Robotic-assisted surgery in reconstructive surgery

Open and laparoscopic radical prostatectomy: experience at our center

Percutaneous access to the upper calyx with patients in the supine position: an initial experience

Erectile Dysfunction and associated risk factors among young Mexican adults: the importance of partner availability

Initial experience with percutaneous nephrolithotomy in the modified Valdivia position for surgical treatment of renal lithiasis patients

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Robotic-assisted surgery in reconstructive surgery

Minimally invasive surgery in Mexico, referring to initial Laparoscopic Surgery, has developed greatly over the last years. Laparoscopic procedures are currently more frequently performed in many centers in our country. These include oncologic surgery, as well as reconstructive surgery, especially in the upper urinary tract, such as laparoscopic ureteropyeloplasty. Now with the availability of robotic-assisted technology, the question is whether we will take it as far as other countries, considering that the open techniques are still the criterion standard, except in the case of ureteropyeloplasty.

It is also true that different surgical areas, such as those of gynecology and coloproctology, among others, have increased their experience in minimally invasive, laparoscopic, and robotic-assisted surgery, which has generated flows of patients that require support in reconstructive procedures.

Robotic-assisted ureteropyeloplasty

The laparoscopic approach described by Shuessler in 1993 with the same indications as for open surgery, is a procedure that requires previous training in laparoscopy of greater technical complexity, the performance of intracorporeal suturing, and when necessary, the placement of intraoperative double-J ureteral stent. However, once experience is acquired, these are movements that can be performed transperitoneally or retroperitoneally. They are facilitated through robotic surgery, reducing the complexity of the reconstruction. The robotic-assisted Anderson-Hynes repair is currently regarded as an alternative with a low complication rate, shorter hospital stay, and faster recovery period.

Robotic-assisted ureteral reimplantation

Ureteral repair due to a variety of causes has been described by different authors. Among them is the laparoscopic Psoas Hitch technique for distal ureter stricture repair. It is clear that reconstructive surgery of both the upper and lower ureter can be performed laparoscopically, including the difficulties of the movements and the manipulation of such a delicate structure, but with a better visualization of it. In their description of the robotics procedure, Mufarrij et al., with their vast experience, propose ureteral reconstruction secondary to ureteropelvic obstruction, ureterolithotomies, and ureteral reimplantations in their series. Robotic-assisted ureteral reimplantation with Psoas-Hitch has been developed by experienced surgeons with excellent results (fig. 1), blood loss of 48 ml, surgery duration of 208 min, and an average hospital stay of 4 days with no conversion data.

Robotic-assisted ureterovaginal fistula closure

Fistula is generally secondary to abdominal or vaginal hysterectomy, cesarean section, or anterior colporrhaphy. Ureterovaginal or vesicovaginal fistulas can also result from urologic surgery, surgery of the colon, and in those patients that have undergone radiation or pelvic trauma surgery and their laparoscopic repair has been performed and described. Nowadays, many groups carry out robotic-assisted hysterectomies on a learning curve, although no significant differences have been demonstrated in surgery passing from benign to malignant pathology management. Radical hysterectomy or surgery for benign pathology is a frequent intervention and is on the rise as a robotic-assisted
procedure. An excellent alternative is simultaneous repair when the lesion is detected, but if they are undetected, the ideal approach is through the same via, which is increasingly being requested by the patients themselves (fig. 2). Robotic surgery offers us three-dimensionality and support in the spaces of the pelvis that enable correct repair, even in complex situations.9

**Robotic-assisted colposacral suspension**

The repair of the different compartments has given rise to different procedures with or without meshes that have been subjects of debate with respect to results, functionality, and complications. The abdominal approach is adequately indicated in those patients with previous vaginal repair, isolated prolapse, or enterocele. It has been reproduced laparoscopically and has been compared with the open technique.10 The robotic-assisted technique has also had similar results, also in obese patients; for many years obesity was considered an impediment.11 Today there are similar results between laparoscopic and robotic-assisted surgery.

With the growth of minimally invasive surgery in its areas of laparoscopy and robotics we are able to reproduce many of the reconstructive techniques that have followed the evolutionary course of surgery from the open technique to robotic-assisted procedures. This should make it clear to us that the therapeutic option exists and that it is reproducible with good results. There should be no obstacles to this surgery when it is the best option for a given case. Many cases require delicate movements and precise reconstructions, which are two of the great characteristics of robotic surgery, together with improving our vision for correctly identifying planes in anatomies that have been modified or seriously compromised.

**References**


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Open and laparoscopic radical prostatectomy: experience at our center

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Abstract

Aims: At the Complexo Hospitalario Universitario de Santiago de Compostela (Spain), retropubic radical prostatectomy has been performed since 1993 and laparoscopic radical prostatectomy since 2006. We decided to analyze our results and compare the two techniques.

Methods: A retrospective observational study was conducted that included all laparoscopic prostatectomies performed within the time frame of January 2011 and September 2013 (62 cases) and all the open prostatectomies performed in 2012 (100 procedures).

Results: We found no statistically significant differences in either the functional (p = 0.15) or oncologic (p = 0.07) results, but there was a statistically significant difference in relation to complications (p = 0.04). The laparoscopic approach is currently the most frequently performed surgical option in our center for the radical approach to prostate cancer.

Conclusions: Laparoscopic radical prostatectomy is a technique with a long learning curve. Nevertheless, we consider that this procedure provides benefits to the patient presenting with prostate cancer, especially with respect to pain, complications, and functional and oncologic results.

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Material y métodos: Hemos realizado un estudio observacional retrospectivo que incluye todas las prostatectomías laparoscópicas desde enero de 2011 hasta septiembre de 2013 (62 casos), y todas las prostatectomías abiertas realizadas en 2012 (100 intervenciones).

Resultados: No hemos hallado diferencias estadísticamente significativas en resultados funcionales (p = 0.15) ni oncológicos (p = 0.07), aunque sí en complicaciones (p = 0.04). En la actualidad el abordaje laparoscópico es ya la opción quirúrgica más frecuente en nuestro centro para el abordaje radical del cáncer de próstata.

Conclusiones: La prostatectomía radical laparoscópica es una técnica con una curva de aprendizaje larga; pese a ello, consideramos que su aprendizaje aporta beneficios al paciente con cáncer de próstata, especialmente en cuanto al dolor, las complicaciones, así como los resultados funcionales y oncológicos.

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Introduction

Adenocarcinoma of the prostate is the tumor with the highest incidence in the male population worldwide1,2 and was the third cause of death by cancer in Spanish men in 2005, with 5,511 deaths.3

Surgical treatment is radical prostatectomy (RP). In 1982, Walsh and Donker introduced open retropubic radical prostatectomy (ORRP), which remained the surgical treatment standard for decades, providing more than 10 years of life expectancy for patients with low-risk tumors.1

In 1992, Schuessler et al. presented the first case series of laparoscopic radical prostatectomy (LRP), concluding that it offered no benefits with respect to ORRP and that the laboriousness of its performance would hinder its future implementation.4

In 1998, Guillonneau et al. introduced descending LRP with transperitoneal access that has shown functional and oncologic results similar to those of ORRP.5 The biggest drawback of LRP is still its technical difficulty. A recent multicenter study reported that a surgeon must perform 750 procedures to complete the learning curve.6

At the Complexo Hospitalario Universitario de Santiago de Compostela we have routinely performed RRP since 1993. The first LRP was carried out in 2006, and since then, the percentage of laparoscopic surgeries has grown each year. The aim of our study was to compare the two techniques to evaluate whether LRP offered more advantages to our patients or whether the 2 surgeries had equivalent results.

Methods

A retrospective, comparative, observational study was conducted that included all the LRP and ORRP performed within the time frame of January 2011 to September 2013 (62 cases, representing 38.3% of the case series that was studied) and all the RRPs performed in 2012 (100 patients, 61.7% of the series). The 2 study groups were attended to at a single center: the Complexo Hospitalario de Santiago de Compostela (Spain).

The following data were obtained from the case records: age, date of intervention, surgery duration, tumor characteristics, perioperative and postoperative complications, and patient progression in the successive check-ups at our outpatient service.

Tumor stage was determined through the TNM classification, both clinical (in all the cases according to physical examination and digital rectal examination) and pathologic (considering the anatomopathologic study of the prostatectomy specimen). Preoperative and postoperative prostate-specific antigen (PSA) levels were also analyzed, along with the Gleason grade of the biopsy samples and extirpated organs that were seen in the majority of patients.

Continence was determined in accordance with absorbents required, asking each patient the number of compresses or diapers used per day.

Sexual potency was evaluated through a directed interview, in which the patient was asked about his capacity to satisfactorily perform sexual relations before and after the procedure, as well as the use of oral, intraurethral, or intracavernous drugs for erectile dysfunction.

The R package was employed for the statistical analysis. The chi-square test was used for the susceptible qualitative variables (utilizing the Yates correction in case of expected frequencies equal to or lower than 5) and the Student’s t test for the quantitative variables. Results with a significance level lower than 5% were regarded as statistically significant (in other words, p ≤ 0.05).

Results

The mean age was 65.12 years (± 5.90) in the patients that underwent ORRP and 63.68 (± 6.04) for the patients that underwent LRP (p = 0.13). The mean PSA level was 8.05 (± 6.57) in the ORRP patients and 6.93 (± 1.95) in the LRP patients (p = 0.098). The predominant clinical stage was cT1c in both groups (p = 0.3755). The Gleason score of the prostate biopsy samples seen in the majority of patients was 6 (3+3), and broken down by technique was 57.94% for ORRP and 70% for LRP (p = 0.0623). It should be mentioned that only 4 patients with a Gleason score of 8 in the biopsy were operated on, all of them through open surgery. Tumor burden in the biopsy, quantified as the number of affected cores, was higher in the LRP group (5 cores as opposed to 4).
Patients were not selected in relation to prostate volume: 38.65 cc (11.93-100) in the ORRP group and 35.53 (15.5-84) in the LRP group (p = 0.6707) (table 1).

There was clear understaging of Gleason grade in the surgical specimen study in both techniques, as well as a majority of organ-confined tumors. Pathologic stage analysis showed localized tumor in 76.41% of ORRP patients and in 84.74% of the LRP patients (p = 0.2048) (table 1).

In regard to surgery duration, ORRP was the faster surgery: 145 min for ORRP compared with 193 min for LRP (p < 0.005). The median hospital stay was 4 days for both techniques (p = 0.12).

There were more complications with ORRP and the difference was statistically significant (p = 0.04). Complications in the conventional approach group were: 3 lymphoceles, one urinary fistula, and 8 re-admissions for different reasons. There were 2 re-interventions in the LRP group for non-urologic causes (table 2). Mean blood loss was 3.4 g/dl (0.8-8.4) in the ORRP group and 3.8 (0.5-7.6) in the LRP group (p = 0.06). Six of the ORRP patients (5.45%) and one of the LRP patients (1.61%) required transfusion.

### Table 1  Epidemiologic data and TNM staging

<table>
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<tr>
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<th>ORP</th>
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<tr>
<td><strong>Age</strong></td>
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<tr>
<td>Mean</td>
<td>65.13</td>
<td>63.68</td>
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</tr>
<tr>
<td>Typical deviation</td>
<td>5.90</td>
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<tr>
<td>Variation coefficient</td>
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<td>0.09</td>
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</tr>
<tr>
<td><strong>Preoperative PSA</strong></td>
<td></td>
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<tr>
<td>Mean</td>
<td>8.05</td>
<td>6.93</td>
<td>0.098</td>
</tr>
<tr>
<td>Minimum</td>
<td>1.43</td>
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<tr>
<td>Maximum</td>
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<tr>
<td>Typical deviation</td>
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<tr>
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</tr>
<tr>
<td>T2b</td>
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<tr>
<td>T2c</td>
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<td></td>
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<td>T3</td>
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<td>&lt;5</td>
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<td>5.00</td>
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<td>6 (3+3)</td>
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<tr>
<td>8 (4+4)</td>
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<tr>
<td>8 (5+3)</td>
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<tr>
<td>8 (4+4)</td>
<td>4.72</td>
<td>1.69</td>
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ORP: open radical prostatectomy; LRP: laparoscopic radical prostatectomy.
Hematuria presented in only 8 patients that underwent the classic approach (table 2). Immediate postoperative progression was evaluated through the visual analogue scale (VAS) for pain in all the patients during the 2 days following the intervention. The ORRP patients had more discomfort (2.19 compared with 1.88 out of 10), but this result was not statistically significant (p = 0.31).

Surgical margins were classified into 3 groups: absent, focal, and extensive. There was a lower percentage of positive margins in the laparoscopic technique (p = 0.07) (fig. 1).

Continence was classified in relation to the number of absorbents required daily. A total of 65.42% patients in the conventional technique group and 73.33% in the laparoscopic group were continent (or used a protective compress) (p = 0.56) (fig. 2).

Sexual potency was evaluated at the most recent consultation for each patient, resulting in favorable results for LRP, with 15% more patients capable of maintaining sufficient erection, compared with the ORRP (p = 0.15) (fig. 3). Due to the patient load, there was scant use of validated questionnaires (such as the International Index of Erectile Function, IIEF-5), but all the patients were interviewed.

**Discussion**

In our center, ORRP is the technique that has been regularly performed during the last 20 years and with good results by both skilled and inexperienced urologists. In contrast, surgeons performing the laparoscopic technique have begun their learning curve in LRP in the last decade. We decided to compare the two groups for the first time, to determine whether the laparoscopic approach, which is more demanding technically, also provided benefits.
Given that this was a retrospective review, there was no case randomization or patient selection for one technique or the other. No statistically significant differences were observed in any of the demographic or clinical staging parameters.1

Clearly significant differences were observed in relation to surgery duration. Even though current laparoscopic surgery duration at our center has noticeably decreased, we believe it will be difficult for the laparoscopic surgical time to equal the duration of conventional surgery.

Complications were analyzed according to the Clavien-Dindo classification7, obtaining better overall results for laparoscopy (p = 0.04) (table 2).

The almost significant oncologic results have been in favor of laparoscopy (fig. 1). We exclusively evaluated surgical margins and their size, but in the literature reviewed, it was not possible to define the relative risk of this anatomopathologic finding in relation to tumor recurrence.

Some studies infer that a positive surgical margin and a Gleason score equal to or above 8 are independent factors for biochemical recurrence,1 but other articles point out that the application of adjuvant radiotherapy to all patients whose anatomopathologic study does not ensure complete prostate tumor extirpation would suppose overtreatment of 60% of patients.8

Therefore, when we have a longer follow-up time, we will analyze our study population in relation to other predictive factors of biochemical progression, such as: PSA upon diagnosis and surgical specimen stage or perineural infiltration.9

The functional results (continence and sexual potency) have also been favored by the laparoscopic technique, but not with enough significance to demonstrate its superiority (figs. 2 and 3). It should be mentioned that due to a lack of precision in the medical history and the existence of different classifications, an effort was made to minimize bias by gathering the functional result data by telephone.2,12-13

And finally, we observed that the patients presented with less pain and had a lower complication rate with the laparoscopic technique, and the oncologic and functional results, especially, were more encouraging.

As often is the case with such prevalent diseases, there are numerous treatment options.

RP is considered an ideal treatment for low-risk or intermediate tumors (Grade A recommendation) and its use is thought to be reasonable in high-risk tumors (Grade B recommendation). Currently, exeresis of the prostate is mainly performed as a retropubic, laparoscopic, or robotic procedure, with no technique being able to show superiority over the other.14

In this context, we decided to compare our case series, made up exclusively of retropubic surgeries and transperitoneal laparoscopies in order to detect the statistically significant differences between the two techniques.

The study was retrospective, and there has not been a long enough follow-up period, but our results have shown that there is better surgical margin control and a greater probability of recovering continence and potency with the laparoscopic technique, in the hands of the skilled surgeon. And therefore, in our center, LRP is the standard radical surgery for prostate tumors, excepting individual cases that still are managed through the classic approach.

In the future, when we have a larger case series and longer follow-up periods, we will reanalyze our results, adjusted by new parameters such as clinical and biochemical recurrence, radiotherapy (adjuvant or rescue), or the different therapies of penile rehabilitation. We also hope to be able to bring robotic-assisted therapy to our center; it is less demanding technically and is showing encouraging functional results.2

**Ethical responsibilities**

Protection of persons and animals. The authors declare that no experiments were performed on humans or animals for this study.
Data confidentiality. The authors declare that they have followed the protocols of their work center in relation to the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

Financial disclosure
No financial support was received in relation to this article.

