1 Towards organised prostate cancer testing in Sweden

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Introduction & Objectives: The European Randomized study of Screening for Prostate Cancer (ERSPC) has previously demonstrated that prostate-specific antigen (PSA) screening decreases prostate cancer (PCa) mortality with and increasing benefit over time. At 16 y follow-up, PCa mortality reduction in those who attended at least one screening round was 25% and in the Swedish branch of ERSPC 35% at 18Y follow-up time (Hugosson et al Eur RUol 2019, Hugosson et al Scand J Urol 2018). Attempts to reduce overdiagnosis and overtreatment in Sweden have been presented by the STHLM3 study group by introducing a protein and genetic biomarker test (Grönberg et al Lancet Oncol 2015) and recently in combination with MRI (Ekelund et al NEJM 2021, Nordström et al Lancet Oncol 2021). In 2018, the Swedish National Board of Health and Welfare recommended against screening for PCa with a PSA test, but they recommended Regional Cancer Centers to work on organised PCa testing. The Swedish guidelines for prostate cancer recommend MRI prior to prostate biopsy and to include PSA density (PSA-D) with a cut-off at 0.15 before decision on biopsy but biomarkers like four kallikrein score, STHLM3, PHI, PCA3, Select MDx and Confirm MDx are not recommended as a clinical routine.

Materials & Methods: Based on a political decision in Southern Sweden, a program for organized PCA testing (OPT) started with a pilot study in 2020 of 1000 randomly selected men at age 50, 56 and 62. All men between 50 and 74 years will be invited the coming years. An algorithm is based on recommendations in the national guidelines including MRI and PSA density and a fully digitalized system has been developed in collaboration with the Western region of Sweden. Based on the level of the PSA test, men will get an automated reply to never take another PSA test, to repeat the test at certain time intervals or to continue with further examination based on the algorithm.

Results: The first results from the pilot test indicate only minor adjustment needed in the digitalised system. As expected, 42% of men went for a PSA test, despite the Covid-19 pandemic. The number of men with elevated PSA level, and the proportion subsequently diagnosed with prostate cancer was also close to estimation. The introduction of OPT in Sweden is about to start in several regions.

Conclusions: Based on results from ongoing studies, organised testing for prostate cancer in Sweden is likely to be implemented but the best algorithm has yet to be identified and the timing is unclear. The use of different algorithms will make it possible to find a way towards an optimal system for early detection of potentially harmful prostate cancer. Artificial intelligence (AI) and big data can play a important role in the interpretation of MRI, incorporation of biomarkers and to identify the best algorithm. A key question is to find the optimal approach for biopsies, targeted versus systematic.

2

Focal high-intensity focused ultrasound vs. active surveillance for ISUP grade 1 prostate cancer: Medium-term results of a prospective matched-pair comparison

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Introduction & Objectives: Focal therapy (FT) for localized prostate cancer (PCa) aims to reduce side effects from radical whole-gland treatments while maintaining the oncologic benefits of those treatments. FT is gaining ground among PCa clinicians and patients, and the number of treated men and available studies are growing rapidly. Nonetheless, current guideline panels do not recognize FT as a standard option and recommend that its use be limited to clinical trials and prospective registries. We investigated whether fHIFU yields oncologic advantages over Active Surveillance (AS) for low-risk PCa.

Materials & Methods: We included 2 prospective series of 132 (fHIFU) and 421 (AS) consecutive patients diagnosed with ISUP 1 PCa between 2008 and 2018. The primary outcomes were (1) freedom from whole-gland or ADT treatment and (2) time to whole-gland or ADT treatment. Secondary outcomes included (1) freedom from any treatment, comprising radical, repeat focal, or palliative (ADT) treatment; (2) time to any treatment; (3) systemic progression free survival and (4) overall survival (OS).

Results: Median fHIFU follow-up was 50 months (interquartile range, 29-84 months). Among matched variables, no major differences were recorded except for AS having more suspicious digital rectal examination findings (P = 0.0074) and recent enrollment year (P =0.0005). Five-year survival from RT or ADT was higher for the fHIFU cohort (67.4% vs 53.8%; P = .0158). Time to treatment was approximately 10 months shorter for AS than for fHIFU (time to RT, P =0.0363; time to RT or ADT, P =0.0156; time to any treatment, P =0.0319). No differences were found in any-TFS (fHIFU, 61.4% vs AS, 53.8%; P =0.2635), OS (fHIFU, 97% vs AS, 97%; P =0.9237), or metastasis (n=0 in fHIFU and n = 2 in AS; P = 0.4981). Major complications were rare (n = 4), although 36.4% of men experienced complications. No relevant changes were noted in continence (P =0.3949) and erectile function (P =0.0098).

Conclusions: At a medium-term follow-up fHIFU for mainly low-risk PCa (ISUP grade 1) is safe, may decrease radical treatment or ADT need and allow longer time to treatment compared to AS. Nonetheless, no advantages are seen in PCa progression and/or death (OS).

3 Clinical implementation of pre-biopsy magnetic resonance imaging pathways for the diagnosis of prostate cancer

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Introduction & Objectives: To assess the outcomes of pre-biopsy magnetic resonance imaging (MRI) pathways, as a tool in biopsy-naïve men with suspicion of prostate cancer, in routine clinical practice. Secondary outcomes included a comparison of transrectal MRI-directed biopsy (TR-MRDB) and transperineal (TP)-MRDB in men with suspicious MRI.

Materials & Methods: We retrospectively assessed a two-centre cohort of consecutive biopsy-naïve men with suspicion of prostate cancer who underwent a Prostate Imaging-Reporting and Data System version 2 (PI-RADS v2) compliant pre-biopsy MRI in a single, high-volume centre between 2015 and 2019 (Centre 1). Men with suspicious MRI scans underwent TR-MRDB in Centre 1 and TP-MRDB with additional random biopsies (RB) in Centre 2. The MRI and histopathology were assessed in the same institution (Centre 1). Outcomes included: (i) overall detection rates of Grade Group (GG) 1, GG ≥2, and GG ≥3 cancer in men with suspicious MRI; (ii) Biopsy-avoidance due to non-suspicious MRI; and (iii) Cancer detection rates and biopsy-related complications between TR- and TP-MRDB. To reduce confounding bias for MRDB comparisons, inverse probability weighting (IPW) was performed for age, digital rectal examination, prostate-specific antigen (PSA), prostate volume, PSA density, and PI-RADS category.

Results: Of the 2597 men included, the overall GG 1, GG ≥2, and GG ≥3 prevalence was 8% (210/2597), 27% (697/2597), and 15% (396/2597), respectively. Biopsy was avoided in 57% (1488/2597) of men. After IPW, the GG 1, GG ≥2 and GG ≥3 detection rates after TR- and TP-MRDB were comparable at 24%, 57%, and 32%; and 18%, 64%, and 38%, respectively; with mean differences of -5.7% (95% confidence interval [CI] -13% to 1.4%), 6.1% (95% CI -2.1% to 14%), and 5.7% (95% CI -1.7% to 13%). Complications were similar in TR-MRDB (0.50%) and TP-MRDB with RB (0.62%; mean difference 0.11%, 95% CI -0.87% to 1.1%).

Conclusions: This high-volume, two-centre study shows pre-biopsy MRI as a decision tool is implementable in daily clinical practice. Compared to recent trials, a substantially higher biopsy avoidance rate was achieved without compromising GG ≥2/GG ≥3 detection and coinciding with lower over detection rates of GG 1 cancer. Prostate cancer detection and complication rates were comparable for TR- and TP-MRDB.

4 The importance of lesion conspicuity in prostate cancer risk assessment

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Introduction & Objectives: Prostate cancer risk stratification continues to be an outlier, in that no consideration of prostate cancer volume is incorporated into our risk models - nor is it applied to our TNM classification. Another anomaly, again exclusive to prostate cancer, is our habit of declaring 'invisible' disease 'significant'. This does not occur in any other solid organ cancer. And most are considerably more lethal than prostate cancer.

Materials & Methods: Data from numerous sources (clinical trials; molecular analyses; case-matched patient studies; modelling) will be presented to argue that MRI conspicuity is an important tumour-attribute that should be incorporated into future risk models.

Results: In our published series of MRI-directed active surveillance, we show the importance of disease conspicuity (the presence of a visible MRI-lesion) in predicting the risk of disease progression. For instance, non-visible 3 plus 4 seems to behave like visible Gleason 3 plus 3. In our detailed analyses of the world's best-characterized research cohorts (such as PROMIS and PICTURE studies) that incorporate both imaging and detailed pathological sampling (>1 core per cc of tissue), we are able to show the relationship between cancer conspicuity and the underlying tissue microstructure and molecular landscape.

Conclusions: The hypothesis that MRI-lesion conspicuity may be among the most important tumour attributes will be presented for discussion.

5 Risk estimation of metastatic recurrence after prostatectomy: A model using preoperative MRI and targeted biopsy

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Introduction & Objectives: Prostate cancer metastatic risk is correlated to its volume and grade. These parameters are now best estimated preoperatively with MRI and MRI-guided biopsy. To estimate the risk of metastatic recurrence after radical prostatectomy (RP) in our model versus conventional clinical EAU classification. Secondary objective is biochemical recurrence (BCR).

Materials & Methods: Retrospective study of cohort of 713 patients having underdone, MRI-guided biopsies and RP between 2009 and 2018. The preoperative variables included PSA, cT-stage, tumor volume (TV) based on the lesion's largest diameter at MRI, the percentage of Gleason Pattern 4/5 (%GP4/5) at MRI-guided biopsy and volume of GP4/5 (VolGP4/5) calculated as TV x %GP4/5. The variables' ability to predict recurrence was determined in univariable and multivariable Fine-and-Gray models, according to the Akaike criteria information (AIC) and Harrell's C-index.

Results: Overall, 176 (25%), 430 (60%) and 107 (15%) had low, intermediate and high-risk disease according to the EAU classification. During a median follow-up period of 57 months [32-91], we observed 132 (18.5%) cases of BCR and 48 (6.7%) of metastatic recurrence among the 713 patients. During the follow-up period, metastatic recurrence was observed in 48 patients with 5-year probability of 5.6% [95%CI 3.9-7.7]. VolGP4/5 (categories: <0.5; 0.5-1.0; 1.01-3.2; >3.2 ml) was the parameter with the lowest AIC and the highest C-index for metastatic recurrence 0.82 [95%CI 0.76-0.88] and for BCR 0.73 [95%CI 0.68-0.78]. In a multivariable model that included %GP4/5 and TV, C-index was 0.86 [95%CI 0.79-0.91] for metastatic recurrence and 0.77 [0.72-0.82] for BCR. Same results for EAU classification were 0.74 [0.67-0.80] and 0.67 [0.63-0.72] respectively. Limitations were in short follow-up and absence of PSMA-PET/CT availability.

