Meeting the challenges in urogenital diseases
EU Health Commissioner Andriukaitis urges stronger collaboration

By Joel Vega and Erika de Groot

To the rhythm, high energy beat of the synchronized, four-man Copenhagen Drummers band, the 33rd Annual EAU Congress opened yesterday with European Commissioner for Health and Food Safety, Prof. Vytenis Andriukaitis (LT) urging the audience to collaborate in the European Reference Networks (ERNs).

“This flagship project reflects not only the need to further strengthen our collaboration, but also the fact that we can and have achieved a lot if we put together our resources, knowledge and commitment,” said Andriukaitis. He emphasized that the synergies of expert centres are invaluable and will come a long way in providing better healthcare, particularly to those with rare diseases.

Andriukaitis thanked EAU Secretary General Prof. Chris Chapple for his personal efforts and commitment to ERNs with the involvement of urological expertise in the eUROGEN network which currently numbers 29 active units in 11 EU member states.

Chapple also highlighted the crucial role of the EU in creating the ERNs which he said will lead to better data collection and mutual collaboration among European scientists and clinical professionals. “To ensure the sustainability of this project we need to form partnerships and work on common goals,” he said.

The Opening Ceremony traditionally highlights the EAU’s honorary members and awardees. Chapple conferred the title of Honorary Members to Gunnar Aas (SE), Patrick Colby (FR), Mani Manon (US) and Aij Tave (IN). Prof. Vicenzo Mirone (IT) received the EAU Willy Gregoir Medal 2018. Prof. Didier Jacqmin (FR) was awarded the EAU Frans Debruyne Lifetime Achievement Award, while Prof. Selucik Silay (TR) won the EAU Crystal Matala Award.

“For urologists our biggest concern is how to boost our medical and surgical techniques, and balance these without neglecting our core competencies,” said Mirone.

EU Ernest Desnos Prize for his contributions to urological history, while Hashim Ahmed (GB) was awarded the EAU Prostate Cancer Research Award.

New agents and imaging to improve PCa therapies
Experts’ forecasts at ESO Prostate Cancer Observatory

There is a range of new agents, molecular markers and improved imaging techniques that over the coming years will help doctors to further optimize their management of prostate cancer patients, particularly those with advanced or high-risk disease.

During the 5th European School of Oncology (ESO) Prostate Cancer Observatory held yesterday, a panel of prostate cancer (PCa) specialists presented their evolutions for promising medical approaches that aim to boost the current management of PCa.

The multidisciplinary presentations covered new developments and forecasts for research, surgery, active surveillance, imaging, pathology, and medical oncology. The perspective and concerns of patient groups were also discussed by Prof. Louis Denis (BE) as a representative for these groups.

“My expectations for 2018 and next year are further results from STAMPEDE and the potential changes in the standard of care for metastatic hormone-naïve prostate cancer (mHNPC) patients,” said medical oncologist Dr. Ananya Choudhury (GB) who gave the prostate cancer (PCa) presentation for neonatal MC in Europe, Canada and the United States.

Prof. Steven Joniau (BE), who co-chaired the session with Prof. Ricardo Valdagni (IT), said: “For me, the session showed that we need to better understand the disease with the aid of the many tools we have now such as PSMA, MRI and others, in combination with the standard tests such as PSA. Tools such as PSA still have their use despite the entrance of new methods. It is important to avoid over-treatment and instead focus on the detection and treatment of high-risk cancers.”

Joniau reiterated Touijer’s key message as he stressed the importance of AS to avoid over-treatment of low-risk PCa.

Dr. Ivo Schoot (NL) discussed prostate MRI and its diagnostic accuracy, noting that a limitation of MRI is disagreement among radiologists. “There are now proposed adjustments to the PI-RADS test,” said Schoot. “Looking back, to 2017, prostate MRI shows maturation with its strength and limitations.”

Prof. Roldolo Monfreti (IT) discussed developments in pathology such as the update of PCa grading, intraductal carcinoma of the prostate, the routine molecular markers used by pathologists with multiple clinical purposes, and the potential of liquid biopsies such as urine and blood.

African and European views on HIV and circumcision

By Erika de Groot

Ethics and human rights. Medical safety concerns. These are factors that differentiate African and European views on the role of circumcision in HIV prevention as discussed today in the Joint Session of the European Association of Urology (EAU) and the Pan-African Urological Surgeons Association (PAUSA) chaired by Dr. Allen Chiora (ZW) and Prof. Dr. Rien Nijman (NL).

In his lecture Successes and Challenges of Male Circumcision in the HIV era, Dr. Tonderayi Mangwiro (ZW) stated that male circumcision (MC) averts a greater incidence of ulcerative sexually-transmitted infections (STIs) and the susceptibility of the foreskin to abrasions during intercourse.

Additional benefits include lower incidence of urinary tract infection in infants, penile hygiene, and prevention of balanitis and phimosis. The risk of penile cancer is also lowered. Mangwiro said that MC is “not a silver bullet.” It has a 60% efficacy and should be used as part of a comprehensive HIV programme.

According to Mangwiro, the VMMC (voluntary medical male circumcision) programme has done well; it has achieved its scale up targets and is currently developing a new strategy that will introduce a sustainability component.

Dr. Nicolai Lothe (DK) listed varying recommendations for neonatal MC in Europe, Canada and the United States.
Robots not a priority in developing world
Joint EAU-SIU session tackles controversial issues in urology

By Joel Vega

Costly robot-assisted surgery is not viable in the developing world considering that there is no convincing data on the superiority of these expensive robot technologies, says a UK-based expert.

During the Joint EAU-SIU (Société Internationale d’Urologie) session, part of the Urology Beyond Europe programme, experts clashed on the perceived benefits of robotic procedures.

“Strive to become a better surgeon, particularly if you are in the developing world. Stop obsessing about technology… There are no differences in outcomes,” said Prof. Prakash Dasgupta (GB). “Only 5% of surgical procedures require robotics, so the cost of robot-assisted procedures rose by 13% in three years, resulting in an additional cost of $2.5 billion in additional healthcare costs. The robot is unnecessary laury in the developing world.”

Dasgupta rebuked the arguments of Dr. Sudhir Rawal (IN) noting that a centre needs to perform over 200 cases of robot-assisted surgery in order for it to be cost-effective. He also examined the issue of a shorter hospital stay, stating that hospital stay depends on the country where the patient lives.

“I have nothing to do with the surgery,” said Dasgupta, adding “a fool with a tool is still a fool.”

Conversely, Rawal anchored his arguments within the context of the Indian experience where he said there is a clear need for a more efficient alternative to open and laparoscopic approaches. He noted that there are opportunities to save money with robotic surgeries, and mentioned that robotic procedures in India are much less expensive when compared, for instance, with the United States. He also insisted that there are clear benefits in terms of blood loss, wound closure time, and a shorter learning curve for surgeons compared to laparoscopy.

The session also covered some other key controversies in uro-oncology. Prof. Axel Bex (IN) argued that lymphadenectomy in renal cancer is unnecessary, against the pro-statements of Dr. Frederic Pouliot (CA), whilst Profs. Shin Egawa (JP) and Fred Witjes (NL) debated the merits of metastasectomy in urothelial cancer and Profs. Peter Wilkink (SE) and Paolo Gontier (IT) discussed the necessity of intracorporeal diversion.

Bex said the likelihood of lymph node involvement is small and the overall rate of local recurrence does not seem to be altered by lymphadenectomy.

“Between 58 to 95% of patients with lymph node involvement eventually die of their disease, and the cost of treatment far exceeds the costs of treatment for patients who do not have lymph node involvement.”

Biomarkers: A new pillar in diagnosis of BCA?
Major shift in EAU Guidelines anticipated

By Leek Keizer

The interconnectedness of urology in Europe is exemplified by the collaboration evident in the Scandinavian countries and the Scandinavian Association of Urology in particular.

On the first day of EAU18, the 33rd Annual EAU Congress, held this year in Copenhagen, the EAU History Office welcomed prominent Danish and Scandinavian speakers to give the audience a flavour of the long history of regional cooperation, as well as some biographies of eminent Danish urological pioneers.

Establishing a Nordic Society
Prof. Christian Beisland (NO) spoke about the extensive history of urology in the Scandinavian countries as well as the establishment of an international urological association for the region.

Beisland said: “The Nordic Surgical Society (NKF) was first founded in 1859, making it one of the oldest surgical societies in the world. It was a relatively slow process of separating urology from general surgery, with the first national societies being established in the 1920s and 1930s.”

In 1950, the Scandinavian Association of Urology laid its foundations as an informal group, a ‘travelling club’ for urologists in Denmark, joined later by urologists from Norway, Sweden and Finland. In 1956, a proposal was made to formalise this arrangement in a proper Association, albeit with some initial scepticism by representatives from Norway and Sweden. Beisland: “In the end, the Association was famously founded in the sauna of Professor Tuuvinen’s summer house in Ojakalla, Finland.”

Prof. Beisland, speaking about the history of the Scandinavian Association of Urology initially, the Association had a fixed quota of members from each country, although over time this arrangement was replaced by automatic membership when a urologist joined their respective national society. Ireland joined the Association in 1996.

Since 1995, the official language of the Association has been “bad English” (as opposed to “bad Swedish” – the words of Prof. Jens Andersen (DK)). The decision to switch to English was made in order to be more inclusive to the Finnish delegates and also to attract greater international interest. Prof. Andersen recollected that board of the Scandinavian Association had a lot of discussion at the time, amid fears of a loss of national identity.

Holm and Holm: Drs. Jørgen Kristensen (DK) and Jørgen Nordling (DK) presented biographies of Profs. Hans Henrik Holm and Tage Holm (DK), noting their extensive history of urology in Denmark, and their role as influential and respected urologists. Holm was a pioneer in interventional ultrasound, combining urology and interventional radiology, treatment of cysts and percutaneous nephrostomy in the 1960s.

Tags Hold: The 1999 Willy Gregoire Award Winner, was a founding member of the International Continence Society, and was tasked with establishing uniform terminology in that field. “He was a much-admired tutor and he supervised a huge range of topics as Professor at Herlev Hospital,” Nordling concluded.

Biomarkers: A new pillar in diagnosis of BCA?
Major shift in EAU Guidelines anticipated

Prof. Arnulf Stenzl (DE), Scientific Congress Office Chairman looked back on a well-attended Specialty Session on bladder cancer on Friday, the first day of EAU18. The session consisted of a series of case-based debates on some of the biggest names in uro-oncology.

The wide variety of debates had a common theme: biomarkers are maturing as a third pillar in diagnosis. Stenzl: “We don’t want to rely just on the pathological, so we’ve used clinical assessment as well. And now the use of biomarkers is evolving into a feasible third pillar.”

“All these discussions took place in areas where the EAU Guidelines are not conclusive. Urologists need to find more data, and we are getting closer. You could almost say that it’s done. Several speakers and audience members are already using molecular markers, despite not being in the guidelines.”

Despite not being part of the EAU Guidelines recommendations yet, Prof. Stenzl anticipates a “major shift” in the coming years. “This is a pressing issue, there’s a lot of uncertainty at the moment. We know that these things will be changing, there’s not been a change for decades in bladder cancer Guidelines. Studies with thousands of patients are being published. There is an unmet need, and there is good data. I expect a change to the EAU Bladder Cancer Guidelines soon.”

“EAU Bladder Cancer Guidelines soon.”

Debate “winners”
Experts like Profs. David McCrory (USA), Juan Falou (ES), Maurice Broust (FR) and Jim Catto (GB) presented cases and led discussions on topics like cystoscopy, treatment options following neoadjuvant classification and what to do when BCG fails.

“It’s hard to say that there were winners in these ‘debates’. Prof. Stenzl conceded. “This topic is much too sophisticated and grey to have clear winners”. Nevertheless, this session was one of the most important and well-attended of the day. These kinds of case-based debate sessions could be something we will be seeing more of at the Annual Congress.”
Raising the next generation of key opinion leaders
Young Academic Urologists report on recent achievements

By Jen Tidman

The Young Academic Urologists (YAU) showcased the achievements of their talented and already-renowned members at a specialty session. Dr. Michiel Sedelaar (NL) introduced Chairman Prof. Selçuk Silay (TR) who has not only expertly guided the YAU over the past two years, but is also this year’s Crystal Matula award winner.

Silay ran through the accomplishments of the group over the six years since its inception. 84% of YAU members are presenting at EAU18, 44.7% have received a local or international scientific award, 32.7% are journal editors or associate editors, 19.4% have presentation or hands-on tutor responsibilities at ESU courses, 50.6% are involved in the EAU Sections, 23.6% are involved in Guidelines panels, four members have won Matula awards, and over 80 PubMed papers have been published (22 in 2017). The group has also contributed to EAU Section and Regional meetings, organised its own specific meetings, and at EAU18 will be running courses on presentation and leadership skills.

Through teamwork and the formula of “enthusiasm + trust + respect”, the YAU is raising the next generation of key opinion leaders, award winners and Association of Academic European Urologists members. “The future belongs to those who believe in the beauty of their dreams,” said Silay, quoting Eleanor Roosevelt. He encouraged EAU members under 40, affiliated to an academic institution, and with at least five publications to their names, to apply to join the group.

Prof. Chris Chapple (GB), giving the Secretary General’s perspective of the role of YAU within EAU, said the Executive and Board were very keen to include members in all activities, but they should be proactive in getting involved: “Things don’t just happen, they have to be made to happen. You are at the stage in your careers when you have to make things happen.”

He said members should join the Sections to build expertise, get involved with the Research Foundation, submit to the three EAU journals, work on ESU courses, and contribute to the Guidelines and Patient Information groups. He stressed the importance of networking, evidence-based rather than eminence-based medicine, and embracing the whole field in order to maintain control as a urologist rather than becoming a technician.

“At the end of the day, the future is in your hands,” said Chapple, “Look on the website for grants, activities, how to get involved, and help the EAU achieve its mission statement.”

Dr. Panagiotis Kaldis (GR) said it was difficult to report on all of the YAU non-urology working groups’ achievements over the past 12 months into a ten-minute presentation, but managed to show that the Functional, Men’s Health, Paediatrics, Trauma & Reconstructive, and Endourology-Lithiasis groups all made robust contributions to the peer-reviewed literature, academic meetings, educational courses, and ongoing research. “There is a lot of work being done in these groups. All of these people are going to develop themselves and provide something better for our specialty.”

Dr. Gaëlle Blouard (FR) said that the technology (uroTechnology and Robotics) and oncology (Bladder, Renal and Prostate) working groups had been similarly successful in the same areas, “Last year was very good for these groups. I am sure 2018 will be even better.”

The following YAU awards were presented by Prof. Hein Van Poppel (BE):

•  EAU Willy Gregoir Medal
•  EAU Honorary Membership
•  EAU Prostate Cancer Research Award
•  Best paper published in 2017 by the Prostate Cancer YAU group – Dr. Roderick Van den Bergh (NL)
•  Best poster presented at EAU 2018 by the Mens Health YAU group – Dr. Georgios Ivan Ruscio (IT)
•  Reviewer of the year from YAU – Prof. Andrea Necchi – collected by Prof. Evangelos Liatsikos (GR) on behalf of winner

“Things don’t just happen. You have to make things happen.”

Dr. Sedelaar and Prof. Silay chaired the meeting of the Young Academic Urologists.

Award Gallery

C. Chapple awards V. Mirone with the EAU Willy Gregoir Medal

S. Silay receives the EAU Crystal Matula Award from C. Chapple and M. Prassezza from LABORIE

C. Chapple congratulates G. Aus with his EAU Honorary Membership

D. Jaquim receives the EAU Frans Debruyne Life Time Achievement Award from C. Chapple and E. Dourver from KARL STORZ

H. Ahmed accepts the EAU Prostate Cancer Research Award from C. Chapple and F. Schröder from the FHS FOUNDATION

C. Chapple恭喜es F. Colby with his EAU Honorary Membership

C. Chapple congratulates M. Mencen with his EAU Honorary Membership

S. Musalli receives the EAU Ernest Deanna Prize from C. Chapple

D. Delfs accepts the EAU Hans Meckler Award from C. Chapple and E. Douwen from KARL STORZ

Prof. C. Chapple congratulates A. Vaze with his EAU Honorary Membership

If you want to find out more about our upcoming meetings and projects, please visit the EAU Wall in the Green Area.

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Congress news

Congress highlights

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Complications after open radical cystectomy

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Low-intensity ESWT

Shared decision-making in prostate cancer care
BAVARIAN NORDIC IS STRIVING TO BRING NOVEL TARGETED VACCINES TO MAXIMIZE IMMUNOTHERAPY IMPACT FOR CANCER PATIENTS

Our innovative oncology platform is designed to specifically target a variety of challenging tumor types. We have developed a portfolio of active cancer immunotherapies, designed to alter the disease course by eliciting a robust and broad anti-cancer immune response while maintaining a favorable risk-benefit profile.

Multiple clinical trials are ongoing in collaboration with the NCI, NIH, academia and industry partners. Through numerous industry collaborations, we seek to explore the potential synergies of combining our immunotherapies with other immune-modulators.
Endocrine disrupting chemicals (EDCs) influence our health, including male genital development and male reproduction. There is an increase in most western societies in male reproductive disorders: the most striking ones are the decline in sperm quality and the increase in testicular cancer.

These problems arise from a maldevelopment of the testes during early pregnancy, also known as testicular dysgenesis syndrome (TDS). Both in wildlife observations and in animal experiments TDS develops after exposure to EDCs, resulting in abnormal genital development, a short anogenital distance and infertility. Data from ongoing longitudinal studies in children confirm that our western lifestyle is a major contributing factor in the etiology of male genital development disorders.

Male genital development

The male genitalia develop between week 7 and week 14 of pregnancy. The activity of the sex region of the Y chromosome (SRY gene complex) results in differentiation of the fetal gonad into a fetal testis. Already early in pregnancy the fetal testis starts producing hormones, like testosterone, anti-Müllerian hormone (AMH) and Insl-3 (Figure 1). Testosterone plays a central role in the further differentiation of the male genitalia, either direct (development of the epididymis and vas deferens) or after conversion into dihydrotestosterone (DHT, development of the external genitalia and prostate). Male under-virilization can be caused by different defects in this system, including low fetal testosterone production, absence of 5α-reductase and malformation of the androgen receptor.

Maldevelopment of the fetal testes and low fetal testosterone production can result in birth defects, like cryptorchidism and hypospadias. In adult men, these defects will result in men who will have small testes, low testosterone production (congenital hypogonadism), defective spermatogenesis and an increased risk for testicular cancer (Figure 2).

Epidemiology and etiology of TDS

The incidence of cryptorchidism and hypospadias is rising in some western countries. Both conditions have mixed etiology, including genetic factors and intra-uterine exposure to pseudo-estrogens and anti-androgens. Recently, it was shown that the use of paracetamol during pregnancy doubles the risk of cryptorchidism. Other exposures possibly involved in male maldevelopments are air pollution (diesel, maternal and paternal smoking). Children born after IVF have an increased risk of hypospadias.

In animal studies different industrial chemicals have been shown to cause maldevelopment of the male genitalia. These chemicals have a similar structure to estrogens and are also named pseudo-estrogens or xeno-estrogens. They can easily pass the placenta and act as estrogen, disrupting testicular development. Other chemical compounds have an anti-androgenic action in the male fetus. EDCs are common in our daily environment and are used in many products, including plastics, flame retardants, cosmetics and pesticides.

The number of diseases potentially linked to early life EDCs exposure is substantial and include:

1. obesity and diabetes (congenital hypogonadism),
2. female reproduction (premature ovarian failure),
3. male reproduction (cryptorchidism, hypospadias, male infertility, male hypogonadism),
4. hormone-sensitive cancers in males and females (breast cancer, testicular cancer, ovary tumors, thyroid cancer),
5. neurodevelopment and neuroendocrine system disorders (ADHD, Autism),
6. immune system defects (asthma, food allergies).

Many of these diseases will only appear later in life, thus making it difficult to prove a causal relation with prenatal EDCs exposure. However, in the last years both animal and human studies have strongly indicated this relationship. Animal studies and observation in wildlife provide strong evidence that manmade chemicals can disrupt the hormone dependent pathways responsible genital development.

