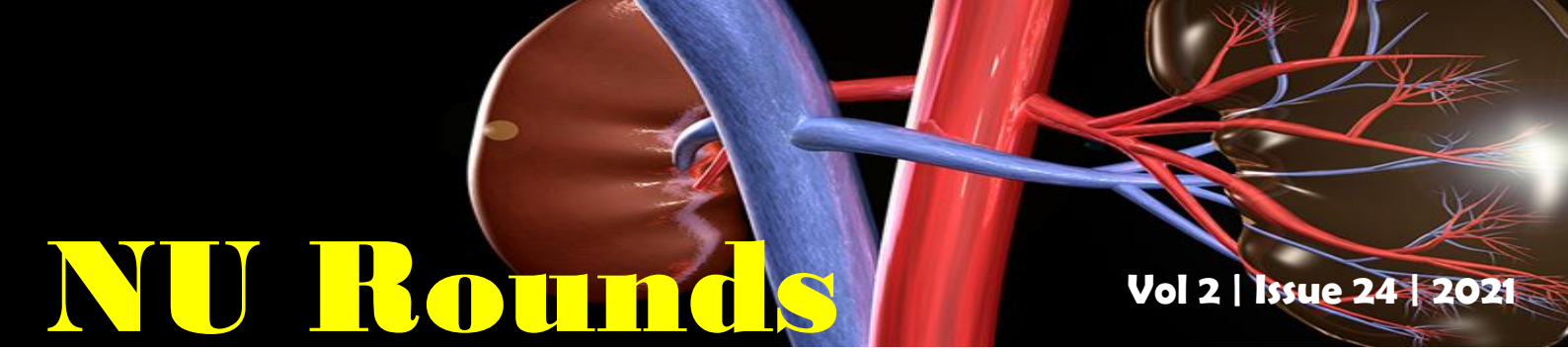

NU Rounds

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you "**NU Rounds**" which contains latest and interesting news in the field of Urology.

Inside This Issue:

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

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Incidental diagnosis of non-functional bladder paraganglioma: a case report and literature review

Introduction

Paraganglioma of the urinary bladder (PUB) is a rare disease, accounting for 0.06% of all bladder tumors. The PUB symptoms are correlated with over secretion of catecholamine or tumor impact. It is classified into functional and non-functional. Functional PUB usually exhibits symptoms such as headache, syncope, palpitation, and sweating. However, 10–15% of these tumors are non-functional and in 10%, hormone activity does not manifest clinically. Non-functional PUB might have symptoms such as frequency and urgency of urination, intermittent painless whole course gross hematuria, and lumbar discomfort. In addition, histological characteristics such as the death of focal transparent cells and burnt muscle infiltration might be easily diagnosed as bladder cancer. The present study reported a case of a female patient who underwent bladder tumor resections two times due to the confusion of bladder cancer and whose histopathological and immunohistochemical results confirmed paraganglioma.

Case Presentation:

A 62-year-old female presented with the symptoms of stomach ache, frequent micturition, and urination pain for 20 days. Diagnosed with high blood pressure 1 year ago, administered Amlodipine besylate tablets 5 mg po qd occasionally, did not check blood pressure; denied any tumor observation in the family history. Colour ultrasound of the urinary system showed a 38 mm × 34 mm hypoechoic mass on the right side of the bladder, CDFI: in the masses, blood supply was sufficient.