Conclusions: We developed a preoperative risk tool integrating the volume of GP4/5 based on MRI and MRI-guided biopsies to predict metastatic recurrence after RP. Our model showed higher accuracy over conventional clinical risk models. These findings might enable physicians to provide more personalized patient care.

6

Intraoperative NeuroSAFE in robot-assisted radical prostatectomy increases nerve-sparing surgery without affecting oncological outcome

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Introduction & Objectives: Radical prostatectomy (RP) is frequently complicated by erectile dysfunction and urinary incontinence. Nerve-sparing surgery (NSS) improves functional outcomes, but could compromise oncological outcome. This study validates the impact of neurovascular structure-adjacent frozen-section examination (NeuroSAFE) on oncologic and clinical outcome.

Materials & Methods: 1756 prostate cancer patients underwent robot-assisted RP, of whom 959 (54.6%) with NeuroSAFE (2019-2020), and 797 (45.4%) without (historical control cohort 2016-18). Clinical-pathological parameters and biochemical outcome were analysed.

Results: Men in the NeuroSAFE cohort had higher tumour grade (p<0.001) and clinical stage (p<0.001) than in the control cohort. NeuroSAFE enabled more frequent NSS in both pT2 (92.8% versus 75.9%; p<0.001) and pT3 disease (82.8% versus 54.8%; p<0.001). In adjusted analysis, NeuroSAFE resulted in more frequent uni- (odds ratio (OR) 3.9; 95% confidence interval (CI) 2.9-5.3; p<0.001) and bilateral (OR 5.2; 95%CI 3.9-7.0; p<0.001) NSS. While the positive surgical margin (PSM) rate decreased from 50.7% to 42.1% in pT3 stage (p=0.031), NeuroSAFE was not an independent predictor for PSM status (OR 0.85; 95% CI 0.68-1.06; p=0.151) in the entire cohort. Patients who underwent NeuroSAFE had improved biochemical recurrence free survival (HR 0.62; 95% CI 0.45-0.84; p=0.002). In 272 men, the PROMS showed that 91.5% of patients in the NeuroSAFE cohort used 0-1 pads after 12 months. A Dutch nationwide study (ProZIB) in 2015-2016 showed that 79% of the men used 0-1 pads 12 months after RP.

Conclusions: NeuroSAFE enables more unilateral and bilateral NSS without negatively affecting surgical margin status and biochemical recurrence. Twelve months after RP the NeuroSAFE cohort showed a better continence rate as compared to the ProZIB data.

7 Tissue engineering in urological surgery

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Introduction & Objectives: Tissue engineering/bioengineering is a very topical issue as applied to the bladder and urethra, and there are no products that are widely accepted at present as being appropriate for introduction into clinical practice. In this presentation, I will review our own experience with the development of tissue-engineered material for the treatment of stress incontinence and review the evidence for the use of bioengineered oral mucosa based on our past experience and current work which is underway. This presentation will provide a global overview of the subject of tissue engineering. In particular, I will review the evidence for tissue engineering as applied to the lower urinary tract. Following the initial work that we carried out on providing a bioengineered substitute for oral mucosa, a subsequent project using mucocele has been produced with limited license for use in Germany. The initial data relating to this material, although reported as potentially encouraging, on close review is not compelling and this will be discussed in detail. The use of biomaterials, in particular the use of polypropylene for stress urinary incontinence has proven to be a very contentious subject in recent years. For the last 15 years we have been working on developing alternative materials which could replace polypropylene which was never adequately studied prior to introduction and where a number of problems were encountered with the use of this material when used for abdominal hernia repair.

Conclusions: Bioengineering (tissue engineering) is a subject which requires close interdisciplinary working between clinicians and scientists. The potential for this is enormous. At this time, contemporary evidence for the use of these materials has to be treated with caution until comprehensive pre-clinical and clinical studies have been carried out. It is important that we learn the lessons from the past and do not make the same mistakes for the future.

8 Clinical application of circulating microRNAs in urological malignancies

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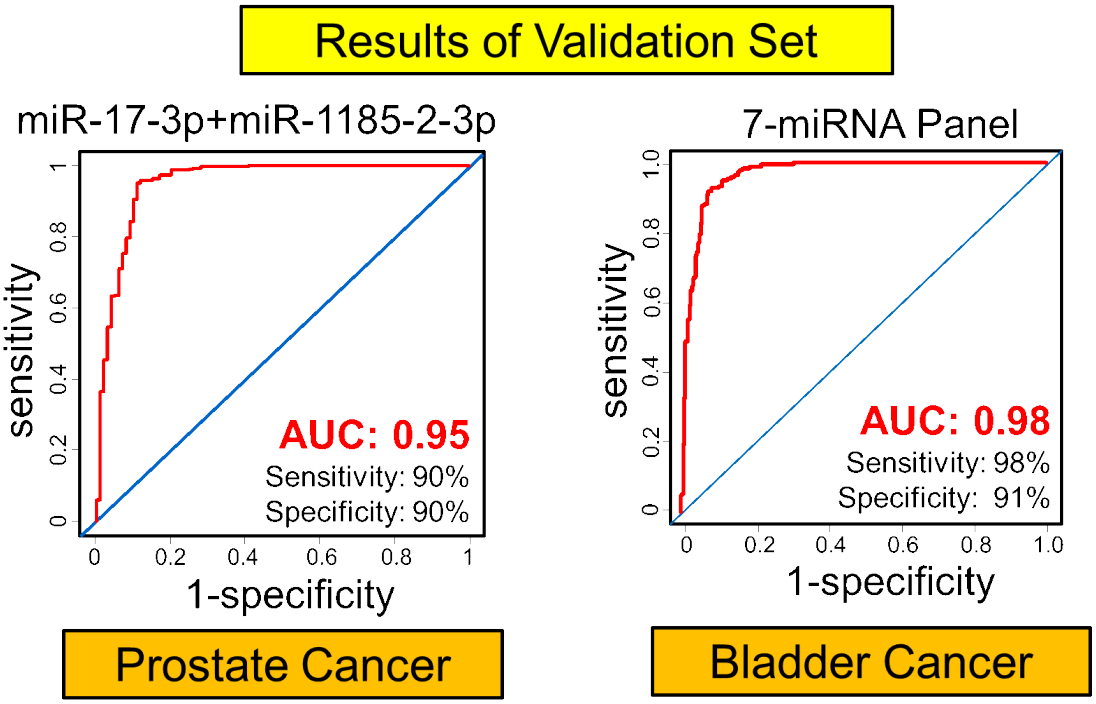
Introduction & Objectives: Early detection of cancer is crucial for its ultimate control and prevention of malignant progression. In Japan, a nationwide project was conducted between 2014 and 2019 to develop novel cancer detection tools using serum microRNAs (miRNAs). Using the National Cancer Center Biobank, we collected more than 10,000 serum samples from patients with urological cancers. Subsequently, comprehensive miRNA microarray analyses were conducted for all these samples. This serum miRNA database provides insights regarding miRNA biomarker candidates. In this presentation, I would like to share the summary of the project.

Materials & Methods: In prostate cancer, we investigated the potential of serum miRNAs as an accurate diagnostic tool in patients with suspected malignancy. Serum samples from 809 patients with known prostate cancer and 241 patients with negative prostate biopsies were obtained from that Biobank. Forty-one healthy control samples were obtained from two hospitals in Japan. Comprehensive microarray analysis was performed for all samples. Samples were randomly divided into three sets. Candidate miRNAs for prostate cancer detection were identified in the discovery set. A diagnostic model was constructed using combinations of candidate miRNAs in the training set. The performance of the diagnostic model was evaluated in the validation set.

Results: In the discovery set, 18 candidate miRNAs were identified. A robust diagnostic model was constructed using a combination of two miRNAs (miR-17-3p and miR-1185-2-3p) in the training set. A high diagnostic performance, with a sensitivity of 0.90 and a specificity of 0.90, was achieved in the validation set regardless of the Gleason score or clinical TNM stage. In another exploratory analysis for bladder cancer, we could also establish a mathematical model with a seven-miRNA panel, achieving a decent performance (AUC: 0.98; sensitivity: 0.98; specificity: 0.91). The diagnostic accuracy was high, regardless of stage and grade of bladder cancer.



Conclusions: Through our project, we found that serum miRNA analysis was highly accurate in discriminating between cancer and non-cancer samples. We believe that miRNA-based test could drastically change the landscape of urological cancer diagnostic strategies in the near future. In this presentation, I also would like to introduce our current prospective study and discuss the perspective of liquid biopsy in urological cancer management.

9

Role of prior nephrectomy for synchronous metastatic Renal Cell Carcinoma (mRCC) on efficacy in patients treated with Avelumab + Axitinib (A + Ax) or Sunitinib (S): Results from JAVELIN Renal 101

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Introduction & Objectives: Cytoreductive nephrectomy (neph) remains controversial in the management of mRCC; the role of neph before immune checkpoint inhibitor treatment is unknown. In this follow-up analysis of the phase 3 JAVELIN Renal 101 trial (NCT02684006), we assessed the role of prior neph in patients (pts) with mRCC with synchronous metastases at diagnosis treated with A + Ax or S.

Materials & Methods: Efficacy outcomes were assessed from the third interim analysis in pts with mRCC who had M1 disease at diagnosis and had prior neph or no neph in the A + Ax and S arms. Multivariate Cox regression analyses were used to assess hazard ratios (HRs) for overall survival (OS) and progression-free survival (PFS; investigator assessment per RECIST 1.1). Logistic regression was used to obtain odds ratios for objective response (OR; investigator assessment per RECIST 1.1).

Results: 412 of 886 pts in JAVELIN Renal 101 had M1 disease at diagnosis, of which 126 (A + Ax) and 147 (S) had prior neph, and 72 (A + Ax) and 67 (S) had no neph. A higher proportion of pts in the no neph vs prior neph group were older (42% vs 32% were ≥65 years), had impaired PS (ECOG PS 1, 54% vs 40%), and had poor prognosis (40% vs 16% by IMDC criteria); fewer pts had PD-L1+ tumors (40% vs 77%). To assess the impact of prior neph, these parameters were adjusted in the multivariate model. Post hoc analyses showed that in the A + Ax arm, observed PFS and OS were numerically improved in the prior neph vs no neph group (PFS, HR [95% CI] 0.785 [0.531-1.161]; OS, HR 0.593 [0.379-0.930]); however, no differences were observed in the S arm (PFS, HR 1.146 [0.773-1.699]; OS, HR 0.859 [0.551-1.341]. Confirmed OR was numerically higher in pts with neph vs no neph in the A + Ax arm (odds ratio 2.669 [1.315-5.414]) but not in the S arm (odds ratio 2.018 [0.824-4.941]).