Consequences of TDS in adult life

A decline in sperm quality has recently been confirmed by a large meta-analysis of more than 5,000 publications: the authors found a 50–60% decline in sperm counts among men unselected by fertility from North America, Europe, Australia and Asia in the period without signs of “leveling off” in more recent years (Levine et al.). A recent study from China in more than 30,000 young men found a decline in sperm concentration of 10% in a 17-year study period. Studies in humans now also show a negative effect of EDCs on male fertility: in a recent study the effects of pesticides exposure in early life resulted in a decline of sperm quality of 30% later in life compared to men that were not exposed. In the same period, we have observed an significant increase in the incidence of testicular cancer (TC) in western countries. In the Netherlands, as in most other European countries, the incidence of testicular cancer has more than doubled in the last two decades. Although the number is good in terms of disease survival, many of these men will be hypogonadal after treatment. Infertility is high in these men: at time of diagnosis 10% of these men have low sperm quality and 12% are azoospermic.

At Erasmus MC we have shown that the origin of testicular cancer occurs during fetal life. TC arises from embryonic germ cells that have failed to mature appropriately. Those precursor cells of TC are known as carcinoma in situ (GCS). Only after puberty, when testostereone levels increase, TC will develop. Multiple genes that play a role in embryonic development of the testes are also involved in the developments of carcinoma in situ of the testes: OCT3/4, SRY, SOX3, SOX17, KIT-ligand. Novel insights indicate a subtle interplay of specific single nucleotide polymorphisms (SNPs), environmental factors, and epigenetic alterations in the etiology of germ cell cancers.

Late consequences of TDS

Male infertility and primary hypogonadism are related to health problems later in life. These men have an increased risk for obesity, type 2 diabetes mellitus, cardiovascular disease and depression. Men with azoospermia have a 2.2 fold increased risk of developing cancer later in life, including germ cell cancers, prostate cancer and lymphomas. Poor semen quality and low testosterone are biomarkers for future health problems. Life expectancy is shorter in these men.

Action needed against EDCs

The World Health Organization and the Endocrine Society have urged policymakers to take measures against EDCs. The estimated costs of inaction against the effects of EDCs of male health in Europe are estimated to be 592 million euros per year (Nordic Council report 2010). Well-designed studies are needed to show how EDCs exposures in early life are the basis of many diseases later in life.

The Health commission of the EU has invited research groups to initiate further investigations and €50 million euros are made available within the program Horizon 2020 for this type of studies. However, more action is needed: we need to reduce and eliminate those EDCs that have already been shown to be harmful to human health (Bisphenol A, DEHP, flame retardants, parabens, PCB’s). Hundreds of manmade substances in our daily environment have been indicated to act as EDCs. Furthermore, public awareness needs to be improved, such as explaining to pregnant women and young mothers how to limit and avoid exposures to EDCs. Campaigns have already been launched: www.endocrine-disrupting-chemicals.org. Special attention is focused on alternatives for pesticides and plastics.

References

2. Skakkebaek NE, Rajpert-De Meyts E, Main KM. Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects. Hum Reprod 2010; 25: 975-78

Saturday, 17 March 2018 08:35–10:00: Plenary Session 1. Hot topics, quality evidence and advances in andrology
Complications during or after radical cystectomy are frequent with delayed diagnosis and treatment resulting in severe chronic morbidity. Therefore, its management requires a high level of knowledge and experience as this surgical procedure may cause severe morbidity in fourth of the patients with mortality rates rapidly increasing with complications.

This article summarizes recent studies with high level of evidence in this field.

Intraoperative blood loss
Open radical cystectomy is still the mainstay of treatment for muscle-invasive bladder cancer. It has been consistently shown that open radical cystectomy, as a major surgical procedure, is associated with a higher estimated blood loss during surgery compared to robotic surgery2. Therefore, reducing blood loss has come to the focus of surgeons experienced in open techniques. In a double-blinded trial randomized trial, intraoperative blood loss was lower in patients with pelvic venous pressure decreased significantly after removing abdominal packing and abdominal lifting at all time points during cystectomy. Of note, no correlation was reported between pelvic venous pressure and complications.

Venous thromboembolism (VTE)
Venous thromboembolism (VTE) occurs in 2.5-10% of all patients undergoing radical cystectomy for bladder cancer1. The wide range in reported rates is possibly related to an under-reporting bias across different countries which, in turn, is likely due to under-registration of thromboembolic events after cystectomy in different health care systems. It is important to note the that the majority of thromboembolic events occur after discharge of the patient1.

Pulmonary complications
The occurrence of pulmonary complications is often associated with patient risk factors. Approximately 6% of patients develop postoperative pulmonary complications after cystectomy. Risk factors for postoperative pulmonary complications were reported to be higher age (75 years and older), very low (≤18.5) or very high (>30) body mass index (BMI), smoking, chronic obstructive pulmonary disease, insulin-treated diabetes and low albumin levels (<35 g/dL). Therefore, some efforts have been undertaken to reduce the risk of pulmonary complications postoperatively. One strategy that has been investigated was to compare the rate of complications using either a low or high positive end-expiratory pressure and accelerometer based maneuvers during surgery. Looking into the literature there is divergent data on whether this anesthesiologic strategy during surgery may have beneficial effects on pulmonary function postoperatively.

In the largest study, Hemmes et al. did not find a significant impact of this manoeuvre on outcomes after major abdominal surgery. On the contrary, a trend towards improved outcomes was noted when a strategy with low tidal volume and low positive end-expiratory pressure without recruitment manoeuvres was used. In a meta-analysis, low tidal volume was also reported to be most protective against the development of postoperative acute respiratory distress syndrome1. The most widely accepted practice for ventilation during radical cystectomy is nowadays to avoid high-end expiratory pressures and high tidal volumes during surgery whenever possible.

Surgical complications
The construction of urinary diversion is the main reason for postoperative complications after cystectomy. One strategy that has been described for reconstruction of the urinary route using, i.e. a rectoureterostomy, was shown to significantly reduce the rate of major complications (10% vs. 39%) and 30-90 mortality rates (5.9%/6.8% vs. 7.7%/13%) in patients aged 75 years and older. In this regard, protocols for enhanced recovery after surgery have nowadays been adopted in clinical practice and found to be associated with significantly improved perioperative gastrointestinal and lower rates of complications5.

In some studies additional benefits were reported with the adoption of ERAS protocols resulting in shorter time intervals on intensive care units, lower rates of wound healing disorders and VTE events. Moreover, a randomized study revealed that total parenteral nutrition for the first five days after surgery resulted in higher number of postoperative complications which was mainly due to a higher rate of infectious complications3.

Summary
Given the tumor aggressiveness of muscle-invasive bladder cancer open radical cystectomy is nowadays still the most effective treatment option for the treatment of muscle-invasive bladder cancer. The increasing use of neoadjuvant and adjuvant treatment modalities mandates further attempts to reduce the rate and severity of perioperative complications.

In recent years an increasing number of randomized trials have addressed critical issues of perioperative care. Further well-designed trials are warranted in this major urological field of surgery to improve our understanding in refinements of perioperative care for improved functional and oncological outcomes after cystectomy.

References

Gastrointestinal complications
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Editorial Note: Due to space constraints, the reference list can be made available to interested readers upon request. Please send an email to: communications@uroweb.org

Saturday 17 March 10.00-11.30: Joint meeting of the EAU Section of Oncological Urology (ESOU), the EAU Robotic Urology Section (ERUS), the EAU Section of Uro-Technology (ESUT) and with the ESSO, ESTRU, EUGU, EORTC GUCG and SUO.

Complications in treatment of urological cancers
Antibiotic resistance in Gram-negative uropathogens is increasing worldwide. A compilation of worldwide surveillance data in patients at urological departments with health-care associated urinary tract infections (HAUTI) Resistance towards most uropathogens against all tested antibiotics were high, particularly with regards multidrug resistance (Figure 1). In many countries the resistance rate of Gram-negative uropathogens alone is below 10%, a threshold used for empiric therapy of severe infections, such as sepsis. A worrying finding in the FIGU study was also that the severity of HAUTI is also increasing, 25% being urosepsis in recent years.

Need for novel antibiotics
Because of uncontrolled nosocomial old antibiotics, such as fosfomycin trometamol, nitrofurantoin, and nitroxoline are still recommended for complicated and especially HAUTI in recent years. Fosfomycin trometamol, nitrofurantoin, and cefuroxime axetil have been effective for the empirical treatment of UTI and may offer an alternative to carbapenems in this setting.

3. Meropenem / Vaborbactam
Vaborbactam is a novel cyclic boronic acid inhibitor of many class A β-lactamases. Vaborbactam has a potent inhibitor of serine carbapenemases, and KPC in particular. In-vitro data suggest that meropenem-vaborbactam (M-V) is highly active against KPC-producing Enterobacteriaceae, little effect on A. baumannii containing OXA-type carbapenemases was observed12.

In a phase-3 study TANGO-2 (TANGO-2: efficacy, safety, and tolerability of M-V (bismotec)) compared to doripenem (DOR) in the treatment of cUTI/APN in adults. M-V (meropenem 2 g plus vaborbactam 2 g) administered IV q8 h vs P (ceftazidime 2 g plus tazobactam 1 g), administered IV q8 h for five days. Microbiologic response was observed in M-V vs 182/193=94.3% and 98.2% with clinical cure. P in 137/139=99.3% of the patients. M-V was non-inferior to P. Microbiologic eradication was observed in 162/165=98.2% with M-V and 162/165=98.2% with P. Clinical outcomes were >90 across all MVCs.

Of 552 subjects randomized, 394 (71.9%) included in the m-ITT population: 232 in M-V group and 260 in P group. Microbiologic response was similar for subjects with susceptible and non-susceptible isolates. The most common adverse reactions in patients taking M-V were headache, infusion site reactions and diarrhea. Efficacy of M-V is associated with serious risks including adverse reactions and seizures12.

In a phase-2 study TANGO-2 (TANGO-2: efficacy, safety, and tolerability of M-V (bismotec)) compared to IV colistin plus IMP/CS (IMP/CS-MVC) in patients with Gram-negative pathogens were randomized 2:1 to receive colistin (IV q6h) vs IV colistin plus IMP/CS q48h. The treatment group showed improvements in microbiologic cure and clinical response at TOC in 72% of patients (n=252) which was superior to IMP/CS (54.4%)(p<0.0001), difference 17.6% (95%CI:10.7-24.5). M-V was non-inferior to IMP/CS. Serious adverse events (SAEs) occurred in 14 patients (4.7%) who received colistin and 12 patients (8.1%) who received IMP/CS15.

4. Imipenem / Relbeactam
Relbeactam is a non-beta-lactam serine β-lactamase, similar to aizabactam, that has inhibitory activity against class A β-lactamases. In-vitro carbapenem-resistant Enterobacteriaceae isolates demonstrated that MICs were significantly lowered with aizabactam in combination against KPC-K-producing K. pneumoniae. Compared to IMP alone, little reduction in imipenem-relbeactam MBC was observed in OXA-23 producing P. aeruginosa or OXA-23 producing A. baumannii, suggesting that relbeactam, unlike aizabactam, does not have significant activity against the class D enzymes14.

Phase 2 clinical trials investigating the safety, tolerability, and efficacy of IMP/CS-relbeactam in hospitalized patients with cUTI and complicated intra-abdominal infections have been completed.

A phase-3 trial (RESTORE-IMI-I) is underway investigating efficacy and safety of IMP/CS + relbeactam vs colistin + IMP/CS due to IMP-resistant pathogens18. Group: 1: IMP/CS - relbeactam IV (200mg/100mg to 300mg/150mg depending on renal function) q8h and placebo. Group: 2: CMS (colistimethate base activity (CMA) 300mg) IV loading dose, followed by CMA 75mg to 150mg IV q8h and relbeactam (200mg/100mg to 450mg/225mg IV infusion) in a total of 3 patients with IMP- and colistin-resistant pathogens received open-label IMP/CS - relbeactam (250mg/125mg IV q8h) for 7 days. Treatment duration: five to 23 days (https://clinicaltrials.gov/ct2/show/NCT02452047).

5. Cefeporel
Cefeporel (5-9Mg6-14) is a novel parenteral siderophore encapsulated conjugated with a caged moiety at the third-side chain. Cefeporel utilizes a novel mechanism of entry into the periplasmic space of Gram-negative bacteria and is stable to ESBLs and carbapenemases in vitro activity of cefeporel against Pseudomonas aeruginosa was enhanced under iron-depleted conditions, whereas that of cefeporel was not affected. Cefeporel was shown to have potent chelating activity for ferric iron, and extracellular iron was efficiently transported into P. aeruginosa cells in the presence of cefeporel as well as siderophores. Cefeporel forms a chelating complex with iron, which is actively transported into P. aeruginosa cells via iron transporters, resulting in potent antibacterial activity of cefeporel against P. aeruginosa16.

In total, 38 non-farmamentive Gram-negative bacteria (23 Acinetobacter baumannii and 82 Pseudomonas aeruginosa) and 282 Enterobacteriaceae were studied. Cefeporel exhibited greater antimicrobial activity against Gram-negative bacteria than several comparator antibiotics16.

In a phase-2 study efficacy and safety of IV cefeporel versus IV IMP/CS was tested in hospitalized adults with cUTI/APN. Patients with Gram-negative pathogens were randomized 2:1 to receive cefeporel(0.75 g, q6h) or oral HCTZ and IMP/CS. Serious adverse events (SAEs) occurred in 14 patients (4.7%) who received cefeporel and 12 patients (8.1%) who received IMP/CS16.

6. Plazomicin
Plazomicin (PLZ) is a novel aminoglycoside that was synthetically derived from sisomicin. Like other aminoglycosides, it is a bactericidal agent that works primarily through inhibition of protein synthesis. PLZ is structurally similar to the traditional aminoglycosides (amikacin, gentamicin, tobramycin), though modified to resist aminoglycoside-modifying enzymes that are often present in CRE. PLZ is not affected by carbapenemase production and has good in-vitro activity against carbapenem-resistant isolates of K. pneumoniae, E. coli, and Enterobacter species and produces a variety of carbapenemases and ESBLs. The presence of 16S RNA methyltransferase in Enterobacteriaceae, which modifies the ribosomal site that binds PLZ, leads to plazomicin resistance. PLZ is more potent than other aminoglycosides in treating Enterobacteriaceae19.

A phase-3 study evaluating eravacycline 1.5∕mg/kg versus 750∕mg IV for the treatment of cUTI/APN due to IV and oral (7) was for the treatment of CRE. PLZ was randomized 1:1 into one of three treatment groups. The study lasted 2±2 days with examinations on Day 5±1 on day 7±2 days (TDC).

The treatment success (combined clinical and microbiologic response) for the m-ITT population was 70.0% (95%CI: 61.6-78.2%) in the FINA05 group, 67.6% (95%CI: 59.8-75.8%) in the FINA05 group and 53.4% (95%CI: 41.5-65.2%) in the CP-PRO group. Finafloxacin dosed for five or did not showed higher treatment success rates than cefeporel dosed for five, due to a higher rate of AEs. Cefeporel versus ciprofloxacin was lower in patients with acidic urine-pH as compared to those with alkaline increasing the AEs, while finafloxacin's microbiologic eradication rate was equal high at either pH range on Day 3. The safety profiles of the three treatment groups were comparable, the majority of the AEs were mild to moderate in severity and regarded to be unrelated to study medication.

8. Eravacycline
Eravacycline is a novel synthetic fluorouquinolone that is active against almost Gram-negative species. In vitro eravacycline is two- to four-fold more potent than ticagycline against CRE.

A phase-3 study evaluating eravacycline 1.5∕mg/kg versus 750∕mg IV for the treatment of cUTI/APN (IGNITE) with an oral step-down treatment provided non-inferiority. These data remain unpublished to date and thus further studies are needed to establish the role of eravacycline in treating CRE.

Crucial role of antimicrobial stewardship
Several antibiotic substances are currently under development, or in the late clinical phase of development. Nevertheless, unique novel substances are rare, therefore antimicrobial stewardship plays an important role to preserve the antibiotic substances available.

Editorial Note: Due to space constraints the reference list has been omitted. Interested readers can email at EUT@uroweb.org for a complete listing.
Novel modalities for nodal staging in prostate cancer

Burden of nodal disease is linked with poorer outcomes

Dr. Henk van der Poel
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Co-Author: Dr. Nikos Grivas (GR)

In prostate cancer, nodal metastases are an initial step in the development of distant disease in the vast majority of men. Moreover, disease recurrence after local therapy is most frequently caused by the presence of nodal metastases. These observations support the notion that nodal metastases do develop early in the progression process of prostate cancer.

Nodal metastases and survival

Still the precise moment of nodal metastases development remains illusive. Yet, understanding how and when nodal disease develops is crucial in understanding cancer progression and determining timing of treatment as opposed to active surveillance. Prognosis of men with nodal metastases-only is far better than that for men with metastases to other sites and the majority of men are alive 10 years after diagnosis14. Moreover, recent analyses suggested a survival benefit of early nodal metastases treatment15.

The number of removed nodes as well as the number of nodes containing metastases is predictive of survival outcome16-20.

Imaging

In prostate cancer, nodal metastases conventional imaging has long been limited due to its inadequacy to detect pelvic nodal lesions smaller than 7-8mm. With the advent of novel imaging modalities, even smaller nodal metastases can be detected using either 68Ga-PSMA-PET or USPIO (nano-)MRI4. Sensitivity of metastases of 2mm can be detected using either techniques very efficiently introduced by the group of Tobias Maurer21.

Although interesting to guide towards nodes most likely to contain metastases, this method still will leave untreated the nodal metastases which are under the detection threshold. A nodal-template directed treatment rather than targeting visible nodal metastases could improve outcome. This would not only allow to apply men with macroscopic nodal metastases but might also improve outcome in men with microscopic or molecular metastases where a benefit may even be higher as implied by the observation that men with less nodal metastases have generally better outcome after surgical treatment.

Nodal template

A template of specific tracers depicting nodal drainage patterns such as those applied in the sentinel node biopsy method has the potential to tailor the surgical treatment. A nodal-template directed treatment rather than targeting visible nodal metastases could improve outcome. This would not only allow to apply men with macroscopic nodal metastases but might also improve outcome in men with microscopic or molecular metastases where a benefit may even be higher as implied by the observation that men with less nodal metastases have generally better outcome after surgical treatment.

These lymph node tracers currently consist of both radioisotopes such as 99mTc and fluorochromes such as indocyanine green (ICG). The former allowing for lymph drainage imaging preoperatively using scintigraphy, whereas ICG provides intraoperative near infra-red (NIR) imaging22 (Figure 2). In a systematic review the diagnostic accuracy of sentinel node techniques far exceeded that of any preoperative imaging technique for the detection of nodal metastases beyond extended lymph node dissection as reference standard23.

Moreover, molecular staining by RT-PCR showed nodal metastases in up to 1/3 of men with routinely assessed node negative disease and these men were at risk of disease recurrence24. On the other hand, 68Ga-PSMA-PET scanning had high accuracy in detecting non-local recurrences after radical prostatectomy25 even at PSA levels below 0.5 ng/ml. This strongly suggests that PSMA-PET scanning may help to select men for salvage local radiotherapy after prostatectomy25-27.

Surgery

From surgical studies on lymph node dissection we already know that the removal of more nodes during an extended (lymph) node dissection results in a higher yield of nodal metastases and potentially longer biochemical recurrence-free survival26. Even though an extended dissection of nodal tissue may result in better outcome when compared to no or limited dissection, the added value of adjuvant radiotherapy and androgen ablation further improved outcomes27,28.

These observations from retrospective series seem to support two notions: a. that imaging of all relevant nodal metastases is not feasible with current imaging modalities; b. that complete ablation of nodal metastases will require more than removing visible metastases only. Considering these observations it can be hypothesized that thorough imaging may direct treatment to specific nodal zones where metastases are most likely, better predictors of nodal metastases are needed to fully eradicate remnant disease. This seems to apply to the use of radio-guided-PSMA tracer directed surgery as recently elegantly introduced by the group of Tobias Maurer21.

We therefore studied the role of a lymph drainage tracer in detecting extended lymph node dissection and we observed both an improved nodal metastases yield as well as decreased biochemical recurrence rates in comparison to a historic control population29.