Conflict of interest
The authors declare that there is no conflict of interest.

References
Percutaneous access to the upper calyx with patients in the supine position: an initial experience

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KEYWORDS
Percutaneous nephrolithotomy: Supine position; Renal lithiasis; Upper pole

Abstract
Background: The correct choice for the percutaneous puncture site is key to the success of any percutaneous nephrolithotomy. The ideal puncture should maximize the effectiveness of the procedure in terms of stone-free rate and minimize the risk for complications. It is necessary to correctly choose the calyx to be accessed; in certain cases the upper calyx is the ideal site.

Aims: To report our experience with the percutaneous approach to the upper pole with patients in the supine position.

Methods: A retrospective, observational, descriptive study was carried out on patients with stones in the renal pelvis or upper calyx treated through percutaneous nephrolithotomy.

Results: A total of 17 patients were included in the study, and 17 kidney units were treated. All 17 patients (100%) underwent general anesthesia. Nine (53%) of the patients were men and 8 (47%) were women, with a mean age of 45.8 years (range: 18-72). Stone site was the right kidney in 10 (59%) patients and the left in 7 (41%). A total of 13 (76%) patients were symptomatic. The mean body mass index was 27 kg/m² (range: 20-34). ASA classification was I in 13 (76.4%) patients, II in 3 (17.6%) patients, and III in one (5.8%) patient. Eight (47%) patients underwent previous treatments. Procedure success or stone-free rate was achieved in 14 (82.3%) patients with the first treatment and in 17 (100%) with the second treatment.

Discussion: Current knowledge of the pleural and diaphragmatic anatomy, the use of real time ultrasound for percutaneous puncture, and the development of new surgical techniques have considerably reduced the risk for intrathoracic complications.
Accesso percutáneo al cáliz superior en posición supina: experiencia inicial

Resumen
Antecedentes: La correcta elección del sitio de punción percutánea es un punto clave para el éxito de cualquier nefrolitotomía percutánea. La punción ideal debe maximizar la efectividad del procedimiento en términos de tasa libre de cálculos y minimizar el riesgo de complicaciones. Es necesario elegir correctamente el cáliz a abordar; en algunas ocasiones el cáliz idóneo es el superior.

Objetivo: Reportamos nuestra experiencia en posición supina en el abordaje percutáneo del polo superior.

Material y método: Estudio retrospectivo, descriptivo, observacional. Se incluyeron pacientes con cálculos renales en la pelvis o el cáliz superior que fueron tratados mediante nefrolitotomía percutánea.

Resultados: Se incluyeron un total de 17 pacientes y 17 unidades renales fueron tratadas. Se llevó a cabo anestesia general en las 17 (100%) cirugías. Nueve pacientes eran varones (53%), y 8, mujeres (47%), con una edad media de 45.8 (rango: 18-72) años. Sitio del cálculo derecho/izquierdo: 10 (59%)/7 (41%). Pacientes sintomáticos: 13 (76%). Índice de masa corporal 27 (rango: 20-34) m2. ASA I, 13 (76.4%), ASA II, 3 (17.6%), ASA III, uno (5.8%). Ocho pacientes habían sido sometidos a tratamientos previos (47%). Tamaño del cálculo: 28.5 (15-42) mm. Éxito del procedimiento o tasa libre de cálculo: 14 (82.3%) en el primer tratamiento y 17 (100%) en el segundo.

Discusión: El actual conocimiento de la anatomía pleurodiafragmática, el uso del ultrasonido en tiempo real para la punción percutánea y el desarrollo de nuevas técnicas quirúrgicas ha reducido notablemente el riesgo de complicaciones intratorácicas.

Conclusión: El acceso al cáliz superior en posición supina es seguro y reproducible. Este acceso ofrece una excelente visión de todo el sistema pielocalicial y solo se debe reservar para casos en donde el cáliz inferior no resulta ser la mejor opción.

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Conclusions: Access to the upper calyx with the patient in the supine position is safe and reproducible. This approach provides excellent vision of the entire pyelocaliceal system and should be reserved for cases in which the lower calyx is not the best option.

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Introduction

The correct choice of percutaneous puncture site is a key point for the success of any percutaneous nephrolithotomy (PNL). The selection of the best calyx for entrance to the urinary tract should be planned preoperatively based on computed tomography and other imaging studies. The ideal puncture should maximize the effectiveness of the procedure in terms of stone-free rate and minimize the risk for complications, especially bleeding and visceral damage.

An undisputable advantage of the supine position is that prior to puncture, diagnostic flexible ureteroscopy can be performed for the purpose of knowing the best puncture site (calyx), stone characteristics (if it is impacted or not), dilation capacity of the pyelocaliceal system, size of the infundibulum, and even a change in treatment criterion (PNL to flexible ureteroscopy or vice versa). PNL is the method of choice for the treatment of large volume stones, complex stones, or when another treatment has failed or is likely to fail.

In order for percutaneous treatment of kidney pathology to be successful, the calyx for approach must be correctly chosen and in some cases the ideal one is the upper calyx (UC). Either because the urologist is not accustomed to this approach or due to the risk for intrathoracic complications, intercostal approaches in the prone position are not frequently employed, and even less so, in the supine position.

The aim of this study was to report our experience with the supine percutaneous approach to the upper pole utilizing 3 different techniques:
1) Caudal displacement of the lower pole
2) Intercostal puncture guided by fluoroscopy and ultrasound
3) Intercostal puncture guided by fluoroscopy and controlled ventilation

Methods
A retrospective, descriptive, observational study was conducted that included a total of 17 patients, and consequently 17 kidney units, diagnosed with kidney stones predominantly in the UC or that had the highest success rate with UC access. The variables included were: age, sex, affected kidney, ASA, body mass index, prior treatment failure, stone size, technique employed for UC puncture, surgery duration, transfusion rate, use of nephrostomy or not, use of Holmium laser or not, success rate, hospital stay, and complications. All the patients were operated on by the same surgeon (JAZG). Patients with incomplete case records or that had 2 or more percutaneous tracts were excluded from the study.

Preoperative protocol
The following studies were done on the patients: Computed axial tomography, urine culture, and preoperative antibiotic management in all patients. Postoperative protocol: Measurements were made using the visual analogue scale for pain, use or administration of simple analgesics for all patients, removal of the nephrostomy tube, and computed axial tomography to evaluate stone clearance (success rate).

Technique
1) Caudal displacement of the lower pole
The previously described position and percutaneous access technique were used. General or regional anesthesia were indiscriminately utilized. The modified Galdakao or Valdivia positions were used. After cystoscopy and the placement of a 6 Fr straight catheter to perform retrograde pyelography or diagnostic flexible ureterorenoscopy, we made an initial subcostal incision to the lower calyx (LC) with an 18 G diamond-tip Chiba needle. We introduced a hydrophilic guidewire and then we shifted the proximal end of the needle in a cephalad direction achieving caudal displacement of the kidney (fig. 1). We attached this needle with a Kelly forceps and proceeded in a subcostal manner to the puncture of the upper pole with a new needle, thus achieving a kidney displacement of 3 cm, on average.

A completely subcostal puncture of the upper calyx was made with the previously described “one shot” technique (fig. 2).10–11

The Endovision technique is sometimes employed for puncture precision and safety (fig. 3). The majority of times we use ultrasound to identify the pleura or the colon. In the nephrostomy we generally use a Foley or a 16 Fr Nelaton catheter.

2) On some occasions the intercostal approach can be imminent. Through ultrasound, we locate the upper pole, ensuring that there is no pleural interposition, and guided by fluoroscopy, we access the upper calyceal system. The transducer is placed perpendicular to the major axis of the kidney for correct visualization of the UC.

3) Fluoroscopy-guided intercostal puncture with controlled ventilation (fig. 4): when intraoperative ultrasound is not available, we reproduce the described technique for puncture in the prone position,12 puncturing the skin and perirenal tissues during expiration, and puncturing the collecting system during inspiration. Theoretically,

Figure 1  Retrograde pyelography image of the patient with a duplex collecting system.

Figure 2  Caudal displacement of the left pole and tract identification.
this reduces the risk for pleural puncture. After puncture, we place a Roadrunner® guidewire and dilate it in one shot to 24 Fr (fig. 5). Flexible nephroscopy is routinely carried out at the end of the procedure, regardless of the calyx accessed.

Results

A total of 17 patients were included in the study, representing the treatment of 17 kidney units. General anesthesia was used in the 17 (100%) surgeries. Nine (53%) of the patients were men and 8 (47%) were women. The mean age was 45.8 (range: 18-72) years. Stone laterality was: 10 (59%) right side and 7 (41%) left side. Symptomatic patients: 13 (76%). The mean body mass index of the patients was 27 (range: 20-34) kg/m². ASA 1: 13 (76.4%), ASA 2: 3 (17.6%), and ASA 3: 1 (5.8%) (table 1). Patients that underwent previous treatments: extracorporeal lithotripsy/ureteroscopy/failed PNL: 8 (47%). Partial staghorn stones: 5 (29.4%). Mean stone size: 28.5 (range:15-42) mm. Ultrasound assistance for making the tract: 12 (70.5%) patients. UC percutaneous access: 17 (100%) patients. 24 Fr operating tube was used in 17 (100%) patients. Double-J catheter was left in 100% of the patients and nephrostomy was done in only 14 (82.3%) patients. Mean surgery duration

<table>
<thead>
<tr>
<th>Table 1 Preoperative patient values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients/surgeries performed, n</td>
</tr>
<tr>
<td>Age (years), mean (range)</td>
</tr>
<tr>
<td>Sex W/M, n</td>
</tr>
<tr>
<td>Stone side (R/L), n</td>
</tr>
<tr>
<td>BMI 1/2/3, n</td>
</tr>
<tr>
<td>BMI, m² body surface area, n (range)</td>
</tr>
<tr>
<td>Previous treatment, n (%)</td>
</tr>
<tr>
<td>Symptomatic patients, n (%)</td>
</tr>
<tr>
<td>Stone size in mm, mean (range)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2 Procedure results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puncture technique, n (%)</td>
</tr>
<tr>
<td>Fluoroscopy alone</td>
</tr>
<tr>
<td>Fluoroscopy + ultrasound</td>
</tr>
<tr>
<td>Lower pole distraction technique</td>
</tr>
<tr>
<td>Surgery duration (min), mean (range)</td>
</tr>
<tr>
<td>Laser use n (%)</td>
</tr>
<tr>
<td>Success at first event, n (%)</td>
</tr>
<tr>
<td>Success at second event, n (%)</td>
</tr>
<tr>
<td>Complications, n (%)</td>
</tr>
<tr>
<td>Urosepsis n (%)</td>
</tr>
<tr>
<td>Urocutaneous fistula</td>
</tr>
</tbody>
</table>
was 91.5 (55-140) min. Laser lithotripsy was carried out on 3 (17.6%) patients. In regard to procedure success or stone-free rate: 14 (82.3%) with the first treatment and 17 (100%) with the second treatment. Three patients underwent a second look in the second treatment. Mean hospital stay was 2 (range:1-4) days. There were complications in 2 patients (11.7%): urosepsis 1(5.7%), urinary fistula 1(5.7%), and there were no transfusions (0%) (table 2). A transurethral catheter was placed in the patient with urinary fistula for 7 days and the fistula was resolved.

The UC was punctured using the technique of caudal kidney displacement in 4 (23%) patients.

The controlled ventilation technique was used in 4 (23%) patients.

Three (17%) patients had intense pain, making it necessary to remove the nephrostomy tube in fewer than 24 h.

Postoperative pain was routinely treated in the postoperative period with 90 to 120 mg of ketorolac daily.

Discussion

The supine position for percutaneous approaches is not new. In 1954, radiologists described kidney punctures for the purpose of performing pyelography. Later, Valdivia-Uria et al. described access in the supine position finding the same results in relation to clearance and complication rates.

It is widely described that supracostal approaches imply a risk for pulmonary and intrathoracic injury and this risk progressively increases the “higher” the puncture.

The choice of which calyx to puncture is based on the ability to provide maximum stone clearance through a point of entrance with minimum trauma to the parenchyma or adjacent organs. Once the operating tube has been placed, the UC offers the best course for checking the entire pyelocalceal system.

In comparison, with the LC approach, the operating tube has less torque, less reach, and less stability.

Current knowledge of pleuropulmonary anatomy, the use of real time ultrasound for percutaneous puncture, and the development of new surgical techniques have noticeably reduced the risk for intrathoracic complications. The great versatility of upper access for resolving pathology of the calyceal systems and the ureter are reached more easily, especially the upper pole of the right kidney is surrounded by the eleventh rib and in the tenth intercostal space. It can move caudally as much as 2 vertebral bodies during inspiration in the prone position. During total expiration, 80% of the upper polar lies above the twelfth rib and at the end of expiration, when the supracostal approach is being used, the pleura can be passed through on the right side in 29% of the cases and on the left side in 14% of the cases.

With these anatomic data, it could be said that puncture above the twelfth rib could be safe, but there never should be puncture above the eleventh rib, and much less above the tenth.

The following recommendations have been described for reducing the incidence of complications during intercostal puncture:

1. Maintain a puncture site as medial as possible, outside the lateral edge of the erector-spinal muscle.
2. The puncture should be made at the lateral half of the rib.
3. With the patient in total expiration, the surgeon penetrates the retroperitoneum, whereas entrance to the collecting system is carried out during total inspiration, a maneuver that caudally displaces the kidney.

Some case series have reported the UC approach through a subcostal puncture of the LC, despite the risks and limitations that the oblique course of the tract could have. Rigid instruments could damage the peri-infundibular vessels when attempting to introduce them into the UC due to the sharp angle between that calyx and the renal pelvis.

With respect to the UC approach, the literature is clear about possible intrathoracic complications. Access above the tenth rib has a high complication rate and it should never be used. There are many techniques that describe access to the UC in the prone position, none of which have been shown to be better than the other, and these same techniques have been extrapolated to the supine position with similar results. Falahatkar et al. describe pulmonary insufflation as a puncture method, thus abandoning the supracostal punctures. Goyal et al. describe the technique of caudal displacement of the lower kidney pole, stating that they managed to caudally displace the kidney 3.2 cm, on average, thus avoiding intercostal punctures.

An advantage of *Endoscopic Combined IntraRenal Surgery* is that there is no need for intercostal punctures or multitracts. Theoretically, retrograde access enables better revision of the collecting systems. The use of flexible instruments and the “pass the ball” technique has resulted in the UC approach not being frequently used, something we do not agree with.

In the supine position, access to the UC is much shorter than to the LC. The tract is more stable and the rest of the calyceal systems and the ureter are reached more easily, but it has the disadvantage that it is not very mobile and in general the immediate postoperative period is more painful than with access to the LC. Perhaps this is due to trauma to the periosteum of the ribs with the dilators or to the rupture of the intercostal muscles.

There are not many reports in the literature in regard to the UC approach. In fact, Nour et al. state that puncture in the UCs is almost impossible with the patient in the supine position and tends to only be used for treating staghorn stones.
The majority of the reports state that it is preferable to access the kidney through the LC in either the prone or the supine position, because it is safer in terms of intrathoracic complications. Despite this, the upper and middle calices should be accessed when it is deemed necessary. In the case series by Neto et al., UC access was used in 5.7% of their patients, which was a very similar result to ours. 10, 25

There are also few reports on complications of the UC approach in the supine position. However, the prone position has been associated with a higher complication rate than the subcostal approach. Punctures in the prone position above the eleventh rib have a particularly high complication rate. More than 23% of those cases present with pneumothorax and hemotherox, as well as with pleural fistula. This is related to the fact that it is a transthoracic and transpleural puncture, despite being performed with the lung in the expiratory phase.