Conclusions: Pts who presented with M1 disease at the time of diagnosis and had undergone prior neph had numerically improved efficacy outcomes vs no neph with A + Ax but not with S.

10

Real-World data of patients with synchronous metastatic renal cell carcinoma treated with nivolumab and ipilimumab and the primary tumour in place

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Introduction & Objectives: Following CARMENA and SURTIME, upfront cytoreductive nephrectomy (CN) is no longer standard of care. Intermediate and poor risk patients receive systemic therapy with the primary tumour (PT) in place with the option to perform deferred CN in responding patients. This paradigm continues in the era of immune checkpoint inhibitor combination in frontline for metastatic renal cell carcinoma (mRCC). We assessed the safety and efficacy of this approach in a real-world setting.

Materials & Methods: A retrospective clinical audit from 3 institutional datasets of patients treated with first-line Nivolumab and Ipilimumab (N+I) combination and the primary tumour (PT) in place was performed. Patients and tumour characteristics, International Metastatic RCC Database Consortium (IMDC) risk, overall response rate (ORR) in the PT and metastatic sites according to RECIST 1.1, time to response (TTR) of the PT, PT- and immune related- (ir) adverse events (AE), deferred CN rate, progression free- (PFS) and overall survival (OS) were analysed.

Results: We identified 71 primary mRCC patients (42.3% IMDC poor risk; 43.6% > 3 metastatic sites). Baseline mean primary diameter was 9.3 cm. Of 69 patients with at least 1 follow-up CT scan, 23 (33.3%) had a partial response (PR) of the primary after a median of 4.8 months which was associated with a 91.3 % overall response rate at metastatic sites (MS) and absence of progressive disease, irrespective of IMDC risk. The complete response (CR) rate at MS (n=7 (10.1%)) is similar to the CR rate in the pivotal front-line registration trial CheckMate 214. Thirteen deferred CN were performed (18.8%) after a median of 13 months, rendering 4 patients disease-free. Only 4.3% of primaries progressed, grade 3-4 immune-related adverse events occurred in 31.9%. Irrespective of IMDC risk, patients with a PR in the primary had a 89% 1-year overall survival rate versus 67% in those without (p=0.012).

Conclusions: A partial response in the primary tumour following immune checkpoint inhibitor combination therapy with nivolumab and ipilimumab in patients with metastatic kidney cancer is associated with superior response at metastatic sites and survival irrespective of IMDC risk.

11 Perfusion areas-based 3D virtual models: the “rainbow kidney” as a new tool to optimize the clamping strategy during robot-assisted partial nephrectomy

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Introduction & Objectives: Selective clamping is nowadays under investigation among the strategies to optimize functional outcomes after nephron sparing surgery (NSS). As already demonstrated, the planning and intraoperative assistance of 3D virtual models (3DVM) resulted in a higher rate of selective clampings, leading to optimize the renal function of the operated kidney. However, in some cases the strategy planned with 3DVM fails intraoperatively, forcing the surgeon to switch to global clamping. This issue might be related to the empirical definition of vascular regions boundaries inside the kidney, based on the direction of arterial branches entering the renal sinus. Our aim was to develop new 3DVMs considering their different perfusion areas instead of vascular regions empirically estimated, to evaluate their accuracy intraoperatively and to assess if there are factors influencing the tumor location relative to these perfusion areas.

Materials & Methods: We implemented our 3DVMs together with the Voronoi diagram, an Euclidean distance-based mathematical tool used to calculate vascular dominant regions in other organs. A perfusion areas-based 3DVM was built for all the renal masses scheduled for NSS from 2019 to 2021. On its basis a selective clamping limited to the peritumoral area was performed when feasible. Near-infrared-fluorescence imaging (NIRF) was used to confirm the regions maintaining vascularization. To demonstrate the concordance between virtual and real areas, an automatic superimposition of the 3DVMs over the real anatomy was performed, comparing their extent on bidimensional images via k-Cohen test. At last, each lesion location was evaluated in relation to the number of its crossing perfused areas and a multivariate regression model (MLR) was fitted to assess potentially related preoperative factors.

Results: 48 patients were prospectively enrolled in the study. In 100% of them the renal pedicle management strategy was conducted as preoperatively planned. 68.7% of them underwent selective clamping. The concordance between the NIRF enhanced areas and their corresponding 3DVM areas was confirmed (k=0.94). Distribution of perfused areas crossing the tumor was as follows: 16.6%, 29.1%, 43.7%, 8.3%, 2.4% for 1, 2, 3, 4 and 5 crossing areas respectively. At MLR the clear cell histotype was the only factor related to a lower number (<3) of perfusion areas crossing the tumor, while tumors larger in size were related to a higher number (>3) of perfusion areas.

Conclusions: The implementation of mathematical algorithms to 3DVMs allows a precise estimation of the perfusion area of each arterial branch feeding the organ, leading to perform an effective pedicle management. Moreover, with this new technology it is possible to open new perspectives on the knowledge of renal tumors features, considering their growth in relation to their surrounding environment.

12

Improved long-term outcome of patients with non-muscle invasive, low and medium risk bladder cancer between 1997 and 2014; A Swedish population-based study

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Introduction & Objectives: The most common form of urinary bladder cancer is the low and intermediate risk of stage Ta. This patient group has a high recurrence rate but progression is rare. The aim of this study was to investigate recurrence and survival in a large population-based setting with respect to possible prognostic factors and during different time periods.

Materials & Methods: BladderBaSe is a database which links information from the Swedish National Register of Urinary Bladder Cancer (SNRUBC) with a number of national health care and demographic registers through the use of the personal identification numbers. In 1997-2014 in Sweden, a total of 26808 patients were diagnosed with NMIBC, of whom 16599 were low (G1) and intermediate (G2) risk Ta cancer. Times to recurrence and cancer specific death were analyzed with regard to differences in age, gender, grade, region and hospital type. For temporal analysis we used 3, six-year periods.

Results: The mean age was 70 years and 74 % were males. Low risk according to grade constituted 56 % while 44% had intermediate risk. Recurrence rate was 52% overall for the median follow-up time of 63 months and main risk factor was higher risk category. The rate was similar between the first two time periods but became substantial lower in the most recent period. Five percentage died of the disease and risk category was the main prognostic variable.

Conclusions: Risk of recurrence decreased in the last time period. Risk category based on grade was the most important prognosticator for outcome.

13 Outcomes of EAU affiliated live surgical events from 2015 to 2020: An overview from the EAU live surgery committee

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Introduction & Objectives: The EAU live surgery guidelines were established in 2014 and our objective was to look at the outcomes of EAU affiliated live surgical events, to check if these were being implemented.

Materials & Methods: Between January 2015 to January 2020, patients from EAU affiliated LSEs were included for all surgical procedures carried out. All these events were pre-evaluated by the EAU Live Surgery committee and met the criteria for an EAU-LSE, with outcomes recorded and submitted to the registry. Data was collected for type of procedure, intraoperative, short and long-term complications.

Results: A total of 246 procedures were performed across 18 live surgery events and ranged from 19-74 procedures/year. It included 109 (44.3%) robot assisted procedures, 21 (8.5%) laparoscopic procedures, 10 (4%) transurethral bladder procedure, 11 (4.4%) prostate enucleation procedure, 72 (29.2%) endourological procedures, and 23(9.3%) andrology/reconstruction procedures. A total of 77 different surgical techniques or variations for 55 different types of surgeries were performed as LSE over the last 5 years. A total of 44 (17.8%) short-term complications and 9 (11.3%) long-term complications were seen, of which Clavien III/IV complications were seen in 5.2% and 7.5% over a short and long term follow-up respectively.

Conclusions: The 5-year outcomes of EAU live surgery events show that they are safe and follow previous guidelines set by the panel. It seems likely that a fine balance of patient safety and educational value might lie in LSEs being performed by local surgeons in their parent hospital with patients and staff they know, and technological advances will make live streaming a seamless process.

14 Intrarenal backflow during endoluminal irrigation visualized by dynamic Gadolinium-enhanced MRI

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Introduction & Objectives: Ureteroscopic procedures (URS) are currently increasing dramatically. Although URS is generally considered safe, serious complications, including sepsis, do occur. It is assumed that septic complications are due to intrarenal backflow (IRB) with leakage of fluid into the venous and lymphatic system as a result of irrigation-induced increased intrarenal pressure (IRP). The mechanism of IRB and at what pressure levels it occurs is still unknown. We evaluated a new method to document and visualize IRB as a function of IRP and time in a pig model.

Materials & Methods: The animal protocol was approved by The National Animal Experiments Inspectorate (Copenhagen, Denmark). The ureteropelvic junction was occluded with a balloon-catheter through which IRP was measured in 45-kg female pigs. Irrigation with a Gadolinium/saline solution was performed at increased IRP intervals. MRI including T1-maps of the kidneys was performed with 5-minute intervals.

Results: MRI showed backflow of Gadolinium into the kidney cortex in all cases (Fig. 1). The measured baseline pressure before initiation of irrigation was 9.6 mmHg (range: 5-13 mmHg). The mean time to first visual damage was 15 minutes (range: 5-25 min) and the mean registered pressure at first visual damage was only 21 mmHg (range: 16-25 mmHg). Uniformly, for all cases MR showed early signs of intrarenal backflow into the cortex of the kidneys clearly visualised as pyramid shaped changes first appearing in the upper and lower poles. Subsequently, similar shaped changes appeared in all other regions until large areas were affected at the end of MR scan.

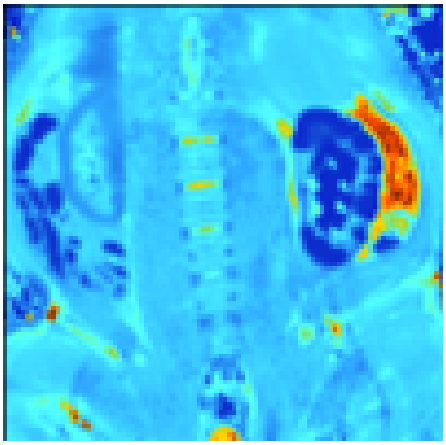

Fig. 1: Gadolinium irrigation in the left kidney showing intrarenal backflow and perirenal fluid accumulation

Conclusions: Gadolinium enhanced MRI provided new detailed information about IRB. IRB takes place at even very low pressures, and the level of IRB was documented to be a function of both IRP and time. This emphasizes the importance of keeping IRP and OR time low during ureteroscopy.