Prognostic prediction

Older studies showed a non-linear correlation between androgen receptor expression in nodal metastases and overall survival30. For immunohistochemical detection of lymph node metastases from prostate cancer Gamez et al.16 suggested to use PSA, PSMA and androgen receptor expression. In light of PSMA tracing it is interesting to note that the percent of PSMA-positive cells was similar for primary tumor and nodal metastases, but the levels of expression per cell were lower in nodal metastases31.

Bostrom et al.2 reported that although PTEN loss was an independent predictor of outcome in men with node positive disease, TMM56s/ERG fusion status was not. Cell proliferation had an additional prognostic value to the number of positive nodes. Interestingly, neuroendocrine differentiation as assessed by chromogranin A expression was found more frequently in nodal metastases (2.6% of cells) compared to the primary tumor (1%), in particular in Gleason pattern 5 tumors (>7% vs.1.4% of cells)32.

Clearly, management of nodal metastases in prostate cancer is still in its infancy. Routine radiation of nodal basins in localized prostate cancer was not associated with improved survival33 but selective radiation of nodal basin seems to be more effective than standard radiation. Moreover, the true role of nodal dissection is still debated34. A nomogram to predict outcome showed the presence of Gleason sum score >7 was the strongest risk factor predicting cancer-specific survival in men with nodal metastases. These men were 5x more likely to die of disease35. In the same series, with each positive node removed cancer-specific mortality increased by 10%.

Locally treating nodal metastases

In prostate cancer an increase in the burden of nodal disease is associated with poorer outcome. Local treatment of nodal metastases with surgery or radiotherapy may improve outcome, but clinical and in particular molecular predictors are only poorly understood. Template-guided surgery based on novel pre- and intraprostatic imaging may improve nodal dissection.

References
Following a recent suggestion by the American Society of Clinical Oncology (ASCO), precision medicine in oncology aims to improve efficacy, to minimize side effects and to overcome acquired resistance of anti-cancer therapies by delivering "the right cancer treatment to the right patient at the right dose and the right time".

To achieve these aims, appropriate prognostic and predictive biomarkers are required. Prognostic biomarkers may stratify patients according to their individual risk in order to decide whether systemic therapy is justified balancing potential toxicities against possible benefits ("who to treat"). Predictive biomarkers may predict treatment responses to be expected by individual treatment approaches ("how to treat").

Clinical use of appropriate biomarkers not only requires their identification by modern "pan-omics" methods (whole-genome sequencing, transcriptome analysis, proteomic and metabolomics approaches) but also their bioinformatic and functional integration in the pathophysiologic framework of the according neoplastic disease.

Precision oncology approaches have already been adopted or are getting more and more adopted regarding the treatment of a variety of malignancies (e.g. chronic myelogenous leukaemia, breast cancer, advanced non-small cell lung cancer). Recent high-throughput analyses may provide the scientific basis for a potential future functional implementation of precision oncology in the treatment of bladder cancer as well1-3.

In the palliative setting, initial responses are observed only in up to 70% of patients and long term-survival resistance of anti-cancer therapies by delivering precision oncology in the treatment of bladder cancer as well4-6. Currently, unselected platinum-based combination therapies are the mainstay both in the curative perioperative systemic treatment of muscle-invasive non-metastatic bladder cancer as well as in palliative treatment of non-resectable or metastatic bladder cancer. However, neoadjuvant (NAC) or adjuvant (AC) perioperative chemotherapy, using cisplatin-based regimes, improves oncological outcome only marginally (4-10% improvement in five-year overall survival)7.

In the palliative setting, initial responses are observed only in up to 70% of patients and long term-survival is below 20%. These observations in perioperative and palliative systemic treatment imply that in many UC patients a subpopulation of cancer cells evades cytostasis or cell death by inherent or acquired resistance to systemic treatments. This is apparently also true for recently introduced immune-oncological therapeutic approaches. Accordingly, validation of these data in a prospective clinical setting is still missing as is integration of these data in the pathophysiologic mainframe of bladder cancer in order to allow tailoring individual diagnostic and therapeutic approaches are essential.

Intra-tumor heterogeneity While advances in precision oncology in the perioperative systemic treatment of bladder cancer clinical may be expected in the medium term, implementation in the metastatic, especially in the post-platinum, setting may be limited not only by inter- but also by intra-tumor heterogeneity. In this context, a recent comparative analysis of primary and metastatic tumor tissue before and after platinum-based chemotherapy demonstrated the evolution of distinct molecular features during growth and metastasis as well as before and after systemic therapy.

In summary, important initial steps towards precision oncology in bladder cancer therapy have been taken. Nevertheless, validation of these data as well as integration of these data in the pathophysiologic mainframe of bladder cancer in order to allow tailoring individual diagnostic and therapeutic approaches are essential.

References

Figure 1: Diagnostic and therapeutic algorithm as proposed by the TCGA consortium as a framework for prospective hypothesis testing in clinical trials.
Today’s European Urology Events

ESU Writing Course Part 1
March 17th
8.30 – 10.30
Orange Area, Room 1 (Level 0)

ESU Writing Course Part 2
March 17th
12.00 – 14.00
Orange Area, Room 1 (Level 0)

Platinum hour
March 17th - 18th
16.00 – 18.00
European Urology booth #C3-C29

How to write the introduction and methods

Aims and objectives:
Understand how to construct a well written introduction and methods section for your manuscript. Learn how to work through examples of good and bad practices, and understand key points when writing. Obtain insight from editors on what they expect to see.

• To understand what makes a good introduction
• To understand what makes a good methods section
• To understand about systematic reviews and meta-analysis
• To learn from experienced editors

1. Welcome
Jim Catto, Sheffield (GB)
2. How to write an introduction
Giacomo Novara, Padova (IT)
3. Group working I
4. How to write the methods section
Christian Gratzke, Munich (DE)
5. Key features for a systematic review
Marcus Cumberbatch, Sheffield (GB)
6. What to look for in the statistics section
Christian Gratzke, Munich (DE)
7. Group working II
8. Questions and answers

How to write results and discussion

Aims and objectives:
Learn the best way to draft the results and discussion section of a scientific paper. Understand how to work through examples of good and bad practices, to find the key points of the manuscript. Obtain insight from editors on what they expect to see.

• To understand what makes a good results section and how to best present your data
• To understand what makes a good discussion
• To learn from experienced editors

1. Welcome
Jim Catto, Sheffield (GB)
2. How to write the results chapter
Stephen Boorjian, Rochester (US)
3. Choosing and presenting your statistical analyses
Melissa Assel, New York (US)
4. Group working I
5. Writing the discussion section
Jean-Nicolas Cornu, Rouen (FR)
6. What the editor looks at when reviewing the results and discussion
Stephen Boorjian, Rochester (US)
7. Group working II
8. Questions and answers

We would like to invite you to attend the Platinum Hour drinks reception to meet and greet the editors, authors and reviewers of the European Urology family of three: European Urology, European Urology Focus and European Urology Oncology. Please join us to toast to the family’s new sister journal European Urology Oncology.

This new journal complements the family by delivering high quality research while pursuing the goal of a multi-disciplinary approach. Urology, Medical Oncology, Radiation Therapy, Imaging, Pathology and Basic Research working together with the same final aim: to improve patient care. If you’ve got practice changing, groundbreaking research in urological oncology, you can directly submit your original article via this link: ees.elsevier.com/euonco.

We look forward to answer any questions about the new journal, or another member of the European Urology family, during the drinks reception at our booth!
Infectious complications and fURS

fURS procedure may lead to severe infectious complications if crucial measures are not properly taken

Surgical management of renal stones has substantially changed in the last two decades where endourological procedures, such as percutaneous nephrolithotomy (PCNL) and flexible ureterorenoscopy (fURS) became the standard treatment options for the minimal invasive removal of renal stones.

Related with this issue, increasing experience gained in the ureteroscopy management of upper urinary tract stones as well as the marked improvements in the instrument technology have increased the popularity of fURS as a safe and acceptable treatment alternative for small-to-moderate sized renal stones up to 20 mm.

Published data on this aspect so far has clearly demonstrated that fURS in experienced hands may reveal potentially higher stone-free rates (SFR) than extracorporeal shock wave lithotripsy (ESWL) and lower morbidity than PCNL in the treatment of such stones. Moreover, flexible ureterorenoscopic laser disintegration and successful removal of these stones with high SFR did reduce the morbidity and hospital stay to a certain extent in the majority of the cases.

However, despite its minimal invasive and efficient nature, fURS procedure is not completely complication-free and some certain problems could be encountered either during and/or early post-operative follow-up period. Such problems could be partly explained with the rapid expansion of URS indications to larger and more complicated stones and to elderly patients with significant comorbidities originating from such a high success rate and low complication rates obtained.

Relevant studies indicated well that inappropriate widening of the indications might result in a higher incidence of severe complications, including febrile urinary tract infection (UTI), need for blood transfusion, renal dysfunction or septic shock.

Related with this issue, by using the Clinical Research Office of the Endourological Society (CREDS) database in their original study, De la Rette et al., analyzed 1388 patients treated with URS (consisted of data from 31 centers in 32 countries) and reported the stone-free rates as well as post-operative complications rates to be 89.4 % and 3.5 % respectively².

The most frequent complication noted was fever (1.2 %) in that study. Of the complications noted so far after fURS, while infection affecting up to 1.8 % of patients undergoing flexible ureterorenoscopy and laser lithotripsy has been reported. More recently, Fan showed in a retrospective study that the incidence of infectious complications following fURS may range between 1.2 and 18.9 %³.

Several subsequent studies have also reported that unopacified stones may be a major problem for management despite the use of appropriate antibiotics prior to the endourological procedures⁴. As previously mentioned, infectious complications following fURS remain a decisive issue and it has been reported that this procedure may still have unforeseen postoperative systemic and sometimes life-threatening infection despite a well-performed appropriate pre-operative antibiotic therapy along with the use of ureteral access sheath (UAS) which effectively reduces the likelihood of pyelocalyceal or pyelovenous backflow. Access sheaths also allow for continuous irrigation of the renal pelvis and improved stone clearance, as well as lower renal pelvic pressure that may be protective against pyelocalyceal and pyelovenous backflow⁵.

Regarding the risk of infectious complications after a successful fURS, while it is highly crucial to postpone the treatment of stones in the presence of an urinary tract infection, a well-confirmed negative pre-operative urine culture prior to procedure however has not been found to guarantee the absence of post-operative infection.

fURS procedure could be associated with higher risk of post-operative infection in cases with infected stones, longer operative times, and the presence of residual fragments as well as fever⁶. On the other hand, again higher intrapelvic pressure levels during fURS procedure could be associated with post-operative sepsis and Zhao et al. demonstrated that the patients who had sustained an intrapelvic pressure > 100 mmHg were more likely to develop post-operative fever⁷.

However, although the URS reduces the renal pelvic pressure and may help to reduce the operative absorption of leakage fluid, the authors did not find any increased risk of infective complications when it was used (p > 0.47). In the several reports they have not found any association between intrapelvic pressures and the incidence of post-operative fever after PCNL⁸.

Regarding the other possible risk factors for infectious problems after fURS, in their original study Marto et al.¹⁰ have reported that the patients with such infectious complications had significant comorbidities (coronary heart disease, CVD, alteration of lipid metabolism, anticoagulant therapy) at univariate analysis. An increased risk of infectious complications following fURS was found to be associated with some concomitant conditions such as Crohn’s, cardiovascular disease, high ASA score and high stone burden.

Thus, the increased risk of infectious complications among cases with greater comorbidities emphasizes the importance of judicious patient selection for this type of procedure. Additionally, Fan et al. found that pyuria, operative duration, and infections stones were independently related to infectious complications⁹.

On the other hand, and equally important, intraoperative stone culture has been found to be more relevant than a pre-operative urine culture in guiding the antibiotic therapy and we do not develop sepsis and also identifying patients at risk for post-operative sepsis. These results have clearly outlined the importance of obtaining an intra-operative stone culture in a routinely performed manner.

Studies have shown that 8 % of the patients with positive stone cultures developed sepsis and this value was significantly greater than the percentage with negative stone cultures who developed sepsis (1 %). As a result, from the data of the stone culture were found to be critical in determining the treatment in these patients and more importantly, the stone culture seemed to have a higher association with post-operative sepsis than did the pre-operative culture (301).⁶

Additionally, published data do indicate that the proper and careful use of an appropriately sized ureteral access sheath during the procedure may allow a successful and, more importantly, infection-free procedure.⁶

In summary, culture antibiotic-based appropriate antibiotic administration, lower irrigation pressure during the procedure along with an unobstructed peri-operative urinary drainage, obtaining intra-operative urine or stone culture are the established important factors in effectively preventing postoperative infectious complications, including sepsis.

References


Surgeons should be aware of potential serious infectious complications arising from fURS procedures and the corresponding management strategies.

Prof. Kemal Sarica
Chairman
Department of Urology
Ege/University
Kars (TR)

Saturday, 17 March 2018
EUF Congress News
Ernest Desnos: Honouring urology historians

Historical Exhibition features artefacts from Desnos’ career and much more

By Leah Keizer

Last night saw the presentation of the first EAU Ernest Desnos Prize for contributions to the field of the history of urology. The EAU History Office unanimously voted to honour Prof. Sergio Musitelli (IT), long-term expert of the Office and co-author of several unique volumes dedicated to the earliest history of urological procedures.

Musitelli, who turned 90 this year, was Visiting Professor of the History of Urology, Sexology and Andrology at the University of Pavia for many years, following a long career in philosophy, ancient arts, oriental literature and languages and the history of ancient science and medicine.

Since the start of the EAU History Office, Musitelli functions as a professional history expert and participates in all activities. Based on his position as an expert in history, he was one of the most active contributors to the work of the EAU History Office, not only with numerous articles and books but also in reviewing submitted articles for the annual De Historia Urologiae Europaeaueae volumes. Furthermore, he was responsible for selecting and reliable index of all published volumes of these series.

In the words of EAU History Office Chairman Prof. Philip Van Kerrebroeck (BE): “Sergio’s own accomplishments are co-founding the AFU and later the SIU, as well as treating Emperor Napoleon III for a bladder stone in 1873 and major pioneering work on prostate brachytherapy.

However his most significant contribution was in the field of the History of Urology. Therefore his ‘magnum opus’ is the first book on the History of Urology ever. This book was published in 1914 as “Histoire de l’Urologie” (History of Urology, Paris. Doin éditeur, 1914). The large volume presents, in 294 pages with 196 beautiful black and white illustrations and nine coloured reproductions, a complete overview on the origins to the beginning of the 20th century.

Historical Exhibition

This year’s Historical Exhibition, which is open at the EAU Booth in the Exhibition Hall this morning features several items from Desnos’ impressive oeuvre. His most notable historical works, some personal artefacts, and the original Desnos medal from the early 20th century on which the EAU Ernest Desnos Prize is based.

In honour of our host country this year, the exhibition also features several highlights from the history of urology in Denmark and the Scandinavian countries. It is completed with items related to the First World War, the end of which was one century ago this year. The First World War disrupted the development of urology, and particularly the international cooperation within the field just as it was reaching maturity. Several prominent British urologists were veterans of the Great War, and the exhibition explores their time of service and subsequent accomplishments in urology.

New publications

A good opportunity to visit the Historical Exhibition would be when you collect your copies of the latest EAU publications. EAU members can collect their copy of the 25th Anniversary Edition of De Historia Urologiae Europaeaueae, the congress gift for This Relief. Much Thanks! by Dr. Johan Mattelaer, as well as other membership benefits, depending on your entitlements.

Mattelaer’s latest publication explores the depiction of urination in art, both classical and contemporary. It is a beautifully illustrated colour table book that celebrates our field and offers unique insights.

De Historia Urologiae Europaeaueae

The original Desnos medal from the early 20th century on which the EAU Ernest Desnos Prize model is based

The 25th Anniversary Edition of De Historia features contributions from past editors, special attention for the inaugural Ernest Desnos Prize winner, as well as the usual wide-ranging articles that cover the history of urology.

The Historical Exhibition is located across the EAU Booth (H69). Publications can be collected at the EAU Booth. The EAU Booth is open on the following days:

Saturday 17 March, 09:30-18:15
Sunday 18 March, 09:30-18:35
Monday 19 March, 09:30-15:30

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"I've found the ChM Urol to be both challenging yet achievable, providing me with the tools to achieve lifelong learning at a very high level, all aided by a world-class faculty and super support team."

Class of 2015 graduate

"I think without the ChM Urol program, I could have struggled with my fellowship training, maybe failed completely. The ChM Urol has been key to this fellowship success. It is one of the reasons why I am a qualified urologist today!"

Class of 2017 graduate
Adherence to national and international guidelines is sub-optimal throughout Europe. In fact, significant gaps currently exist in terms of the application and use in clinical practice of the EAU Guidelines, even though they are based on standardised high-quality methodology and are endorsed by all 28 European Member States.

For example, we are aware that in some countries, approximately one out of four men with prostate cancer received androgen deprivation therapy despite the fact it is not recommended by the EAU Guidelines. This in turn increases the risk of short- and long-term side effects in these patients, and the costs related to disease management.

In addition, studies have reported that despite clear EAU guideline recommendations advocating the use of intravesical chemotherapy post-surgical resection in non-muscle invasive bladder cancer, adherence to these guidelines is low and varies widely, with estimates ranging from 22% to 71% in a sample of five European Union countries. There are also similar concerns regarding non-adherence to non-oncological guidelines in urology. A study conducted to assess adherence to non-oncological guidelines in five European Union countries.

Another limitation in relation to guidelines development is that guideline panels are often limited to those with clinical and methodological expertise. The voice of the other stakeholder groups in the design and delivery of healthcare (e.g. patients, carers, charitable organisations and industry) is often missing from these discussions. Given the emphasis on patient-focused outcomes and the need for guidelines to be responsive to stakeholder needs, strong arguments exist for the inclusion of all of the key stakeholder groups in the guidelines development process. Achieving true stakeholder engagement in the Guidelines development, delivery and implementation process will:

- Guarantee that all stakeholders have confidence in the guidelines development process and as such the resulting recommendations;
- Ensure that the recommendations are appropriate, achievable and can be translated into corresponding health behaviour leading to better treatment compliance and better health outcomes; and
- Result in recommendations and guidelines which facilitate person-centred care.

Guideline developers need to ensure that guidelines have a clear structure and local applicability in order for guidelines to be useful in different settings and healthcare systems. Although guidelines have the potential to improve care by promoting effective interventions and discouraging ineffective ones, publication of guidance alone is unlikely to optimise practice. Development of guidelines must be supported by an effective dissemination and implementation strategy. The EAU have successfully developed an effective mass dissemination platform through Twitter. The EAU Twitter platform has also been used to estimate adherence to EAU guidelines recommendations. The EAU Guidelines Office ‘IMAGINE’ project (IMpact Assessment of Guidelines Implementation and Education) has been developed to effectively tackle the issues of non-adherence and implementation with the ultimate goal of ensuring all patients across Europe receive the best evidence-based standardised care.

Why should we improve clinical practice guidelines adherence?

If evidence-based best practice recommendations are not disseminated effectively and knowledge is not actively transferred, variations in practice are likely to occur. Where variations in practice occur, healthcare is unequal within nation states and across European member states, whilst health systems are most likely inefficient. Furthermore, if all stakeholders, including patients, are not meaningfully included in consultations to prioritise research areas, to determine which outcomes are the most important, and to ensure recommendations are phrased appropriately, then they are denied informed shared-decision making.

There is an urgent need to harmonise clinical practice throughout Europe and guidelines are the ideal framework for doing so. The key to this is to ensure the availability of high-quality European-wide guidelines, which are robustly established, fit for purpose and comprehensive. The EAU guidelines are an excellent demonstrator model for achieving harmonisation across all EU member states. It is fundamentally important that such guidelines have a high degree of visibility, uptake and adherence by clinicians and healthcare providers.