With respect to punctures above the twelfth rib (or intercostal), the incidence of hydron pneumothorax has been reported at an incidence of 4-15% and at 0% with subcostal access. 19, 26

In relation to the differences we have found regarding a subcostal approach in the supine position, the following stand out: 1) the kidney is less mobile or floating at the time of performing the puncture in the UC, 2) one shot dilation generally is more resistant, 3) the operating tube has much less mobility, 4) intraoperative blood loss could be considered a bit higher, and 5) pain at the puncture site is more intense in the postoperative period. This coincides with the observations stated by El Harrech et al. 11

Despite the accumulated literature on the subject, it is still uncertain which of the 2 positions is the best (prone vs. supine) and intercostal access in the supine position is defined even less. Based on the CROES results, it is more probable to receive an UC puncture in the prone position than in the supine position (11.4% vs. 4.0%), as well as punctures at multiple sites (9.0 vs. 4.1%). Supracostal access (above the twelfth rib) is much more common in the prone position than in the supine position (11.4 vs. 4.0%), as well as punctures at multiple sites (9.0 vs. 4.1%). Subcostal approach in the supine position, the following stand out: 1) the kidney is less mobile or floating at the time of performing the puncture in the UC, 2) one shot dilation generally is more resistant, 3) the operating tube has much less mobility, 4) intraoperative blood loss could be considered a bit higher, and 5) pain at the puncture site is more intense in the postoperative period. This coincides with the observations stated by El Harrech et al. 11

In their work with more than 300 cases of percutaneous nephrolithotomy, the authors declare that there is no conflict of interest.

References
Percutaneous access to the upper calyx with patients in the supine position: an initial experience


Erectile Dysfunction and associated risk factors among young Mexican adults: the importance of partner availability

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Abstract
Objective: To determine the prevalence of ED and associated risk factors among young Mexicans between 18-40 years of age.

Methods: An observational, cross-sectional, descriptive and analytic study was conducted. Data collection was achieved through a questionnaire. Participants completed the Urologic Health Survey for Men and the International Index of Erectile Function (IIEF-5) questionnaire. The study also included sociodemographic, clinical, and sexual behavior variables.

Results: Of the 373 questionnaires filled out, only 160 were answered completely and used for the analysis. The mean age was 25.59 ± 5.45 years. The prevalence of ED was 33.7% (mild 17.5%, mild-to-moderate 8.1%, moderate 6.3%, and severe 1.9%). The mean score for non-ED males was 24.38 ± 0.94 versus 15.41 ± 4.81 in the ED group. Univariate analysis showed a significant difference in the items of age (p<0.01), having a stable sexual partner (p<0.01), sleeping with the sexual partner (p<0.01), sexual orientation (p=0.04), and the number of sexual intercourse episodes per week (p<0.01). In the multivariate analysis “Not having a stable sexual partner” remained a significant risk factor (p=0.027, OR=2.60 [CI 1.11-6.08]).

Conclusions: In our study, young Mexican adults had an ED prevalence of 33.7% and most of the cases were mild (17.5%). Partner availability was important. No organic variables were related to ED.

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Erectile Dysfunction and associated risk factors among young Mexican adults: the importance of partner availability

Introduction

Erectile dysfunction (ED) prevalence increases with age and severely affects quality of life [1]. Despite being a frequent reason for urologic consultation, it is considered underestimated by patients, as well as under-diagnosed and under-treated, particularly in young patients. There are approximately 20 million young adults in Mexico [2] and ED [3] is increasingly being diagnosed in this age group, yet little specific information is available. International studies reported an ED prevalence of 30-35% for males between 18-40 years of age [4,5]. A survey by Barroso-Aguirre et al. reported a prevalence of 9.7% in Mexican young adults [6]. Several risk factors have been described for ED such as diabetes mellitus, obesity, smoking, hyperlipidemia, hypertension, low urinary tract symptoms, and low physical activity [4,7]. However, given that young adults have a lower prevalence of these comorbidities, other risk factors may play a greater role. The aim of this study was to determine the prevalence of ED and its associated risk factors among Mexican adults between 18 and 40 years of age.

Methods

An observational, cross-sectional, descriptive, and analytic study was designed. Proper approval by our local Ethics Committee was obtained. Young male volunteers between 18 and 40 years of age answered the Urological Health Survey for Men, together with the International Index of Erectile Function (IIEF-5) questionnaire [8]. The survey included sociodemographic, clinical, and sexual behavior variables. Participants from Mexico City were invited by e-mail or social networks to anonymously access a secure web site-hosted survey (www.surveymonkey.com/s/ESUMasculina). Invitations were sent to addresses included in databases from universities in Mexico City. ED was graded using the IIEF-5 score, according to previously reported criteria. Patients with a score ≥ 22 points were considered not to have ED [3]. ED was classified into 4 groups: mild (17-21), mild-to-moderate (12-16), moderate (8-11), and severe (5-7) [8]. Univariate analysis using the Student’s t and chi-square tests was performed, and a logistic regression multivariate analysis model was used to calculate the risk factors for ED. Statistical significance was stated as p < 0.05. Analysis was done using the Statistical Package for Social Sciences, version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 373 surveys were obtained. One hundred and sixty subjects completed the entire questionnaire and had been sexually active in the previous month, and so were included as the final sample of our study (fig. 1). The mean age of the participants was 25.6 ± 5.4 years. The prevalence of ED was 33.7% (n=54) according to the IIEF-5 (fig. 2) and the distribution for each severity group was 17.5% (n=28), 8.1% (n=13), 6.3% (n=10), and 1.9% (n=3) for mild, mild-to-moderate, moderate, and severe, respectively (fig. 2). The mean IIEF-5 score for healthy males was 24.4 ± 0.9 vs. 15.4 ± 4.8 in the ED group. Seventy-eight percent of subjects were single and 21.8% were married or living with a partner (common law). In
of sexual level, 86.9% were in college or higher and 13.1% had only elementary or high school education. According to sexual orientation, 80.6% patients were heterosexual, 13.8% homosexual, and 5.6% bisexual. One hundred thirty-three (83.1%) patients initiated sexual activity before 20 years of age and the mean of previous sexual partners was $9.9 \pm 16.1$. Condom use had always been null in 21.2% of the subjects and 15.5% were unsatisfied with the size/thickness of their penis. In this group, 28.8% of the subjects were circumcised.

A univariate analysis comparing ED versus healthy groups showed a significant difference in age ($p<0.01$). Patient comorbidities related to ED diagnosis are shown in Table 1, and there were no significant differences. No difference in educational level was found.

Table 2 shows the sexual behavior and sexual experience variables. Having a stable sexual partner ($p<0.001$), sleeping with the sexual partner ($p<0.001$), sexual orientation ($p=0.04$), and the number of sexual intercourse episodes per week ($p<0.001$) were statistically different among the groups.

All significant variables from the univariate analysis were included in a logistic regression multivariate model, which is shown in Table 3. The only variable that remained significant as a risk factor for ED was “not having a stable sexual partner” ($p = 0.027$, OR $= 2.60 [CI 1.11-6.08]$).

**Discussion**

The prevalence of ED in young men and the associated risk factors have been described for different populations. Table 4 shows the reported prevalence of ED in our country and in international studies. Laumann et al., one of the first authors to investigate sexual dysfunction, surveyed 1,410 men 18-59 years of age in the National Health and Social Life Survey (NHSLS). He found a 7% prevalence of ED in the group of subjects 18-29 years old and 9% in the group of 30 to 39-year-olds [9]. Ponholzer et al., in a series with 2,869 patients from Austria, reported an ED prevalence of 25.5-28.9% in patients between 20 and 50 years of age [7]. The evaluation method may modify the prevalence [10]. In a paper by Martín-Morales et al., an 8.48% prevalence of ED in the group of 25 to 39-year-olds was found using 6 questions
### Table 2  
Univariate analysis of sexual behavior and sexual experience variables related to Erectile Dysfunction Diagnosis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unit</th>
<th>Total&lt;sup&gt;a&lt;/sup&gt;&lt;br&gt;n = 160</th>
<th>Erectile dysfunction&lt;sup&gt;a&lt;/sup&gt;&lt;br&gt;n = 54</th>
<th>Healthy&lt;sup&gt;a&lt;/sup&gt;&lt;br&gt;n = 106</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total previous sexual partners</td>
<td>n</td>
<td>9.9 ± 16.1</td>
<td>7.1 ± 9.1</td>
<td>10.2 ± 16.5</td>
<td>0.12</td>
</tr>
<tr>
<td>Sexual partners (previous month)</td>
<td>n</td>
<td>1.2 ± 1.2</td>
<td>1.0 ± 0.9</td>
<td>1.3 ± 1.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Episodes of sexual intercourse (previous week)</td>
<td>n</td>
<td>1.5 ± 0.9</td>
<td>1.0 ± 0.7</td>
<td>1.9 ± 1.0</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

### Variable                                      | Reference | Total [n (%)]<br>n = 160 | Erectile dysfunction [n (%)]<br>n = 54 | Healthy [n (%)]<br>n = 106 | p value |
| Circumcision                                   | Yes       | 46 (28.8)                   | 11 (20.3)                        | 35 (33.0)                     | 0.21    |
| Contraception (condom)                         | Never     | 34 (21.2)                   | 12 (22.2)                       | 22 (20.8)                     | 0.18    |
|                                               | Sometimes | 51 (31.8)                   | 14 (25.9)                       | 37 (34.9)                     |         |
|                                               | Always    | 75 (46.9)                   | 28 (51.9)                       | 47 (44.3)                     |         |
| PDE5 inhibitor                                 | Yes       | 18 (11.3)                   | 5 (9.3)                         | 13 (12.3)                     | 0.76    |
| Drug abuse                                     | Yes       | 5 (3.1)                     | 3 (5.5)                         | 2 (1.9)                       | 0.57    |
| Stable sexual partner                          | Yes       | 113 (70.6)                  | 26 (48.1)                      | 87 (82.1)                     | <0.01   |
| Sleeps with sexual partner                     | Yes       | 69 (43.1)                   | 13 (24.1)                      | 56 (52.8)                     | <0.01   |
| Marital status                                 | Married<sup>b</sup> | 35 (21.8) | 8 (14.8) | 27 (25.4) | 0.06    |
|                                               | Single    | 125 (78.2)                  | 46 (85.2)                      | 79 (74.6)                     |         |
| Sexual orientation                             | Heterosexual | 129 (80.6) | 35 (64.8) | 94 (88.7) | 0.04    |
|                                               | Homosexual | 22 (13.8)                   | 14 (25.9)                      | 8 (7.5)                       |         |
|                                               | Bisexual  | 9 (5.6)                     | 5 (9.2)                        | 4 (3.8)                       |         |
| Satisfaction with size/thickness of penis      | Satisfied | 135 (84.4)                  | 41 (75.9)                      | 94 (88.7)                     | 0.18    |

<sup>a</sup> Mean ± standard deviation.
<sup>b</sup> Including living with a partner (common law).

### Table 3  
Logistic multivariate analysis: risk factors for ED.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference</th>
<th>OR</th>
<th>CI (95%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>&lt;30</td>
<td>0.45</td>
<td>0.12-1.67</td>
<td>0.29</td>
</tr>
<tr>
<td>Marital status</td>
<td>Married/cohabitation</td>
<td>0.52</td>
<td>0.11-2.49</td>
<td>0.41</td>
</tr>
<tr>
<td>Sexual orientation</td>
<td>Heterosexual</td>
<td>1.61</td>
<td>0.64-4.07</td>
<td>0.30</td>
</tr>
<tr>
<td>Stable sexual partner</td>
<td>Not having one</td>
<td>2.60</td>
<td>1.11-6.08</td>
<td>0.027</td>
</tr>
<tr>
<td>Sexual intercourse per week</td>
<td>Fewer than 3 episodes</td>
<td>6.84</td>
<td>0.85-54.89</td>
<td>0.07</td>
</tr>
<tr>
<td>Sleeps with partner</td>
<td>Yes</td>
<td>1.83</td>
<td>0.61-5.47</td>
<td>0.27</td>
</tr>
</tbody>
</table>

### Table 4  
Reported erectile dysfunction prevalence in young adults in Mexico and the rest of the world.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>n</th>
<th>Age</th>
<th>Prevalence (%)</th>
<th>ED measurement</th>
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<td>9.7</td>
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<tr>
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<td>2001</td>
<td>Spain</td>
<td>2476</td>
<td>25-39</td>
<td>8.48</td>
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<tr>
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<td>2004</td>
<td>Israel</td>
<td>5836</td>
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<td>2005</td>
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<td>2869</td>
<td>20-30</td>
<td>25.5-28.9</td>
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<td>Rynja&lt;sup&gt;9&lt;/sup&gt;</td>
<td>2009</td>
<td>Netherlands</td>
<td>151</td>
<td>17-35</td>
<td>33.6</td>
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<td>Martins&lt;sup&gt;17&lt;/sup&gt;</td>
<td>2010</td>
<td>Brazil</td>
<td>1947</td>
<td>18-40</td>
<td>35</td>
<td>Direct question</td>
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<td>Bayraktar&lt;sup&gt;2&lt;/sup&gt;</td>
<td>2011</td>
<td>Turkey</td>
<td>5438</td>
<td>18-39</td>
<td>1.9</td>
<td>IIEF</td>
</tr>
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(1-5 and 15) from the IIEF; the prevalence changed to 3.92% when a single direct question was used [11].

Using a validated questionnaire (IIEF-5, IIEF 1-5+15, SHIM) generally results in discrete discrepancies in ED prevalence across populations. Heruti et al., from Israel, found a prevalence of 26.9% from a sample of 5,836 men 25-55 years old [12]. Rynja et al. showed a prevalence of 33.6% in a sample of 151 men aged 17-35 years from the Netherlands [5]. Laumann et al. reported a prevalence of 9% in the group of 30 to 39-year-olds [9]. Martins et al. published a study done in Brazil, where a 35% ED prevalence was reported in subjects from 18 to 40 years of age [13].

Besides differences among evaluation methods, ED prevalence variations could be explained by the following factors: sociocultural differences, life-style, education, author biases, selection criteria, statistical analysis, and efficiency of health services. We evaluated a particular population sample with specific characteristics. Our participants came from Mexico City, an almost 100% urban area with access to the Internet, so people with a mid-high socioeconomic status and mid-high educational level were included. We acknowledge this limitation. However, despite being a limited sample, its characteristics and behavior can be transferred to other similar populations.

Classic papers by Laumann et al. and Ponholzer et al. described risk factors that have been confirmed by other authors. They include age, educational and socio-economic status, comorbidities, depression, sexual abuse history, and lower urinary tract symptoms [7,9]. However, we found that partner availability and previous sexual background were significant factors for ED in this population. On the one hand, having a stable sexual partner to sleep with was related to normal sexual function. Also, having fewer sexual partners (previous month) and fewer episodes of sexual intercourse (per week) was related to ED. Sexual preference was also a significant variable, with a greater homosexual and bisexual predilection in the ED group.

In regard to the relation between sexual preference and sexual dysfunction (SD), there are previous reports in a specific population of men that have sex with men (MSM). Two representative studies used items from the NHLSLS, obtaining a prevalence of 74-79% of subjects with at least one SD symptom. They found that symptoms, such as performance anxiety, low sexual desire, erection problems, or sex not being pleasurable were related to SD [14,15]. On the other hand, Lau et al. found that 42.5% of Chinese MSM had at least one SD symptom (pain during sex, 13.8%; premature ejaculation, 10.4%; anxiety, 18.7%; erectile problems, 6.3%; no pleasure, 13.8%; no orgasm, 5.6%; hypoactive sexual desire, 8.3%) [16]. Breyer et al. reported a higher rate of ED in homosexual men, compared with heterosexual men (24% vs. 12%, respectively, p = 0.019) [17].

Partner availability emerges as an important risk factor in this age group. Previous reports describing “lack of partner availability” as a risk factor for ED are described in older adult populations. They mainly focus on the impact of marital status and partner’s health status [18,19]. Our results show that having an available partner is also important in this particular age group. It may have an impact on the frequency of sexual intercourse, as well as the experience and comfort gained with the partner. Interestingly, younger age was a risk factor for ED in our analysis. We believe that it is mainly related to stable partner availability, but it could also be related to what we might call “developed sexual skills”. Despite the fact that we cannot prove a causal relationship, we feel that more frequent intercourse and a wider variety of sexual partners may aid in developing a more satisfactory sexual practice.

ED has been related to organic diseases such as hypertension or diabetes mellitus. A validated comorbidity index questionnaire was not included. However, given the low prevalence of chronic diseases in this age group, we consider it may not have influenced our global results.

Another weakness of our study was the lack of a global evaluation of psychosocial factors. Since only depression was directly queried and was not recognized as a risk factor, a complete psychological evaluation would have been ideal. Recent studies suggest that poor mental health, stress, anxiety, or alexithymia may have an impact on ED [20,21]. The method by which the survey was completed precludes an easy evaluation, but we plan to include at least a validated questionnaire in future studies.