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Report of the First in Man Study of a novel, minimally invasive treatment for Lower Urinary Tract Symptoms (LUTS) secondary to Benign Prostatic Hyperplasia (BPH)

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Introduction & Objectives: The ProVee Expander is a nitinol implant designed to be deployed between the bladder neck and the verumontanum to mechanically open the prostatic urethra without ablation, resection or piercing of the prostate. The first in man evaluation of the ProVee Expander was conducted to demonstrate the safety and feasibility of the procedure and implant. The Primary Endpoint was successful deployment of implant. Secondary endpoints included 1) the rates of complications in the peri-operative period and in the immediate postoperative and follow-up periods and 2) preliminary assessment of the effectiveness in alleviating LUTS using IPSS, QoL and Qmax measurements.

Materials & Methods: This was a prospective, non-randomised, 10 patient safety and feasibility study carried out after ethical approval. Males ≥ 50 years, IPSS of > 15, Qmax of <12 mL/s and prostate volume of 30-80 cc were enrolled. No wash out period for medications was mandated by the protocol and it is noteworthy that 7 of the 10 subjects enrolled, were on BPH or OAB drug therapy immediately prior to the procedure and discontinued their medication from the day of the index procedure onwards. Follow up visits were performed at 2 weeks, 1, 3, 6, and 12 months using the IPSS, Qmax, residual urine, the International Index of Erectile Function (IIEF), pain assessment via the Faces Pain Scale and flexible cystoscopy at 3, 6 and 12 months.

Results: Age range was 58 – 75 with a mean IPSS of 23 and mean Qmax of 8 ml/s. The ProVee urethral expander was successfully deployed in all 10 patients, all men voided following the procedure and no catheterisations were required. Reported postoperative AEs were typically mild and transient and postoperative CT assessments demonstrated that the implant expanded to a minimum diameter of 37F in the prostatic urethra. All 10 subjects have completed 12 month follow up and all data has been independently monitored from source. The device was well tolerated with no unexpected procedural or device related adverse events or complications and no migration was detected. There were no reported cases of de novo retrograde ejaculation. The trial was not powered to demonstrate efficacy with any significance. All 10 patients had an improvement in IPSS through 12-months. There was a 63% Improvement in Qmax at 12-months. All men not on LUTS medication prior to the procedure showed a ≥40% improvement at 12-months. Overall, 8/10 subjects showed an IPSS improvement of ≥30% through 12-months post being treated with ProVee.

Conclusions: The ProVee Expander can be safely and reliably deployed in the prostatic urethra. The 12-month data from this First in Man (FIM) study of 10 subjects demonstrates the ProVee Expander can safely alleviate LUTS in BPH patients. Further larger clinical studies are planned for 2022.

16

Could the high-power laser increase the efficacy of stone lithotripsy during retrograde intrarenal surgery?

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Introduction & Objectives: The aim of the study is to compare a high-power setting holmium yttrium aluminum garnet (Ho:YAG) laser lithotripsy to the established low-power setting approach during Retrograde Intrarenal Surgery (RIRS).

Materials & Methods: Our study analyzed the data of consecutive patients managed with RIRS. The patients were divided into 2 groups according to the employed laser settings of power, energy and frequency; dusting (20W=0.5Jx40Hz) (Group1) and stone “self-popping” (60W=1.5-2Jx30-40Hz) (Group 2). Perioperative outcomes including operative time (OT) and stone disintegration time (SDT) were compared between groups. Stone-free rate (SFR) was evaluated 1 month after the surgery.

Results: Overall, 174 patients with 179 renal units were included. The dusting mode was utilized in 98 patients (100 renal units), whereas 76 patients (79 renal units) underwent the stone “self-popping” technique. The SFR was 82.1% for both groups. The OT and SDT were 60.1 ± 18.6min and 32.6 ± 9.4min respectively for Group 1, and 44.9 ± 15.5min and 16.5 ± 4.7min respectively for Group 2. According to the final analysis, laser lithotripsy using stone the “self-popping” technique was significantly faster compared to the dusting technique with a coefficient value of 14.12min (CI = 8.8 – 19.44) and 15.84min (CI = 13.44 – 18.2) for OT and SDT, respectively.

Conclusions: The stone “self-popping” technique with power at 60W, the frequency at 30-40Hz and energy at 1.5-2.0J is a safe and effective modality for the active treatment of renal stones. In comparison to the dusting mode, it resulted in significantly faster procedures (14.12min) possessing similar SFR.

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Optimization of laser pulse shape to reduce retropulsion in lithotripsy procedures

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Introduction & Objectives: Retropulsion effect is a significant problem in laser lithotripsy. It decreases stone ablation efficiency due to movement of the stone during and between the laser pulses, limits practically usable laser pulse energy, thus making the procedure sub-optimal, and makes treating small stones especially difficult, thus increasing risk of missing them and increasing chances of recurrence. Recently introduced Thulium Fiber Laser (TFL) has a potential for substantially reducing the retropulsion effect due to the optimal peak power and its inherent capability of precise control of the laser pulse.

Materials & Methods: In this work, we accessed feasibility of retropulsion suppression using TFL with pulse shape optimized or minimal retropulsion, in a controlled lab environment, using Bego stone phantoms. A specially designed setup allowed to record stone movement after individual laser pulse or during a series of pulses using a high-speed high-resolution video camera. A prototype TFL (IPG Medical, Marlborough, MA, USA) with pulse shape modulation capability has been employed for experiments. Standard (rectangular) and the optimized pulsed shapes were compared. Furthermore, we compared TFL with a leading commercial Ho:YAG lithothripter (short, long, and Moses pulses). In addition, stone ablation efficiency was measured as well.

Results: Optimized Pulse of TFL decreased the retropulsion-caused stone displacement of 5x5x5 mm Bego stone after 0.5 sec laser exposure with 15 W power and energies 0.2, 0.5, 1, and 1.5 J as follows (respectively): 1) 1.2, 1.5, 1.6, and 1.6 times lower compared to regular pulses of TFL with the equal energies; and 2) 1.3, 1.9, 2.9, and 2.9 times lower compared to long pulses of Ho:YAG laser with the equal energies. Ablation efficiency of the optimized pulse of TFL for moving 5x5x5 mm Bego stone after laser exposure with 15 W power and energy 0.2-1.5 J was: 1) About equal to regular pulse of TFL; 2) 2 to 3 times higher compared to long pulse of Ho:YAG laser. For Ho:YAG laser, significant improvement of retropulsion was achieved with long and Moses pulses (vs short pulses), with no practical difference between long and Moses pulses.

Conclusions: Optimization of peak power and pulse shape of Thulium Fiber Laser allows decreasing retropulsion and increasing ablation efficiency. High energy optimized laser pulse can be used for ablation without increasing retropulsion effect. Clinical validation of MRP is necessary.

18

Predictive factors for recurrent urolithiasis formation in patients with exstrophy-epispadias complex

Eur Urol Open Sci August 2022;42(Suppl 1):S19

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Introduction & Objectives: Patients with exstrophy-epispadias complex (EEC) have an increased formation of urolithiasis with an estimated incidence of 10-52%. Our objective is to determine which factors may contribute to the recurrence of stone events.

Materials & Methods: A prospectively maintained database on 150 patients with EEC was reviewed. We selected 35 patients who underwent treatment for urolithiasis. Data was collected to determine demographics, type of urinary reconstruction, presence of continent catheterizable conduit (CCC) or bladder neck reconstruction (BNR), location and size of stone, debut, CIC, time to first stone treatment, surgical approach, latency time until recurrence, rate of recurrence. Bivariate analysis was performed.

Results: Urinary reconstructions of the patients were: 65,7% enterocystoplasty (30.4% reservoir), 20% ureterosigmoidostomy and 14.3% maintained their native bladder. 48.6% had CCC and 45.7% BNR. Only significant factors to recurrent urolithiasis were CCC (OR:10,2, p=0,042) and CIC (OR:14.0, p=0.021). 77.1% minimally invasive procedure and 22.9% open surgery were performed, but the surgical approach did not affect the stone recurrence. The highest rate of recurrence (33.3%) was seen in enterocystoplasty patients with CCC, since the highest median of total urolithiasis surgeries (Me=10) and shortest time-to-first recurrence event (Me=9 months) was identified in reservoir. The location of stone was 51.4% in bladder and 45.7% in UUT and no-statistically significant factors were found for recurrence (88,9% and 66,7% repectively) , but patients with recurrent UUT stones where more likely to debut with acute pyelonephritis (45.5%, p=0.02). Median time to first urolithiasis treatment was 8.6 years (IQR 2.6-13.7) in bladder and 23 years (IQR 7-33) in UUT.

Conclusions: These data suggest that urolithiasis in the exstrophy-epispadias complex is related to risk factors associated with CCC and CIC as well as the presence of enterocistoplasty. The role of metabolic abnormalities that may predispose to urolithiasis is unknown but under investigation. Standard treatment is effective but stone recurrence remains a significant problem.

19

The future of neuromodulation for Lower Urinary Tract Symptoms: Possibilities and challenges.

Eur Urol Open Sci August 2022;42(Suppl 1):S20

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Introduction & Objectives: Neuromodulation by stimulation of a sacral nerve (SNM) is an established therapy for LUTS. Percutaneous tibial nerve stimulation (PTNS) is potentially an alternative method. New technical and surgical possibilities are emerging. These increased facilities create new clinical challenges.

Materials & Methods: SNM with a recharge-free device (InterStimTM II, Medtronic, Minneapolis, MN) was the standard approach for years, but was only approved for magnetic resonance imaging (MRI) head scans. Recently a new MRI-safe InterStim device (InterStim II MRI-neurostimulator in combination with the InterStim SureScan™) provides full-body MRI safety.
Two rechargeable and conditional MRI-safe devices (the Axonics r-SNM SystemTM and the Medtronic InterStim® Micro-neurostimulator) have been marketed. A rechargeable battery allows for a much smaller volume implantable pulse generator (IPG) and potentially more comfort for patients.

The battery life of rechargeable devices has been estimated at 15 years compared to the longevity of the current InterStim II, which is about 5–7 years. As a result, rechargeable IPGs will be associated with a reduced need for reoperation. Hence life expectancy of patients will be an important factor when considering rechargeable devices, besides cognition and patient's dexterity.

Recently a new approach to sacral nerve stimulation has been developed, consisting of a miniature implantable stimulator and proprietary wireless mid-field powering unit (AHLLevees System, Neuspera Medical Inc, San Jose, CA).
Additionally several companies are developing miniature battery less and leadless implantable devices for tibial nerve stimulation, that allow for external, self-controlled, activation of the device for application of stimulation. A pilot long term trial with the Renova iStim^{TM} system (BlueWind Medical, Herzliya, Israel), using an open procedure and a leadless electrode, shows good clinical results.