Whilst the EAU guidelines are now endorsed by all EU member states, European Union/European Commission endorsement would undoubtedly increase the recognition of the importance of guidelines in general, as well as their visibility, dissemination and implementation. If this integrated model for the development, dissemination and implementation of European-wide guidelines for urology could be achieved, the potential for other clinical areas to apply this cohesive model would be promising with the prospective overwhelmingly positive impact on harmonisation and a far more effective healthcare provision in Europe.
Update in vaginoplasty technique

Prospective randomized studies need to identify ‘ideal’ vaginoplasty

Regarding nontransgender vaginoplasty; the Frank method, which was described in 1938, involves the use of repositioned vaginal epithelium to form a neovagina. The vaginoplasty is achieved by creating a vaginal “roof” of peritoneum (Davies et al.). The Davydov technique, which may also be used for vaginal reconstruction, is a classical surgical technique that involves the use of a urogenital sinus flap to create the vaginal opening (Horbach et al.). The Frank method is considered to be the gold standard for the creation of a neovagina in non-transgender patients (Colebunders et al., Perovic et al.).

The main goals of vaginoplasty are to achieve an aesthetically and functionally ideal perineal complex that will satisfy the patient (Bizic et al., Karim et al.). The neovagina should be moist, elastic and hairless, with a capacity of at least 12 cm and a diameter of 3-4 cm. The clitoris should be small, reduced and sensitive to enable complete arousal. Labia minora and majora should resemble the female vulva as much as possible. Innervation of the new genitalia complex should be functionally intact in order to offer the patient a feeling of erogenous stimulation during sexual intercourse (Bizic et al., Karim et al., Selvaggi et al.).

Transwomen who prefer an aesthetic outcome, in contrast to vaginoplasty for the insertion of a non-functional vagina, can undergo labiaplasty and clitoroplasty. Some authors used 7 cm as the cut-off for vaginal length and width for the patients who were reconstructed by STG alone.

1. Skin grafts

Local nongential skin flaps, full-thickness skin grafts (FTG) or split-thickness skin grafts (STG) have been used for neovagina formation. Hage and Karim harvested FTG from the lower abdomen and a used a mold to insert it in the neovaginal cavity. They reported no significant cosmetic and functional complications after a follow-up duration of seven months. All of their patients (n=6) were reported to be “subjectively” pleased with the cosmetic and functional outcome. Mean neovaginal depth and width was 12 cm, and 3 cm, respectively (Horbach et al., Hage et al.).

Siemsen and Matzen used FTG of penile skin, STG or a combination of both in a group of 11 patients. They reported no significant cosmetic and functional complications after a follow-up duration of seven months. All of their patients (n=11) were reported to be “subjectively” pleased with the cosmetic and functional outcome. Mean neovaginal depth and width was 12 cm and 3 cm, respectively (Horbach et al., Hage et al.).

2. Penile skin inversion technique

Penile skin inversion technique remains the method of choice for vaginal reconstruction in MTG (male to female) patients. Currently, penile skin inversion technique is the most frequently performed and hence the most extensively studied surgical procedure within the context of MTG gender reassignment. Hernio; the inverted penile skin on an abdominal or more inferior pedicle is used as an outside-in technique for the creation of the neovagina (Bizic et al., Horkab et al.).

Preserved-vascularization of the penile skin, its mobility, non-hair-bearing surface, sensate nature, thin connective tissue and relatively minimal tendency to contract represent the main advantages of using penile skin-based flaps (Bizic et al.). In cases where the penile skin is deficient (circumcision, microepis, etc.), several technical refinements can be applied as such as combining the penile skin flap with scrotal (Bizic et al., Selvaggi et al.) and/or urethral flaps (Bizic et al., Perovic et al.). Utilizing a penile flap together with a scrotal graft in addition to penile skin may also serve well to lengthen the neovaginal cavity (Kocjanic et al.).

Van Noort et al. combined penile skin with a scrotal full-thickness skin graft and/or a posteriorly based scrotal skin flap. The major drawback of this modification was the introduction of hair-bearing scrotal skin within the posterior lining of the vagina if hair removal has not been done peroperatively. To avoid this, permanent epilation can be accomplished before the vaginoplasty via laser therapy or electrolysis in patients with a limited amount of penile skin. Alternatively, the graft can be meticulously cleared off adipose tissue and hair follicles immediately after harvest at the back beneath the scrotum. Perovic and Djordjevic has described another technique in which a spatulated urethral flap was fixed onto the penile skin flap to increase neovaginal length and width. This addition also served as a surgical technique of a hidden suture line (Bizic et al., Selvaggi et al.). Although flaps contract much less often than grafts, patients are still required to use a dilator postoperatively for at least one year to prevent neovaginal and introital strictures.

Buncamper et al. used additional fullthickness skin graft in the penile inversion vaginoplasties of women who have a penile skin length of less than 1 cm in an effort to obtain a neovaginal depth and create an esthetically superior vagina. In their case-control study (n=100, 32 with and 68 without additional FTG), none of the tested parameters differed significantly between the two groups. Recently, Papadopoulo et al. assessed the surgical outcome of their combined vaginoplasty technique in which a constructed urethra together with a scrotal skin graft was used in addition to the penile skin flap to form the neovagina. The main aim of this procedure was to achieve the largest possible vaginal depth and width, increasing the lubrication level of the neovagina and providing a more esthetic mons pubis by decreasing the pronounced abdomen that might be more pronounced within solely penile skin was used for reconstruction. They also created a “clitoral hood” with an esthetic prepuce by dividing the foreskin into an inner and outer layer in an effort to prevent clitoral desensitization. Measured postoperative neovaginal depth ranged from 11.37 to 14.9 cm, depending on the size of the dilator used (25-40 mm). All of the patients further reported intact and favorable vaginal, clitoral and labial sensations.

Denovilliers fascia should be opened to create a space for the neovagina. Speculum should be carried out up to the level of the pouch of Douglous and the ischial spines laterally. This type of extended dissection of the rectoprostatic space allows for omission of the neovaginal and introital stenosis.

3. Pedicled small or large bowel segments (intestinal vaginoplasty)

Intestinal vaginoplasty has become a valid option that can be used for constructing a neovagina. Especially in regions where hair-bearing scrotal skin is available for grafting, intestinal grafts provide a good alternative. Some authors used 7 cm as the cut-off for penile skin length below which bowel-based options should be offered (Buncamper et al.). A lack of penile and scrotal skin is often present in transwomen who started hormonal therapy (puberty blockers) at a younger age. Buncamper et al. can also be used when prerin neovaginal reconstructive attempts with skin flaps and/or grafts failed in transgender patients. The need to elongate the vagina in transwomen requiring greater depth after a previous neovaginal construction is another indication to proceed with intestinal vaginoplasty.

Use of pedicled bowel segments offers some advantages regarding cosmesis and sexual function. First of all, it provides sufficient amount of tissue for optimal vaginal depth and width. Moreover, this tissue is self-lubricating given the secretory potential of the intestinal mucosa. Additionally, intestinal inner lining resembles the vaginal mucosa in texture and appearance. Lastly, the lumen of the isolated intestinal segment has little tendency to shrink which eliminates the need for lifelong postoperative vaginal dilatation which is almost always necessary in intestinal grafts/flap based neovaginal constructions (Bouman et al., DeMarco et al.). Intestinal vaginoplasty has also some inherent disadvantages such as; the need for intestinal anastomosis, the risk of postoperative
For current medical LUTS treatment, one can choose between several medications. When considering medical LUTS treatment, one should take into account the risk of progression of the underlying BPH, the invalidating nature of the symptom complex, the predominant symptom(s), the risk of side effects and the cost of the treatment4.

Prior to considering treatment, it is evident that symptoms should be bothersome for the patient. Patients with light to moderate symptoms should be reassured and given lifestyle advice1.

The risk of progression is easily defined as increasing LUTS (for the majority of patients). In a subset of patients, acute urinary retention (AUR) and need/ demand for surgical treatment defines progression. Patients who are at risk for progression, might benefit from hormonal treatment with 5-alpha-reductase suppressive therapy. Prostatectomy will proven risk reduction for surgery and AUR. Certainly when morbidities put the patient at risk for surgical treatment, this treatment should be offered. Easily detectable factors for progression are age, prostate volume, PSA level and presence of PVR1.

Voiding symptoms
The nature of the symptom complex will determine the medical treatment. The majority of patients will have voiding symptoms as part of male LUTS. Voiding symptoms in the presence of a small prostate will direct the clinician to the use of alpha-blocking agents or phosphodiesterase-5 inhibitors. The presence of storage symptoms will direct the clinician to treatment with antimuscarinic agents or beta-3-adrenoceptor agonists depending on the size of the prostate, also hormonal therapy with y-5-alpha-reductase inhibitors can be considered. In the case of bothersome nocturia, desmopressin could be an option.

There are several reasons to combine different agents of the above-mentioned treatment options in one patient. A first reason is to tackle the different aspects of the symptom complex.

Most male LUTS is caused by benign prostatic Hyperplasia (BPH) which, in turn, is linked to benign prostatic enlargement (Photo: Getty images)

For the right patient.

The majority of male LUTS is still caused by benign prostatic hyperplasia (BPH). The use of BPH is associated with benign prostatic enlargement (BPE). When patients seek help for invalidating LUTS due to BPH, the clinician should elucidate certain elements in order to select the right treatment for the right patient.

Firstly, the clinician should confirm that the patient is suffering from uncomplicated BPH-related LUTS. The functional lower urinary tract disorder should not be associated with complications, such as the lower urinary tract (such as high PVR, bladder stones, bladder diverticula, recurrent bleeding and recurrent infections) or complications of the upper urinary tract (such as hydro-ureteronephrosis, renal function deterioration or ascending urinary tract infections). These cases mandate (surgical) treatment.

In the case of uncomplicated BPH-related LUTS, patients generally prefer medical treatment over surgical treatment. In the last decades, the incidence of surgical treatment for BPH-related LUTS has significantly declined. The incidence of medical treatment however has increased significantly1.

Update in vaginoplasty... Continued from page 14

bowel-related complications (ileus, anastomosis leak, peritonitis), as well as, the mucosal origin, intussusception, intussusception, bleeding after intercourse, malodor and also ancedential the potential for developing dissection colitis, ulcerative colitis and cancer.

The basic steps of intussusception vaginoplasty can be summarized as: harvest of the segment (through median or Pfannenstiel laparotomy, laparoscopic-assisted laparotomy and total laparoscopic incision). The incidence of storage symptoms is low. The sigmoid colon and ileum are the most commonly preferred intestinal segments for vaginoplasty. Sigmoid colon possesses the advantages of having a long, larger diameter, better tolerance to trauma and more similarities to the vaginal lining in terms of appearance, texture and natural lubrication (Elshehemy et al.). Despite being stated as an advantage of intestinal segments, mucous production may lead to excessive discharge and be the cause of malodor, especially when ileum is used.

Laparoscopic harvest of the bowel for vaginoplasty was introduced in order to minimize the inevitable morbidity associated with open transperitoneal surgery. The length of harvested segments varies considerably, ranging from 3.5 to 14.5 cm. Vaginoplasty with different folding techniques (U-pouch, J-pouch, detubularization and retubularization technique) can be utilized to create a new vaginal pouch. Depending on the vascular anatomy of the patient, the intestinal graft can be transferred to the perineum in an isoperistaltic or antiperistaltic fashion to minimize the tension on the vascular pedicle (Bouman et al.). Usually a two-finger- wide space between rectum and urethra is created by blunt dissection. Fixing the neovagina to the sacral promontory, the uterosacral ligament and adjacent muscle fascia of the pelvic floor are the commonly applied maneuvers to prevent prolapse (Bouman et al., Moulaert et al.)

In a recent review, which included 22 retrospective studies and 894 patients, the prevalence and severity of perioperative complications were reported to be low after intestinal vaginoplasty4,4.3% for sigmoid-derived and ileum-derived vaginoplasties, respectively). Intestinal stenosis, necessitating revision surgery, was the main postoperative complication and this was seen in 3.3% and 1.2% of the sigmoid-derived and ileum-derived vaginoplasties, respectively (Bouman et al.). The rate of sexual satisfaction, which was usually assessed in a subjective fashion and without the use of Female Sexual Function Index (FSFI), was reported to be 85% (Davies et al., Hensele et al.).

Integrative multidisciplinary approach
Gender dysphoria and patients complaining about this disorder have started to be recognized by the community which translated into increased number of patients engaging into this transition and seeking treatment. Different organizations have established standards related with the diagnosis and management (medical and surgical) of gender dysphoria as example an integrated multidisciplinary approach. Vaginoplasty represents the last step of the MTF transition process. Penile skin inversion technique is the most investigated and therefore the most evidence-based technique for vaginoplasty. Surgical outcome and sexual outcomes associated with this technique are generally acceptable to good. Using additional urethral and penoscrotal flaps may provide benefit in terms neovaginal depth and lubrication. Intestinal vaginoplasty is a viable alternative, especially for secondary procedures. Overall, the outcomes of penile skin incision treated with pedicled bowel segments does not seem to be inferior to the penile skin inversion technique. There is a need for prospective randomized studies with standardized surgical procedures, larger patient cohorts and longer follow-up period in order to make a valid comparison between the available vaginoplasty techniques and identify the “ideal” one.

Editorial Note: Due to space constraints, the reference list can be made available to interested readers upon request by sending an email to: communications@uroweb.org

Saturday 17 March 23.15-25.35: Meeting of the EUU Section of Genito-Urinary Reconstructive Surgeons (EUGRUS); Updates in genito-urinary reconstruction

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Residual fragments - an ongoing headache after fURS

Patient follow-up and counselling are crucial in renal stone cases

The widespread use of SWL led to the introduction of the term “clinically insignificant residual fragments” (CIRF) in urologic vocabulary. These stone fragments are defined as post-fragmentation disintegrates measuring ≤0.4mm or less in diameter. From the practical perspective, it is assumed that these fragments pass spontaneously through the urinary tract without causing the patient any clinically relevant conditions. Residual fragments (RF) may also remain in the collecting system after any kind of surgical intervention also, especially after shock wave lithotripsy (SWL), percutaneous nephrolithotomy (PCNL), and reoperation intramural surgery (RIRS).

In recent years a shift has occurred worldwide towards RIRS as represented by flexible ureteroscopy (fURS) in combination with laser lithotripsy. fURS enables relatively “straightforward” and rapid access to the upper urinary tract, allowing the endourologist to inspect all its areas and target stones easily.

This trend is affecting both the absolute number of fURS procedures for urolithiasis-related interventions and stone size. Large renal stones (RIRS) also tend to be treated by RIRS. Because of the retrograde route’s anatomical limitations, namely a relatively thin ureter diameter and access sheaths (UAS) smaller than those used in open surgically, extraction can become very time-consuming. To overcome this obstacle, several disintegration concepts have been developed. One recommends the creation of very small pieces of stone dust, or sand that pass spontaneously after treatment.

Admittedly, little is known about the natural history and clinical relevance of RF on patients’ course or their impact on subsequent stone-related events (SRE). Little has been published on long-term outcomes, and the evidence level in what has been reported is low. Most publications discuss case series, and even the RF definition, size, detection, and follow-up strategies are quite heterogeneous. In the literature, the postoperative observation of patients with RF ranges from five months to one year. More interestingly, are re-treatment rates between 19.6 and 58.6% during follow-up.

Status quo

Is the presence of RF after stone interventions a reason to worry? Several investigations were conducted to answer this question. Our group assessed stone-related events (SRE) requiring retreatment in a series of 100 consecutive patients treated by fURS for renal stones and evaluated potential risk factors thereof. We defined RF as fragments measuring ≤0.4mm (i.e., fragments too small for retrieval). Our primary outcome was the incidence of SRE requiring medical or surgical interventions and SWL to treat upper urinary tract urolithiasis. Patients presenting RF at risk for (ipsilateral) SREs requiring medical and/or surgical interventions.

The lessons we learned from this evidence are that:• the current surgical management of urinary stones should always aim for total stone clearance, and• that patients with miniscule RFs should not be declared stone-free.

What has the future in store for us?

Several technical improvements have been validated in vitro and in small case series. SWL technology is providing new camera systems for continuous monitoring of SWL head coupling during the procedure, which might significantly decrease the number and energy levels of shockwaves to achieve comparable results and high stone-free rates. Publications addressing new lens designs have also reported greater focusing precision and efficacy.

Interestingly, a novel technology described as “burst wave lithotripsy” might also enhance SWL’s efficacy.

Some interesting future developments should be discussed concerning the RFs technologies now leading among the modalities applied in modern stone therapy.

First, innovations in disintegration technology are most welcome and important if RFs are to be avoided. Present-day Ho:YAG lasers are the gold standard in endoscopic lithotripsy in both RIRS and PCNL. The latest technological innovations are aiming for safer and faster disintegration achieving similarly-sized fragments. Holmium laser devices now offer higher energy and frequencies, but also longer pulses, causing less retroperitoneal and producing smaller fragments (dust, stone sand).

Second, we need better retrieval instruments such as graspers and baskets. The size of novel endoscopic instruments requires new concepts and designs of extraction devices. New grasper designs cannot be simply adapted from open stone surgery or semi-rigid ureteroscopy for ureteral fragments. Ultimately, completely new approaches RFs need to be developed. These include irrigation and suction devices, gluing agents, magnetic extractors, etc.

Lately but not least, the slow fusion of flexible ureteroscopy with master-slave robotic platforms is currently a hot topic, similar to urologic laparoscopy. ureteroscopy with master-slave robotic platforms is currently a hot topic, similar to urologic laparoscopy.

Our study’s most important finding was that 33.3% of the low-risk stone-patient with RFs after RIRS experienced an ipsilateral SRE, while low-risk individuals with no RFs suffered no SRE on the ipsilateral side (p = 0.005). After the initial euphoria that accompanied the introduction of highly miniaturized endoscopic instruments and advanced lithotripsy systems allowing safe, rapid, and precise treatment of urinary stones, the underestimated problem of RFs might indeed give the endourologist a headache.

There is now evidence that endoscopically-determined RFs are an independent predicting factor for SRE in low-risk stone formers, and that they threaten the postoperative course especially over longer follow-up periods. Thus every effort must be made to achieve complete stone clearance after endoscopic interventions and SWL to treat upper urinary tract urolithiasis. Patients presenting RF at risk for (ipsilateral) SREs requiring medical and/or surgical interventions.

Figure 2: High-risk (A) and low-risk (B) stone formers with (green line) without RF (blue line) (according to Hein et al. 2018).

Our study describes a significant ergonomic improvements. Conventional master-slave systems for laparoscopic surgery in urology such as DaVinci® might also prove useful for stone retrieval, particularly for large and very large renal and ureteric calculi.

Residual fragments are clinically important. There is now high evidence and knowledge regarding RF after RIRS that confirm that RFs are clinically important. They affect significantly the patient’s post-interventional clinical course. Low-risk stone formers benefit especially from complete stone clearance. Differences between patients with or without RF become apparent over the long term, probably due to a delayed Nidus effect in recurrent stone formation. The term “clinically insignificant rest fragments” (CIRF) should therefore be abandoned.

The awareness that RF may not always be avoidable means that continuous patient follow-up and counselling are extremely important in case of RF after treatment.

References


Saturday 27 March 10:35-10:40: Meeting of the EAU Section of Urolithiasis (EULIS): Management of stones: Advancing technology, increasing experience and changing concepts. Where are we in 2018?

Saturday, 17 March 2018
18:00–18:05
Pr Morgan Rouprêt
Optimising patient management in urogenital cancers

The management of patients with urogenital cancers continues to advance, driven by the success of new clinical trials and the progress of sustainable interventional and emerging techniques. For the treatment of prostate cancer, hormones manipulation remains a key therapeutic strategy. Recent data has provided new insights on the impact of androgen deprivation therapy on treatment outcomes, compared with subcutaneous androgen-suppressing hormone therapies. The role of novel agents and changes to treatment guidelines have optimised management of patients with advanced prostate cancer.

