, Ken Herrmann, University Hospital Essen, Germany, and a team of researchers analysed the efficacy of a new treatment, Lu-PSMA-617, discussed at the EAU21 congress.

Lu-PSMA-617 targets the molecule PSMA, which can be found elevated on the surface of PCa tumour cells. This unique treatment involves using beta radiation to destroy PSMA and the surrounding microenvironment. The researchers aimed to discover whether Lu-PSMA-617 was more effective than standard care. To begin with, they recruited 831 patients with metastatic

and castration resistant PCa. The patients were randomised to receive Lu-PSMA-617 plus standard care or standard care only.

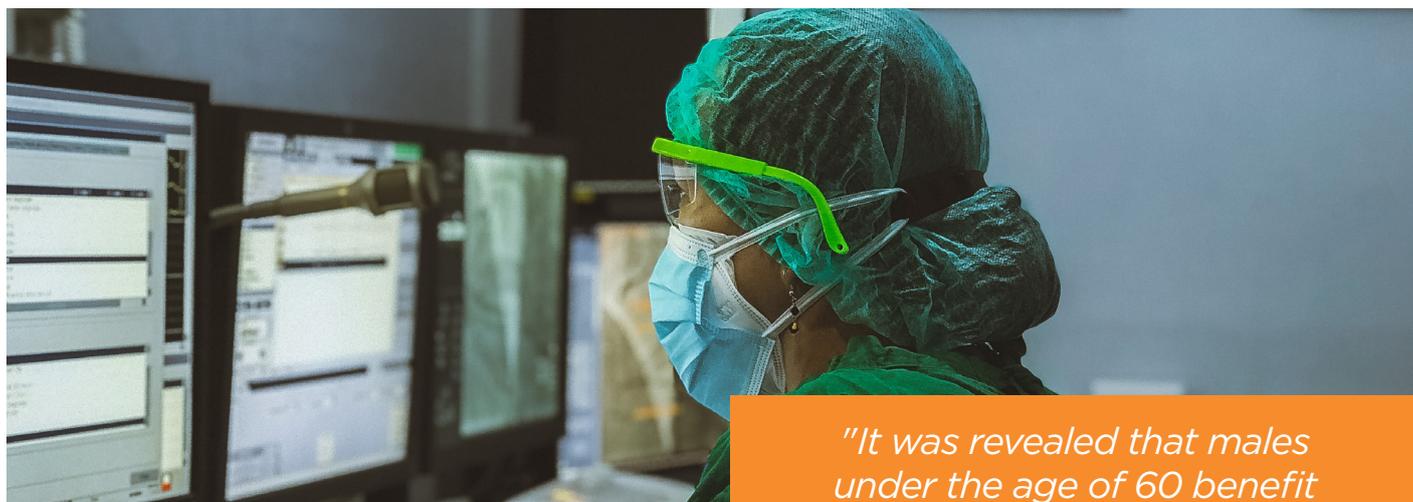
Interestingly, the patients treated with Lu-PSMA-617 had significantly improved survival time. The median survival time was 15.3 months in patients treated with Lu-PSMA-617 and 11.3 months in individuals receiving standard care only. Overall, survival time improved by an average of 4 months. Additionally, progression-free survival also showed promising results and became longer with Lu-PSMA-617 treatment (8.7 months versus 3.4 months). What is more, the safety profile showed that the quality of life was not negatively impacted.

This novel treatment could be valuable in patients where standard treatment has been ineffective or in individuals with high levels of PSMA. Herrmann concluded, "Lu-PSMA-617 can improve the lives of many men with advanced prostate cancer and their families." Due to the positive results, this treatment is being reviewed by the NHS in England and Wales for approval. ■

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Monitoring Low-Risk Prostate Cancer Proves More Effective Than Active Treatment



"It was revealed that males under the age of 60 benefit very little from active surveillance in terms of survival, whereas those over 60 were seen to survive for at least 10 years with no additional treatment."

ENCOURAGING evidence has surged proving that men over 60 diagnosed with low-risk prostate cancer could benefit from monitoring their disease with no additional treatment. This method of 'active surveillance' involves close monitoring of their cancer, and was presented at the EAU Congress, which took place on 8th to 12th July 2021 following its success in two recent studies.

Due to the novel nature of active surveillance, scientists from the University of Gothenburg and Uppsala University, Sweden, developed a new statistical technique to combat the lack of available long-term data. Researchers began looking at the number of patients on active surveillance who progressed to other forms of treatment, rather than focusing on those who died of prostate cancer. Due to the wide use of treatments such as radiotherapy and surgery, existing long-term follow-up data allowed scientists to predict the outcomes for patients on active surveillance up to 30 years following diagnosis. The model showed the percentage of sufferers who died from the disease, as well as the number of years they spent without treatment.

The principal aim was to identify those who benefitted the most from active surveillance. Eugenio Ventimiglia, a urologist from San Raffaele Hospital, and a PhD student from Uppsala University explained "the older you are and the lower risk your cancer, the greater the benefit. But

we saw a real divide at age 60." It was revealed that males under the age of 60 benefit very little from active surveillance in terms of survival, whereas those over 60 were seen to survive for at least 10 years with no additional treatment.

The method of active surveillance also reduces the risk of side effects, including incontinence and erectile dysfunction, which are commonly experienced with radiotherapy and surgery. Research from the Europa Uomo Patient Reported Outcome Study (EUPROMS), which included around 3,000 males saw 45% of those on active surveillance experience erectile problems, compared to 70-90% on other treatments. The importance of this statistic was explained by Lionne Venderboc, a postdoctoral researcher at Erasmus MC "Lack of sexual function affects patients' quality of life more than any other reported side effect. The survey shows that active surveillance has the least impact on sexual function of all possible treatment options." There is hope that this method encourages men to overcome their reluctance to be tested for prostate cancer, as the later the disease is diagnosed, the more severe the impact of treatments on quality of life. ■