Conclusions: Several technical innovations in the field of urological neuromodulation have emerged in recent years and continue to be evaluated. Two major approaches are available: a sacral or a tibial nerve. Furthermore, energy can be delivered through an implanted recharge-free or a rechargeable battery. All these innovations necessitate specific algorithms for patient selection. As long as these are not available careful clinical evaluation, should guide the selection of a specific technique and approach in individual patients.

20

Characteristics of women with acute pyelonephritis in a historic five-year cohort and predictors of ultrasound abnormalities among women treated for acute pyelonephritis in outpatient care: a prospective study

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Introduction & Objectives: Urinary tract infections (UTIs) are common but their hospital burden are uncertain. Pyelonephritis can be complicated and may need a rapid drainage of the kidney. Unfortunately, the risks factors remain unknown. This study aimed to estimate the national incidence of hospitalized UTIs in France. We focused on pyelonephritis and confirmed the risk factor on a prospective population treated in an ambulatory setting.

Materials & Methods: The phase 1 of the study is a historic five-year cohort of adult patients hospitalized with UTIs in France that was extracted from the medico-administrative databases using an ICD-10 code algorithm built by a multidisciplinary team. The performance parameters were estimated blindly, by reviewing 1122 cases. The national incidence of UTIs was then estimated. We then analyzed the characteristics of women who were hospitalized for a acute pyelonephritis (AP). The risk factors of needing a renal drainage (ureteral stent, double J stent or nephrostomy) were analyzed. The phase 2 of the study is a prospective univariate and multivariate analysis to identify predictors of ultrasound abnormalities in a huge AP population managed in an outpatient care network.

Results: In the phase 1 study, a total of 2,083,973 patients with UTIs were hospitalized over the period, giving an adjusted incidence rate of 900 cases/100,000 inhabitants, stable over the period, higher in females and increasing with age. AP represents 23.6%. More than three-quarters of patients had at least one comorbid condition (76.8%). Of the 527,671 patients hospitalized for AP, 65,870 needed a renal drainage (12.5%, stable over the period), more often for men (20.6%) than for women (10%), and for patients between 50 and 69 years old (20% drainage). The proportion of patients with a complication was higher with a drain (26%) than without a drain (9.4%). The morbidity of patients who underwent a renal drainage (7.7%) was higher than that of patients without (6.2%). In the phase 2 study, 2,054 women were treated for AP. Among them, 32.5 % (n=667) had history of urinary tract infection and 5.8 % (n = 120) an uropathy. The most frequent uropathogen was E. coli (n=1,432; 69.7%), ESBLs were found in 39 (1.9%) urine cultures. Ultrasound was abnormal in 7.3% (n=149). Age over 55 (OR=2.23; 95%CI 1.58-3.15; p<0.0001) and uropathy (OR=3.69; 95%CI 2.26-6.01; p<0.0001) were independently identified as predictors of ultrasound abnormalities. The risk increased by 1.8 % (95 % CI 1.0-2.6) each additional year of age.

Conclusions: This national cohort study is the first to date to estimate the incidence of UTI-related hospitalizations in France. We identified age and uropathy as an independent predictor of abnormal ultrasound in outpatient AP in outpatient women with AP. This population may need rapid renal drainage.

21 PLANET (Planning Appropriate Nocturia Evaluation and Treatment); Deriving consensus on primary management of nocturia from all causes

Eur Urol Open Sci August 2022;42(Suppl 1):S22

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Introduction & Objectives: Understanding the causative conditions in individual nocturia patients may allow identification of a medical condition, providing an opportunity to direct treatment appropriately. Frustratingly, most GPs attribute nocturia to bladder or prostate disease, and may overlook the basic evaluations to consider polyuria, so referral to urologists is an early step. Unfortunately, urologists are not trained to evaluate the medical causes of nocturnal polyuria, which includes chronic kidney disease, hypertension, obstructive sleep apnoea (OSA) and many others. Hence harmful or futile treatments might be offered, while therapy outcomes may be disappointing.

Materials & Methods: The PLANET project undertook five systematic reviews in relevant medical areas (Cardiovascular, Nephrology, Endocrine, Sleep Medicine, Neurology) and used these to inform expert consensus panels from the applicable specialties, which derived mechanism/assessment and therapy consensus using Nominal Group Technique (NGT) methodology. The conclusion of the project is the development of an overarching algorithm based on the evidence synthesis and a further NGT consensus.

Results: The practical priority of the algorithm is to support practitioners who may have to assess a patient with nocturia caused by a mechanism with which the practitioner is not familiar. This includes the patient's first presentation to the general practitioner (GP), or referrals to an inappropriate specialty (e.g. a patient referred to a urologist where the mechanism turns out to be obstructive sleep apnoea). Basic widely-available assessments and low risk therapy is emphasised. The prime focus is on empowering the GP to appreciate the likely underlying mechanism, so that therapy can be offered in primary care, and any specialist referrals are justified and sent to the appropriate expert.

Conclusions: Causes of nocturia are so diverse that no single specialty encompasses the potential contributors. The NGT discussions identified that even specialists may not recognise how conditions they manage could influence urine production. For example, the cardiology NGT showed that nocturia is not considered a cardiovascular symptom even though heart failure, hypertension and several cardiac medications can generate diuresis and natriuresis. Hence, follow-on funding has been secured to adapt and evaluate the PLANET main algorithm for real-life practice by integrating it into primary care computer systems (Nocturia Evaluation and Treatment; Implementing Assessments and Consolidating Therapy in primary care).

22

Efficacy and safety of sacral neuromodulation for neurogenic lower urinary tract dysfunction: a randomised, sham-controlled, double-blind, multicentre clinical trial

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Introduction & Objectives: Although neurogenic lower urinary tract dysfunction (NLUTD) is a highly prevalent and disabling condition, standard treatments remain often unsatisfactory. Sacral neuromodulation (SNM) is a well-established therapy for non-NLUTD, but there is a lack of randomised controlled trials in neurological patients. We therefore assessed efficacy and safety of SNM for NLUTD in randomised, sham-controlled, double-blind, multicentre clinical trial.

Materials & Methods: Patients with refractory NLUTD and intended SNM were eligible for this sham-controlled, double-blind multicentre randomised controlled trial. After minimally invasive bilateral tined lead placement into the sacral foramina S3 or S4, patients underwent SNM testing. If successful (≥50% improvement in key bladder diary variables), the neurostimulator was implanted for permanent SNM. For two months, the effectiveness of SNM was optimized using sub-sensory stimulation with individually adjusted parameters. Participants were then randomly assigned in a 1:1 ratio to either SNM verum or sham stimulation and re-evaluated after a two-month double-blind intervention phase. The primary outcome was success of SNM verum versus sham stimulation compared to baseline.

Results: Of 124 patients undergoing SNM testing, 65 (52%) tested positive and 60 (median age, 49.5 years; 17 men) were randomised. After two-month intervention, SNM remained successful in 22 (76%) of 29 patients receiving verum and in 13 (42%) of 31 receiving sham stimulation (odds ratio, 4.35; 95% confidence interval, 1.43–13.21; P=0.009). During the entire study period, there were 10 adverse events (6 resulted in dropout). No dropout occurred during the intervention phase.

Conclusions: SNM is effective and safe for treating refractory NLUTD in well-selected neurological patients. These findings support the implementation of SNM into the care pathway of NLUTD.

23 Sacral neuromodulation for management of severe bladder dysfunction due to endometriosis: experience from a tertiary reference center

Eur Urol Open Sci August 2022;42(Suppl 1):S24

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Introduction & Objectives: Endometriosis is a highly prevalent disease in females and can be associated with lower urinary tract symptoms (LUTS), as well as bladder pain syndrome and bowel dysfunction. Bothering LUTS are challenging to manage for urologists as the clinical picture is often blurry with a variety of symptoms. One of the most difficult situation is persistent voiding symptoms after deep infiltrating endometriosis (DIE) surgery (seen in around 10% of cases), that may lead to clean intermittent catheterization (CIC). Our goal was to report our experience with sacral neuromodulation (SNM) as a treatment of persistent voiding symptoms after DIE surgery.

Materials & Methods: All patients who underwent SNM between 2011 and 2020 for persistent LUTS after DIE surgery were included in the present analysis. The analysis was retrospective, based on prospective data collected in our tertiary reference center. Data collected included age, date and type of DIE surgery, characterization of LUTS (questionnaires, uroflowmetry, post void residual and urodynamics if available). Details of SNM surgery were also evaluated (results of test phase, complications of surgery). The criterion for device implantation was improvement of symptoms of 50% or more during the test phase. Patients were followed at the clinic at 1, 3, 6, 12 months and yearly thereafter. Primary endpoint was success of the procedure at last follow-up, defined by device in place, functioning and persistent improvement of voiding LUTS.

Results: Twenty-one patients were included. Mean age was 36±3.5 years. Mean number of surgical interventions for DIE was 1.75±1.4, 12 patients had associated bowel surgery. Median time interval between index DIE surgery and SNM was 21 months. Before SNM, all patients had voiding difficulties confirmed by urodynamics and 10 were using CIC daily. Following test phase, two patients had infection and explantation of the device, and 15 were implanted. After a median follow-up of 16 months, 11 patients had a successful outcome with device still in place. 5 out of 10 patients who practiced CIC at baseline were free from CIC at last follow-up. A few patients mentioned improvement of their bowel symptoms under SNM.

Conclusions: SNM seems to be a valuable option for severe voiding symptoms after DIE surgery, harboring a 50% success rate and a standard risk of complications. Better understanding of the complex underlying pathophysiology of LUTS after DIE surgery may improve patient selection in the future.

24 Developing varicoceles in experimental animals: What we have learned

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Introduction & Objectives: To evaluate the unknown effects of varicocele on testicular function and sperm capacity to induce appropriate embryonic development for implantation, varicoceles were surgically induced in Wistar rats.

Materials & Methods: Surgical procedures to induce an experimental model of left varicocele (LV) in Wistar rats (n=60; group A) were performed. We attempted to induce varicoceles in rats by performing partial ligation of the left renal vein and by ligating all of the anastomotic branches of the left testicular vein (LTV) as we have previously described (Eur Urol, 1992; 22:44-52). Rats of the same age were sham-operated and served as a control group (n=10; group B). Eight weeks after the surgical procedure for varicocele induction, nine rats of group A did not demonstrate dilation of the LTV. At that time, rats of group B underwent a second sham-operation procedure and subpopulations of the remaining varicocelized rats of group A underwent a) left varicocelectomy (LVRMY; group A1;n=16; 8 weeks after the varicocele induction surgery) or b)ligation of the right testicular vein (LRTV; group A2;n=14) or c)a sham operation (group A3; n=21; varicocele group without additional surgical treatment). Within each group, developed blastocysts from IVF methods, using epididymal caudal spermatozoa, were transferred to synchronized pseudopregnant female recipients. Student t-test or chi-square test were used for statistical analysis. A probability P smaller than 0.05 was considered as statistically significant.