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Vascular Targeted Photodynamic Therapy

Marketing Authorization (EMA) granted by European Commission November 10th 2017

TOOKAD® (padeliponin)

Non Thermal Light3

Chairman: M. Wirth, Dresden (DE)

M. Wirth, Dresden (DE) Welcome 17:44 - 17:50

F. Montorsi, Milan (IT) Clinical Results (Ph. III) 17:50 - 18:10

A. Scherz, Rehovot (IS) Focal Therapy & Non Thermal light 18:30 - 18:50

A.R. Azzouzi, Angers (FR) Procedure & Practical training 18:50 - 19:10

I.S. Gill, Los Angeles (US) Active surveillance & TOOKAD® 19:10 - 19:15

M. Wirth, Dresden (DE) Conclusion 19:10 - 19:15

Sunday March 18 17:45 – 19:15
Blue Area, Room 5 (Level 0)

Symposium: Date & Time: Location:

M. Wirth, Dresden (DE)

TOOKAD® (padeliponin) 184 mg or 364 mg powder for solution for Injection

Abbreviated prescribing information - please consult the full summary of product characteristics before prescribing.

Chairman: M. Wirth, Dresden (DE)

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Therapeutic indications: TOOKAD is indicated as monotherapy for adult patients with previously untreated, undifferentiated, high-risk, adenocarcinoma of the prostate in excess of 30 years age - Clinical stage T1c to T2a, - Gleason Score 4-7, based on high-resolution biopsy strategies - PSA ≥ 10 ng/mL, - 3 positive cores with a maximum cancer core length of 5 mm in any one or 2 positive cores with 50% of cancer involvement in any one core or a PSA density of 0.15 ng/mL or ≤.

Posology and method of administration: TOOKAD is restricted to hospital use only. It should only be used in a hospital setting by personnel trained in the use of TOOKAD. Photodynamic therapy (PDT) procedure: The recommended posology of TOOKAD is one single dose of 3.46 mg/kg of padeliponin. TOOKAD is administered as part of focal PDT. The PDT procedure is performed under general anaesthetic after rectal preparation. Prophylactic antibiotics and alpha-blockers may be prescribed at the physician’s discretion. Retreatment of the same lobes or sequential treatment of the contralateral lobes of the prostate are not recommended.

Sporadic parameters: In patients with severe hepatic impairment (CTP class C) TOOKAD should be used with caution, in patients with renal impairment or in elderly patients no dose adjustment is needed. The medicinal product contains potassium. Illustration for phototoxicity of TOOKAD. The solution is administered by intravenous injection over 10 minutes. Then the prostate is illuminated immediately for 22 minutes 15 seconds by laser light at 785 nm delivered via interstitial optical fibres from a laser device at a power of 150 mW/cm² of fibre, delivering an energy of 200 J/cm². Treatment should not be undertaken in patients with a Light Density Index (LDI) ≤ 0.1 cannot be achieved. See the SPC for further instructions.

Central indications: Hypersensitivity to the active substance or to any of the excipients. Any previous prostatic interventions when the internal urinary sphincter may have been damaged, including transurethral resection, prostatectomy, or placement using the treatment guidance so that the internal urinary sphincter is in the peri-prostatic area. Simultaneous treatment of both prostate lobes was associated with an inferior outcome in clinical trials. Special warnings and precautions: There is limited biopsy data beyond 2 years after TOOKAD-VTP. There is limited data on long-term outcomes and on potential safety issues associated with post-TOOKAD local scarring in case of disease progression. At present TOOKAD-VTP has been shown to be safe in clinical trials and subject to local notice, long-term follow-up will be required to determine whether TOOKAD-VTP will be curative in a proportion of patients. Following TOOKAD-VTP, patients should continue with regular PSA measurements (to detect early disease relapse), and should have regular digital rectal examinations (DREs) and transrectal ultrasound (TRUS) scans (to assess disease regression). PSA should be tested every 3 months for the first 6 months after the procedure and then every 6 months after that, to detect evidence of residual tumour and/or new disease. Where available, prostate biopsy should be repeated at least once a year after the procedure to assess the cancer status and ensure toxicity does not occur.

Adverse events can be reported to steba@primevigilance.com

1 - EU/CP/TOOKAD European Medicine Agency: November 2017

2 - Community register of medicinal products for human use http://ec.europa.eu/health/documents/community-register_htm/h11268.htm#ID=2644


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Patients should avoid exposure to direct sunlight (including through windows) and all bright light sources, both indoors and outdoors. For specific instructions on light protection measures, see the SPC sect. 4.4. Photodynamic therapy (PDT) may increase the risk of radical prostatectomy is avoided. Some degree of erectile dysfunction is possible soon after the procedure and may last for more than 6 months. Extracorporeal shockwave may be considered if erectile dysfunction occurs even if radical prostatectomy is associated with the bladder and/or rectum, and development of a recto-urethral or external fistula. A urinary fistula has occurred in one case due to incorrect fibre placement. The equipment should be carefully calculated and use the treatment guidance software to reduce the risk of clinically significant extracorporeal shockwave. Intravascular/intraprostatic ultrasound guidance. Patients with a history of unilateral or with urinary flow problems may be at increased risk of poor flow and urinary retention post the TOOKAD-VTP procedure. Urinary incontinence. The risk of post-procedural urinary incontinence is increased in the case of non-corporeal fibre placement using the treatment guidance software. The TOOKAD-VTP procedure is contraindicated in patients with any previous prostatic interventions where the internal urinary sphincter may have been damaged. Inflammatory bowel disease. TOOKAD-VTP should only be administered after careful clinical evaluation, to patients with a history of acute non-radiation bowel disease or any condition that may increase the risk of recto-urethral fistula formation. Use in patients with abdominal clamping. Patients with abdominal clamping may develop excessive bleeding due to the insertion of the needles required to position the light fibres.

Interactions: The use of medicinal products that are substrates of CYP3A4 or CYP2C8 (naproxen, atorvastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin, losartan, glyburide) for which concentration-dependent serious adverse events have been observed should be avoided on the day of TOOKAD infusion for at least 7 days after administration. Medicinal products which have potential phototoxic effects (such as metronidazole, sulfadiazine, quinolones, phenothiazines, sulfonyle hypoglycaemic agents, thiazide diuretics, griseofulvin or antihistamines) should be stopped at least 10 days before the procedure with TOOKAD and for at least 3 days after the procedure. In consequence there is a potential risk of phototoxicity of the laser or placement of the laser or placement of the laser. Nonsensitive laser devices should be avoided. In consequence there is a potential risk of phototoxicity of the laser or placement of the laser or placement of the laser.

Pregnancy and lactation: Contraindication. If the patient is sexually active with women who are capable of getting pregnant, he/she or his partner should use an effective form of both control to prevent getting pregnant during a period of 10 days after the VTP procedure. Pregnancy and Breastfeeding: TOOKAD is not indicated for the treatment of women.

Effects on the ability to drive and use machines: TOOKAD has no influence on the ability to drive or use machines.
**The medical treatment of lower urinary tract symptoms (LUTS) secondary to benign prostatic enlargement (BPE) is mainly focused on medical or surgical treatment in frail elderly patients.**

During the last two decades, the introduction of several pharmaceutical agents has dramatically decreased the related morbidity and mortality, making the LUTS management in the elderly more effective and less invasive than before. However, despite the numerous observational studies (OSs) and randomized controlled trials (RCTs) performed in the last 2 decades, the identification of a single therapeutic approach or procedure suitable for the frail elderly patients is challenging. The frail elderly population is known to be a heterogeneous group within which several health conditions are present. Therefore, the frailty assessment is critical to better stratify patients according to their frailty status, not focused on elderly patients.

**Table 1: Morbidity and Mortality of BPE surgery in elderly patients**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Country and Study</th>
<th>Year of publication</th>
<th>N of enrolled patients</th>
<th>Mean Age (years)</th>
<th>Surgical intervention</th>
<th>Morbidity (%)</th>
<th>Mortality (%)</th>
<th>Comments and Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reich et al.</td>
<td>Germany, 2000-2003</td>
<td>2005</td>
<td>1054</td>
<td>75</td>
<td>TURP</td>
<td>11.10</td>
<td>0.10</td>
<td>Strength: Good sample size, prospective design. Limitations: No qualitative assessment of ageing status, not focused on elderly patients.</td>
</tr>
<tr>
<td>Matani et al.</td>
<td>Germany, 1996</td>
<td>86</td>
<td>80</td>
<td>TURP</td>
<td>6</td>
<td>0</td>
<td>No qualitative assessment of ageing status, not focused on elderly patients.</td>
<td></td>
</tr>
<tr>
<td>Wyk et al.</td>
<td>UK, 1989</td>
<td>96</td>
<td>80</td>
<td>TURP</td>
<td>7</td>
<td>0</td>
<td>Limitations: No qualitative assessment of ageing status, retrospective design.</td>
<td></td>
</tr>
<tr>
<td>Briefy et al.</td>
<td>UK, 1995-1997</td>
<td>90</td>
<td>80</td>
<td>TURP</td>
<td>6</td>
<td>0</td>
<td>Limitations: No qualitative assessment of ageing status, retrospective design.</td>
<td></td>
</tr>
<tr>
<td>Meli et al.</td>
<td>UK, 1978</td>
<td>67</td>
<td>80</td>
<td>TURP</td>
<td>77</td>
<td>0</td>
<td>Limitations: No qualitative assessment of ageing status, retroactive design.</td>
<td></td>
</tr>
<tr>
<td>Marmenini et al.</td>
<td>Brazil, 2008-2010</td>
<td>100</td>
<td>75</td>
<td>75</td>
<td>TURP, Open prostatectomy</td>
<td>20</td>
<td>1</td>
<td>Strength: Prospective design. Limitations: small sample size, different procedures (TURP, PVP, HoLEP) evaluated together in the study.</td>
</tr>
</tbody>
</table>

In conclusion, we should seek alternative therapeutic strategies to TURP in particular in the most vulnerable portion of the elderly population. In recent years, several randomized clinical trials (RCTs) compared different laser techniques versus TURP and open prostatectomy showing lower morbidity of laser procedures and at least equivalent functional outcomes. The advantages of laser prostate surgery included in particular a superior haematological and functional recovery in anticoagulated patients, reduced blood losses and consequently a diminished blood transfusion rate. However, the vast majority of patients enrolled in these RCTs generally at least 65 to 75 years old. A very limited number of studies directly addressed the efficacy and safety profile of laser procedures in over 75 years old patients.

Echali et al. performed a retrospective analysis of their patients who underwent laser prostate surgery between 1998 and 2012. They identified 264 octogenarians, 68.5% of the enrolled population. For this category the mean age at time of procedure was 86±3.5 years. Holmium laser enucleation of the prostate was performed in 71 (66%), holmium laser ablation of the prostate in 16 (15%), holmium laser transurethral incision of the prostate in 13 (15%) and photoselective vaporization of the prostate in 12 (11%). Procedures for octogenarians almost doubled in a decade, passing from 11% at the end of 2002 to 19% at 2012. Likewise, the most recent studies about the safety of TURP in elderly, about 20% of perioperative complications has been recorded even for laser surgery.

During these studies, the surgical therapy seemed to be safe and effective for elderly patients; however, no conclusive recommendations can be drawn in particular in the frailest segment of the elderly population.

From these preliminary evidences laser surgery seem to be an effective and safe option for elderly patients owning morbidity, in particular the high-grade complications. However, no qualitative assessment of ageing status in the above mentioned studies has been performed; therefore no definitive recommendations can be drawn in particular in the frailest segment of the elderly population.

In this subgroup of patients, Prostatic Urethral Lift (PUL) may be more attractive options. In fact as mentioned before elderly patients in general population, these therapeutic alternatives may be performed in almost all cases under local anesthesia as a day case with a very low rate of complications and mortality. The most common adverse events experienced in the studies were dysuria, haematuria, and pelvic pain. These adverse events were mostly self-limiting, typically resolving within two weeks without further sequelae. Nevertheless to our knowledge no studies have specifically assessed the safety of these surgical procedures in frail elderly patients.

**Morbidity and perioperative outcomes**

In this report, we collected the existing evidences about morbidity and perioperative outcomes of different techniques for treatment of BPE among frail elderly patients. In 2008 Reich et al. prospectively evaluated mortality, morbidity and perioperative outcomes in 2,070 octogenarians more than 10,000 patients. The mean age of the enrolled population was 71.1 years old, the mortality rate was 0.1% and the overall morbidity rate was 11.2%. The most common complications during the first month were urinary catheter withdrawal failure (5.9%), re-intervention (3.4%), symptomatic urinary tract infections (2.6%), bleeding requiring transfusions (2.9%), and TURP syndrome (0.4%). Reich et al. did not focus their attention towards frail elderly men in their study; however morbidity was significantly increased by age, polymedication, and preoperative indwelling catheter. Lower complication rates in synthetic, the collected evidences suggest that TURP is burdened by a twofold complication rate in aging patients when compared with general population undergoing the same procedure. However this unfavourable clinical scenario is evolving over time. As suggested by the downward trend in morbidity and mortality in most recent studies, we may speculate that advancement in surgical techniques and devices has probably lowered the risks of complications associated with TURP in frail elderly population. Moreover we should keep in mind that there is a wide heterogeneity within the geriatric patients, with a considerable variability of life expectancy and health status within the same age group.

Therefore, the quantitative assessment of age should not be the only predictive factor to define a therapeutic strategy in the elderly. As yet proposed by the European Urology Association (EUA) in agreement with the Society of Geriatric Oncology (SGO) for the management of prostate cancer, a standardized geriatric assessment that takes into account the multidimensional aging of age would make possible to better identify the heterogeneity of the population and to adopt a therapeutic strategy adapted to the level of vulnerability.

Consequently, we should seek alternative therapeutic strategies to TURP in particular in the most vulnerable portion of the elderly population. In recent years, several randomized clinical trials (RCTs) compared different laser techniques versus TURP and open prostatectomy showing lower morbidity of laser procedures and at least equivalent functional outcomes. The advantages of laser prostate surgery included in particular a superior haematological and functional recovery in anticoagulated patients, reduced blood losses and consequently a diminished blood transfusion rate. However, the vast majority of patients enrolled in these RCTs generally at least 65 to 75 years old. A very limited number of studies directly addressed the efficacy and safety profile of laser procedures in over 75 years old patients.

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However, the vast majority (82.3%) was low-grade complications (Clavien grade I-II), high-grade complications (Clavien grade III) were only17% of the total and no perioperative deaths occurred in the study. A longer operating time was an independent risk factor for perioperative morbidity in octogenarians, while functional outcomes were good and comparable with younger patients.

Similarly, Piao et al. evaluated prospectively the effect of age on the efficacy and safety of HoLEP. In this study, patients 80 years had significantly higher rate of hypertension, higher values of ASA scores, total prostate volumes, higher rates of urinary retention, and use of anticoagulants at baseline. Moreover, the mean operative time and enucleation weight were higher in octogenarians when compared with younger patients. In addition, elderly men had a longer hospital stay time (9±1.6 days) than general population (6±0.7 days; p < 0.001). Nevertheless the morbidity rate assessed by Clavien-Dindo classification (about 15%) and the functional outcomes were comparable regardless of age.

From these recent evidences laser surgery seem to be an effective and safe option for elderly patients owning morbidity, in particular the high-grade complications. However, no qualitative assessment of ageing status in the above mentioned studies has been performed; therefore no definitive recommendations can be drawn in particular in the frailest segment of the elderly population.

**References**

**My journey in prosthetic urology**

**Teaching is the most difficult task in surgery but is also the mark of an expert**

My journey

Mine is the fourth generation of doctors, I was born with Medicine in my blood. When I was a medical student, in 1980, I spent three months in US with a friend of my father who was a urologist. I never thought that I would be a surgeon but it turned out to be my passion too. In those days, I witnessed for the first time in my life a penile implant. The patient was a diabetic with a very large penis and I was astonished with the procedure.

So, I said to myself, I want to do this surgery. When I finished medical school, I started training as a resident doctor in one of the best hospitals in Madrid (Gregorio Marañon) where I spent five years completing a fantastic urology residency. When I was a fourth-year resident I spent a few months in Boston with Bob Krane’s group learning about Sexual Medicine and penile surgery. Irwin Goldstein and Ilnigo Sanz de Toisda were the big names there and I kept up my connection with them for many years. They were the pioneers of Sexual Medicine and I was lucky to be close to them at that time and for many years afterwards, Ilnigo moved to Madrid and although he was not a surgeon he became my mentor and my close friend until his premature death.

When I finished my residency in urology, I took a position as urologist in Gregorio Marañon Hospital and was very fortunate to have a Head of Department, Carlos Hernandez, who wanted to give doctors responsibility very soon. He put me in charge of andrology at a young age. However, I liked surgery more than research, so I got involved in penile implant surgery and Peyronie’s disease surgery and started to publish, to participate in and to organize courses and seminars. As we were based in a University Hospital with residents visiting us, we soon created a “school” with a style of implant that is still used today. We learnt from all the big names in Prosthetic Urology in the world such as Steve Wilson, John Mulcahy, David Ralph or Mariano Rassello just to name a few. But as much as with the masters, I also learned a lot from the people who were once residents and then became masters themselves—Juan I. Martinez-Salamanca, Enrique Lledo, Javier Romero or Agustin Fraile just to mention a few.

Penile prosthetic implantation

Not only the penile prosthetic implantation surgery has an important role in the management of organic end-stage erectile dysfunction. The European Association on erectile dysfunction recommend the implantation of a penile prosthesis. The evidence of high efficacy, safety and satisfaction rates of both patients and partners is robust. Nevertheless, outcomes are not always perfect, complications arise and malfunctions are somewhat frequent.

Mastering the surgical techniques for the implantation of sipirin cases but particularly when complications arise is a must for the modern urologist. Our experience, with around 1,000 penile prostheses implanted in the last 25 years, has allowed us to explore different aspects of prosthetic surgery and to make innovations that improve the surgical outcomes. I would like to share with you my journey in Prosthetic Urology which can be better done from the standpoint of some landmark papers, breakthrough papers, that led to a change in penile prosthetic surgery. I will comment some other publications. These are examples of these papers:

- Buckling of cylinders may cause ... This paper was the first to demonstrate the role of MRI in penile prosthesis to assess the correct position and position of the use of MRI as a diagnostic method for penile prostheses complications is the standard practice. This was my first “impressive” paper, published in *Journal of Urology* and some of the pictures in the paper were used by others to illustrate their presentations. (Figure 1)

**Methodology and clinical application**

**Nipple technique**

1. **Buckling of cylinders may cause prolonged penile pain**

   - **Use of a penile extender**...
   - **Twenty years ago infections were much more common**
   - **Infection was the standard of care for those cases**
   - **The consequence was a fibrotic shortened penis, very difficult to re-implant.**
   - **I worked for the first time the efficacy of a penile stretcher in facilitating re-implantation surgery.**
   - **Now the use of a penile extender is common practice for all patients with any kind of penile fibrosis before surgery.**

   This paper prompted the medical use of a penile extender, now is a recommendation in the EUA Guidelines for the conservative treatment of Peyronie’s disease.

2. **Dual implant in patients...**

   - **The popularity of radical prostaticctomy as a treatment for prostate cancer led to an increasing number of patients with severe ED and stress urinary incontinence.**
   - **The usual treatment is first to correct the incontinence and then proceed with the penile implant in those patients still willing to undergo further surgery.**
   - **The alternative would be to perform this double implant at the same time through the incision.**
   - **We described in this paper our technique of doing this procedure performed by S. Wilson.**
   - **The double implant is also recommended as an option in the EUA Guidelines in such patients.**

   Inflatable Penile Prosthesis Implantation Without Corporal Dilation... Typically, the implant involves the dilatation of the cavernosal bodies to make enough space to insert the cylinders. We demonstrated that this is not necessary in the virgin case, so you can avoid it with all the benefits of being less invasive: it saves surgical time decreasing complications, preserves complimentary erection and avoids retraction of the penis helping to maintain the penile length after implantation. Many implanters in the world are using this technique now.

3. **A new one for you and everyone in the OR (and that’s not good).**

   - **Abdominoplasty and z-plasty...**
   - **This paper on penile prosthesis in these patients with hidden penis opened a discussion about the importance of the cosmetic aspect in penile surgery including Peyronie’s disease, as well as the role of lengthening procedures in patients with a short penis.**

   These papers were innovative in the field and reflected both the insight and the experience of surgeons interested in the search for better outcomes for our patients. It is also true that innovation is wholly linked to constancy and permanence in any medical field. Receiving recognitions like the Nikolay Alekseev Bogoroz Medal awarded by the Russian Association of Andrology in 2010, or the Brantley-Scott Award of Excellence presented during AUA 2015, reflects the appreciation of my peers. In the end you need to analyze your results, particularly when you are far along the journey. When you connect all you learn, you are doing something good for your patients. (Figure 1)

4. **Time probably correlates with being decently good at it but committing in advance for the long haul changes it completely.**

   Commonly we have colleagues who are interested in everything: oncology, lithiasis, incontinence, andrology but they do not focus on anything specific and try different areas. It is very hard to become an expert in anything if you don’t focus on one specific area with the intention of developing that chosen area.