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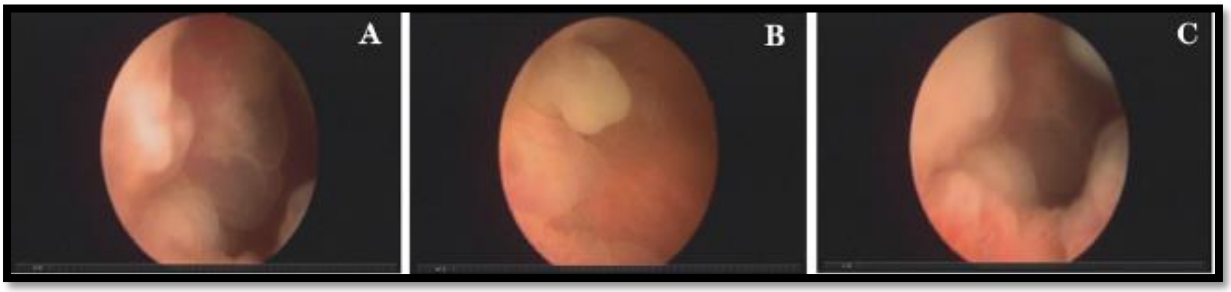
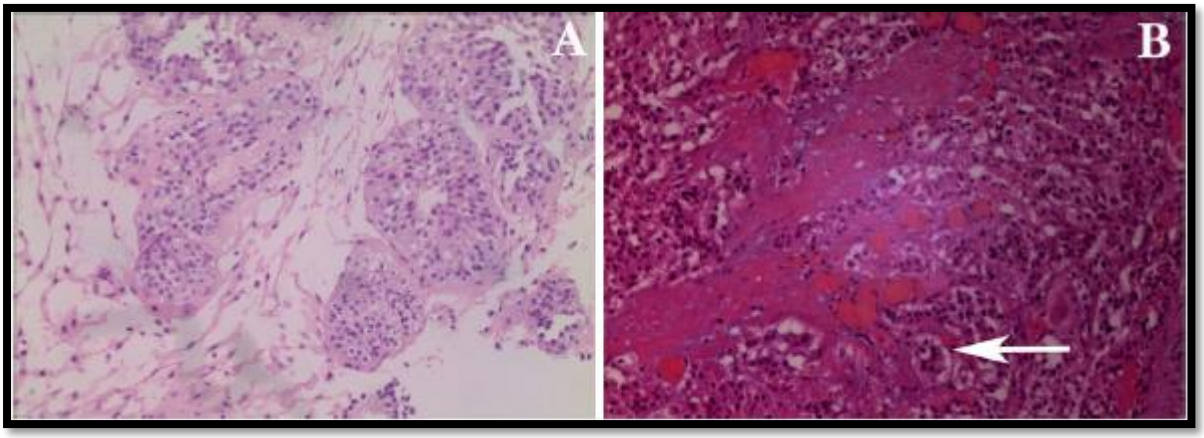


Cystoscope. a, b Large tumor was observed in the right side of the bladder; a large number of growing follicles were observed; dead tissue and broad-based were seen; c the bottom of the tumor continued to the entrance of the right side

Cystoscope showed bladder occupying lesion. Biopsy diagnosis: papillary polypoid cystitis was suspected as a malignant change.



Pathology. a This image showed papillary polypoid cystitis; b arrow showed tumor cells were arranged in small nests, the interstitial blood sinuses were also abundant

Then, the patient was admitted to urological department. Further, computer tomography urography considered bladder cancer. Cystoscopy and biopsy failed to define the nature of the lesions in outpatient department, which prompted a transurethral resection of the bladder tumor. histopathological and immunohisto chemical results were diagnosed as bladder paragangliomas. For the reason, the tumor was removed by partial resection of the bladder. The postoperative recovery and follow-up were uneventful.

Follow-up

Three and six months after the operation, no discomfort was reported. Blood sugar and blood pressure were at normal levels. No obvious abnormality was detected by cystoscopy. However, The patient was advised regular re-examination and lifelong follow-up, with respect to blood pressure, blood glucose, urinary catecholamine, ultrasound, CT, and cystoscopy.

Discussion and conclusion

PUB mainly occurs in young Caucasians, with a male to female ratio of 1:3, mostly single, and common in the anterior wall, posterior wall, and top of the bladder. Cause of the disease is unknown. In the case of a familial paraganglioma, it may be related to the mutation in the succinate dehydrogenase coding gene. Most of the PUB was located in the submucous or muscular layer of the bladder wall; about 37% could penetrate the whole bladder wall or the pelvic wall.