Finally, a validated quality of life analysis was not done. Most of the participants had mild ED, but we did not measure its impact. We did not directly evaluate socioeconomic status, but the survey was web-hosted, which may reflect a relatively higher and educated socioeconomic group.

Conclusions

In our study, young Mexican adults had an ED prevalence of 33.7% and most of the cases were mild (17.5%). We found that a younger age, homosexual orientation, not having a stable sexual partner, not sleeping with a partner, and a lower number of sexual intercourses per week are factors related to ED in the univariate analysis. The only significant risk factor in the multivariate analysis was not having a stable sexual partner. Sexual experience and partner availability are important factors influencing ED in young male subjects.

Ethical responsibilities

Protection of persons and animals. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Financial disclosure

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References


4. Cunningham GR, Rosen RC. Overview of male sexual dysfunction; 2011, June [edn: UpToDate].


Initial experience with percutaneous nephrolithotomy in the modified Valdivia position for surgical treatment of renal lithiasis patients

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Abstract

Background: Renal lithiasis is a very common pathology that has been described since Hippocrates. Its etiopathogenesis involves different theories on formation that include saturation, oversaturation, crystal nucleation, crystal growth, epitaxis, matrix, crystallization inhibitors, epidemiologic aspects, and heredity. Compared with classic lumbotomy, percutaneous nephrolithotomy is a less aggressive technique facilitating kidney stone treatment. Reduced hospital stay, low analgesic use, and a shorter recovery period make this a well-accepted surgical technique by patients and it is considered the first treatment option in many cases.

Aims: To present the experience at our institution with the modified version of the previously described technique.

Methods: All surgical notes on percutaneous nephrolithotomies in the modified Valdivia position performed within the time frame of January to August 2014 were reviewed.

Results: The mean age of the patients was 42 years. Of the 10 patients included in the study, 7 were men and 3 were women. Five of the patients presented with staghorn stones, 2 with pyelic stones, and the rest with pyelic and calyceal stones. Stone size ranged from 2 to 7 cm. A total of 2 (28.6%) stones were in the lower portion of the collecting system, 7 (64%) were in the middle portion, and one (7.1%) was in the upper portion. Estimated surgery duration was a mean of 120.5 min. The complication rate (Clavien-Dindo: I-IV) was 20%, one patient presented with bleeding that was controlled, and 80% of the patients were stone free.
Conclusions: In our experience, percutaneous nephrolithotomy with the modified Valdivia technique is a safe and effective option with a high success rate, anesthesiological advantages, and few complications.

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Introduction
Renal lithiasis is a very common pathology in the area of urology that has been described since Hippocrates. Its etiopathogenesis includes different theories as to its formation (saturation, oversaturation, nucleation of a crystal, growth of a crystal, epitaxis, matrix, crystallization inhibitors, epidemiologic aspects, and heredity). Stones are made up of different components (calcium oxalates, calcium phosphate, magnesium phosphate, uric acid, urates, cystine, and medications) and they can be found at different sites of the urinary tract (kidney, ureter, bladder, and urethra).

In 1974, Brantley and Bissada utilized a panendoscope and flexible forceps to extract kidney stones. Percutaneous nephrolithotomy (PNL) reached its highest degree of perfection in 1981 when the nephroscope, sonotrode, and fascial dilation telescopic set were presented. This equipment has made it possible to have percutaneous access to the kidney, break up the stone, and extract all its fragments in a single surgical act.

Compared with classic lumbotomy, PNL is a fairly unaggressive technique that facilitates the treatment of recurrent lithiasis. Shorter hospital stay, low analgesic medication intake, and shorter work-related recovery period make this surgical technique one that is well accepted by patients and it is considered the first surgical treatment option in many cases.

Percutaneous access to the kidney was originally described by Goodwin et al. in 1955 for performing a temporary nephrostomy in a patient with hydronephrosis. The patient was placed in the prone, ventral decubitus position, most likely in order to prevent colon injury. In 1976, Fernstrom and Johansson performed the first PNL.
The subsequent reports on percutaneous access to the kidney were all described with the patient in the same position for nephrostomy, as well as for kidney stone treatment.5

This approach in the procedures of nephrostomy and nephrolithotomy was popularized and acclaimed and today is the criterion standard for different situations, even substituting open surgery in the treatment of complex stones.2

Since their introduction and up to the present, percutaneous surgery and the equipment utilized have greatly progressed, incorporating technical modifications and modernized medical instruments.7-8

In 1988, Valdivia-Uría et al. published a series of 557 nephroscopy cases, all performed with the patient in the supine dorsal decubitus position, creating an alternative for percutaneous kidney access.3

After the publication of that article, percutaneous kidney surgery in the supine position has gained ground and modifications to the Valdivia technique have been incorporated in some endourology centers.4

The aim of this study was to present a modification of the Valdivia-Uría technique in relation to the position of the patient.

Description of the technique. The patients were placed on the operating table in the total dorsal decubitus position, with the flank to be operated on at the edge of the table. No pillow or any other form of flank elevation was used.

The lower limb ipsilateral to the puncture location was slightly abducted with an approximate 15 cm elevation in relation to the table. The contralateral lower limb remained abducted, similar to the lithotomy position (fig. 1).

The upper limb on the opposite side from the puncture remained extended parallel to the torso. The ipsilateral upper limb was positioned in abduction.

We placed the surgical drapes, leaving the flank to be operated on exposed, where a sterile plastic bag to collect fluids was attached with the plastic adhesive drape (fig. 2).

The table and equipment in the operating room must be arranged so that they facilitate simultaneous cystoscopy and/or ureteroscopy with the percutaneous procedure, opposite the side of the percutaneous access; the radioscopy monitor in the upper area and the laser and video tower (with the video camera, monitor, light source, lithotripter, and recording system) in the lower area. The surgical instrument table is to the left of the surgeon (fig. 3).

All the procedures were performed under general anesthesia. We introduced a 6 Fr open-tipped catheter using a 22 Fr cystoscope. A 16 Fr Foley transurethral catheter was placed. In all the cases retrograde pyelography was carried out and the lower calyx was the puncture site in all the kidney units. Puncture was performed under fluoroscopy and there was no need to use other media, such as ultrasound, in any of the cases.

Figure 1 Modified position with 80 degree angulation axis.

Figure 2 Surgical drape placement and puncture.

Figure 3 Position in relation to the fluoroscope. Final position of the pelvic members.
Methods
A descriptive, analytic, cross-sectional study was conducted in which the surgical notes were reviewed from all the PNL procedures in the modified Valdivia position that were performed within the time frame of January to August 2014. Only patients with the complete protocol were included (table 1).

Results
A total of 10 patients were included in the study. The mean age was 42 years and 7 of the patients were men and 3 were women. Five of the patients presented with staghorn stones, 2 with pelvic stones, and the rest had both pelvic and calyceal stones. Stone size varied from 2-7 cm. Two stones (28.6%) were in the lower portion of the collecting system, 7 (64%) in the middle portion, and 1 (7.1%) in the upper portion. The estimated surgery duration was a mean 120.5 min. There was a 20% complication rate (Clavien-Dindo: I-I V) and one controlled hemorrhage. Eighty percent of the patients were left stone free (table 1).

Discussion
Efficacy: PNL and open surgery are equally efficacious for the treatment of renal lithiasis. For example, in a study on 129 patients with kidney stones, we found that PNL and open kidney surgery were associated with a similar complication and success rate. An important difference is that PNL reduced hospitalization by 60% and enabled the patient to return to work in approximately one week.
compared with more than 3 weeks after open kidney surgery. This less invasive technique also costs 40% less than open kidney surgery.

As many punctures as needed are carried out to leave the kidney in a stone free state. They are facilitated by the distension of the renal pelvis and calyces with the injection of physiologic solution or contrast when necessary. A hydrophilic guidewire is left in all the punctures for later dilation and it should be directed towards the ureter whenever possible. This makes the dilation of the percutaneous tract safer and reduces the risk for puncture miscalculation.

Whenever possible, a safety guidewire that can be positioned at the opening of the Amplatz sheath or outside it should be left in place for working. This facilitates the procedure and increases its safety.

The puncture made at the posterior axillary line is parallel to the infundibular vessels entering at the avascular “Brödel’s bloodless line”, thus reducing the possibility of vascular injury.

Obese patients benefit from the total supine position, mainly because of the anesthetic advantages, as well as not having to be moved after anesthesia.

Stone fragmentation can be performed with an ultrasound, ballistic, or laser lithotripter. The fragments are removed with a trident or foreign body forceps.

The risk for colon perforation with the patient in the supine position should be demythified, given that the colon is pushed against the kidney in the prone position, which theoretically can increase the possibility of an accident.

In relation to the position of the patient and the Amplatz sheath, the infusion of a large quantity of high-pressure fluid is not necessary for visualization. We almost always work in a dry operating field, reducing the risk for water absorption, sepsis, and fragment mobilization for the ureter or other calyces.

The nephrostomy is left in place for 7 days and the double-J catheter for 15 days. The patient is released from the hospital 24-48 h after the operation. At 30 days the patient is seen for an imaging study and laboratory test follow-up.

The stone clearance rate reported in a meta-analysis of the most recent PNL case series is around 78%. In our study, we had an acceptable stone clearance rate of 80%, compared with the 93% reported with the original Valdivia et al. technique. In regard to complications, we should point out that there were significant differences both during the intervention and in the immediate postoperative period in the overall analysis. Surgery duration was a mean 120.5 min longer than that reported with the original Valdivia-Uría et al. technique (85 min), but that is still within an acceptable range, taking into account that ours is a teaching institution. Puncture through fluoroscopy costs less than under Endovision, as described in the original technique. Thanks to the modified position the arch is more easily and freely turned in a C to ensure fewer punctures in the kidney units to be treated. The Amplatz dilators are also re-sterilized, adding to the cost-benefit of the procedure.

The transfusion rate (1%) was similar to that described in the literature and the percentage concurred with that of other supine PNL case series or with the original technique, varying from 3 to 9%. On the other hand, it was slightly lower than the rate reported by a meta-analysis conducted by the AUA for case series of PNL in the prone position. We partially attribute this to our preference in using the high-pressure balloon as the system for dilating the nephrostomy tract.

There were no colonic injuries, the same as with the original technique, this being the great advantage over the prone position, in which the colon is displaced posteriorly and laterally.

And finally, we should point out that the postoperative period was similar in relation to hospital stay and analgesic doses in reference to other similar studies.

One of the main advantages, apart from those already mentioned, is the fact that our center is a teaching hospital, which allows urology residents to participate more actively in the procedure. They can simultaneously work the urinary tract in an anterograde and retrograde manner, optimizing surgery duration and the skills of the professionals in training.

Conclusions

Various modifications have been made on the original technique described 17 years ago, all of them basically in an effort to reduce cost and surgery duration. The benefits over the prone position are indisputable and clearly demonstrated. In our experience, despite being a small case series in relation to the original case series, the results were similar and within an acceptable range. It is our goal to be able to show more advantages in a future study with a larger number of cases and to propose this type of technique as an alternative for the urologic medical community. In our institution, both the prone and supine positions are managed, making it essential to compare the two and manifest the results.

Ethical responsibilities

Protection of persons and animals. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Financial disclosure

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Conflict of interest

The authors declare that there is no conflict of interest.

References


Single-dose piperacillin/tazobactam as prophylaxis in transrectal prostate biopsy

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Abstract

Background: The increasing resistance to quinolones has led to the consideration of other antibiotic options for the prevention of infectious complications in prostate biopsy. We present our experience using a single dose of piperacillin/tazobactam as prophylaxis.

Methods: A retrospective study of transrectal prostate biopsies performed at our institution from 2008-2013 was conducted. All patients received enemas before biopsy and a single 4.5 g dose of piperacillin/tazobactam was administered i.v. a few minutes before the biopsy. Clinical and microbiological variables were analyzed to find out risk factors for complications.

Results: A total of 543 biopsies were included. Ninety-two complications (16.9%) were reported in 74 (13.6%) patients, 4.2% of which were infectious complications. In these patients, the associated risk factors were a previous history of positive urine cultures within a 3-year period before biopsy, the presence of a transurethral indwelling catheter at the time of the biopsy, hospital admission within a month before biopsy, and a preoperative positive urine culture despite antibiotic therapy selected according to the resistance pattern.

Conclusions: Physicians and patients should be aware of the risk for complications, particularly if risk factors are present. A single dose of piperacillin/tazobactam is a reasonable option for prophylaxis, especially in countries with a high prevalence of quinolone-resistant pathogens.

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Introduction

Currently, prostate biopsy (PB) is the standard method for confirming the diagnosis of prostate cancer (PCa). The implementation of widespread screening with prostate-specific antigen (PSA) has increased the number of PBs over the last decades. A rising PSA and/or suspicious digital rectal exam (DRE) are the most frequent indications for a PB.[2] Other indications include persistently elevated PSA with a low PSA free/total ratio, increased PSA velocity, PSA duplication time or PSA density, the histopathologic finding of atypical small acini proliferation (ASAP), prostatic intraepithelial neoplasia (PIN), and active surveillance.[2,4]

PB can be performed either transrectally or transperineally under ultrasound or magnetic resonance guidance. The number of cores taken depends on prostate size, history of previous biopsies, and patient age. In our center, we usually perform ultrasound-guided transrectal prostate biopsies (TRPB) with 12-18 cores at initial biopsy.[5]

The reported complication rate of TRPB is variable: bleeding occurs in up to 50% of cases, although it is usually clinically irrelevant. Nevertheless, serious infectious complications develop in 2-6% of cases, of which nearly 4% require hospitalization and treatment within 30 days after the procedure. Given the severity of infectious complications, some strategies have been recommended in order to lower their frequency, including the use of prophylactic antibiotics.[7] However, there is still controversy regarding the adequate type and dosage of antibiotic. Quinolones are the most widely recommended, because they have good penetration into prostatic tissue.[2] Unfortunately, quinolone resistance rates have increased significantly.[6] In Latin America and other developing areas around the world, the resistance rates to quinolones and cephalosporins have reached alarming figures. For this reason since 2008, we have found it necessary to use an alternative prophylactic strategy based on a single i.v. dose of piperacillin/tazobactam (P-T).[5] In this study we described the complications of TRPB, emphasizing infectious complications, with the use of this prophylactic regime.

Methods

We performed a retrospective study on men that underwent TRPB from January 2008 to June 2013 at our department. Patients without complete clinical records were excluded. We analyzed clinical, laboratorial, and pathological data, as well as follow-up information. Previous evaluation in all patients included PSA, complete blood cell count, blood chemistry, coagulation tests, urinalysis, and urine culture.

As preparation, all patients received the indication to apply a micro-enema the night before and the morning of the procedure. Prophylaxis with a single i.v. dose of P-T 4.5 g was administered 30-60 minutes before biopsy. After measuring prostate and transition zone volumes, core biopsies were obtained with semi-automatic equipment (BARD® MAGNUM® Reusable Core Biopsy System) and an 18-Gauge thru-cut needle in a systematic fashion (12-18...
cores for the first TRPB or extended protocol for subsequent procedures).
Perioperative complications were registered during the procedure and stated in the surgical report. Outpatient visits were scheduled 1 week and 1 month after biopsy. All patients were advised about possible symptoms and to go to the emergency room (ER), if necessary, in the case of further complications. Perioperative and early complications were classified according to the Clavien-Dindo system.10

We intentionally reviewed the past urologic history of the patients, looking for positive urine cultures within 3 years before biopsy and its association to urinary tract infection (UTI) or resistant strains after TRPB.

A univariate analysis was performed to find variables related to the development of infectious complications, and statistical analysis was done using the IBM® SPSS® v. 20 package.

Because of the retrospective nature of the study, ethics committee approval was not necessary. Nevertheless, patient data confidentiality was maintained and there was no violation of the Helsinki Declaration.

Results
A total of 543 men that underwent TRPB were included in the study. Mean age was 65 ± 7.51 years. Median PSA was 7.49 (0.22-3000) ng/ml. Lower urinary tract symptoms (LUTS) were reported by 68% of the patients and 66% were under ß-blocker therapy. The most frequent comorbidities were diabetes mellitus in 165 men (30.4%) and high blood pressure in 258 (47.4%). Thirty-seven patients (6.8%) had a transurethral indwelling catheter at the time of TRPB and 34 (6.3%) had a previous hospital admission within a month before TRPB.