Results: Four weeks after the second surgical procedure, a)bilateral intraabdominal versus intratesticular temperature difference and b)bilateral epididymal caudal sperm concentration, motility, fertilizing capacity (IVF methods had been performed), and sperm capacity to induce embryonic development up to the blastocyst stage were significantly smaller in the group A3 than in groups A1 or B. The above parameters on the right side were significantly smaller in group A3 than in the group A2. The number of offspring per inseminated oocyte on the right side was significantly larger in groups A1, A2, or B than in group A3.

Conclusions: LVRMY improves bilaterally spermatogenesis and epididymal sperm maturation process in rats with LV. LRTV in rats with LV salvages spermatogenesis, epididymal sperm maturation process, and sperm ability to trigger appropriate embryonic development for implantation on the right side. The detrimental effects of LV on the right testis may be attributable to the development of a secondary clinical or subclinical right varicocele after the induction of a primary LV.

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Simulation in Urological Training and Education (SIMULATE): A randomised controlled trial to determine the effect of simulation-based surgical training

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Introduction & Objectives: With increasing challenges in surgical training, simulation has been hypothesised to enhance progression along the initial phase of the surgical learning curve. SIMULATE aims to assess whether supplementary simulation training is superior to the current standard of exclusive OR-based learning in helping residents reach a level of proficiency sooner.

Materials & Methods: This international, multicentre randomised controlled superiority trial recruited urology trainees (n=94) who had performed ≤10 ureterorenoscopy (URS) cases, as a selected index procedure, with no prior simulation experience. Recruits were randomised to simulation-based training (SBT) or non-simulation-based training (NSBT) groups, the latter of which is the current standard of training. Training sessions were conducted for the SBT arm, utilising an expert-developed multi-modality training curriculum. The primary outcome was the number of procedures required to achieve proficiency, defined as achieving a score of ≥28 on an Objective Structured Assessment of Technical Skill (OSATS) assessment scale, on 3 consecutive operations, without complications. Secondary outcomes included number of surgical complications and stone-free status in each arm. All participants were followed up for 25 procedures or over 18 months.

Results: A total of 1140 patient procedures were performed by 65 participants who continued with follow-up from the simulation (n=32) and conventional (n=33) training arms. Proficiency was achieved in 66% of simulation (n=21/32) and 55% of conventional (n=18/33) groups (OR 1.59 [95% CI 0.59-4.33]) over a mean of 9.6 and 10.9 sessions (HR: 1.41 [95% CI 0.72-2.75]). Simulation participants (OR 3.33 [95% CI 1.09-10.24]) required fewer number of procedures to reach proficiency (HR 0.89 [95% CI 0.39-2.02]) in flexible ureterorenoscopy, the more complex form of the index procedure. Significant differences were observed in overall comparison of OSATS scores between groups (27.3 vs 25.9; p<0.0001). Fewer complications (2.5% vs 6.8%) and non-stone-free patients (6.6% vs. 8.6%) were reported in favour of simulation.

Conclusions: Surgical residents undergoing supplementary simulation-based training achieved higher overall proficiency scores than those conventionally trained. They required fewer procedures to reach proficiency in the more complex form of the index procedure and demonstrated better clinically meaningful outcomes.

26 Remote instant prostate pathology based on artificial intelligence enhanced ultrasound (AI-US): From biopsy to diagnosis in 30 min

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Introduction & Objectives: Early diagnosis of prostate cancer (PC) based on rapid histopathological evaluation is an essential step on the way to personalized medicine. For the first time we utilized the combination of AI-US and remote telepathological Fluorescent Confocal Microscopy (FCM) within 30 minutes to identify malignancy and discuss consequences instantly.

Materials & Methods: After informed consent 73 patients (median-age: 73, PSA-range: 1.2 - 1173ng/ml) were scheduled for AI-US targeted prostate biopsy (1-6 cores) between 2020-2021. Cores were stained for FCM analysis and digital images were sent for “real-time” pathology review followed by routine pathological procedure.

Results: Overall PC detection was 34% (25/73 cases). Clinically significant PC (csPC: Gleason ≥7) was found in 56% (14/25 cases). Median time from biopsy to FCM diagnosis was 30 min. FCM diagnosis was confirmed by standard pathology analysis in 88% (64/73) to differentiate between malignant and benign tissue. All csPC were diagnosed by instant FCM, detection rate of insignificant cancer (≤Gleason 6) was 60% (6/10cases). All high-risk patients according to AI-US classification were diagnosed with only 2 targeted cores by FCM analysis.

Conclusions: Combination of AI-enhanced US targeted biopsy and instant FCM is a new tool to personalize the diagnostic approach. Reduction of core number and real-time confirmation of csPC allows reduction of diagnosis-related stress for patients, costs and time.

27 Patient reported outcomes using EPIC-26 one year Post-RP: The impact of surgical approach and training

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Introduction & Objectives: Earlier reports using Patient Reported Outcome Measures (PROMS) have suggested that functional outcomes of RARP are superior to Open (ORP) or Laparoscopic (LRP) approaches. However, an RCT of RARP versus LRP [Stolzenburg, EAU 2021] demonstrated no significant difference in continence outcomes at 1 year, although sexual function remained better following NSRARP. We sought to evaluate the impact of surgical approach and training on functional outcomes, using a validated PROMS, in a single surgeon's practice of Minimal Access RP.

Materials & Methods: PROMS were prospectively collected using EPIC-26 to assess 1-year functional outcomes in 3 groups of contemporaneous patients in a single surgeon practice:. LRP, RARP, and Training RARP (T-RARP). The three groups, LRP (n=50), RRP (n=96) & T-RARP (n=72) were well-matched in all parameters - age, BMI, PSA, GG, T stage, EPIC-26. Relatively few were suitable for bilateral nerve sparing given the selection criteria used for surgery and increasing active surveillance of lower risk disease.

Results: The mean operative time for LRP and RARP was significantly shorter than T-RARP (130.7 and 128.4 v 147.6 mins, p=0.003). Blood loss ranged from 125.7ml-164.5 mL with no significant difference observed between the groups. There were no conversions to open and no blood transfusions. Mean length of hospital stay of 1.5 days in all groups. Oncological outcomes were equivalent with no difference in the positive margin rate observed between the groups. PROMS using the EPIC-26 questionnaire yielded a return rate at one year of 84% in the LRP group and 87.5% in the RARP groups. At 1 year the EPIC-UI (urinary incontinence) score was significantly higher in the LRP group compared to both RARP and T-RARP (76.06 v 62.5 v 57.5, p=0.006). There was no difference between the EPIC-UO for urinary symptoms & EPIC-B for bowel function between the groups. All three groups have shown high scores ranging from 95.6 to 97.3 in the EPIC-S for sexual function.

Conclusions: The learning curve for RP is long and outcomes are known to improve with experience. Stolzenburg et al have shown in an RCT comparing LRP and RARP that outcomes are similar at 1-year, whilst the LAPRO study demonstrated that surgeon experience had a greater impact on outcome than the surgical approach. Our study confirms both these findings in a single surgeon series using a validated PROMS questionnaire at 1-year post-op. Whilst experienced in RARP, the surgeon's experience of LRP is greater, which may contribute to the observed benefit regarding continence outcomes at 1 year in the LRP group. Training had a demonstrable impact with longer operating times and poorer functional outcomes. This study demonstrates that functional outcomes following RP can effectively be assessed with PROMS and confirms that the variables affecting surgical outcomes are complex and influenced by more than just the surgical approach used.

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Estetrol improves quality of life in advanced castration-sensitive prostate cancer: A randomized clinical trial

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Introduction & Objectives: Androgen Deprivation Therapy (ADT) is the standard treatment for locally advanced or metastatic prostate cancer (PC). In de novo metastatic PC ADT can be combined with docetaxel and/or androgen receptor pathway targeting agents such as abiraterone, enzalutamide or apalutamide or in case of low-volume disease with radiotherapy. However, ADT is not devoid of side effects such as sometimes life threatening cardiovascular (CV) risks. ADT also causes hot flushes (HFs) interfering with quality of life and bone loss with an increased fracture risk. This is a consequence of estrogen deficiency since the reduction of testosterone suppresses its metabolite estradiol (E2). In the PCombi trial we assessed the safety, quality of life (QoL) and potential anti-tumor effects of high dose fetal estrogen estetrol (HDE4) in patients with advanced prostate cancer treated with a luteinizing hormone-releasing hormone (LHRH) agonist.

Materials & Methods: PCombi is a phase II, double-blind, randomized, placebo-controlled study, conducted at 4 sites in the Netherlands from March 2018 to May 2020. Patients had regionally advanced non-metastatic or metastatic castration sensitive prostate cancer that required ADT. All patients received LHRH agonist treatment according to investigators choice and were randomized 2:1 to receive a 40 mg oral dose of HDE4 (n=41) or placebo (n=21) for 24 weeks. The primary endpoints were frequency of hot flushes and levels of total and free testosterone (T). Secondary endpoints included assessments of QoL, bone metabolism, PSA and FSH levels.

Results: Of 62 patients randomized, 57 were suitable for the Per-Protocol analysis (37 on HDE4 and 20 on placebo). No E4-related serious cardiovascular adverse events occurred. Daily hot flushes were reported by 55.0% of patients in the placebo group and by 5.9% of patients in the HDE4 group ($P<0.0002$). Compared with placebo, bone turnover (osteocalcin and CTX1) decreased significantly with HDE4 ($P<0.0001$). Total T and free T decreased earlier ($P<0.05$) and free T was lower at all seven time points ($P<0.05$ at 24 weeks). Sex hormone-binding globulin (SHBG) levels increased by 185% ($P<0.0001$). PSA suppression was stronger and occurred earlier ($P<0.003$). FSH levels were suppressed by 98% vs 37% with placebo ($P<0.0001$).

Conclusions: HDE4 was well-tolerated in LHRH agonist treated patients with advanced prostate cancer and did not cause treatment-related cardiovascular adverse events. Hot flushes, bone turnover and other estrogen deficiency symptoms were substantially reduced, improving QoL. Total T, free T, PSA and FSH were suppressed earlier and stronger, all suggesting further disease control by HDE4 co-treatment. These data warrant start of a phase III trial.