Diagnosis:

Colour ultrasound of the urinary system is the first line of investigative modality to detect the silent as well as functioning ectopic lesions. Doppler demonstrates the vascular nature of these tumors. The tumor shows a low-density shadow mass with clear edge, calcium density shadow and uneven enhancement on CT. On magnetic resonance imaging (MRI), these tumors are markedly hyperintense on T2-weighted (T2W) images. In addition to the monitoring of catecholamine or its metabolites, echocardiography, CT, magnetic resonance imaging (MRI), and radiotracer molecular imaging in the clinical suspicion of PUB is essential. The histological characteristics of paraganglioma are similar to those of bladder cancer Histologically, the paraganglioma is usually composed of cells with a “zellballen” pattern with abundant eosinophilic or amphophilic cytoplasm divided by delicate vascular stroma. Biopsy of tumor tissue will confirm diagnosis with diffuse, strong positivity for neuron- specific enolase, synaptophysin, and/or chromogranin.

Treatment:

The PUB is not sensitive to radiotherapy and chemotherapy. The most common treatment is partial cystectomy. Other treatments include transurethral cystectomy and radical cystectomy. The symptoms can be controlled, and low incidence can be achieved by surgical resection. Cytotoxic chemotherapy is feasible for patients with paragangliomas that cannot be resected as they progress rapidly or exhibit marked bone metastasis. The most widely used chemotherapy regimens include CVD (cyclophosphamide, vincristine, and dacarbazine). The survival rate of patients with malignant paragangliomas is variable. According to the study population, the overall 5-year survival rate is 35–60%.

Conclusions:

Nonfunctional bladder paragangliomas are occasionally found on imaging studies with the symptoms of urinary tract infection or/and intermittent painless hematuria. It may present clinical, radiology and pathological features similar to bladder cancer, so knowledge of this generally benign neuroendocrine neoplasm is of great importance to avoid misdiagnosis. It should be accompanied by the clinical and pathological characteristics of the patient and image changes. Partial resection of the bladder can effectively treat this disease.

Source: Tu et al. Incidental diagnosis of non-functional bladder paraganglioma: a case report and literature review. BMC Urol (2021) 21:98

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Robotic radical prostatectomy: diffcult to start, fast to improve? Influence of surgical experience in robotic and open radical prostatectomy

Introduction

Radical prostatectomy (RP) may be a curative treatment option for men with localized intermediate- and high-risk prostatic adenocarcinoma . Open retropubic radical prostatectomy (ORP) is that the longest established procedure for RP. Additionally to ORP, robotic-assisted radical prostatectomy (RARP) has been widely utilized since its introduction in 2000. Studies have shown improvements in surgical outcomes concerning complication rates, blood loss, transfusion rates and hospital stay. Nevertheless, there are numerous studies comparing the oncological and functional outcomes of ORP and RARP with no definite resulting superiority. However, additionally to the high standardization and advancement of technology, there will always be a determinant of surgical experience. Nevertheless, there is the necessity to coach new surgeons. Therefore, there will always be patients undergoing RARP or ORP who are a part of a novice surgeon's learning curve. However, a robotic system may be a specific and different surgical tool reserved for specialised centres and a fewer number of surgeons, while exposure to open surgery may be a common place for all surgeons. Therefore, some experience in open surgery would be expected by any novice ORP surgeon. The way of teaching novice surgeons differs between open and robotic-assisted surgery. Open surgery allows an almost simultaneous and shut action of novice and attending surgeons. In contrast, robotic surgery creates a physical barrier with the necessity to vary position or switch consoles between novice and attending surgeons to perform surgery together in an early learning curve.

Aim: To evaluate the influence of surgical experience on surgical and oncological outcomes by comparing RARP and ORP.