A total of 436 men (80.3%) underwent first-time TRPB, whereas 107 (19.7%) underwent subsequent biopsy. Indications for TRPB included high PSA in 341 cases (62.7%), suspicious DRE in 33 (6.1%), both an elevated PSA and suspicious DRE in 143 (26.3%), ASAP in 11 (2%), active surveillance in 6 (1.1%), and not specified in 9 (1.6%). PSA value was < 10 ng/ml in 246 (45.3%) patients; between 10-20 ng/ml in 81 (14.9%); > 20 ng/ml in 31 (5.7%); and missing in 185 cases. Mean prostate volume was 51.46 ± 29.1 cc. Twelve-core biopsy was performed in 300 men (55.8%), more than 12 in 234 (43.5%) patients, fewer than 12 in 4 cases (0.8%), and not specified in 5.

All patients had a urine culture before TRPB, of which 35 (6.4%) were positive. Treatment was completed according to resistance pattern (fig. 1). We found that 217 (39.9%) of the patients had 2 or more urine cultures within 3 years before the procedure; 48 (22.1%) of them had at least 1 positive urine culture within that period.

Only 3 patients had intraoperative complications: one patient had transient bradycardia, one had transient hypotension (both required interruption of the procedure) and one patient presented with rash presumably due to P-T allergic reaction, in whom the procedure was completed safely.

During the first month, 74 patients (13.6%) reported at least one complication, for a total of 92 events (fig. 2). The Clavien-Dindo Classification is reported in Table 1. Two patients had acute urinary retention (0.36%) and 23 (4.2%) had infectious complications including acute

Table 1 Clavien-Dindo classification of complications within a month after biopsy.

<table>
<thead>
<tr>
<th>Clavien-Dindo classification</th>
<th>No=74 (13.63%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>66 (12.15%)</td>
</tr>
<tr>
<td>Grade II</td>
<td>5 (0.92%)</td>
</tr>
<tr>
<td>Grade III</td>
<td>3 (0.55%)</td>
</tr>
<tr>
<td>Grade IIIa</td>
<td>3 (0.55%)</td>
</tr>
<tr>
<td>Grade IIIb</td>
<td>0</td>
</tr>
<tr>
<td>Grade IV</td>
<td>0</td>
</tr>
<tr>
<td>Grade V</td>
<td>0</td>
</tr>
</tbody>
</table>

![Figure 1](Germs isolated in the last urine culture before biopsy)

![Figure 2](Complications within a month after biopsy)
prostatitis, orchiepididymitis, pyelonephritis, or fever. Sixty-nine (12.8%) patients had a urine culture within the first month, of which 19 were positive (27.5%). Two (0.3%) patients were admitted to receive i.v. antibiotics.

The univariate analysis showed that a previous history of positive urine cultures within 3 years, the presence of transurethral indwelling catheter at the time of the procedure, and preoperative positive urine culture despite antibiotic therapy selected according to resistance pattern were factors associated with infectious complications (table 2).

A positive urine culture immediately before the biopsy, even after guided treatment, was resistant to quinolones.11 The use of a single dose of antibiotic prophylaxis is an appealing strategy15, particularly in countries with a higher prevalence of resistant microorganisms. In recent years, our institutional resistance rate has risen, with 57% of *E. coli* strains being resistant to quinolones.16-17

Our results demonstrate that past medical history with a focus on infectious disease and urological issues is of the utmost relevance. As previously shown, the presence of a transurethral indwelling catheter at the time of biopsy was strongly associated with the development of infectious complications. Therefore, if possible, a TRPB should be avoided while patients are using this device or deferred until completion of proper antibiotic therapy. Other non-modifiable risk factors for infectious complications include a previous positive urine culture or UTI within a 3-year time period before biopsy. Modifiable risk factors are positive urine culture immediately before TRPB or recent hospital admission.

The former requires properly selected antibiotic therapy based on an antibiotic susceptibility test and the delay of TRPB until a negative urine culture is obtained. Moreover, it would be advisable to perform biopsy at least one month after discharge from previous hospital admission. On the other hand, some authors have demonstrated the role of rectal swabs in providing targeted antimicrobial prophylaxis, thus decreasing the incidence of infectious complications.18

We and others have previously reported the experience with a single dose of PT as antimicrobial prophylaxis9,13 or in combination with quinolones.14 The use of a single dose of antibiotic prophylaxis is an appealing strategy15, particularly in countries with a higher prevalence of resistant microorganisms. In recent years, our institutional resistance rate has risen, with 57% of *E. coli* strains being resistant to quinolones.16-17

**Discussion**

In this retrospective analysis of TRPB, we found that the overall rate of early complications was low (13.6%). Although hematuria was frequently reported, it did not require therapeutic intervention. Other well-known complications included hematospermia and rectorrhagia. Infectious complications are particularly relevant, given their life-threatening potential. The prophylactic regime with P-T allowed us to control this type of sequel (4.2%) during the first month. All patients were successfully treated and only two patients required hospital admission to complete their treatment. Sanders and Buchan analyzed 1,421 TRPBs and reported a hospitalization rate of 2.8% (40 cases) within the first month after biopsy. They used a 4-day course of antibiotics as prophylaxis, mostly with ciprofloxacin. More than 50% of isolated *Escherichia coli* strains after biopsy were resistant to quinolones.11 Another retrospective study performed in two hospitals in London, UK, reported 2.1% of infectious complications requiring admission to the ER. They used a 5-day prophylactic course of ciprofloxacin and a single i.v. dose of amikacin before the procedure. The majority of isolated microorganisms, particularly those causing bacteremia, were ESBL-producing strains that were also resistant to quinolones.12

**Table 2** Univariate analysis of factors related to infectious complications.

<table>
<thead>
<tr>
<th>Variables</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of at least one positive urine culture within 3 years prior to the biopsy</td>
<td>4.061</td>
<td>1.48–11.13</td>
<td>0.003</td>
</tr>
<tr>
<td>Transurethral catheter at the time of biopsy</td>
<td>6.235</td>
<td>2.42–16.09</td>
<td>0.001</td>
</tr>
<tr>
<td>Hospitalization within a month prior to the biopsy</td>
<td>3.051</td>
<td>0.99–9.46</td>
<td>0.05</td>
</tr>
<tr>
<td>A positive urine culture immediately before the biopsy, even after guided treatment</td>
<td>5.007</td>
<td>1.87–13.42</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Overall, the infection rate we found was consistent with rates in the literature. However, our figure is of paramount relevance, considering that with this strategy we achieved infectious complication control similar to that in the developed countries, where the use of quinolones or cephalosporins is still safe for PB prophylaxis. Even though these data suggest that a single i.v. dose of P-T does not provide better prophylaxis than other regimens, we believe it is an excellent option for clinical practice in world regions other than the US and Europe, where resistance rates make the use of quinolones prohibitive. Furthermore, besides having a broader-spectrum, in comparison with cephalosporins, P-T induces to a lesser extent the expression of ESBL-producing strains.19

Our study has some limitations, mostly due to the retrospective nature of the investigation. Moreover, the inclusion of a comparative group receiving a different antibiotic would be desirable. However, the strength of this investigation is the fact that all patients underwent a
homogenous evaluation, including a urine culture with an antibiotic susceptibility test prior to biopsy and all received the same antibiotic regime. Moreover, other advantages include the close follow-up based on electronic records and the processing of all urine cultures at our institution, as well as the description of risk factors associated with infectious complications.

We believe a single i.v. dose of piperacillin-tazobactam is an alternative for TRPB in an environment with a high prevalence of quinolone resistance. Being a single dose treatment with a broad spectrum and lower induction of resistant strains, complication rates remain low. Before performing a TRPB, it is advisable to acknowledge the following risk factors for infectious complications: a previous history of positive urine cultures within 3 years, the presence of transurethral catheterization at the time of the procedure, hospital admission within the previous month, and preoperative positive urine culture despite antibiotic therapy selected according to resistance pattern. Future research should aim to analyze these factors in a prospective fashion. Patients with a positive culture should confirm urine sterility after antibiotic treatment.

Conclusions

Prostate biopsies are a necessary procedure for the diagnosis of PCa, but urologists and patients must be aware of the risks. If possible, patients should wait if they have had recent hospitalization and transurethral catheters should be taken out. It is recommendable to have a confirmatory urine culture, even if patients have taken proper antibiotic treatments. Patients with a history of previous urine infections must be aware of the higher risk for infectious complications.

Ethical responsibilities

Protection of persons and animals. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that they have followed the protocols of their work center in relation to the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

Financial disclosure

No financial support was received in relation to this study/article.

Conflict of interest

Dr. Herrera-Cáceres, Dr. Villeda-Sandoval, Dr. Ruiz-Quiones, Dr. De La Rosa-Leiva Dr. Feria-Bernal, and Dr. Galindo-Fraga have nothing to declare. Dr. Castillejos-Molina reports personal fees as a speaker from Lilly and personal fees as a speaker from GSK, outside the submitted work.

Dr. Rodriguez-Covarrubias reports personal fees as a speaker from GSK and personal fees as a speaker from Ferring Pharmaceutical, outside the submitted work.

References


Ejaculation has no impact on prostate-specific antigen levels


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Abstract

Background: Prostate-specific antigen (PSA) is a tumor marker used in the diagnosis of prostate cancer; it is organ-specific but it is not disease-specific. The effect of ejaculation on PSA concentration is controversial.

Aim: To evaluate the impact of PSA values after ejaculation on biopsy indication in a screened population.

Methods: Baseline PSA was measured in 100 patients that had abstained from sexual activity for at least 7 days. A second measurement was carried out 48 h after ejaculation. The numerical differences were compared using the Student’s t test. The McNemar’s test was used to analyze pre and post-ejaculation values and clinical significance was defined as a PSA value above a pre-established limit for biopsy indication.

Results: Mean age of the patients was 52.7 ± 8.6 years. The mean baseline PSA was 1.39 ± 1.43 ng/mL and after ejaculation was 1.48 ± 1.51 ng/mL (p = 0.54). Two patients had PSA values that increased sufficiently for biopsy indication, using a parameter of 4 ng/mL after ejaculation. The McNemar’s test showed no statistically significant differences (p = 0.500).

Conclusions: There was no statistically significant difference in PSA after ejaculation and this change had no clinical relevance.

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La eyaculación no tiene impacto en los niveles de antígeno prostático específico

Resumen

Antecedentes: El antígeno prostático específico (APE) es un marcador tumoral órganoespecífico usado en el diagnóstico de cáncer de próstata, sin ser enfermedad-específico. El efecto de la eyaculación sobre la concentración del APE es controversial.

Objetivo: Evaluar el impacto en los valores de APE posterior a la eyaculación sobre la indicación de biopsia, en una población cribada.

Métodos: Se realizó una medición de APE basal en 100 pacientes con al menos 7 días de abstinencia sexual. Una segunda determinación fue tomada dentro de las 48 h posteriores a la eyaculación. Las diferencias numéricas fueron comparadas utilizando la prueba t de Student, mientras que la significación clínica fue medida (test McNemar) observando los pacientes que debían someterse a biopsia según valores pre y posteyaculación.

Resultados: El promedio de edad fue de 52.7±8.6 años. La media del APE basal fue de 1.39 ± 1.43 ng/ml, y de 1.48±1.51 ng/ml después de la eyaculación (p = 0.54). Dos valores de APE aumentaron suficientemente para indicación de biopsia usando un parámetro de 4 ng/ml posterior a la eyaculación. El test de McNemar no mostró diferencias estadísticamente significativas (p = 0.500).

Conclusiones: No existe diferencia significativa en el APE posteyaculación. Este cambio no fue clínicamente relevante.

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Introduction

Prostate-specific antigen (PSA) is a serine protease and its prostatic origin was demonstrated in 1979. It belongs to the kallikrein family and digests the gel that is formed in seminal fluid after ejaculation. Since its identification, it has been used in screening and in the follow-up of patients with prostate cancer (CaP). Nevertheless, it is organ-specific and not disease-specific and its role as a screening tool has recently been questioned.

A PSA between 4 and 10 ng/ml has a 20% positive predictive value for CaP. The standard cut-off point for prostate biopsy indication is 4.0 ng/ml. At some centers, the level has been reduced to 2.5 ng/ml in an effort to increase its sensitivity. However, there are circumstances other than CaP that can increase PSA values, decreasing its specificity.

Some of the conditions reported in the literature that can increase PSA are digital rectal examination, cystoscopy, prostate biopsy, transurethral catheterization, urinary retention, and bicycling. Ejaculation has also been identified as a factor increasing PSA concentration. There is controversy among different studies analyzing this association, added to the fact that the differences were only observed and evaluated from a numerical, and not a clinical, point of view.

A possible explanation for the post-ejaculation increase in PSA is the augmented pressure in the prostatic ducts, which can cause basal membrane disruption and a consequent leakage of PSA into the circulatory system.

The aim of our study was to evaluate the change in PSA values after ejaculation and its impact on the clinical indication for prostate biopsy in an adult sample of a population that underwent CaP screening.

Methods

The study was approved by our institutional ethics committee. Men between the ages of 40 and 75 years were invited to participate. Those presenting with prostate cancer, having taken 5α-reductase inhibitors within the last 6 months, diagnosed with prostatitis in the last 3 months, or having had prostate biopsy within the last 6 months were excluded from the study. Participants with a past history of pelvic surgery in the last year, radical prostatectomy, congenital urinary tract abnormalities, or International Prostate Symptom Score (IPSS) values above 8, and patients that had undergone urinary tract procedures involving the use of instruments in the last 3 months were also excluded.

All the participants signed statements of informed consent and were questioned in regard to ejaculatory abstinence within the last 7 days. A baseline serum PSA sample was later taken and the IPSS questionnaire was applied. All the samples were processed by the same laboratory. Total PSA was measured through a chemiluminescent bioassay (Abbott, Architect i4000). The second sample was obtained 48 h after ejaculation. External determination was proposed for the patients with PSA values above 4 ng/ml in either of the 2 determinations in order to make a decision from this result.

Baseline and post-ejaculation PSA were compared using the paired Student’s t test, establishing each individual as his own control. Clinical significance was defined as a PSA...
value above the levels considered the limits for prostate biopsy, based on definitions from previous studies: 2.5 and 4 ng/ml. The difference was compared through the McNemar test.

The statistical analysis was done with the Statistical Product and Service Solutions (SPSS) version 17.0 (Chicago Illinois) software. Statistical significance was set at a p < 0.05.

Results

One hundred patients with a baseline PSA sample were recruited for the study. Six of those participants were lost during the follow-up and so were excluded from the final analysis. None of those 6 differed from the participants that completed the follow-up in relation to age range (p = 0.69), IPSS score (p = 0.54), and baseline PSA (p = 0.81).

The mean age was 52.7 ± 8.6 years and the total IPSS score was 3.8 ± 2.4. The mean baseline PSA was 1.39 ± 1.43 ng/ml and after ejaculation was 1.48 ± 1.51 (table 1).

The mean difference between the 2 measurements was not statistically significant (p = 0.054). The absolute mean and percentage of change were 0.08 ± 0.41 ng/ml and 8.7 ± 21.3%, respectively (figs. 1 and 2). The mean time from the last ejaculation to the first PSA determination was 20.49 ± 41.93 days. The mean time from ejaculation to the second serum determination was 17.36 ± 10.16 h.

Ejaculation was achieved through coitus in 68 participants (66.7%), masturbation in 24 (23.5%), and 2 (2%) patients stated through wet dreams. We compared the absolute change percentage in the PSA between coitus and masturbation and found no differences in the absolute change of PSA between the 2 groups (p = 0.11), but there were differences between them with respect to the percentage of change (p = 0.02).

No correlation was found between the time from ejaculation and the absolute change of PSA (p = 0.269) or in the percentage of change of PSA (p = 0.087).

Utilizing the cut-off value of 2.5 ng/ml for biopsy indication, 16 patients would be candidates for undergoing this procedure due to their post-ejaculation result. However, 11 of them already presented with a baseline PSA value above 2.5 ng/ml (fig. 3). The McNemar test showed no differences between patients that would have to be taken for biopsy according to their baseline and post-ejaculation PSA values (p = 0.063).