5. **Study and practice are the basis of the learning process in surgery: understand what to do and do it repeatedly.**

   - **In penile prosthetic surgery you cannot rely: find a mentor who can help you develop that**
   - **The first thing I believe to be fundamental is to get help: find a mentor who can help you develop that**
   - **Reflection can be applied to any discipline in life, it will outline my own experience. Probably this**
   - **Teaching is the most difficult task in surgery but is also the mark of an expert**

   And last but not least, my final reflection is, in my opinion, the most important of all: to teach others what you have learned. Teaching is the most difficult task in surgery; you start by assisting an expert, next step is to be assisted by an expert, then would come being assisted by someone less experienced than you and finally the most difficult is to assist someone less expert than you, making you the expert.

   In surgery, you are at the top when you are mentoring other surgeons. If someone considers you his mentor, his master in surgery, he/she has a doubt of what to do in a difficult case and calls you for an opinion, that is when you can finally consider yourself an expert.

References


New cases of bladder cancer are diagnosed in approximately 110,500 men and 70,000 women each year. In 2018, it is predicted to be the fourth and tenth most common malignancy in males and females, respectively, in the United States. 18,250 patients in the European Union and 12,000 US patients die from urothelial bladder cancer each year.

Mortality rates have remained relatively stable in recent years. At presentation approximately 20-30% of bladder cancers are muscle-invasive and would likely be fatal for patients within two years if left untreated. Radical cystectomy and extended pelvic lymphadenopathy provide the best chance for long-term survival and are considered the standard of care for clinically localized muscle-invasive bladder cancer and high-grade recurrent non muscle invasive disease.

The incidence of bladder cancer increases with advancing age. Considering the increasing life expectancy and the increasing proportion of elderly people in the general population, radical cystectomy will be considered for a growing number of elderly patients. However, radical cystectomy by any approach is complex surgery associated with significant peri-operative morbidity in a susceptible patient cohort who are frequently elderly with associated co-morbidities. The risks of surgery therefore need to be balanced with the benefits of treatment.

Potential advantages of robotic-assisted radical cystectomy (RARC) include reduced complications, less intra-operative blood loss due to the prolonged pneumoperitoneum, quicker return of bowel function, shorter hospital stay and earlier return to normal activities, which would all theoretically allow more immediate resumption of adjuvant chemotherapy if required. RARC has been shown to be advantageous in elderly patients and other susceptible groups with a combination of RARC with an enhanced recovery program has been shown to further reduce the recovery time after cystectomy.

The number of RARC’s performed in the United States is steadily increasing, however, <20% of radical cystectomies are currently performed robotically. Indications are that RARC is gradually being adopted and that the technique is evolving, with an increasing number of centres performing totally intracorporeal RARC.

Despite the apparent advantages of RARC, debate remains as to whether minimally invasive surgery negatively impacts survival outcomes, potentially due to inadequate resection, suboptimal lymph node dissection or alteration of recurrence patterns due to ‘tumour seeding’ related to the pneumoperitoneum or insufflation. A recent multicenter study reporting early recurrences in laparoscopic radical cystectomy (LRC) found 8.7% of patients with favorable pathological characteristics (pT2 No Ro or less) developed disease progression in the first 24 months post-operatively, concluding that the pneumoperitoneum may have contributed to these recurrences.

Oncological outcomes following robotic-assisted RC

Tumour recurrence after RARC linked to biology, not to surgical procedure

Figure 1: RFS estimates from the ESWG multi-institutional database focusing on the centres performing totally intracorporeal RARC

Figure 2: RFS estimate comparing RARC between patients with non-favorable (pT>2 or N+) and favorable pathological characteristics (pT2 No Ra)

A multi-centre RARC series published by the EAU Scientific Working Group (ESWG) identified that early recurrences at any site occurred in 4.2% of patients at three months, 18.8% at 12 months and 25.4% at 24 months, which is equivalent to early recurrence rates seen in ORC series. The ESWG series identified that distant recurrences in the bones, lungs and liver were most frequent and that pelvic lymph node recurrences were the commonest site of local recurrence. This is also consistent with the pattern of recurrences seen in previous studies of ORC and in autopy series. Regarding ‘unusual recurrence patterns’, they identified five patients (0.9%) with peritoneal carcinomatosis and two patients (0.3%) with port site (wound site) metastasis, which are both of low incidence and consistent with published open series.

Whilst debate remains on the potential for detrimental effects from RARC on early recurrence patterns, there is little evidence of an overall higher incidence of early recurrences following RARC. Early RFS rates correlate closely with five-year RFS and overall survival and current evidence from cumulative analysis indicates satisfactory medium and long-term RFS rates and cancer specific survival. In a recent review RFS rates at two years post-operatively ranged from 62-81% in RARC series. Even papers highlighting unusual recurrence patterns as a possible indicator of detrimental effect have not shown an increased incidence of recurrences compared to the ORC, in fact in both these series the overall incidence of recurrence was lower in the RARC group.

Recurrence patterns

Previously hypothesised potential negative effects of RARC, such as insufflation, the pneumoperitoneum and methods of specimen extraction remain unproven. Recurrence patterns attributed to the pneumoperitoneum and insufflation include peritoneal carcinomatosis and port site metastasis. Peritoneal carcinomatosis incidence has been found to be as high as 19% in bladder cancer patients at autopsy, but importantly it is most frequently associated with extensive metastases at multiple sites. In RARC series the incidence of peritoneal carcinomatosis has been found to be low at 3–5%, even with long-term follow-up.

Review of patients in the ESWG series with peritoneal carcinomatosis and port-site metastasis revealed all patients to have high-grade urothelial carcinoma. Four of the five patients with peritoneal carcinomatosis presented with multiple metastases and 80% had upstaging of disease, from organ-confined to non-organ confined disease and only one (20%) received NAC. These findings further indicate that peritoneal carcinomatosis from tumour seeding is related to tumour biology rather than the pneumoperitoneum or other ‘effects’ of a RARC approach. Hypothesising that tumour biology is the main causative factor for early recurrence is also consistent with the laparoscopic cystectomy series that described unusual early disease recurrence patterns among patients with favorable disease characteristics (pT2pN0Ro). This series reported 8.8% of patients with pT2pN0pR0 developed recurrences within 24 months, with most of these patients showing progression to high-volume disseminated metastatic disease. Multi-variate logistic regression analysis identified p7 stage as the only factor significantly associated with early recurrence in this multi-centre study.

The ESWG series reported similar early recurrence rates (See Figure 3). But while you consider that approximately 80% of recurrences occur in the first two years [18,26], recurrence rates of 8.7% in pT2N0Ro in the first two years, equates to the five-year RFS of 89% in pT2N0 patients previously reported in a “Gold Standard” ORC series. Indeed, early recurrences with ‘favorable disease’ can be expected in a proportion of patients, pT2N0 has been shown to be a heterogeneous group with approximately a third being stratified as high-risk, showing oncological outcomes similar to pT3N0 disease.

Accepted early indicators of oncological efficacy include PSM rates and lymph node yields. Several cumulative analyses of RARC series have shown respectable PSM rates and median extended pelvic lymph node yields consistent with open series and RARC series. PSM rates were strongly associated with pathological staging.

Other factors consistently associated with early recurrence are lymph node involvement, advanced pathological stage and positive surgical margin.
rates19. In the ESWG cohort20, we see early recurrences associated with these variables on the Kaplan Meier estimates (See Figure 1), giving further evidence that early recurrences following RARC are primarily related to tumour biology and not the modality of surgical treatment. On regressional analysis of the ESWG series, the risk of recurrence was associated with positive compared to negative lymph nodes (N1 vs N0 HR= 3.6 p<0.0001 and N2 vs N0 HR=5.6 p<0.0001). Pathological non-organ confined, when compared to organ confined disease, was also a significant risk factor for early recurrence (HR=5.8 p<0.0001), as was a PSM (HR 4.5 p<0.0001)19. Female gender was also seen to be a risk factor (HR 1.63 p<0.05) and has previously been identified as an independent adverse prognostic factor for both recurrence and progression of bladder cancer6.

Survival benefits
Whilst reported early and late outcome measures of oncological efficacy will rightly dictate future adoption rates of RARC, current evidence indicates survival benefits of radical cystectomy in elderly or co-morbid patients previously considered unsuitable for major surgery19. The need for oncological efficacy therefore needs to be increasingly balanced with the risks of surgery. It is recognized that an RARC approach is advantageous in elderly patients and other susceptible patient groups19 and there is evidence of changing patient demographics in RARC series19.

The potential additional advantages of a totally intracorporeal RARC technique, include less morbidity from the operation, reduced transfusion rates and enhanced recovery20,21. Quicker recovery following surgery should also result in improved opportunities for earlier administration of adjuvant chemotherapy, when pathological results or early recurrences indicate the need8.

Although the selection biases of patients for optimum management outside of prospective randomized controlled trials can limit direct comparison with alternative treatments, it is also evident that due to the heterogeneity of aggressive urothelial cancer, it is difficult to accurately identify the best prognosis patients prior to surgery. To enable true comparison between treatments, robust molecular or biological markers associated with accelerated disease progression are required, but they are currently lacking in the clinical setting. This inability to accurately predict metastatic risk pre-operatively is a possible explanation for why smaller study numbers have concluded differences in early recurrence patterns between RARC and ORC20.

Oncological efficacy
Indicators of oncological efficacy following RARC, namely PSM rates and PLND yields are comparable to ORC series. Whilst several groups have indicated potential for unusual recurrence patterns after RARC, their findings do not correlate with either an increase in recurrence rates or decrease in cancer specific survival. Current evidence indicates that early recurrence rates and RFS rates following RARC appear equivalent to published ORC series. In all series, positive lymph nodes, non-organ confined disease and PSM’s were associated with poor oncological outcomes, indicating tumour recurrence following RARC are primarily related to tumour biology and not the modality of surgical treatment.

Editorial Note: Due to space constraints, the reference list can be made available to interested readers upon request by sending an email to communications@uroweb.org.
Antibiotic treatment's collateral effects

Antimicrobial stewardship, critical antibiotic use are crucial to minimise bacterial infections

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A priority concern for worldwide healthcare structures is the increased resistance of microorganisms in health-associated infections (HAIs) and also in the outpatient setting. Moreover, the emergence of multidrug-resistant organisms (MDRO) is a worrisome point as the selection of an appropriate antibiotic treatment is a challenging task.

Several definitions for MDRO have been proposed such as those microorganisms with resistance to three or more antibiotic classes. It is recommended to follow the definition by the Centers for Disease Control and Prevention, which contains MRSA microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents. Certain types of microorganisms deserve special attention such as extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae or those resistant to carbapenems. Enterococcus resistant to vancomycin, and Methicillin-resistant Staphylococcus aureus (MRSA).

In recent years, antifungal resistance is also increased, in particular in cases of Candida glabrata and Aspergillus fumigatus. Fungal infections are more common in patients with immunosuppression, those with cancer and transplant recipients. MRSD are also considered as a collateral effect of antibiotic treatment. Another worrisome consequence related to antibiotic treatment is Clostridium difficile infection. Both the isolation of multidrug-resistant bacteria and Clostridium difficile are associated with an increase in morbidity and mortality rates, longer hospitalisation and higher costs. It is estimated that MDRO infections increase hospitalisation cost by 10–30%, and Clostridium difficile infections increase the hospitalisation stay by a mean of nine days.

MDRO are commonly isolated in patients hospitalised in a urology ward with hospital-acquired infections. A study data from France in 2002 (Global Prevalence Study on Infections in Urology) carried out by the EAU Section of Infections in Urology (ESUI) and the Global Alliance for Infections in Surgery Working Group, and with healthcare-associated urinary tract infections, 45% of Enterobacteria and 25% of P. aeruginosa were multidrug-resistant. Moreover, the rate for imipenem was 8% (Figure 1 summarise resistance rate from GPRU study). Higher resistance rates were reported in a case of unresponsiveness.

Furthermore, MDRO are isolated as a hospital-acquired infections in healthcare structures. This term includes when patients were hospitalised within 90 days before the infection, or receives long-term healthcare, intravenous therapy, specialised wound care, or hemodialysis. ESBL-producing bacteria are also isolated in a community setting. Missile and the subsequent use of broad-spectrum antibiotics are related to the growing frequency of microorganisms that are resistant to antibiotics. Inappropriate use of antibiotic agents in human and food producing animals also contribute to the development of antibiotic resistance. In particular, there is a clear connection between the prescription of fluoroquinolones and the incidence of resistant strains.

Therefore, in areas with higher resistance to quinolones, they should be avoided as empirical treatment. Moreover, ESBL-producing Enterobacteriaceae are also frequently resistant to other antibiotics such as fluoroquinolones and aminoglycosides. Carbapenems are usually the antibiotics prescribed in the management of infections due to MDRO, especially those caused by ESBL-producing bacteria. However, carbapenemase-producing bacteria are also emerging, and it is a worrisome problem as up to a 50% mortality rate has been described in patients with bloodstream infections with carbapenem-resistant Enterobacteriaceae.

Furthermore, few treatment options are available for cases of carbapenemase-producing bacteria. However, a correct selection of antibiotics is of paramount importance. Some drugs not frequently prescribed in this setting, such as fosfomycin and nitrofurantoin, are active against strains with a lower resistance rate, and they are considered as an attractive alternative in the management of urinary tract infections with the isolation of ESBL-producing bacteria and MDRO microorganisms. Fosfomycin shows good activity against common uropathogens, including ESBL-Enterobacteriaceae. Parenteral administration of fosfomycin can be effective whether urinary tract infections are caused by ESBL Enterobacter, Pseudomonas aeruginosa, and vancomycin-resistant-Enterococcus. Fosfomycin is not recommended for patients with low concentrations in serum and renal tissues are achieved. Nitrofurantoin also offers good efficacy against Enterobacteriaceae such as E. coli, Klebsiella, and Enterobacter. However, it is ineffective against Proteus and Pseudomonas.

For severe infections caused by MDRO including methicillin-resistant Staphylococcus aureus (MRSA), Acinetobacter baumannii, P. aeruginosa and carbapenemase-producing bacteria, antibiotics such as tigecycline and colistin are indicated. Collaboration with an infectious disease physician is advised for these patients.

Among urological patients, high rate of antibiotic resistance has been reported due to specific risk factors such as urinary catheters and surgery during hospitalisation. According to data from our department there is a high-risk of MDRO isolation in a patient with immunosuppression (OR 2.97), urinary lithiasis (OR 2.93), a prior urinary infection (OR 2.45), and an indwelling urinary catheter prior to admission (OR 1.97). The highest rates of MDRO were found among patients with MHS and a double-J stent and a nephrostomy tube. We have also analysed strains due to carbapenem-producing bacteria in patients hospitalised in our Urology ward, and each of them had an urinary catheter, and two out of 12 had immunosuppression.

A survey carried out in Germany reported that urologists were more confident prescribing the correct dosage and duration of antibiotics. However, both urologists and non-urologists had poor knowledge about antibiotic stewardship.

The main points for minimising resistance to antibiotics, selecting appropriate empirical antibiotic therapy, and optimising outcomes are an adequate knowledge of risk microorganisms, and microbiological and resistance patterns for the isolation of multiple-drug-resistant microorganisms. Moreover, a proper indication regarding prophylaxis is required (indication and no indication, duration, type of antibiotic). When the infection is diagnosed, the selection of antibiotics may be challenging as anywhere from 15% to 45% of infections due to ESBL-producing bacteria are not appropriately managed. On the one hand, broad-spectrum antibiotics should be avoided. Moreover, antibiotics must be selected while taking into account the appropriate dosage, an adequate route of administration, and administration timing. Before selecting an antibiotic treatment, previous cultures must be reviewed as high resistance rates are reported after previous antibiotic therapies.

Antimicrobial prophylaxis according to the recommendation by Best Practice Guidelines (EAU) is recommended in order to minimise the emerging antimicrobial resistance, on the same hand, an adequate empirical treatment must be chosen. On the other hand, broad-spectrum antibiotics should be avoided. Moreover, antibiotics must be selected while taking into account the appropriate dosage, an adequate route of administration, and administration timing. Before selecting an antibiotic treatment, previous cultures must be reviewed as high resistance rates are reported after previous antibiotic therapies.

The main points for minimising resistance to antibiotics, selecting appropriate empirical antibiotic therapy, and optimising outcomes are an adequate knowledge of risk microorganisms, and microbiological and resistance patterns for the isolation of multiple-drug-resistant microorganisms. Moreover, a proper indication regarding prophylaxis is required (indication and no indication, duration, type of antibiotic). When the infection is diagnosed, the selection of antibiotics may be challenging as anywhere from 15% to 45% of infections due to ESBL-producing bacteria are not appropriately managed. On the one hand, broad-spectrum antibiotics should be avoided. Moreover, antibiotics must be selected while taking into account the appropriate dosage, an adequate route of administration, and administration timing. Before selecting an antibiotic treatment, previous cultures must be reviewed as high resistance rates are reported after previous antibiotic therapies.

In summary, the following measures are recommended in order to minimise the emerging growth of multidrug-resistant organisms (MDRO):

- Training regarding MDRO, local microbial prevalence, and resistance patterns, and prescription of antibiotics are required for healthcare providers.
- Informing patients about prevention of infections is not only necessary for healthcare personnel, it should also include everybody in contact with the patient.
- The prescription of antibiotics should be adequately indicated and justifiable, avoiding broad-spectrum antibiotics.
- Antibiotic prophylaxis according to the recommendation by Best Practice Guidelines (EAU) is recommended in order to minimise the emerging antimicrobial resistance. Perioperative antibiotics should not routinely be maintained beyond the first 24 hours after surgery.
- Antibiotic choice should be determined according to a risk factor for MDRO;
- Inappropriate and unnecessary use for prevention, including shortening, when possible, the duration of urinary catheterisation;
- Methods for enhanced microbiological diagnosis with rapid detection of resistance are advisable; and
- Antimicrobial Stewardship Programs dedicated to improving antibiotic use are required and have demonstrated a reduction in the incidence of infections due to selection of MDR and C. difficile infections.

References


Saturday 17 March
10.00-14.40: Joint meeting of EAU Section of Andrological Urology (ESAU) and the EAU Section of Infections in Urology (ESIU) – When basic science meets clinical practice
Office Urology: Meeting the challenges
Prostate biopsy issues top agenda of ESUO

By Joel Vega

The new EAU Section of Urologists in Office (ESUO) will focus on prostate biopsy issues during its “first” annual meeting, following its official launching last year in London. The topic is of prime concern to office urologists with recent and still evolving changes in prostate cancer detection such as new imaging techniques.

“We have headlined our meeting here in Copenhagen as “All about prostate biopsy in office,” as this reflects an important method in urologic office done in all countries,” said ESUO Chairman Prof. Dr. Helmut Haas (DE).

Haas said the session will be moderated by office urologists, with expert lectures by Profs. Maurice Stephan Michel (DE) and (Jochen Walz (FR), and Drs. Stefan Czarniecki (PL), Stefan Haensel (NL), and Robert Schneider (CH). Michel will discuss indications for biopsy, patient’s preparation and biopsy procedures. Walz, meanwhile, will examine TRUS- and MRI-guided biopsies, going through patient selection, benefits, drawbacks and future prospects. Management of biopsy complications will be discussed by Haensel, while Czarniecki will explore the role of biomarkers in prostate cancer treatment. Schneider will look into pioneering experiences and lessons from a fusion biopsy network in Switzerland.

“We aim to have an interactive session as much as possible, stimulating the audience to provide critical views and feedback back to the panel of speakers,” said Haas. Aside from Haas, chairing the session are three ESUO members including Dr. Horst Brenneis (DE), Dr. Stefan Haensel (NL) and Dr. Robert Schneider (CH) who will provide preliminary remarks and lead the case discussions.