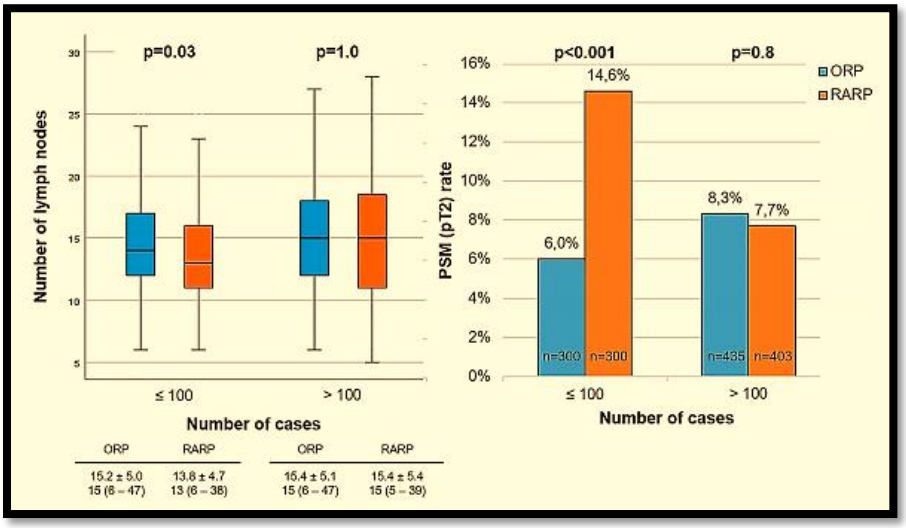
Methods:

Retrospectively analyzed data from 1438 patients who underwent ORP (n=735) or RARP (n=703). For each procedure, the level of experience of three different surgeons was summarized. Perioperative and pathological parameters reflecting surgical performance were compared between both learning curves. RARP data were influenced by new introduction of the robotic system.

Results:

The median patient age at surgery was 66 years (IQR 42–80). Patients in the RARP group were younger ($p < 0.001$) and had a lower oncological risk ($p < 0.001$). Inexperienced RARP surgeons had a higher pT2-PSM rate and lower lymph node yield (13.8±4.7 vs. 14.7±4.8; p=0.03) than inexperienced ORP surgeons. After 100 procedures, RARP and ORP surgeons had the same pT2-PSM rate (8% vs. 8%; p=0.8) and lymph node yield (15.4±5.4 vs. 15.4±5.1; p=1.0).

Lymph node yield and PSM rate of pT2 tumors depending on surgical experience



In multivariate analysis for ORP, surgical inexperience (≤100 cases) was an independent predictor of a longer operating time ((OR 9.0; p<0.001) and higher amount of blood loss (OR 2.9; p<0.001). For RARP, surgical inexperience (≤100 cases) was a predictor of a longer operating time (OR 3.9; p<0.001) higher amount of blood loss (OR 1.9; p=0.004), higher pT2-PSM rate (OR 1.6; p=0.03) and lower lymph node yield (OR 0.6; p=0.001).

Conclusions: Surgical experience has a relevant impact on perioperative and pathological parameters RARP has a higher initial pT2-PSM rate and lower lymph node yield than ORP. This is relevant for patient selection for novice teaching in RARP.

Source: Skarecky DW. Robotic-assisted radical prostatectomy after the first decade: surgical evolution or new paradigm. ISRN Urol. 2013 Apr 3;2013:157379.

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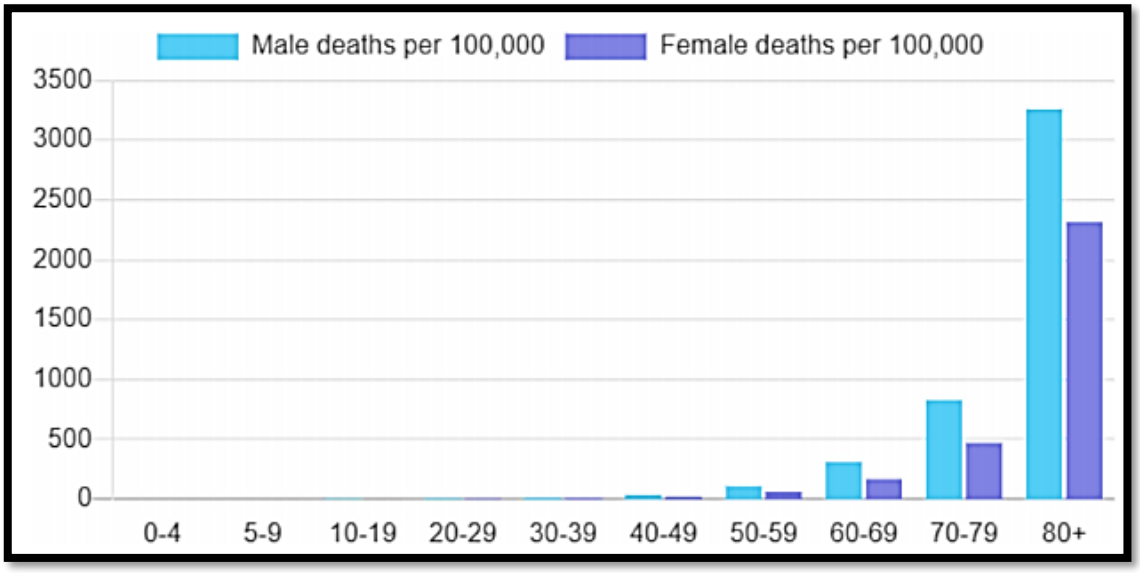
Treatment of Serious COVID-19 with Testosterone Suppression and High-dose Estrogen Therapy