Using 4.0 ng/ml as the cut-off value, 6 of the subjects had elevated post-ejaculation PSA values. Five of these patients already had a baseline PSA above the cut-off value. In fact, an elevated PSA level in one of the patients decreased to below 4.0 ng/ml after ejaculation and the post-ejaculation PSA values reached the criteria for biopsy in only 2 subjects (fig. 3). Once more, the McNemar test showed no statistically significant difference (p = 0.500).

Discussion

The current paradigm is that ejaculation affects the absolute value of PSA and it is common practice to request that the patient abstain from having ejaculation at least 48 h prior to obtaining the sample for PSA determination. Through a search of the PubMed database for clinical studies dealing with this theme, we found that the majority were conducted in the 1990s and their results were inconsistent.
Ejaculation has no impact on prostate-specific antigen levels

Nevertheless, the present day recommendation is based on studies showing significant differences.

In 1993, Simak et al. were the first to analyze the relation between ejaculation and PSA. Their study included 18 young patients and found a statistically significant decrease, despite the small number of patients. They concluded that this variation could have a clinical impact and that further studies were necessary; another study supported their conclusion. On the other hand, some published articles found no changes, whereas others demonstrated an increase. Nevertheless, there were differences between the populations in each of the studies and the methods used.

Tchetgen and Oesterling compared PSA values at 1, 6, and 24 h after ejaculation in 64 adults (mean age of 60 years). Their results showed a statistically significant increase in both the change in absolute levels and the percentage of change, and differed from our results. However, their study utilized very strict measures of time between determinations, which we considered an approach not in accordance with clinical reality. Another important point was that their mean PSA value was below 4 ng/ml (1.8 ng/ml) with a mean change that was higher at the first hour (0.8 ng/ml). In another study by Herschman et al. that also measured post-ejaculation PSA at 1, 6, and 24 h, a statistically significant increase was observed in only 20 patients. However, when the cut-off point was defined at 4 ng/ml, none of the patients needed biopsy due to PSA changes, and when the cut-off point was > 2.5 ng/ml, only one of their participants underwent biopsy. Another 2 patients showed a post-ejaculation PSA value > 2.5 ng/ml, one hour after ejaculation. That PSA determination (1 h post-ejaculation) is not a typical setting and therefore we consider that such a change has no clinical impact.

Other studies found no statistically significant difference and are criticized because they recruited young volunteers or because the exact time between PSA determinations was missing. We consider that knowing the precise variations at different times is important in the field of molecular biology to explain the pharmacokinetics of PSA. However, the main objective of this discussion is the clinical impact.

Stenner et al. conducted a study with 2 cohorts and, similar to our results, found no statistically significant differences. The first cohort consisted of 618 individuals with a self-report on the time of the last ejaculation before PSA determination. The second cohort was of 88 volunteers in whom the second sample was determined within 48 h after ejaculation. The similarity of the study design with ours supports the conclusions of both studies, as well as the reproducibility of the results.

The clinical impact of a change in PSA was analyzed in that study, looking for patients with values above 4 ng/ml. Five of the patients (5.7%) would have to undergo biopsy according to their post-ejaculation PSA. In our cohort only 2 patients (2.1%) would have to undergo biopsy due to the increase in PSA > 4 ng/ml, and even utilizing the cut-off point > 2.5 ng/ml, only 5 patients (5.3%) would be indicated for biopsy from their post-ejaculation PSA determination.

Despite the fact that the Tchetgen and Herschman groups had results that were distinct from ours in relation to the significant difference of the change in PSA, this was only of numerical importance. After reviewing their clinical results, we could conclude that the increase in post-ejaculation PSA values had no clinical impact and that the previous judgments were based only on absolute numerical differences.

Some studies with larger samples show differences from a numerical perspective. This can be explained by the time interval employed for taking the sample. Our study, like that of Stenner et al., was developed based on the daily clinical setting and neither one confirmed a numerical difference or, more importantly, clinical impact.

Conclusions

Sexual abstinence before PSA determination should not be recommended to patients, given that it has few clinical implications. However, an increase in PSA to a value above arbitrary reference values should be complemented with a second sample and its etiology should be studied.

Ethical responsibilities

Protection of persons and animals. The authors declare that the procedures followed conformed to the ethical standards of the responsible committee on human experimentation and were in accordance with the World Medical Association and the Declaration of Helsinki.

Data confidentiality. The authors declare that they have followed the protocols of their work center in relation to the publication of patient data.
Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

Financial disclosure
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Conflict of interest
The authors declare that there is no conflict of interest.

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References
Role of estrogens and their receptors in benign and malignant prostate diseases: Part 1

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KEYWORDS
Estrogens; Estrogen receptors; Estrogen serum levels; Estrogen mechanisms; Benign prostatic hyperplasia; Prostate cancer

Abstract Numerous studies on the molecular basis of prostate cancer focus on the role of androgens, but estrogens have been shown to be linked to prostate cancer development and progression. In the present article, we reviewed the laboratory and clinical evidence, demonstrating that estrogens can be the cause of the development and progression of prostatic hyperplasia and prostate cancer. We also studied the more significant mechanisms related to estrogen action, which include: direct genotoxicity, hyperprolactinemia, inflammation, and receptor-mediated action. In addition, we analyzed the functions of the known estrogen receptors (alpha and beta) in diseases of the prostate. The evidence observed suggests that estrogen receptor alpha plays an essential role in the development of both the normal prostate and the cancer, whereas estrogen receptor beta is related to the differentiation of the prostatic epithelial tissue and numerous antiproliferative actions in prostate cancer. Nevertheless, some of their isoforms are associated with mechanisms of cancer initiation and progression. Finally, we believe that more studies related to estrogen action should be carried out to better understand the role estrogens play in the development of prostate cancer.

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Introduction

Prostate cancer is the fourth diagnosed malignant disease in general, and the second most common in men. It represents approximately 15% of the tumors diagnosed in men. This disease is the fifth cause of death by cancer in men (representing 6.6% of those deaths). The number of deaths is greater in the less developed countries than in the developed ones (165,000 and 142,000, respectively).1

In Cuba, according to the 2013 Annual Statistical Report on Health, this type of tumor is the second in incidence (33.3% adjusted rate) and mortality (50.1% rate). This elevated mortality rate can be explained by the higher number of advanced-stage diagnoses.2

The prostate is like an immense network of homeostatic interaction. The function of this organ is very closely linked to the hypothalamic-pituitary-gonadal axis. It is postulated that the role of androgens in prostatic carcinogenesis is only one side of the problem, given that tumor development commonly occurs in advanced-age patients, in whom testosterone (T) levels are in decline.3 In contrast, estradiol (E2) levels do not decrease with age, but remain unchanged or slightly increase.4 The decrease in the T-E2 ratio is related to the development of prostate cancer.5 6 An association between risk for prostate cancer and a) the polymorphism in the genes involved in 17 ß-estradiol metabolism,7 8 b) increased aromatase expression and the different metabolizing isoenzyme activation,9 10 c) marked alteration in estrogen receptor (ER) expression,11 14 and d) relation to E2 levels in blood13 15 17 has also been demonstrated.

There is now growing evidence that estrogens and their receptors can regulate prostate development and the initiation of cancer and its progression. The aim of our review was to describe the main mechanisms through which estrogens affect the prostate gland and induce carcinogenesis and tumor progression.

Methods

A search was carried out of the databases that specialize in medical themes that included: MEDLINE, PubMed, ScieLo, and DynaMed. The collected information was reviewed to ensure source reliability, aim, reach, audience, prestige and impact factor of the journal, the year of publication, and the level of access to information, for the purpose of carrying out a review of the most up-to-date material of the last 10 years. The information gathered was systematically reviewed using the following descriptors: estrogens, receptor estrogens, serum estrogen levels, estrogen mechanisms, benign prostatic hyperplasia (BPH), prostate cancer. The articles were selected through a collective process and by consensus. Systematic reviews, original articles, and meta-analyses were chosen. A smaller number of articles that met the proposed requirements were found in the databases with Spanish language articles (table 1), which is why 95% of the articles that make up this review are from the PubMed database.

17 ß-estradiol (E2) is a sex hormone from the estrogen group with a broader participation in female than in male sexual development. It is also a vital component in male physiology because it is synthesized from T, mainly in the Leydig cells of mammalian testes by certain germ cells and by Sertoli cells in immature mammals. The main function of E2 is to prevent germ cell apoptosis.18
Relation of estrogens to the normal prostate gland

The role of estrogens in the prostate is not fully understood. It is posited that they are involved in prostate growth, especially in the development of stromal cells and early morphogenic events. Exposure to high levels of estrogen (greater than 60 pg/mL) during the critical period of embryonic development can cause alterations in prostatic morphogenesis and cellular differentiation, known as estrogenization. These disturbances can occur in advanced age and are associated with the increase in prostate lesions correlated with age, such as BPH.10,19

One of the proposed mechanisms to explain E\(_2\)-dependent prostate growth is through prolactin (PRL) released by the pituitary gland. However, not all estrogenic effects can be attributed to the direct action of PRL on the prostate gland.20 It is known that PRL promotes growth11 and inflammation of the normal prostate gland.20 In addition, estradiol exerts a negative feedback loop on the hypothalamic-pituitary-gonadal axis, blocking the secretion of luteinizing hormone and its releaser. Finally, E\(_2\) promotes steroidogenesis of the androgens mediated by the specific aromatase, CYP19A1, of the prostatic stromal cells. This negative regulation was the basis for employing therapy with estrogens at high doses in the primary treatment of prostate cancer (chemical castration)11 (fig. 1).

With age, the level of T production by the Leydig cells diminishes, upon lowering the response to the pituitary LH, and slightly raises the estrogen level due to increases in action of the aromatase enzyme.19,22 Thus an alteration is produced in the E\(_2\)-T balance, favoring the former.5,6

A study conducted on mice suggested that E\(_2\) may contribute to increased lower urinary tract symptoms, through its effect on the urethra and the bladder.21 In humans, there is evidence of an association between elevated baseline E\(_2\) levels and a low risk for undergoing surgery due to BPH.24 In addition, the rapid decline in estradiol levels with age correlates with the increase in prostate volume and obstructive urinary symptoms, just as the elevated E\(_2\)-T ratio is associated with a low risk for developing BPH symptoms.24

Estrogen action is mediated by the specific nuclear receptor (ER), which regulates target gene transcription through binding with its response elements and genomic regulation.23 The second E\(_2\) action mechanism proposed is ligand-receptor interaction. The prostate expresses 2 basic subtypes: a (ERa) and b (ERb).

The physiologic role of ERb is involved with the regulation of glucose metabolism and its homeostasis, insulin signaling, and immunity modulation through the control of inflammation and programmed cell death (apoptosis).13 Moreover, ERb is the negative regulator of ERa and modulates gene expression, depending on the type of tissue.25 Both receptors have a specific arrangement in the prostate. ERa is expressed mainly in the stromal compartment and sometimes in basal or luminal epithelial cells (only 10% is positive) and its expression is associated with cell proliferation signals.27 ERb is expressed in basal epithelial cells and sometimes in luminal cells.

In rodents, prolonged exposure (prenatal or neonatal) to estrogens causes drastic modifications in the prostatic epithelial tissue, inhibiting its growth and resulting in aberrant functioning. This leads to the BPH phenomenon, essentially mediated by the presence of ERa,28 given that its loss is observed in the differentiation of the prostatic stromal compartment.29

Relation of estrogens to prostatic carcinogenesis

In the study conducted on aromatase CYP19A-deficient mice (ArKO mouse), the incidence of prostate cancer decreased when they were exposed to exogenous androgens and estrogens (levels comparable with those in aging), compared with the wild-type mice. This suggested in situ estrogen production, and that it is an essential component for prostatic carcinogenesis.9 Furthermore, a decrease in its activity was observed in the hormone-sensitive prostate cancer cell line (LNCaP) cells that are transformed into a more aggressive phenotype, as well as an increase in the reductive activity of the 17 β hydroxysteroid dehydrogenase enzyme, which catalyzes the interconversion of the most active steroids, e.g., E\(_2\) and T, into the less active estrone and androstanediol.7 In addition, estrogens can induce overexpression of the catalytic subunit of human telomerase and an increase in its activity in human prostate cell lines. This event is associated with unlimited cell proliferation via mutation accumulation.30

Epidemiologic evidence

Serum E\(_2\) levels remain unaltered with age. Nevertheless, the change in the intraprostatic profile is predominated by estrogens in the aging process. In addition, E\(_2\) levels in blood showed differences in relation to race and ethnicity, given that Afro-Americans (greater incidence and mortality) had

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### Table 1  
Summary of the articles found, reviewed, and included in the review

<table>
<thead>
<tr>
<th>Articles found</th>
<th>Medline</th>
<th>PubMed</th>
<th>Scielo</th>
<th>DynaMed</th>
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<tr>
<td>Articles to be included in Part 2</td>
<td>1</td>
<td>48</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

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Databases: Medline, PubMed, Scielo, DynaMed
higher $E_2$ levels than whites, even though they were within the normal range up to 60 pg/mL,\textsuperscript{8,12} whereas the $T$ levels of both groups were comparable.\textsuperscript{31} Epidemio logical data show contradictory results regarding serum $E_2$ levels (table 2). Some results reflect a direct association between high estradiol levels in blood and the risk for prostate cancer,\textsuperscript{3,6,15,17,31-33} whereas others suggest the opposite - a high risk with the growing reduction in $E_2$ levels.\textsuperscript{5} And some studies report a reduced risk for cancer in relation to increased $E_2$ levels in blood.\textsuperscript{34-35}

On the other hand, large randomized studies and meta-analyses found no association with the risk for cancer\textsuperscript{16,36-38} (table 2). However, the latter’s Achilles heel, is the fact that the circadian cycle variations of these hormones was not taken into account when drawing the blood samples at different times during the day,\textsuperscript{39} which could have an influence on negative results.

It is suggested that the differences in the conclusions of the epidemiologic studies is partly due to the fact that prostate tissues have the capacity to produce steroids from androgens in an intracrine manner.\textsuperscript{40} In the transformed tissues, aromatase (CYP19) begins to be expressed in the epithelial cells and not in the stromal cells, and its production is induced in these tissues. This results in an altered T-$E_2$ ratio, which was associated with malignant transformation.\textsuperscript{19,22} The expression of the CYP19A1 isoenzyme is also 30-fold higher in metastatic tissue, compared with primary tumors.\textsuperscript{41}

The theory of the direct genotoxic effect of estradiol on the prostate gland. It has been suggested that estrogens possess a genotoxic effect on the prostate. The proposed mechanism is the conversion of estrogens to catechol estrogens, a hydroxylation mediated by the CYP1\textsubscript{a} and CYP1B1 enzymes. Not until these catechol-estrogens detoxify, can they develop an oxidation-reduction process that contributes to the formation of reactive oxygen species, damaging DNA and contributing to lipid peroxidation and the formation of intermediary metabolites that directly form a molecular complex with the DNA, resulting in mutagenesis.\textsuperscript{42} Human prostate tissues that express elevated quantities of the CYP1B1 isoenzyme are more prone to cancer growth.\textsuperscript{43} Furthermore, it is known that there is high expression of this variant in the prostate tissues of the peripheral zone, where the largest number of tumors are developed. In addition, in prostate cancer patients there is an increase in the range of the estrogen-DNA adducts and
Table 2  Epidemiologic studies of the last 10 years on the relation between estradiol levels in blood and the risk for prostate cancer