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Stratification by risk group reveals the superiority of the robot-assisted technique in the prostatectomy with respect to surgical outcome

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Introduction & Objectives: The robot-assisted technique allows for improved visualisation of the surgical field, and thus potentially better control of the surgical planes of dissection. Prostate cancer is about optimising the balance between radicality and preservation of function, and the aim of the surgery varies with the risk category of the disease. Nevertheless, comparisons of open and robot-assisted techniques have analysed the effects across all risk groups. We have re-analysed a prospective cohort study stratifying by risk category to assess any potential heterogeneity in the outcomes by risk category.

Materials & Methods: We analysed 2650 men with prostate cancer from seven open (n=805) and seven robotic (n=1845) Swedish centres between 2008 and 2011 in a prospective non-randomised trial, LAPPRO. Urinary continence recovery was defined as change of pads less than once in 24 h. Information was collected through validated questionnaires. Rate of positive surgical margins (PSM) and biochemical recurrence (BCR), defined as prostate-specific antigen (PSA) > 0.25 mg/ml, were recorded. Positive surgical margins (PSMs), biochemical recurrence, urinary continence were assessed stratified by two risk groups (low-intermediate and high risk) based on the D'Amico risk classification system.

Results: The outcomes in the two surgical arms were clearly heterogeneous when assessed by risk group. Among men with high-risk prostate cancer, we found significantly higher rates of recovery of urinary continence at 24 months after RRP compared to RALP (66.1% vs 60.5%) RR 0.85 (CI 95% 0.73–0.99). while PSMs were more frequent after RRP compared to RALP (46.8% vs 23.5%) RR 1.56 (CI 95% 1.10–2.21). Overall, biochemical recurrence was significantly more common after RRP compared to RALP at 24 months (9.8% vs 6.6%) RR 1.43 (CI 95% 1.08–1.89).

Conclusions: The results from this observational prospective trial suggest that the robot-assisted technique is associated with less positive surgical margins and less biochemical recurrence but also a higher frequency of urinary continence problems among men with high-risk disease. These data may indicate that the robot-assisted technique allows for better precision in the choice of the dissection plane, and thereby for better opportunities to adapt the surgical approach to the characteristics of the patient's tumor. Moreover, we suggest that future studies of comparative effectiveness should as a rule plan for analyses stratifying by risk category in order to assess whether or not the target of the surgery is met.

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Nerve sparing radical prostatectomy in high risk prostate cancer patients is feasible with good functional results without impairing oncological outcomes: A longitudinal long-term single center study

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Introduction & Objectives: High risk prostate cancer is associated with higher incidence of extra prostatic disease. This has led to the concept that nerve sparing (NS) should be avoided to prevent positive surgical margins as they may increase risk of cancer recurrence. Not only owing to anticipated inferior oncological but also functional outcomes RP has not commonly been offered to men with high risk PCa. Whether NS RP should be attempted in these patients remains a matter of debate. The aim of this study was to assess oncological and functional outcomes in high risk PCa patients following RP.

Materials & Methods: We included consecutive patients at a single, academic centre undergoing open radical prostatectomy for HR-PCa (preoperative PSA > 20 ng/ml and/or Gleason score ≥ 8 and/or ≥ pT3 and/or pN1). We calculated a propensity score and used inverse probability of treatment weighting to match baseline characteristics of high-risk prostate cancer patients undergoing nerve-sparing radical prostatectomy (NSRP) to those having non-NSRP. We analyzed oncological outcome as time-to-event and calculated hazard ratios (HR). In addition we assessed functional outcomes (urinary continence (UC), erectile function recovery (EFR)) at 3, 6, 12 and 24 months by multivariable logistic regression analyses.

Results: A total of 726 patients were included in this analysis of which 84% (n=609) underwent NSRP. There was no difference in positive surgical margins between the NSRP and non-NSRP groups (47% vs 49%, p=0.64). Likewise, there was no difference in the need for post-operative radiotherapy amongst men who underwent NSRP compared to those who did not have nerves spared (HR 0.78, 95%CI 0.53–1.15). NSRP did not impact the risk of any recurrence (HR 0.99, 95%CI 0.73–1.34, p=0.09) and there was no difference in survival for men who underwent NSRP (HR 0.65, 9%%CI 0.39–1.08). There was also no difference in cancer-specific survival (0.56, 95%CI 0.29–1.11) nor progression-free survival (H) 0.99, 95%CK 0.73–1.34). In multivariable analysis adjusted for potential confounders attempted NS was predictive of higher UC and EFR compared to patients with no-NS at all time points. Furthermore, patients with attempted NS were less in need of erectile aid compared with no-NS. Overall and cancer specific survival and local recurrence-free survival were not inferior in patients with attempted NS.

Conclusions: Our study found that NSRP can be safely performed in carefully selected patients with high-risk prostate cancer without compromising long-term oncological outcomes. Attempted NS in patients with high risk PCa is associated with favourable UC and EFR-rates after RP without impairing oncological outcome.

31 Testosterone and COVID-19 :A key hormone's link with the increased mortality in men

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Introduction & Objectives: Worldwide mortality from COVID-19 is nearly 3 times higher in men. We reviewed the incidence of mortality from COVID-19 and its link with co-morbidities and Testosterone deficiency.

Materials & Methods: Patients admitted and dying from COVID-19 in our hospital and in numerous publications from various international institutions were reviewed.

Results: Among patients admitted and dying from COVID-19 more than 70% were men. Co-morbidities like obesity, diabetes, cardiac conditions, obstructive sleep apnea were highly prevalent in COVID-19 hospitalized patients and associated with Testosterone deficiency and death. These figures are comparable to those reported in most large international studies published in the recent literature.

Conclusions: Testosterone deficiency has been shown to play a significant role in modulating the immune response to viral infections like COVID-19. Testosterone is associated with increased pro-inflammatory cytokines involved in viral infection reactions. Androgen receptor activation influences the Transcription of a Trans-Membrane Protease Serin 2 (TMPRSS2) involved in the transmission of COVID-19 infection. A better understanding of the impact of. Testosterone deficiency in the higher severity and mortality of COVID-19 in men underlines the potential of modifying Testosterone levels as a protection of the severity of outcomes in men.

32 Predictors of Corporo-Venocclusive Dysfunction (cvod) in men with bilateral nerve-sparing Radical Prostatectomy (rp)

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Introduction & Objectives: Nerve-sparing status (NSS) during RP is a significant predictor of erectile function recovery (EFR). Poor nerve sparing is associated with collagenization of cavernosal smooth muscle and CVOD development with typically poor response to PDE5 inhibitors (PDE5i) and intracavernosal injection therapy (ICI). This study aimed to define factors predictive of CVOD in men with bilateral NS RP.

Materials & Methods: Study population consisted of (i) men who underwent bilateral NS (defined by the surgeon using an institutional grading system) RP (ii) with poor response to PDE5i and ICI (iii) ≥2 years post-RP (iv) who underwent penile duplex Doppler ultrasound (DUS) (v) using a vasoactive agent redosing schedule. CVOD diagnosis was made with end-diastolic velocity (EDV) values ≥5 cm/sec bilaterally. ADT and radiation therapy were exclusions. We used multivariable modeling to define factors predictive of CVOD. Factors included in the model: patient age, history of diabetes, history of obstructive sleep apnea, number of vascular comorbidities, baseline EF, peri-RP total testosterone (T) level, and total T at DUS (within 3 months).

Results: 201 men with a mean age of 66 ± 7 years. 25% of the patients reported 3 or more vascular comorbidities, 17% had diabetes, 36% obstructive sleep apnea, 39% were current or former smokers. Mean baseline PSA and pre-RP total T was 6.7 ± 6 ng/mL and 410 ± 211 ng/dL, respectively. Median baseline EFD score was 24 (13, 29). 49% of the men had an erection less than penetration rigidity during the DUS procedure with a mean total dose administered of 87 ± 21 units of trimix. 69% received 100 units. CVOD was diagnosed in 76%. Mean total T at DUS was 386 ± 177 ng/dL. 32% had low T. Significant predictors of CVOD after RP in men with BL NSS were: OSA (OR = 3.8, 95% CI = 1.7-8.7), ≥ 3 vascular comorbidities (OR = 5.0, 95% CI = 1.7-14.8), age at the time of DUS (per 10 years increase, OR = 1.9, 95% CI = 1.2-3.0), and pre-RP EF domain score (per 1 unit increase, OR = 0.93, 95% CI 0.88-0.98). There was a signal that in a larger sample size, diabetes may be a significant predictor of CVOD in this group of patients (OR = 2.7, 95% 0.9-8.0).

Conclusions: Baseline clinical comorbidities pre-RP have a significant impact on EFR post-RP, in particular, the presence of venous leak. Despite BL NSS, older patients, men with OSA, higher number of comorbidities pre-RP, and lower pre-RP EF increased the likelihood of developing CVOD post-RP.

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Immunological markers and somatic mutations as predictors for therapy selection in metastatic renal cell carcinoma

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Introduction & Objectives: In clinical practice, there is currently a lack of biomarkers to predict the response of renal cell carcinoma (RCC) to systemic therapy. The aim of the analyses was to systematically investigate the expression of immunological markers in primary tumors and corresponding metastases.

Materials & Methods: 111 primary tumors (101 clear cell RCC, 6 papillary RCC, 2 chromophobe RCC, 1 mixed type, 1 non classified) and 230 metastases (FFPE) from 111 patients were included. Samples were analyzed immunohistochemically with validated antibodies against BTLA, hTim3, and PD-L1, evaluated in a standardized manner using Definiens Tissue Studio® software, and correlated with clinicopathological data. In addition, somatic mutation analysis was performed using a gene panel with 33 renal cell carcinoma candidate genes.

Results: There was no correlation between protein expression of BTLA, hTim3, and PD-L1 in the primary tumor and TNM stage, tumor grading, and survival. Only for PD-L1, protein expression was higher in metastatic tissue than in the corresponding primary tumor tissue and thus independent of the site of metastasis ($p<0.01$). BTLA was most strongly expressed in local recurrences (n=18), lymph nodes (n=32) and adrenal gland (n=17), whereas significantly lower expression was detected in lung (n=53) and bone (n=24). There was a non-monotonic association between PD-L1 protein expression in clear cell RCC metastases and survival (for OS $p=0.081$ and for CSS $p=0.044$) with high risk at low and high PD-L1 expression and lower risk in a small range in between (n=210). No significant association with survival was found for BTLA and hTim3. Association analyses revealed significantly higher PD-L1 expression at the protein level with more mTOR variants ($p=0.03$), while PD-L1 expression was significantly decreased when a VHL mutation was detected ($p=0.03$).