Haas said that as a new office under the auspices of the EAU, the section is taking all efforts for it to achieve its aims.

“Aside from promoting the ESUO to other EAU section offices and affiliates, we have conducted several surveys not only to find out the basic issues that concern office urologists but also to expand our contacts. We appreciate every little effort from our partners, both current and potential, that will help us expand the network of office urology,” Haas said.

“For all office urologists, send us an e-mail (esuo@uroweb.org) with your expectations.”

Special route itinerary

During the congress this week, the section has created a “route itinerary” that will track and identify various meetings or sessions that are relevant or of interest to office urologists.

“Our section has created an itinerary here in Copenhagen which flags and scores the congress’ sessions according to their importance for office urologists. This will help our members or other office urologists to easily identify which sessions can add as priority to their congress agenda,” he said.

Sharing its expertise

He also mentioned that aside from collaboration with other offices, the ESUO is also ready to offer its own expertise.

“Our section offers collaboration, especially based on the fact that most of the new developments in diagnostics and non-surgical therapy have to be transferred to outpatients under outpatient conditions. This means either in outpatient departments or in urologic offices. Office urologists know best the medical and patient-related considerations and administrative rules under which this can be done successfully,” Haas explained.

Haas said ESUO has been invited by the Slovak Urological Society to participate in the Slovak meeting of office urologists in April, where he will not only present the ESUO’s goals and projects but also the challenges and developments in office urology issues.

Nevertheless, he emphasized that a lot needs to be done by the ESUO for it to adequately cover all the issues faced by office urologists.

Meeting Tip!

ESUO Session. All About Prostate Biopsy, Saturday 17 March 10.15-14.00

Prostate biopsy is a core procedure in urologic office. During the meeting all relevant aspects of prostate biopsy in an office setting will be presented by recognized specialists: indication, procedures, the management of complications, and modern imaging. The session is chaired by office urologists who will focus on the outpatient situation.

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Product videos and 360° views:
New journal to offer a multidisciplinary view of GU cancer treatment

By Loek Keizer

The EAU is gearing up to offer a new scientific journal based on the established titles of European Urology and European Urology Focus. We spoke to the Editor-in-Chief of European Urology Oncology, Prof. Alberto Briganti (IT) about the journal’s mission, its intended audience and place in the landscape of medical journal publications.

“This is a new journal, and the EAU’s first official journal that is fully devoted to the research of genitourinary (GU) cancers,” Briganti explained.

“The novel idea is to assemble an editorial team of specialists from different GU-related disciplines who will work together to create a multidisciplinary journal in which different aspects of GU cancers such as medical oncology, radiation therapy, urology, imaging, pathology, molecular pathology are all represented.”

The journal will feature a range of sections, encompassing original research and reviews, discussions and some Guideline reviews. Briganti: “In GU cancers, prostate, kidney and bladder cancer are of course most prevalent, but we will also feature testicular, penile and other rarer cancers. We will have new research coming in, and we are also commissioning reviews on several ‘hot’ topics. We actively commission systematic reviews, meta-analysis, as well as opinion papers, on topics in which there is interest.”

In terms of target readers, European Urology Oncology is designed to serve every medical expert dealing with GU cancers and their research, including urologists, medical oncologists, radiation therapists, imaging specialists and general research scientists.

“Naturally, our core audience is the urologist,” Briganti said. “Urologists are among the main actors in GU treatment and represent majority of our readers. But the scope of our journal goes beyond urology and this might attract attention from other disciplines. Our ultimate aim is to have a wide audience including also non-surgical communities.”

European Urology Oncology will have an impact factor, every other month. EAU members will automatically get access to the new journal. Briganti: “The first edition is coming up soon. We are currently working on the first batch of papers that was accepted.”

Editorial team

Chosen as the EU Oncology’s editorial party due to his previous editing experience, Briganti previously served on the European Urology editorial board, and co-founded EU Focus, together with Mr. James Catto (GB). He also served as guest editor for various issues of other medical journals.

Serving as Associate Editors are medical oncologist Dr. Laurence Algibes (FR), urologist Dr. Gianluca Giannaris (IT), Prof. Ashok Kamal (US) who is involved in Urologic Oncology & Cancer Research and radiation oncologist Prof. Paul Nguyen (US). Managing Editor Ms. Emma Redley is based in Sheffield (GB), where the editorial team of European Urology is also based.

“We have a dream team of editors with different backgrounds from all over the world, who are also key opinion leaders in their respective fields,” Briganti said. “Together, we will endeavor to make this journal essential for those publishing in the field. Competition is very high and we believe that if we insist on quality and rigorous peer reviews, the journal will improve and reach high standards.”

Motivation

The genesis of European Urology Oncology came from the wealth of GU research that is submitted to European Urology. Roughly 80% of these submissions are related to genitourinary cancers, with many of the submissions deserving of an audience. Briganti: “If you consider the number of papers submitted to the main journal, the numbers of straight rejections or rejections after peer review, so many of these are rejected despite their quality. These papers may be given another chance for publication under the EUA’s banner.”

“Authors who might initially not have their research accepted by the editors of European Urology, but who produce good quality papers are then given a chance to be considered for EU Oncology. I believe there is a lot of research which cannot always be allocated (due to space constraints) to the main journal. This is common practice in the industry, and many journals have sister publications in this way.”

“Ultimately, our goal is to publish innovative and high-quality papers which are of course distributed and well-read among the GU community. The journal’s high-quality evidence should ultimately translate into practice-changing data.”

Initially, EU Oncology will draw on submissions to European Urology. “Ultimately, we hope to receive more and more direct submissions, but as the journal is in its infancy, James Catto and I decide which article should go be considered for EU Oncology after rejection from European Urology,” he added.

Whether the emergence of a new, GU cancer-focused journal would affect the current balance of contents of European Urology is difficult to say. “I don’t foresee such a change,” Briganti said. “GU cancer research is so wide, and there are so many developments in terms of clinical and translational research. There will always be sufficient material for both journals. The main journal will continue publishing high-quality material in the field of GU cancers.”

“There is no intention to have any competition now or in the future. Both journals will cover research in uro-oncology. Additionally, European Urology also covers benign diseases, which we will not cover. It has the highest impact factor as it is the most highly-cited, most-read, most-distributed journal in the field. We are a small journal compared to European Urology, and there will not be any competition between us.”

Briganti anticipates more of a divergence between the journals, but not in the short-term. “It takes time to set up a new journal and make it fly properly. In the future, as we begin to receive more direct submissions, we may end up featuring more and more articles within the area of pure medical oncology or translational research,” he said. “Ultimately, our goal is to publish innovative and high-quality papers which are of course distributed and well-read among the GU community. The journal’s high-quality evidence should ultimately translate into practice-changing data.”

Role of medical journals

Translating the research published in medical journals into practice-changing data is exactly the goal of medical journals. “The literature that an EAU membership provides should be useful for any urologist. This way they can stop up to date and be aware of changes in practice or future directions of practice,” Briganti said. He noted that a journal’s ultimate aim is to help improve patient care by publishing and circulating high-quality research, and direct the reader’s attention to new and evidence-based medicine. “We contribute to increasing the adherence to good treatment by practicing urologists,” he said.

European Urology, and soon, European Urology Oncology, are not only widely-cited journals, but are also discussed at meetings, eventually helping shape medical guidelines. Briganti: “The ability to improve and change guidelines is the best that any journal can do. It means you are influencing the rules for good clinical practice. This makes a journal great.”

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EUT Congress News Saturday, 17 March 2018
Predicting resistance to BCG therapy
Emerging therapies for non-muscle invasive bladder cancer

For decades, Bacillus Calmette-Guerin (BCG) immunotherapy has been utilized to prevent recurrence and progression of the disease after tumour resection, in non-muscle invasive bladder cancer (NMIBC) patients. Despite the efficacy of this treatment, a significant fraction of patients will ultimately develop recurrence and progression.

Patients who fail BCG therapy can also incur higher medical costs due to the need for multiple procedures and closer surveillance for recurrence. Furthermore, patients who develop disease progression often have a poorer chance of survival.

Clinicopathological parameters such as tumour grade, stage, multiplicity, recurrence rate, the concomitant presence of carcinoma in situ (CIS), gender, and age have been linked to the response to BCG. However, should be noted that these risk factors are not unique to BCG but are associated with unfavorable NMIBC outcomes as well. Therefore, new genetic and genomic tools have also been investigated, and may have a role to anticipate BCG immunotherapy failure.

Detection for chromosomal aberration using urinary fluorescent in situ hybridization (FISH) shows potential as a predictive tool of BCG failure. During BCG therapy, patients with positive FISH results after induction therapy were shown to have higher cancer recurrence risk (3.5 fold) and progression risk (1.2 fold).

Some studies have also attempted to associate tumour antigen expression with BCG response. However, correlation of a single tumour biomarker with BCG response is confounded by the inherent mutation rate of bladder cancer and complex immunological cascade induced by BCG, p53, Retinoblastoma protein, Survivin, B-cell lymphoma 2, E-cadherin, and the Rb protein, which are typical tumour markers being investigated.

Patients innately immune to mycobacterium, tested using purified protein derivative on skin, and clinical symptoms such as fever have also been considered as possible predictors, though reports have not been consistent.

BCG immunotherapy induces an immunologic response. Following BCG instillation, an increase in leukocytes in urine has been associated with better BCG response. However, immunohistochemical analysis of immune cells in tumour tissue have also been correlated with response to therapy. A panel of cytochemical markers (CD4, CD8, IL-6, IL-8, IL-10, IFN-gamma, IL-27p0 and TNF-alpha), detected in the urine, with a high predictive value for BCG response was also being validated. Increased expression of immune presenting molecules, major histocompatibility complex class I and II, and ICAM, has also been linked to favorable therapy outcomes. BCG induced antitumor immunity is multifaceted and many molecules are linked with response to therapy. Constant monitoring of these molecules during BCG treatment may be challenging.

Genetic variants
Genetic differences between BCG therapy responders and non-responders is another area of research interest. Studies have centered around genes involved in the mechanisms of action of BCG. Genetic variants such as Single Nucleotide Polymorphisms (SNP) in immune response-associated genes have been correlated to BCG response. For example, allelic variants in Human glutathione peroxidase 1 (GPX1) and single-nucleotide associated macrophage protein 1 (NRAMP1) has been associated with bladder cancer recurrence after BCG immunotherapy. NRAMP1 plays an essential role in host-mediated macrophage defense against intracellular mycobacterial infection. The NRAMP1 promoter variant rs1944489 allele 3 was also found to be associated with higher progression risk (p<0.01) (unpublished data). Vitamin D is known to be important in macrophage-mediated mycobacterial infection and response. A recent study showed SNP’s with vitamin D receptor (VDR) in strong linkage disequilibrium, rs10735813 and rs7312334 were correlated to recurrence risk in an Asian cohort of NMIBC patients (unpublished data).

In the same cohort, polymorphisms in cytokine genes such as IL12 (rs3227553) and IL18R1 (rs17712172) were also found to associate with BCG immunotherapy response (unpublished data).

Additionally, studies have also begun to evaluate epigenetic changes, which can alter gene activity and expression outside of gene sequence changes, as predictors of patient response to BCG. In one study using a cohort of BCG treated NMIBC patients, the methylation profile of a panel of tumor suppressor genes (TSG) was assessed and differential methylation patterns of several TSG between patients with recurrence and progression were found.

Differences between populations
The allele frequencies of SNPs between populations of different geographical background and ethnicity should be taken into consideration when developing SNPs as predictive markers of response to BCG therapy. Genetic association studies are usually performed in a homogenous cohort. Whether these genetic predictors can be applied globally requires validation. For example, a Southern European population study reported a panel of eight immune response-associated SNPs predictive of BCG outcome. However, only two SNPs from the panel (rs12203529 and IL18R1 rs17712172) correlated to BCG immunotherapy response in an Asian population; as allele distributions were different between the two populations. This was also observed in NRAMP1 SNP associations and deviation between the Canadian and Asian reports may be due to allele distribution differences of the SNPs analyzed.

Thus, a better strategy may be to evaluate gene transcription or function rather than SNPs. However, this is rather difficult to do as it requires the development of predictive assays that correlate with the gene’s functional response to BCG therapy. Furthermore, the response to BCG is complex, as it is likely that many genes and proteins are involved, and therefore evaluating assays single proteins may be of limited value. Although the evaluation of the global response of patient immune cells to BCG prior to therapy, using array-based technologies monitoring the transcriptional responses or protein response to BCG may be a better approach, these platforms are still quite expensive to run. The development of targeted arrays may reduce the cost in the future.

Emerging therapies
Newer therapies on the horizon include an adjuvant cancer vaccine (MAGE-A3), which was safely administered with standard BCG therapy in NMIBC patients, in a Phase I trial, and it is the first in to show an increase in local T cell response11. Other intravesical immunotherapies in Phase 2 and 3 trials, include the combination of BCG and vaccines (intradermal HS-410 or PANVAC), genetically engineered BCG and modified adenovirus as monotherapy12.

The identification of regulatory T cells and immune suppressive immune cells in tumour tissue has also led to the evaluation of immune checkpoint blockers (ICB) such as anti-PD-L1 and anti-PD-1, which is programmed death-1 receptor is expressed on activated T cells and binds to its ligand PD-L1. This ligand is expressed on normal cells by binding PD-L1 the immune limits the immune response.

PD-L1 expression is found in some bladder tumour cells, especially the higher grade ones, thus the tumour cells are able to block immune activation and escape removal by immune cells. PD-L1 expression is reported to increase after chemotherapy or immunotherapy, and thus it may be a good candidate for intervention. Another immune checkpoint blocker, CTLA-4 (Cytotoxic T lymphocyte associated protein 4), also blocks T cell activation by competing with CD28 for binding to B7 ligands (CD80/CD86). In normal immune processes, it serves to limit immune responses but in cancer it limits T cell activation. The PD-L1 and CTLA-4 pathways do not overlap. Systemic ICB therapy with atezolizumab and durvalumab (anti-PD-L1 and CTLA-4 pathways do not overlap. Systemic ICB therapy with atezolizumab and durvalumab (anti-PD-L1) and pembrolizumab (anti-PD-1) are being evaluated in ongoing phase 2 monotherapy studies. Both are associated with lower immune-related adverse events compared to systemic anti-CTLA. Thus, anti-PD-L1 and anti-PD-1 therapies may provide additional treatment options for BCG-unresponsive and relapsing NMIBC.

There are also phase 1 and 2 studies in progress, that combine BCG with either atezolizumab or pembrolizumab for the treatment of NMIBC13,14.

However, a cautionary point to note is that the use of ICBs should be limited to patients with tumours expressing these proteins. Molecular analysis of patient tumours and immune cells will determine the best therapy for patients.

References

Editorial Note: Due to space constraints the reference list has been shortened. Interested readers can email at communications@uroweb.org for the full list.

Sunday 16 March
09.15-12.15: Urology Beyond Europe, Joint Session of the European Association of Urology (EAU) and the Federation of ASUML European Associations (FAUE)

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EUT Congress News 25
Radical cystectomy remains a procedure associated with high morbidity. A recent contemporary study that analyzed 6,510 patients over a six-year period (2010-2015), reported that 31.5% of patients experienced a complication and 40.3% of patients required a blood transfusion. The length of stay decreased over time from 10.6 days in 2010 to 9.2 days in 2015 (p<0.01), however readmissions increased slightly over the time period to 21.4% in 2015 (p=0.22).

The use of the robotic-assisted approach, for the surgical management of bladder cancer and reconstruction of a urinary diversion, has increased since its description in 2003. Contemporary studies on radical cystectomy series, report that 28.9% to 39.4% of patients underwent a robotic assisted approach. Since more than five years ago, in our institution, as well as in others, 100% of the radical cystectomy and urinary diversions are performed using the robotic assisted technique. Multiple studies, including randomized controlled trials, have demonstrated that Robotic assisted radical cystectomy (RARC) is comparable to open radical cystectomy (ORC) with regards to: surgical margins, number of lymph nodes resected, five-year cancer-specific and overall survival, as well as, local and distant recurrences. Although, RARC may take longer (especially during the learning curve), it has demonstrated less estimated blood loss, less risk of blood transfusions, and shorter length of stay.

It is widely known that most postoperative complications following radical cystectomy arise from the urinary diversion reconstruction. Complications (30 and 90 day; Grade 3-5) have been comparable with both approaches (Open versus Robotic). However, all the randomized control trials reported, have compared ORC to RARC with extracorporeal urinary diversion.

Intracorporeal urinary diversion reconstruction may improve complications rates, and shorten even more the length of stay. Performing a diversion intracorporealy may influence gastrointestinal complication rates by reducing bowel manipulation, mobilization and exposure. A series of series demonstrated that intracorporeal urinary diversions reduce gastrointestinal (23% to 10%; p=0.05) and infectious complications (38% to 10%, p=0.031), as well as; 30-day (5% to 5%; p=0.031), and 90-day readmission (39% to 12%; p=0.047).

Since more than five years ago, in our institution, we perform a pure robotic-assisted radical cystectomy with intracorporeal urinary diversion (abdominal wall or orthotopic). There is a need for the entire generation of robotic surgeons to familiarize themselves with anatomical landmarks, to prevent complications related to the approach of the pelvis, for the ablative oncological part of the procedure such as the extirpation of bladder cancer and lymph node dissection. Finally, diffusion of surgical hints for the creation of intracorporeal urinary diversions is necessary to prevent complications related to the fully intracorporeal reconstruction of the urinary tract.

**Surgical technique**

Pituitary placement starts with a 2 cm longitudinal incision, 5 cm above the umbilicus. Through this incision the peritoneal cavity is opened and a 12 mm balloon trocar is introduced. After pneumoperitoneum is achieved at a maximum pressure of 15 mmHg, at high flow, a 12 mm (or 30 degrees) hand-held robotic camera is inserted, to assist in placing the other trocars under direct vision. Three 8 mm robotic metallic ports, one 12 mm assistant port, and one 15 mm assistant port (for insertion of endoscopic articulating staplers) are placed. (See Figure 1)

**Radical cystectomy and bilateral extended pelvic lymph node dissections**

For the oncological part of the surgery, which includes the robotic cystectomy and bilateral extended pelvic lymph node dissection, it is important to identify three avascular spaces: the periureteral space, the lateral pelvic space and the anterior rectal space. Once these spaces are identified: 1. The ureters are clipped (Hem-o-lok with vicryl suture attached to them) accordingly, to aid in an exact estimated blood loss count; dilating them for an easier reconstruction of the urinary tract afterwards; and preventing possible cancer cell seeding, specially if ureters are stented prior to surgery. 2. The pelvic pedicles can be identified to either staple them with endovascular articulating staplers, or dissect them and secure them with hem-o-loks (selectively when preserving neurovascular structures). 3. The rectum can be dissected away from the posterior bladder wall, the posterior Denovillier’s fascia can be incised, and the rectum can be dissected away from the prostate from base to apex under direct vision.

Once the posterior dissection is completed, the anterior exposure and apical dissection are performed by: 1. Incising the median and lateral umbilical ligaments to release the bladder from the anterior abdominal wall. 2. Opening of the endopelvic fascia bilaterally and suture ligamentum of the deep dorsal venous complex. Once the proximal membranous urethra is skeletonized, the urethral catheter is removed and a Hem-o-lok clip is applied just distal to the apex to prevent urine spillage. (Figure 2) After incision of the urethra the specimen is placed in a retrieval bag and removed from the pelvic cavity.

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**Intracorporeal urinary diversion (Abdominal wall or orthotopic)**

The reconstruction part of the surgery starts by the retroperitoneal transfer of the left ureter to the right side. The posterior attachments (mesocolon) of the colon are freed beginning at the sacral promontory in the presacral space providing an unobstructed passage or tunnel. The sigmoid colon is retracted superiorly and anteriorly, and a blunt to grasp suture is passed under the surface of the mobilized colon at the level of the sacral promontory. The suture tied to the hem-o-lok attached to the distal ureter is grasped and passed underneath the sigmoid loop and brought to the contralateral side. Pulling on the suture transposes left ureter retroperitoneally from left to right. Care is taken not to twist the ureter nor to cause kinking.