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Result</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severi et al.</td>
<td>2006</td>
<td>Elevated ( E_2 ) levels (almost double the normal range) were associated with a 30% decrease in the risk for prostate cancer and were inversely proportional to the appearance of high-grade tumor.</td>
<td>36</td>
</tr>
<tr>
<td>Rohrmann et al.</td>
<td>2007</td>
<td>They reported differences in serum ( E_2 ) levels according to ethnicity. African-Americans had the highest circulating ( E_2 ) levels associated with the highest prostate cancer incidence. Hispanics had intermediate values and whites had the lowest levels.</td>
<td>32</td>
</tr>
<tr>
<td>Roddam AW et al.</td>
<td>2008</td>
<td>In this meta-analysis no association was found between circulating hormone levels and the risk for prostate cancer.</td>
<td>37</td>
</tr>
<tr>
<td>Giton F. et al.</td>
<td>2008</td>
<td>They found an association between serum ( E_2 ) levels and the risk for prostate cancer that presented with a Gleason grade above 4+, as well as a relation to poor prognosis.</td>
<td>33</td>
</tr>
<tr>
<td>Sher DJ. et al.</td>
<td>2009</td>
<td>They conducted a cohort study whose univariate analysis produced no relation between high-grade carcinoma determined by biopsy after radical prostatectomy and the total estradiol levels and total testosterone levels, as well as the T:E2.</td>
<td>38</td>
</tr>
<tr>
<td>Daniels et al.</td>
<td>2010</td>
<td>A cohort study that showed a correlation between high serum estrone levels and high-grade carcinoma, but no association between cancer and serum estradiol levels.</td>
<td>34</td>
</tr>
<tr>
<td>Yao et al.</td>
<td>2011</td>
<td>This study for prostate cancer prevention found no association between serum ( E_2 ) levels and the risk for prostate cancer in the control group, whereas moderate risk for developing cancer with a Gleason score &lt; 7 in patients with elevated ( E_2 ) was found in the group treated with finasteride.</td>
<td>16</td>
</tr>
<tr>
<td>Salonia et al.</td>
<td>2011</td>
<td>Serum ( E_2 ) levels ≤ 50 pg/mL were observed in the majority of the cancer patients, but those with levels &gt; 50pg/mL had 3.24 more possibility of risk for high-grade carcinoma. The authors concluded that serum ( E_2 ) levels serve as an independent predictive high-grade tumor marker.</td>
<td>15</td>
</tr>
<tr>
<td>Salonia et al.</td>
<td>2012</td>
<td>A cohort study in which patients with high-risk cancer showed low levels of T, ( E_2 ), and T:E2 (all ( p \leq 0.02 )) and these levels were associated in the univariate analysis with the risk for high-grade cancer (all ( p \leq 0.006 )).</td>
<td>5</td>
</tr>
<tr>
<td>Tsilidis et al.</td>
<td>2012</td>
<td>A cohort study that found no association between ( E_2 ) and T levels and the risk for prostate cancer.</td>
<td>39</td>
</tr>
<tr>
<td>Abd Elmageed et al.</td>
<td>2013</td>
<td>A correlation was found between elevated serum ( E_2 ) levels and a high Gleason grade in cancer patients (( p=0.043 )) that was significantly higher in descendants of African-Americans compared with descendants of Caucasians.</td>
<td>12</td>
</tr>
<tr>
<td>Qin et al.</td>
<td>2013</td>
<td>The recovery of ( E_2 ) levels and an increase in T:E2 were associated with risk for androgen deprivation therapy failure, especially in castration-resistant patients (( p &lt; 0.001 )).</td>
<td>6</td>
</tr>
<tr>
<td>Usuro et al.</td>
<td>2015</td>
<td>African cancer patients had higher ( E_2 ) levels than BPH patients or controls (( p=0.05 )) and exhibited the lowest T:E2 ratio. There was a strong association between ( E_2 ) levels and the risk for prostate disease (cancer and BPH).</td>
<td>17</td>
</tr>
</tbody>
</table>

BPH: benign prostatic hyperplasia; \( E_2 \): estradiol; T: testosterone; T:E2: testosterone:estradiol ratio
I. García-Figueroa et al

conjugated metabolites that promote the initiation of cancer.44

The above information gives us an idea of how estrogenic metabolites can be genotoxic agents and thus contribute to prostatic carcinogenesis.

Hyperprolactinemia

The direct action of PRL in prostate cancer is the subject of debate, due to the fact that the levels of this hormone in serum are not related to an increased risk for prostate cancer.45 Nevertheless, in vitro studies have demonstrated that there is an increase in the signal of intraprostatic PRL through its receptor21, and the activation it mediates, that is associated with the risk for prostate cancer.21

In a model of induced carcinogenesis in the rat, with the exogenous administration of T and E₂, the majority of the changes in gene expression were attributed to hyperprolactinemia induced solely by E₂.21 Dagvadorj et al., also demonstrated that in patients with prostate cancer, the signal induced by PRL was an essential factor in neoplastic transformation.46 All these findings stress that it is the local levels of PRL, and not the serum ones, that are the most significant in prostatic carcinogenesis.

Changes mediated by the estrogen receptor and hormonal deregulation

Ricke et al., demonstrated in an ERα expression-deficient mouse (aERKO mouse) that treatment with T and E₂ did not induce high-grade intraepithelial lesions or prostate cancer, whereas the ERβ-deficient mouse (bERKO mouse) displayed behavior that was similar to that of the normal mouse, and therefore did develop a tumor.46 A similar study, but on rats, showed that T alone was not sufficient for high-grade intraepithelial lesion development; they only developed when treated with ERα agonists and not with ERβ agonists.47

In human prostate tissue, ERα was detected in the epithelial tissue of high-grade intraepithelial lesions, cancer, and in the hormone-refractory phenotype,14,48 and was therefore related to cell proliferation and tumor cell survival.49

Thus it was proposed that the paradigm involving the role of ERs in the prostate is precisely that ERα is pro-carcinogenic,
as discussed above, whereas ERb has a predominant protective, anti-carcinogenic, pro-apoptotic effect\(^\text{22}\) and prevents cancer invasion because it avoids the transition of epithelial tissue to mesenchymal tissue\(^\text{26,49}\) (fig. 2).

Figure 2 shows the protective role of ERb, inducing apoptosis and inhibiting EMT, thanks to the positive regulation of PHD2. This protein suppresses the HIF-1a levels, inhibiting the pathways related to it. However, when there is a hypoxia stimulus, PHD2 expression, and thus its function, are inhibited. Together with this event, there is a differential splicing in the ERb genes that increases the expression of ERb2, which binds to HIF-1a and stabilizes it, therefore preventing its hydroxylation and degradation. In this manner ERb2 contributes to EMT and prostate cancer progression.

COX2: cyclooxygenase-2; E2: estradiol; FOX3a: forkhead box; HIF-1a: hypoxia inducible factor; H2O2: hydrogen peroxide; NO: nitric oxide; PHD2: prolyl-hydroxylase domain-containing protein 2; PUMA: proapoptotic factor; TWIST: transcriptional factor; VEGF: vascular endothelial growth factor. Adapted from Nelson et al.\(^\text{26}\) and Dey et al.\(^\text{52}\)

A decrease in ERb was observed in the prostate cells that were subject to a neoplastic transformation and then developed high-grade cancer. This supports the idea of the suppressor role of this receptor.\(^\text{26}\) In addition, the specific ligand for this receptor (5α-androstan-3b,17b-diol [3b-Adiol]) can suppress the transformation of epithelial tissue into mesenchymal tissue induced by transforming growth factor b or by hypoxia, hence the cells maintain their epithelial phenotype in prostate cancer.\(^\text{27,50}\) (fig. 2).

There was also an inhibitory effect of ERb on the activation of angiogenesis, given that it inhibited the transactivation of the androgen receptor, suggesting that it acts as a co-regulator of angiogenesis\(^\text{48}\) (fig. 2). This interaction causes a decrease in tumor size and prostate-specific antigen levels.\(^\text{27}\)

However, there is evidence of the presence of ERb in bone and lymph node metastases.\(^\text{31}\) Likewise, the ERb isoforms, ERb2 and ERb5, are correlated with poor outcome.\(^\text{27}\) Additionally, ERb1 acts as an oncogene in hormone-refractory cells that have castrate levels of T, and under E\(_2\) treatment, demonstrating that there is a mechanism by which estrogens facilitate proliferation in this type of cell. This might mediate the change from hormone-sensitive to hormone-refractory,\(^\text{27}\) since estrogens contribute to tumor proliferation through favoring the transition of epithelial tissue to mesenchymal tissue in collaboration with ERa\(^\text{52}\) (fig. 3). Thus, there is a change in the conventional paradigm of the mechanism mediated by the ERs in relation to prostate cancer, which will be widely discussed in the second part of this review.

**Final comments**

Knowledge of the function of estrogens in the pathogenesis, prevention, and treatment of prostate cancer is evolving. After reviewing the different studies, we can state that the role of androgens in the progression of prostate cancer is only one side of the transformation to malignancy. The
studies carried out in vitro and on animals identified a series of mechanisms that included the participation of potentially carcinogenic estrogens, including direct genotoxicity, hyperprolactinemia, chronic inflammation, and changes in the hormonal balance mediated by estrogen receptors. In reference to the latter, ERα was shown to reduce androgen production, which contributes in the long term to the development of BPH, which is a product of inflammation, to cancer. We must not forget there is a conversion of androgens to estrogen, causing an imbalance in the T-E2 proportion, which favors the development of prostate cancer. There was also evidence that ERβ can have the dual effect of both a protector against the development of cancer and an inducer of the change from hormone-sensitive to hormone-refractory disease. This explains the conflicting results in the epidemiologic studies that attempt to confirm the relation between estrogens and the risk for prostate cancer.

The main limitation of this review was the small number of databases consulted due to the low level of access to scientific information.

Nevertheless, we consider that a greater number of studies should be developed, especially epidemiologic studies with fuller designs that focus on the analysis of the complex and multifactorial relation between estrogens, androgens, and the development of prostate cancer.

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Conflict of interest

The authors declare that there is no conflict of interest.

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References


CLINICAL CASE

Robotic-assisted inguinal lymphadenectomy in penile cancer

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KEYWORDS
Robotic-assisted inguinal lymphadenectomy; Minimally invasive; Penile cancer

Abstract. Squamous cell carcinoma is a rare tumor, making up from 2 to 5% of the urogenital tumors. However, because our hospital is a referral center that manages large volumes of patients, approximately 5-7 cases are seen per year. Inguinal lymph node dissection is one of the treatments for these lesions and is being performed more frequently as a minimally invasive procedure.

Our aim was to describe the surgical technique for robotic-assisted inguinal lymphadenectomy in cancer of the penis. We present herein the case of a 73-year-old man with symptom progression of one year and 6 months and increased volume at the level of the glans penis. A biopsy was taken, after which he underwent radical penectomy with perineal urethrostomy. The histopathologic study reported well differentiated verrucous squamous cell carcinoma that invaded the corpus spongiosum and the urethra (T3N0M0G1). Four weeks later he underwent robotic-assisted inguinal lymphadenectomy of the superficial and deep lymph nodes.

Robotic-assisted inguinal lymphadenectomy, aside from its high cost, is a feasible technique when carried out in specialized centers that reduces morbidity, blood loss, and hospital stay.

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Cancer of the penis is a rare neoplasia with an estimated 1,570 cases in the United States in 2012. It represents 0.4% of the cancers in the U.S. and less than 1% worldwide, with an incidence of 0.1-0.9 new cases per 100,000 men per year. Spread to the inguinal lymph nodes is predictable and only 1-2% of patients will present with distant metastases. The primary drainage lymph nodes are in the inguinal region and the secondary nodes are in the pelvic region and they are involved in part of the treatment of penile cancer under different indications.

Radical resection of the inguinal metastases of cancer of the penis is standard treatment and offers excellent regional disease control. It is a potentially curative treatment for carcinoma of the penis. However, this technique has been adapted to minimally invasive surgery, resulting in an underuse of open inguinal lymph node dissection due to the high 50-90% incidence of morbidity that includes lymphedema, skin necrosis, lymphocele, wound dehiscence, and infection.

Micro-metastatic disease presents in 20-25% of patients with non-palpable lymph nodes that undergo prophylactic lymphadenectomy, whereas 50-80% of patients with palpable lymph nodes have metastasis.

The technique of video endoscopic inguinal lymphadenectomy initially described by Bishoff in 2003 and performed by Tobias-Machado in 2005 attempts to reduce the morbidity of open lymph node dissection without compromising the oncologic results.

Up to now, fewer than 200 cases of endoscopic inguinal lymphadenectomy for cancer of the penis have been reported in the medical literature. Robotic-assisted lymph node dissection was reported by Sotelo et al. in 2013 and by Kharadjian et al. in 2014 and we now present herein a description of robotic-assisted inguinal lymphadenectomy as a feasible technique.

Aim

Our aim was to describe the surgical technique of robotic-assisted inguinal lymphadenectomy in cancer of the penis.

Case presentation

A 73-year-old man, resident of the State of Mexico was referred from his home to continuous admission consultation. He had a remarkable past history of occasional smoking, social drinking, type 2 diabetes mellitus of 8-year progression under medical treatment with 850 mg of metformin taken orally/24 h, with poor treatment adherence. Symptom onset was approximately one year 6 months prior, presenting with progressive increase in volume of the glans penis and purulent secretion. He sought medical attention from numerous physicians that began antimicrobial and analgesic treatments with no improvement. He had multiple episodes of bleeding at the lateral surface of the penis that remitted spontaneously, but nevertheless were persistent. The patient also presented with asthenia, adynamia, vertigo, and fatigue, resulting in his hospital admission. Physical examination revealed tegumental pallor, penile tumor, and fetid secretion from the glans penis. Inguinal lymph nodes were not palpated. Directed biopsy was performed under the fetid, purulent, and sclerosing zone of the glans penis and the report stated well-
differentiated verrucous squamous cell carcinoma. Pelvic
tomography and magnetic resonance imaging were carried
out (fig. 1). Radical penectomy with perineal urethrostomy
was performed and the histopathologic study reported well-
differentiated verrucous squamous cell carcinoma
measuring 6 cm at the largest diameter located on the glans
penis and invading the corpus spongiosum and penile
urethra, with lymphatic and vascular invasion. The surgical
site did not show evidence of neoplastic cells, there was
extensive flat lichens on the skin of the prepuce, and
cytopathic changes associated with human papilloma virus
infection staged according to the 2010 AJCC TNM as
T3N0M0G1. Superficial and deep robotic-assisted inguinal
lymphadenectomy was performed with no intraoperative
complications. The patient had satisfactory postoperative
progression and was released on the following day with
Drenovak drains in place that were removed on day 10 of
the outpatient consultation.

**Procedure description:** First, the position of the operating
table was defined, along with that of the da Vinci surgical
system, to the right of the patient. With no repositioning, a
second docking at the time of the extremity change was done,
with an approximate 45 degree turn in the direction of the da
Vinci system (arm cart) (fig. 2). The patient was in the dorsal
decubitus position with abduction of both thighs (fig. 3). The
femoral triangle zone was defined and an approximately 3 cm
incision was made at its vertex with Metzenbaum scissors. The
lateral plane of the adductor longus muscle and the sartorius
muscle was then digitally dissected and an 8 mm robotic port
was placed, the internal one closer to the femoral triangle
vertex and the right one 1 cm higher (inversely in the right
pelvic member). A triangle was formed between the 12 mm
trocar of the initial incision and the robotic trocar of the
external surface of the left leg that would be used for sending
clips and for leg aspiration (fig. 4). Optic port closure was done
with 1 Vicryl and insufflation with CO₂ at 10 mmHg was begun.

Once the above was carried out, the da Vinci surgical system
was advanced and docked. A bipolar fenestrated robotic
forceps was used in the left hand and a monopolar robotic
scissors in the right hand.

Lymphadenectomy was performed under the open
approach principles adapted to the VEIL technique (Video
Endoscopic Inguinal Lymphadenectomy), sparing both
saphenous veins. Metal clips measuring 10 mm were placed
at some of the effluents from the saphenous arch. Surgery
duration was 230 min with a 50-ml blood loss.
Robotic-assisted inguinal lymphadenectomy in penile cancer

Potential of resecting all inguinal lymph nodes at risk for diseases, while minimizing the complications. Minimally invasive surgery reduces the possible adverse effects that present with conventional surgery.

Robotic-assisted inguinal lymphadenectomy is the evolution of a key oncologic surgical procedure in carcinoma of the penis. Our initial experience with robotic-assisted surgery had the disadvantage of high cost.

Ethical responsibilities

Protection of persons and animals. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that they have followed the protocols of their work center in relation to the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

Financial disclosure

No financial support was received in relation to this study/article.

Conflict of interest

The authors declare that there is no conflict of interest.

References


Discussion

Carter et al. performed 19 endoscopic inguinal dissections with a mean of 11 lymph nodes per side, a surgery duration of 177.8 (132-400) min, one day hospital stay (1-12 days), and 25 days with drain (8-101 days). The major complication in the patients included one re-admittance for drainage, pneumomediastinum with no sequelae, and superficial cellulitis.