Conclusions: Our findings reveal a heterogeneous expression pattern of the immune checkpoints BTLA, hTIM3 and PD-L1 with differential effects on survival. The mutational analyses suggest, that combined treatment with mTOR inhibitors and PD-L1 antibodies appears promising and may also explain the lack of synergism of TKI-IO combination treatment in metastatic RCC observed in clinical trials.

34 Nutritional status impairment due to neoadjuvant chemotherapy predicts post radical cystectomy complications

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Introduction & Objectives: Radical cystectomy (RC) is the standard treatment for muscle invasive bladder cancer (MIBC). Neoadjuvant chemotherapy (NAC) improved patient's outcome. The impact of NAC on nutritional status is understudied, while the association between malnutrition and poor surgical outcomes is well known. The aim of this study is to examine the association between NAC, nutritional status impairment and post-operative morbidity.

Materials & Methods: We included MIBC patients who underwent RC and received NAC. Cross sectional imaging was used to measure the psoas muscle area (PMA) and the pre and post NAC PMA difference was calculated (represents nutritional status change). The primary outcomes were post RC ileus, post operative infection and a composite outcome of any complication. Logistic regression models were fit to identify independent predictors of the outcomes. Power analysis required a minimum of 69 patients with a McFadden-R2 = 0.2, alpha = .05 and power = 0.80.

Results: Ninety-one patients were included in the study. Median change in PMA was -122 (-272, -10) mm2. PMA decline was significantly higher in patients with post RC complications (-18 vs -203, $p < 0.001$). PMA change was an independent predictor of all complications, ileus, infection and other complications. The accuracy of PMA change for predicting all complications, post operative ileus, post operative infection and other complications was 0.86, 0.9, 0.77 and 0.86 respectively.

Conclusions: NAC impairs nutritional status as estimated by the change in the psoas muscle area which in turn confers an increased risk of complications after RC. Our results hint towards the need for nutritional intervention during NAC prior to RC.

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Gut microbiota signatures associate with prostate cancer risk

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Introduction & Objectives: Prostate cancer (PCa) is the most common male cancer, but its incidence varies significantly geographically. In contrast, there is less variation in global detection rates of indolent PC. Reasons for these observations may relate to differences e.g. in genetic factors and healthcare policies, but also for differences in lifestyle, such as diet. Currently we do not properly understand the mechanism how lifestyle affect PC risk. Gut microbiota, i.e. a collection of all microbes in the gastrointestinal tract, is acknowledged to affect many metabolic pathways and pathogenetic processes in the human body. Further, the state of gut dysbiosis i.e. disequilibrium of the microbiota, has been linked to many pathological conditions, even in organs distant to intestines. As of today, the role of gut microbiota in prostate carcinogenesis is not well documented.

Materials & Methods: Within a clinical prospective multicenter trial (multi-improd, NCT02241122), the gut microbiota were assessed from 181 men with clinical suspicion of PC (PSA 2.5 to 20.0 µg/l, and/or an abnormal DRE) utilizing 16S rRNA gene sequencing (Illumina) from rectal swabs collected at the time of TRUS-biopsy after MRI. Microbiota sequences were assigned to operational taxonomic units (OTUs), and differential abundance analysis, α- and β-diversities, and predictive functional (PICRUST) analyses were performed. Further, plasma steroid hormone levels were correlated to predicted microbiota functions.

Results: PC was diagnosed in 60% (108/181). Apart for less smoking among subjects with PC, there were no life-style differences between the groups. The gut microbiota profiles of men with PC differed significantly from those without cancer. For example Prevotella 9, members of family Erysipelotrichaceae and potentially pathogenic Escherichia-Shigella were increased, and e.g. Jonquetella, Moryella, Anaeroglobus, Corynebacterium and CAG-352 were reduced in PC cases. Predictive functional analyses revealed increased 5-α-reductase activity (5-AR), copper absorption and retinal metabolism as functional results of different microbiota. Plasma testosterone negatively correlated with predicted microbial 5-AR activity (Wilcoxon rank sum p=0.057) and in a subgroup of men taking 5-AR inhibitors (n=17), plasma estrone (p=0.027), and estradiol (p=0.054) levels were higher in men with predicted increased microbial 5-AR function.

Conclusions: Based on our knowledge, this is the largest and most detailed clinical trial studying the gut microbiota and PCa. We demontrated a significant difference in gut microbiota composition in men with PCa compared to men with benign biopsies. It is of great interest, that steroid hormone metabolism is a potential mechanistic explanation. These findings could partly explain the association of life-style effects and geographical differences observed in PC and warrant further studies with potential for diagnostic and preventive strategies.

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Comparison between laparoscopic sacrocolpopexy with hysterectomy and subtotal hysterectomy in advanced pelvic organ prolapse

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Introduction & Objectives: The primary objective of this study was to compare the efficacy and safety of laparoscopic sacral colpopexy associated with total (L-SCP+TH) or supracervical hysterectomy (L-SCP+SH).The secondary objective was to evaluate the functional and sexual outcomes, and impact of surgical procedures on quality of life (QoL).

Materials & Methods: This single-centre prospective series included women with symptomatic advanced pelvic organ prolapse (POP) who underwent laparoscopic sacral colpopexy associated with total (L-SCP+TH: Group 1) or supracervical hysterectomy (L-SCP+SH: Group 2). The preoperative evaluation included history, pelvic examination, supine stress test, urodynamic test. All operations were performed by one senior surgeon. Patients were followed up at 1, 3, 6, and 12 months postoperatively and then annually using the tests of the preoperative assessment protocol. The follow-up was performed by examiners who had not been involved in the surgical procedures. Patients completed: Prolapse-Quality of Life Questionnaire (P-QoL); Female Sexual Function Index (FSFI); Patient Global Impression of Improvement scale (PGI-I). This study was approved by our Institutional Review Board Committees. Statistical analysis: Mann-Whitney; Wilcoxon tests; McNemar Chi-square; Fisher's exact test ($p<0.05$ statistically significant).

Results: From September 2012 to September 2018, one hundred and nineteen consecutive patients with symptomatic POP> stage 2 were invited to participate. Nineteen out of the 119 patients were not included. One hundred patients were included in the analysis 46 patients in Group 1, 44 in Group 2. In Table 1 and 2 the preoperative and postoperative anatomical and functional results and complications in both groups were reported. The mean follow up was 50 months (range 36-108 months). At last visit there were no statistically significant differences of the cure rates in all compartments between the two groups (anterior compartment: 91.3% in Group 1 vs. 90.9% in Group 2, p=0.54; central compartment : 93.5% in Group 1 vs. 93.2% in Group 2, p=0.9; posterior compartment: 95.7% in Group 1 vs. 93.2% in Group 2, p=0.2). Vaginal mesh exposure only occurred in Group 1 (4.3%). The stress urinary incontinence (SUI) reduced in both groups without statistic difference between the two approaches. In addition, there were 7 cases of grade 1 de novo SUI. All patients underwent pelvic floor rehabilitation with satisfactory results. No surgical correction of SUI was required. The overactive bladder (OAB) and voiding symptoms reduced statistically in both populations without significant difference between the two groups (Table 1 and Table 2). De novo OAB appeared in 3 patients, they were treated with antimuscarinic agent. Constipation disappeared in 12 out of 18 patients in Group 1 and 8 out of 18 patients in Group 2. The total FSFI score improved markedly after surgery in both groups. QoL improved significantly in all domains in both groups. We observed a statistically significant differences between the two groups in the VAS score (mean value 8.84 in Group 1 vs. 9,45 in Group 2 – p=0.0263) and in PGI-I score (mean value 1.56 in Group 1 vs. 1.20 in Group 2 – p=0.046).

Table 1. Pre- and post-operative anatomical and functional results, and complications in both groups

Parameters	**L-SCP + TH Group 1 No 46**			**L-SCP + SH Group 2 No 44**		
	Pre-op	Post-op	p*	Pre-op	Post-op	p*
Point Ba >stage 2, no (%)	46 (100)	4 (8.7)		44 (100)	4 (9.1)	
Point C >stage 2, no (%)	46 (100)	3 (6.5)		44 (100)	3 (6.8)	
Point Bp >stage 2, no (%)	12 (26.08)	2 (4.3)		13 (29.54)	3 (6.8)	
Total vaginal length (cm)						
Subjectively SUI, no (%) - *de novo* SUI	18 (39.1)	14 (30.4) 3 (6.5)	.3865	16 (36.4)	14 (31.8) 4 (9.1%)	.2636
Objectively SUI	16 (34.8)	10 (21.7)	.4187	14 (31.8)	9 (20.5)	.3651
UUI, no (%) - *de novo* UUI	13 (28.3)	7 (15.2) 3 (6.5)	.1489	13 (29.5)	6 (13.6) 4 (9.1)	.1815
Dry OAB, no (%) - *de novo* dry OAB	32 (69.6)	4 (8.7) 0	**.0000**	22 (50)	6 (13.6) 3 (6.8)	**.0014**
Voiding symptoms, no (%)	39 (84.8)	2 (4.3)	**.0000**	34 (77.3)	3 (6.8)	**.0000**
Heaviness	46 (100)	3 (6.5)	**.0000**	46 (100)	3 (6.8)	**.0000**
Constipation, no (%)	18 (39.1)	8 (17.4)	.0162	18 (40.9)	12 (27.3)	.0439
Qmax, ml/s (mean±SD)	12.56±3.5	22±2.9	**.0048**	13.01±4.1	23±3.5	**.0052**
Post void residue >30% of volume (no,%)	33 (71.7)	1 (2.2)	**.0000**	30 (68.2)	1 (2.3)	**.0000**
Mesh erosion, no (%)		2 (4.3)			0	

Table 2. Comparison of post-op results between the two groups

Parameters	**L-SCP + TH Group 1 No 46**	**L-SCP + SH Group 2 No 44**	**P value**
	Post-op	Post-op	p*
SUI, n° (%)	14 (30.4)	15.9)	.1904
UUI, n° (%)	7 (15.2)	6 (13.6)	1.0000
Dry OAB, n° (%)	4 (8.7)	6 (13.6)	.7518
Voiding symptoms, n° (%)	2 (4.3)	3 (6.8)	1.0000
Constipation, n° (%)	8 (17.4)	12 (27.3)	.4533
Pont Ba >stage 2, n° (%)	4 (8.7)	4 (9.1)	.5465
Pont C>stage 2, n° (%)	3 (6.5)	3 (6.8)	.9123
Point Bp>stage 2, n° (%)	2 (4.3)	3 (6.8)	.2207

Conclusions: This study demonstrates that both operations are equivalent in results for anatomy, function and QoL. However, L-SCP+TH has a higher incidence of mesh-related complications than L-SCP+SH.