For an abdominal wall diversion such as an ileal conduit, the bowel including the cecum, ileocecal junction, and ileum is identified. A 20 cm ileal loop segment is isolated about 15 cm proximal to the ileocecal valve by placing marking sutures (3-0 Silk on SH needle for the distal end of the ileal segment and 3-0 vicryl on an SH needle for the proximal end of the ileal segment, where the ureteral intestinal Anastomosis is going to be done). The length of the bowel is determined by the running the bowel and placing an umbilical tape cut to 15 cm.

Care is taken to maintain good vascularity of the isolated bowel segment by visual inspection of the mesentery, as well as transplantation of help identify the mesenteric vessels. In some cases, we have used also intravesical indoxycyanine green (ICG) to identify major mesenteric vessels. Once the 20 cm of ileal segment is identified, and the major mesenteric vessels visualized, the segment is isolated by the use of an Endo-GIA stapler. The restoration of bowel continuity is performed with a stapled side-to-side ileocolic anastomosis. We use a 60 mm and an additional 45 mm Endo-Gia stapler for the side-to-side ileocolic anastomosis. Another, 60 mm Endo-GIA stapler is used transversally, to close the open ends of the ileal limbs. The mesenteric trap defect is closed using running 3-0 vicryl sutures.

We then put into stretch both ureters by pulling on the sutures attached to the hem-o-loks clipped to both ureters, using the Pragprog forces. Once the ureters are lined-up one next to the other, a 3 cm longitudinal incision is made along the anterior aspect of the distal ends (spatulation), to create a wide anastomosis in a Wallach fashion. This is done using a 2-0 monocryl mercurial needle suture. Once this is performed we cut the staple line of the proximal end of the ileal conduit segment selected to perform the ureteral ileal anastomosis in a tension-free manner. First the posterior anastomosis is performed starting proximal at the spatulation site of the right ureter. Running 4-0 monocryl sutures are used for the anastomosis. A Pragprop stabilizes the Wallace Plate and facilitates the anastomosis in a tension-free manner. (Figure 5)
The selection of the ileal segment to be utilized is started by placing a 2-0 silk on an SH needle on the ileum, at least 15 cm away from the ileo-cecal valve. An umbilical tape is cut to 15 cm, measurements of the first, second, third and fourth limbs, are performed and secured by placing 3-0 vicryl stitches on SH needles for identification of each limb of the “W”. At the end of the fourth limb we measure an additional 10 cm for the isoperistaltic limb, and place a 3-0 colored vicryl stitch.

We then perform resection and isolation of the 70 cm ileal segment, as described for the intracorporeal ileal conduit technique. After performing a side to side-ileal anastomosis using Endo-GIA staplers, the “W” neobladder is stabilized. The stabilization of the “W” neobladder is facilitated by passing two 0 silk straight Keith needles suprapubically percutaneously, and passing them through and through both vertexes of the “W”. This keeps the “W” shaped ileum stretched toward the pelvis. With the third arm, and using a Prograsp, the vicryl stitches placed on the antimesenteric border of the ileum. We then proceed to the second limb. At the vertex of the “W” are also grabbed and retracted toward the head. This perfect stabilization and stretching of the “W” shaped ileum, facilitates the organized opening of the ileum in the antimesenteric border. (Figure 6)

The ileum is always opened in a standard organized fashion starting with the right limb of the “W”, and proceeding to the second limb. At the vertex of the “W”, the incision in the antimesenteric boarder (first limb) is brought close to the mesentry, creating a nice wide flap of ileum (2-3 cm in length without stretch and 6 cm wide without stretch) that will be the area where the urethral neobladder neck anastomosis will be done. After finishing the opening of the two first limbs, a 2-0 single needle barbed absorbable suture (V-loc) is used to close the posterior wall of the two open limbs, in a running fashion. Once this is finished we continue opening the third and fourth limbs at the level of the antimesenteric border of the ileum. We then close the posterior wall again of the neobladder with a running 2-0 V-loc suture, in an organized fashion. A total of three lines of continuous sutures are used to finish closing the posterior wall of the neobladder. (Figure 1 A, B)

During all this time, the ileum is stretched and stabilized, facilitating the opening and closure of the posterior wall of the “W” neobladder. Prior to cutting both traction sutures and passing the urethral neobladder neck sutures, a posterior reconstruction of the Denonvillier’s Fascia is performed to bring the urethral stump further into the pelvis (an extra 2 cm more into the pelvis). This reconstruction is performed with a 3-0 V-loc continuous suture.

After closing the neobladder neck sutures, a posterior reconstruction of the urinary tract, following strict anatomy, and adherence to oncological principles, is performed and secured by placing 3-0 vicryl stitches for identification of each limb of the “W”. This keeps the “W” shaped ileum and passing them through bilaterally, closing the “W” neobladder is stabilized. The stabilization of the urethral neobladder neck anastomosis is performed from outside-in, into the neobladder and from inside-out, into the urethral stump. Both needles are passed twice in the neobladder and the urethra, prior to pulling them bilaterally and approximating the neobladder neck to the urethra. Once this is performed, the anastomosis is completed and prior to closing the neobladder anteriorly, a 2-0 french Foley catheter is inserted into the urethra. (Figure 8 A, B)

After closing the bladder neck with the Quill stich, the anterior wall of the neobladder is closed with a 2-0 V-loc in a running fashion. A total of three lines of continuous sutures, a posterior reconstruction of the urethra and closure of the urethral neobladder neck anastomosis is performed with a 2-0 V-loc continuous suture. We then remove the 15 mm assistant port and passed into the ureter and into the isoperistaltic limb, into the neobladder. (Figure 7 A, B)
Best Abstracts: First prize winners
British study bags oncology prize while a multi-centre study from France tops non-oncology

First Prize for the Best Abstract (Oncology) Abstract No: A968-526


Introduction & Objectives
The role of post nephro-ureterectomy treatment for UTUC is unclear. POUT (CRUK/12/027; NC9700075) is a UK led trial that addresses whether adjuvant chemotherapy improves disease free survival (DFS) for patients with histologically confirmed pT2-pT3 No UTUC.

Materials & Methods
Patients (maximum n=345), WHO performance status ≤ 90 days post NU were randomised (1:1) to 4 cycles of gemcitabine-cisplatin (gemcitabine-cisplatin in 40% of patients) or surveillance with chemotherapy given on recurrence if required. Patients had 6 monthly cross sectional imaging and cystoscopy for the first 2 years, then annually to 5 years. Toxicity was assessed by CTCAE v4. The primary endpoint was DFS. The trial was powered to detect a metastasis-related survival (MRS) benefit (HR=0.65; 1-sided alpha=5% power=80% (assessed by EORTC QLQ-C30 and EQ5D)).

Results
Between 31st May 2012 and 5th September 2013, 248 patients were randomized (121 surveillance; 127 chemotherapy) at 57 UK centres. In October 2013, the independent trial oversight committee recommended POUT close to recruitment as data collected thus far (data snapshot 5th September 2013) met the early stopping rule for efficacy. At the time of interim analysis, median follow up was 16.6 months (IQR 75-73.6). Patients had median age 69 years (range 36-88), 38% pT2, 65% pT3; 94% pN0. Grade ≥3 toxicities were reported in 66% chemotherapy patients and 24% surveillance patients. During the treatment period the most common grade ≥3 [a] toxicities in chemotherapy patients were neutropenia 29% [vs. 6% surveillance] and thrombocytopenia 7% [vs. 1%] (surveillance) and 29/153 (chemotherapy) DFS events were reported; unadjusted HR = 0.47 (95% CI: 0.29, 0.74) in favour of chemotherapy (log-rank p = 0.003). Two year DFS was 56% for surveillance (95% CI: 39, 66) and 70% for chemotherapy (95% CI: 58, 79).

Conclusion
Adjuvant chemotherapy is tolerable and improved metastasis-free survival in UTUC. Recruitment to the POUT trial was terminated early because of efficacy favouring the chemotherapy arm; follow up for overall survival continues. POUT is the largest randomised trial in UTUC and its results support the use of adjuvant chemotherapy as a new standard of care.

First Prize for the Best Abstract (Non-Oncology) Abstract No: A968-377


Introduction & Objectives
Management of non-penetrating renal trauma (NPRT) associated with urinary tract rupture (AAST Grade IV-V) is not clearly codified regarding the usefulness of upper tract drainage with stent insertion. The aim of this study was to compare the outcomes of an early upper urinary tract drainage (ED) to a conservative management (CM) after a NPRT with a urinary extravasation (UE) at initial CT-scan assessment.

Materials & Methods
A multicenter retrospective national study was conducted, including all patients treated for renal trauma in 16 centers from 2005 to 2015. Patients who had a UE at the initial CT-assessment delayed phase were considered for inclusion. Penetrating trauma, hemodynamically unstable patients and those who were initially treated with nephrectomy were excluded. Patients were divided into 2 groups: ED defined by drainage of upper urinary tract of the injured kidney within the 48 hours following the admission and CM. The persistence of UE at repeat CT-scan, the need for delayed drainage, length of stay, complications rate and specific death related to the trauma were analyzed.

Results
Among a total of 390 kidney trauma over the studied period 268 patients met the inclusion criteria. The median age was 25 years and 51% (79%) patients were male. Clinicians performed an ED with ureteric stent insertion for 69 patients (26%). A persistent UE was found in 56 patients (39%) of the CM on the repeat CT in mean delay of 6 days. This persistent leak required a delayed ureteric stent insertion in 23 patients (39%). The mean length of staywas longer after ED 21 vs. 14 days after CM (p<0.05). There was no difference in complications rate and death related to the trauma between the 2 groups.

Conclusions
Our results suggest that CM should be considered for the management of renal trauma associated with urinary extravasation at the initial CT-assessment. CM was associated with good outcomes as 83% of the patients didn’t required any drainage of their upper tract and the urinary extravasation at repeat CT was still present for 36% of the patients only. Initial clinical monitoring and repeat CT-scan to re-assess the urine leak might be useful and less invasive than a systematic ED.

Table: Results after NPRT with urinary extravasation

<table>
<thead>
<tr>
<th>Early urinary drainage</th>
<th>Conserve urinary drainage</th>
<th>Delayed drainage</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early urinary drainage</td>
<td>30/41 (73.2%)</td>
<td>37/69 (53.6%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Percutaneous urinary extravasation at ED</td>
<td>3/30 (10%)</td>
<td>3/37 (8.1%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Delayed urinary drainage</td>
<td>2/17 (11.8%)</td>
<td>2/34 (5.9%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Length of stay(days)</td>
<td>27.1±22.2 (22.2)</td>
<td>27.6±22.4 (22.4)</td>
<td>0.92</td>
</tr>
<tr>
<td>Haematoma related to trauma</td>
<td>27/15 (18%)</td>
<td>34/41 (82.9%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Mild complications</td>
<td>17/30 (56.7%)</td>
<td>26/37 (70.3%)</td>
<td>0.22</td>
</tr>
<tr>
<td>Severe complications</td>
<td>3/30 (10%)</td>
<td>3/37 (8.1%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Suicide</td>
<td>1/30 (3.3%)</td>
<td>2/37 (5.4%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Kidney</td>
<td>8/30 (26.7%)</td>
<td>6/37 (16.2%)</td>
<td>0.27</td>
</tr>
</tbody>
</table>

Interactive, Insightful and Independent Education
Learning from Experts in Onco-Urology

Applying for the best prize winners

What is STEPS?
STEPS, or “Sessions To Evaluate Progress” in the management of urological cancers”, is a programme specifically designed for recently specialised uro-oncologists who want to learn directly from world-leading experts in bladder, prostate, renal and testicular cancers. The CME-accredited programme is a fundamental part of the EAU/ESOU strategic partnership with Ipsen. It is founded on our shared commitment to the education of young urologists.

Bringing together a multinational group of medical professionals across several areas of expertise, and with different experiences, allows the fellows to see a variety of new treatment possibilities. It can highlight the pitfalls and solutions provided by diverse approaches. It also opens the door to creating international ties among medical practitioners, and a networking opportunity that can prove invaluable for the careers of young clinicians.

“STEPS connects younger urologists from different countries – it’s very interactive with lots of new information and data discussed” STEPS fellow 2018

Todate, 20 different internationally recognised experts, supported by the ESOU Board, have inspired 138 fellows from 29 countries – and our objective is to continue supporting STEPS to help improve the management of all patients with urological cancers.

Who should apply?
Recently specialised clinicians with a firm interest in the management of urological cancers, who:
- Can demonstrate support from their Head of Department
- Are keen to participate in ESOU and EAU programs
- Understand and speak English fluently

“Within STEPS I really like the enthusiasm of the delegates and the interaction I can have with them as an expert” Peter Mulders, STEPS mentor 2018

Find out more about STEPS from the ESOU website: http://uroweb.org/section/esou/information/
ESU Masterclasses: Designed and aimed to educate
Participants’ feedback is crucial to continually improve the masterclass format

Progress is inevitable; what we know now as urologists in terms of research, technologies and procedures will eventually need an upgrade. We need to grow alongside this advancement, for our patients and for our practice. Hence, the inception of the European School of Urology (ESU).

ESU’s primary goal is to increase what we know and to broaden our skills through various activities designed to meet our educational needs while taking our challenging schedules into account. The high-level ESU Masterclasses are one of the ESU’s most prominent activities.

Why choose the masterclass format?
Although ESU Courses offer frontline lectures, the ESU Masterclasses, in collaboration with the EAU sections of the EAU, are created to be more in-depth. These masterclasses cover urolithiasis, non-muscle-invasive bladder cancer, to focal therapy, among other topics. The ESU Masterclass format is a consolidation of cutting-edge lectures, typical or sometimes challenging clinical cases, and informative semi-live and live surgeries. The programme also feature riveting discussions and hands-on demonstrations.

Even the setting is conducive to learning. Each Masterclass has a defined number of participants – small enough for optimal learning for good, solid interactions and large enough for productive brainstorming. Its commendable faculty is comprised of top experts who provide the best and the latest updates in their respective fields.

ESU Masterclasses
At present, there are seven Masterclasses which are as follows:

- **ESU-ESUT Masterclass on Operative management of Benign Prostatic Obstruction** focuses on relevant, minimally-invasive alternatives for BPH treatment;
- **ESU Masterclass on Female and Functional Reconstructive Urology** covers the management of functional disorders such as lower urinary tract diseases, and other diseases that affect the pelvic floor and related organs;
- **ESU-ESUT Masterclass on Focal therapy for localised prostate cancer** provides a comprehensive review of the rationale for FT and the modalities of patients selection;
- **ESU-ESUT Masterclass on Lasers in Urology** offers the mastery of basic concepts of each laser treatment, identification of suitable candidates per approach, and management of complications;
- **ESU-ESUT Masterclass on Non-Muscle-Invasive Bladder Cancer** delivers modern techniques of transurethral surgery from en-bloc resection, new imaging technologies to new generation lasers.
- **ESU-Weill Cornell Masterclass in General urology** is comprised of theoretical courses on stone and cancer management, conservative treatment of lithiasis, and extracorporeal and interventional management;
- **ESU-ESTU Masterclass on Kidney Transplant** is the latest installment to the masterclass series designed to offer high-level theoretical and practical training, and detailed updates on kidney transplantation.

Benefits for the participants
Completion of an ESU Masterclass means improved proficiencies of participants in terms of practical diagnosis, specific techniques, decision-making and management.

The feedback received from each Masterclass continue to show overall satisfaction from participants. They indicated noticeable improvements with their skills and a boost in their clinical practice after incorporating take-home messages and concepts.

Up-to-date, practical tips and tricks they have acquired from the Masterclasses greatly benefited their patients.

A pre-test and post-test are implemented to boost quality and to evaluate the efficacy of the masterclasses and the faculty (what works and what needs improvement), and to gauge the knowledge of participants.

Plans
There is a steady increase in the demand for ESU Masterclasses since its establishment and up to this day. This is truly encouraging. Through these Masterclasses, participants are given the opportunity to access the best resources in urology. The ESU aims to expand starting next year the number of topics to meet increasing demand.

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Surgery in Motion School presents you with a selection of the best Live Surgeries from EAU18

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With top notch videos of urological procedures
By the best surgeons in the world

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Your guide to video-based urological training
Low-intensity ESWT
An Asian tsunami breaking the horizon

Dr. Colie Tan
Dept. of Urology
Rhosock Pratt Hospital
Singapore (SG)

The use of Low-intensity shockwave therapy (LiESWT) has been making waves in Asia. In the short span of the last few years, we see a rising trend in the use of LiESWT in Asia as more machines and available models are acquired by many urology practices.

We see an increasing confidence in patient outcomes encouraging more Asian urologists to embrace and include Extracorporeal Shockwave Therapy (ESWT) in the treatment of erectile dysfunction (ED) in Asian countries.

The use of ESWT has been a popular treatment for patients with Erectile Dysfunction (ED) and Chronic Pelvic Pain Syndrome (CPPS).

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Shared decision-making in prostate cancer care

Encouraging patient’s role in decision-making or ensuring their preferred level of involvement?

Imagine you informed Jack, a patient with localized prostate cancer, about his treatment options. After you discussed the benefits and side-effects of the options, Jack asks you to make the treatment decision. What do you do? Do you encourage Jack to be actively involved in treatment decision-making? Or do you suggest a treatment to ensure that the patient plays the decision-making role he prefers?

If you consult the literature about this dilemma, you will find conflicting results. Several studies suggest that patients who prefer either more or less involvement in decision-making than they actually experience have worse decision- and health-related outcomes than those for whom their preferred and experienced role match1. But other studies concluded that patients who are actively engaged in their decisions, regardless of role preferences, have better care experiences2.

To examine which of these strategies resulted in the most positive outcomes in a sample of patients with prostate cancer, we performed a prospective, multi-centre, observational study. We investigated whether active involvement in decision-making regardless of role preferences or concordance between preferred and experienced role is the strongest predictor of more favourable patient-reported outcomes. About 450 patients with localized prostate cancer answered questions about their preferred role in decision-making (before treatment) and about the role they experienced (three months after treatment).

The large majority of patients (89%, n=403) preferred active involvement in decision-making, with the remaining 11% (n=56) indicating a preference for passive involvement. A similar distribution was observed for the experienced role in decision-making (active involvement=90%, n=393; versus 10% passive involvement, n=66).

Most patients (n=376, 83%) experienced a role in decision-making that matched their preferred role. However, more than half (69%) of the patients who preferred passive involvement reported having experienced active involvement (preferred less involvement than experienced, n=74). Conversely, of those who preferred active involvement, 11% experienced passive involvement (preferred more involvement than experienced, n=46).

“These findings indicate that patients with localized prostate cancer who indicated that they had been actively involved in treatment decision-making were better informed about their cancer and its treatment, experienced less uncertainty about the treatment decision...”

Active involvement was associated significantly with more prostate cancer (PC) knowledge (Cohen’s $d=0.35$), less decisional conflict ($d=0.52$), and less decisional regret ($d=0.34$). Role concordance was not associated significantly with PC knowledge or decisional regret. However, we did observe an association with decisional conflict ($d=0.41$), indicating that patients who preferred more involvement than they experienced had more decisional conflict when compared to those who initially preferred less involvement or those who experienced a match between their preferred and experienced role.

These findings indicate that patients with localized prostate cancer who indicated that they had been actively involved in treatment decision-making were better informed about their cancer and its treatment, experienced less uncertainty about the treatment-decision, and had less regret about the chosen treatment, compared to patients who reported having experienced passive involvement. Our results do not support previous studies that reported that a match between decision-making preferences and experienced role results in more favourable health care experienced.

In summary, while it may seem desirable to tailor the patients’ role in decision-making to their initial preference, and particularly to a preference for deferring to the advice of the clinician, this does not result in less decisional conflict or regret. Rather, in patients with localized prostate cancer, our results support a strategy of shared decision-making to increase patients’ knowledge about their disease and its treatment, their sense of certainty about the treatment decision, and their satisfaction with the chosen treatment.

Study Members: M.A. Van Stam, MSc; A.H. Pieters, PhD; H.G. Van Der Poel, PhD, M.D.; J.I.H.R. Bosch, PhD, M.D.; C.N. Tiliere, MANP; S. Horenbals, PhD, M.D.; N.K. Aaronson, PhD

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