In comparison to females, males more frequently experience severe acute respiratory syndrome (SARS) caused by SARS-CoV-2 and also die more frequently from COVID-19, especially for the cohort older than 50 yr.

Incidence of male and female deaths per 100 000 population by age group in years



At this age, the foremost important endocrine difference by sex is that the 10–20-fold higher testosterone levels among males, starting from 12 to 35 ng/ml, while levels among females range from 1 to 3 ng/ml. Estrogen levels don't differ between men and ladies after the age of fifty year. Testosterone has inhibitory effects on the system in terms of both cytokine production and lymphocyte proliferation. Apart from these general effects, there are two specific testosterone-dependent host cellular proteins associated with viral cell entry and to serious COVID19 disease. First, the SARS-CoV-2 virus uses ACE2 to enter the host cell. Second, the viral spike protein is primed by TMPRSS2, which is an androgen-regulated protease, and inhibition of TMPRSS2 employing a PI blocks viral cell entry. Serious COVID-19 is characterized by deterioration of lung function, and testosterone-

stimulated TMPRSS2 expression within the lung may explain the greater susceptibility to serious COVID-19 lung infections among men. Suppression of ACE2 and TMPRSS2 by inhibition of testosterone synthesis could also be an efficient treatment for COVID-19, by interfering with viral cell entry or activation. It has been shown that suppression of testosterone via androgen deprivation therapy (ADT) for the treatment of advanced prostatic adenocarcinoma also partly protects against serious COVID-19 infection. Estrogens can blunt innate immune inflammatory responses and cytokine storms and may stimulate B-cell responses and antibody production, all expected to possess a positive effect on the course of COVID-19. In contrast to testosterone, estradiol reduces ACE2 expression and TMPRSS2 activity, thereby inhibiting viral cell entry and increasing viral clearance in females. These considerations have led to two ongoing clinical studies with the estrogens, estradiol and estetrol in patients with COVID-19, focusing on clinical improvement in the acute stage of the disease (ClinicalTrials.gov NCT04359329 and NCT04801836). Recently, during a population of 1 863 478 women, significantly lower likelihood of all-cause mortality from COVID-19 has been reported for postmenopausal women using estrogen replacement therapy (adjusted odds ratio 0.22, 95% confidence interval 0.05–0.94). On the idea of those data, we propose to research the efficacy of ADT and high-dose estrogen (ADET) for the treatment of great COVID-19 disease. We recently investigated this combination therapy for the treatment of advanced castration-sensitive prostate cancer, and observed strong antitestosterone and positive estrogenic effects. The proposed ADET combined treatment will use gonadotropin-releasing hormone (GnRH) antagonists instead of luteinising hormone–releasing hormone agonists to avoid the initial testosterone increase that happens with the latter [5]. To test the ADET hypothesis, we propose a clinical study in male and feminine patients admitted to an medical care unit (ICU) due to SARS-CoV-2 infection. Patients would be randomized to no additional treatment or combined treatment with the GnRH antagonist degarelix and transdermal estradiol patches. All patients within the study would receive anticoagulant treatment. The primary endpoints would be death and duration of ICU stay.

Source: Coelingh Bennink HJT, et al. Treatment of Serious COVID-19 with Testosterone Suppression and High-dose Estrogen Therapy. Eur Urol (2021).