Zhou et al. performed 11 endoscopic lymphadenectomies on 7 patients. There were a total of 135 lymph nodes with a mean of 12.3. Mean drainage was 50.8 (5-130 ml) ml/day. Hospital stay was 10.8 (7-15) days. There were 2 cases of minor complications; one was a 50 ml seroma in the left leg and the other a 180 ml lymphocele in the left limb.

Early lymphadenectomy proved to be an independent prognostic factor for disease-specific survival (3-year survival of 84% compared with 35% in the late lymphadenectomy group). In addition, patients with penile cancer managed with extensive lymphadenectomy (more than 8 lymph nodes) had an overall survival greater than 5 years, compared with patients managed with less extensive lymphadenectomy.

Conclusions

Despite the advantages of early and extensive lymph node dissection, open inguinal lymphadenectomy, and in fact, lymphadenectomy in general, remains a little-used procedure, probably due to the morbidity associated with it. Even in centers where lymphadenectomy is routinely performed, there is a substantial complication rate. The laparoscopic approach to the inguinal region has the potential of resecting all inguinal lymph nodes at risk for diseases, while minimizing the complications. Minimally invasive surgery reduces the possible adverse effects that present with conventional surgery.

Robotic-assisted inguinal lymphadenectomy is the evolution of a key oncologic surgical procedure in carcinoma of the penis. Our initial experience with robotic-assisted surgery had the disadvantage of high cost.

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Conflict of interest

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References

CLINICAL CASE

Locally advanced clear cell renal cell carcinoma with associated renal tuberculosis


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Abstract The association of renal cell carcinoma (RCC) and renal tuberculosis (TB) is uncommon. Whereas the incidental discovery of RCC in tuberculous kidneys is well described, the discovery of tuberculous lesions after radical nephrectomy for cancer is exceptional. The aim of this article was to report a case of locally advanced clear cell RCC whose histologic study revealed associated TB. There are very few published cases of kidney cancer and TB. A case of squamous cell carcinoma of the renal pelvis in a kidney with TB and a case of renal adenocarcinoma and TB have been reported. The present case describes locally advanced RCC with high tumor burden and retroperitoneal adenopathy that, before surgery, suggested metastatic disease to the lymph nodes. However, only histopathologic changes due to TB were found. No clinical or pathologic correlation has been found between these 2 entities, but clinical studies on the subject are lacking.

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Introduction

Tuberculosis (TB) and cancer are 2 processes that can be clinically related, but there can also be an intimate association between TB and cancer. TB can precede a cancer, can appear synchronously, or can occur after the diagnosis and treatment of neoplasia. The association of TB and lung cancer has been well known for years. The synchronous appearance is infrequent and represents 1-3% of neoplasia and renal TB. However, the association of renal TB, laryngeal neoplasia and laryngeal TB, or renal cell carcinoma and TB is unusual. Whereas the incidental discovery of renal cell carcinoma in tuberculous kidneys is well described, the finding of tuberculous lesions after radical nephrectomy due to cancer is exceptional.

Case presentation

A 40-year-old woman from Chiapas, Mexico, lives in overcrowded conditions with 5 people in a room, a dirt floor, has been exposed to wood smoke since her infancy, and exposed to persons that are TB positive. Disease onset manifested with unintentional weight loss of 18 kg in 9 months, fatigue, nocturnal diaphoresis, and oppressive abdominal pain in the hypochondrium and left flank irradiating to the back with a 6/10 intensity with no attenuating or exacerbating factors. Physical examination revealed a thin patient with a body mass index of 18 kg/m² and normal vital signs. She had generalized weakness, well-ventilated pulmonary fields, and no pleuropulmonary syndrome. There was a palpable abdominal mass in the left hypochondrium and flank, painful upon palpation, and no signs of peritoneal irritation. Figure 1 shows the imaging studies that were carried out.

The patient underwent a left radical nephrectomy plus colectomy of the transverse and descending colon, total gastrectomy, partial esophagectomy, splenectomy, Roux-en-Y distal pancreatectomy plus end-to-end esophageal jejunostomy and end-to-end colon-to-colon anastomosis (fig. 1).

The histopathologic study result was a 9 x 7 x 9.5 cm Fuhrman 4, multifocal, clear cell renal cell carcinoma with lymphovascular invasion. It had a rhabdoid component of 80%, no sarcomatoid component, and there was invasion of the renal sinus, Gerota’s fascia, the adrenal gland, colon serosa, pancreas, and muscularis propria of the stomach. Surgical margins were negative. Lymph nodes: 0/26 positive. TB was found in the renal parenchyma, lymph nodes, and spleen. Histochemistry and immunohistochemistry studies were negative and the polymerase chain reaction was positive for TB (fig. 2). Antituberculosis treatment was begun, but suspended when the patient presented with hepatic encephalopathy and toxic hepatitis with an increase in transaminases. Treatment was reinitiated 14 days later, once the patient’s liver function tests were normal. Her progression was good and she was released from the hospital 42 days after surgery.

Discussion

The incidence of renal TB varies according to the prevalence of pulmonary TB in a given geographic location. Approximately 8-10% of the patients with pulmonary TB location develop renal TB. Renal location is the most frequent, following disease in the lung. Renal TB is a serious pathology of chronic progression that can compromise both kidneys, resulting in kidney failure and the possible death of the patient. The main causal agent is Mycobacterium tuberculosis, which reaches the kidneys via the bloodstream, and exceptionally, via the lymphatic system. The bacilli are housed in the cortical medullar zone in the form of granulomas and do not produce kidney
Locally advanced clear cell renal cell carcinoma with associated renal tuberculosis

Figure 1  A, B: CT-urography revealed an enhanced, lobulated and homogeneous 13 × 13.6 × 11 cm lesion dependent on the middle and upper third of the left kidney, boxing in the splenic vein and artery, invading the left renal vein, and infiltrating the spleen, stomach, left adrenal gland, and the body and tail of the pancreas. The vena cava was confluent and permeable. Parahilar lymph nodes, the largest measuring 1.5 cm. C: Pulmonary parenchyma with multiple bilateral calcified granulomas. D: 99mTc ABP scintigram was negative for bone metastases. E: Microscopic specimen. F: Polymerase chain reaction positive for tuberculosis.

Figure 2  A: Clear cell renal cell carcinoma. Neoplastic cells with abundant clear cytoplasm and pleomorphic nuclei with prominent nucleolus alternating with a delicate vascular marking. B: Clear cell renal cell carcinoma with rhabdoid areas. The cells present with marked pleomorphism and abundant eosinophilic cytoplasm with rhabdoid characteristics. C: Pancreatic invasion by the rhabdoid component. D: Lymph node with chronic granulomatous reaction and Langhans giant cells.
disease in the majority of cases. Nevertheless, they can become reactivated 10 to 12 years later and cause an infection that progresses up to the destruction of the renal parenchyma. The disease is insidious and the symptoms are varied. The patients generally present with dysuria, micturition urgency, and flank pain. This pathology should be studied when urinary sediment examination reveals leukocyturia or hematuria and cultures are repeatedly negative for other germs. The isolation of microorganisms through culture is difficult due to the fact that the bacillary population in the patient is scarce. The constitutional symptoms can be observed in up to half the cases. Almost all patients present with a positive reaction to tuberculin and a positive culture for Koch's bacillus in urine. In our case, we did not have the tuberculin test or culture for microbacteria. In relation to imaging study results, 70% of the patients have a manifestation in chest x-ray that includes microcalcifications. Koch's bacillus in urine. In our case, we did not have the polymerase chain reaction tests were positive for Mycobacterium tuberculosis.

From the anatomopathologic viewpoint, the lesion begins as a granuloma that later becomes caseous and then ulcerates. Microscopic detection (Ziehl-Neelsen stain) of alcohol acid-resistant bacilli has very good specificity (above 90%), but a low sensitivity (22%), due to the small quantity of bacilli found in chronic lesions. Amplification techniques such as polymerase chain reaction are currently the most sensitive and specific diagnostic method. The histopathologic study of resected lymph nodes and remnant of the renal parenchyma of our patient showed the presence of granulomas with central caseous necrosis and giant Langerhans cells. The Ziehl-Neelsen stain was negative, but the polymerase chain reaction tests were positive for Mycobacterium tuberculosis.

There are very few published cases of renal cancer and TB. Al-Assiri et al. described one case of squamous cell carcinoma of the renal pelvis in a kidney with tuberculosis and Fernández-Arjona et al. reported a case of renal adenocarcinoma and TB. Our case was one of locally advanced clear cell renal cell carcinoma with a large tumor burden and multiple adenopathies in the retroperitoneum that before surgery were suggestive of metastatic disease to the lymph nodes, but only histopathologic changes due to TB were found. No clinical or pathologic correlation has been found between these 2 entities. A future prospective study searching for TB in renal cancer could provide important information with respect to the biologic behavior of the concomitant form of these 2 diseases.

Ethical responsibilities

Protection of persons and animals. The authors declare that the procedures followed conformed to the ethical standards of the responsible committee on human experimentation and were in accordance with the World Medical Association and the Declaration of Helsinki.

Data confidentiality. The authors declare that they have followed the protocols of their work center in relation to the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

Financial disclosure

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Conflict of interest

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References

CLINICAL CASE

Mixed epithelial and stromal tumor of the kidney: a case report and literature review

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Abstract Mixed epithelial and stromal tumor of the kidney is a rare benign kidney neoplasia that predominantly occurs in middle-aged women. It presents as a well-defined biphasic lesion with solid and cystic components in both tomography and magnetic resonance imaging, reflecting the proliferation of the stromal element and the presence of multiple cysts that are the manifestation of the epithelial element. Malignant transformation, recurrence, and metastasis are rare, but isolated cases and small series have been reported in the literature.

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Keywords Mixed epithelial and stromal tumors of the kidney; Neoplasia; Benign; Biphasic; Cysts

Palabras Claves Tumores mixtos epiteliales y estromales del riñón; Neoplasia; Benigna; Bifásica; Quistes

Tumor mixto epitelial y estromal del riñón. Presentación de un caso y revisión de la literatura

Resumen Los tumores mixtos epiteliales y estromales del riñón comprenden un grupo de neoplasias benignas del riñón, poco frecuente, que principalmente aparece en mujeres de mediana edad. Se presenta como una lesión bien delimitada bifásica, con un componente sólido y quístico tanto en la tomografía como en la resonancia magnética, que refleja la proliferación de componente estromal así como la presencia de múltiples quistes como principal manifestación del componente epitelial. La transformación maligna, recurrencia y metástasis son raras, sin embargo recientemente se han descrito casos en la literatura.

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Introduction

Mixed epithelial and stromal tumors (MEST) of the kidney are biphasic tumors with complex stromal and epithelial elements that were first described by Michal and Syrucek in 1998. They are considered a relatively new pathology and recent reports have described their pathologic clinical characteristics. These tumors, together with cystic nephroma, were grouped into the mixed epithelial and mesenchymatous tumors in 2004, according to the World Health Organization classification of renal tumors. Following several studies, the unifying term renal epithelial and stromal tumors was proposed that would include the 2 pathologies. They are uncommon entities representing 0.20-0.28% of all renal neoplasias and have been reported as isolated cases or in small case series, totaling 100 reports in the international medical literature. The mean age at the time of diagnosis is 46 years and the woman:man ratio is 6:1. These lesions are incidental findings in 25% of the cases and they tend to be asymptomatic. Macroscopically, they are solid, brownish-grey areas and a multilocular cyst with a smooth surface. The cysts vary in size from millimeters to various centimeters at their largest diameter. Their microscopic characteristics show stromal and epithelial components. The appearance of MEST in imaging studies is nonspecific and they can be confused with complex cystic lesions. Surgical resection of the lesion is curative in the majority of cases.

The behavior of these tumors is usually benign, although there are reports of malignant sarcomatoid or carcinomatous transformation that generally progress with a high mortality rate.

Clinical case

An asymptomatic 40-year-old woman had an unremarkable family history. She was a tobacco smoker for 20 years with a smoking index of 20. Physical examination revealed no relevant data and laboratory tests were within normal parameters. During the routine medical evaluation, a right complex renal cyst was identified through ultrasound (fig. 1). The study was complemented with a contrast-enhanced abdominopelvic tomography scan that identified a right renal cystic lesion with 7 HU in the non-enhanced abdominopelvic tomography scan. Afterwards, a control contrast-enhanced tomography scan revealed a Bosniak IV cyst (fig. 2) and the decision was made to perform a partial nephrectomy with complete lesion resection. Macroscopically, the tumor measured 1.7 x 1.5 cm, was well-defined, with pale rose-colored and brownish-grey areas and a multilocular cyst with a smooth and shiny surface. Intraoperative pathologic study reported a benign cyst. The definitive study identified biphasic stromal and epithelial proliferation (fig. 3). The stromal component was made up of fusiform cells with homogeneously chromatic oval-shaped nuclei and scant cytoplasm arranged in short fascicules similar to ovarian stroma. The epithelial component was made up of small, round tubules and cystic dilation (fig. 4). Both the tubules and cysts were covered with cells that went from cubical to flattened, some of which were tuck-shaped. The stromal component expressed vimentin, smooth-muscle actin, and desmin, as well as estrogen and progesterone receptors (figs. 5-7).

At the third month of follow-up, the patient is asymptomatic and awaiting control studies.

Discussion

MEST is a recently described neoplasia that, despite its low incidence, should be considered in the differential diagnosis of renal tumors. It shows predilection for the female sex, peri-menopausal women, or patients with a history of hormone therapy.

There are 8 cases reported in men, and the relevant history in the majority of cases is hormone deprivation therapy for prostate cancer. These tumors are generally asymptomatic, but the most frequent clinical manifestations are palpable mass (31.8%), gross hematuria (27.3%), and flank pain (22.7%). They present as a central lesion of the kidney with expansive growth and frequent compression of the renal pelvis. However, no destructive invasion into the pelvic wall or adjacent parenchyma has been demonstrated, but there is occasional invasion of the renal sinus fat.

MEST is a biphasic tumor composed of a mixture of solid areas formed by stromal components with spindle cells and epithelial components that can vary from small tubules to complex glandular structures and the formation of cysts. It presents with thick septa and a greater percentage of the stromal component (54.6%). The lesions have a mean size of 4.5 cm (1.7-18cm). It presents with thick septa and a greater percentage of the stromal component (54.6%).

The lesions are similar to those of the ovary and can even present data of hyalinization and luteinization. Immunohistochemical study usually shows expression of the stromal component with desmin, smooth-muscle actin, caldesmon, and estrogen and progesterone receptors, such as CD10, whereas the epithelial component generally is expressed through CK7. The connection between sex hormones and the expression of estrogen and progesterone receptors in the stromal cells of these tumors suggests that the hormonal influence is a significant factor in the development of MEST.

Given the similarity between the stroma of MEST and the stroma of the Müllerian tubules in the majority of cases, the presence of ectopic Müllerian stroma in the kidney has also been proposed as the possible origin of these lesions. This suggests that these tumors develop from the neoplastic transformation of the kidney stromal cells that have Müllerian stromal characteristics, with or...
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without melanocytic differentiation. These stromal cells that are similar to Müllerian stroma have the potential to stimulate growth of the epithelium through contact, inducing Müllerian differentiation in the renal tubules involved. Several theories could explain the extragonadal presence of Müllerian stroma; one posits the presence of primitive fetal mesenchyme in the kidney, pancreas, liver, and other sites that can respond and proliferate when there is a hormonal imbalance, and another suggests the abnormal migration of ovarian stromal cells during embryogenesis.

The behavior of these tumors is benign, but some cases of malignization have been reported, including carcinomatous or sarcomatous transformation. Malignant transformation can be observed in both the epithelial and stromal components, characterized by increased cellularity, cytologic atypia, ovoid and vacuolated nuclei with a prominent nucleolus, and high mitotic index (15-25 mitoses per 10 high power fields). Macroscopic observation usually includes hemorrhage and necrosis.

According to authors of small MEST case series, diagnosis should be considered in: a) middle-aged female patients, b) women with a history of hormone replacement with estrogen, c) cystic renal tumors with delayed enhancement after contrast medium administration, and d) lesions originating in the renal pelvis with negative urinary cytology.

MEST is considered in the differential diagnosis of complex cystic lesions such as cystic nephron in the adult, multilocular cystic renal cell carcinoma, and angiomyolipoma with epithelial cysts, among others. Appearance in imaging studies is nonspecific and a Bosniak III or IV cyst is usually reported, described as a single solid lesion or cystic tumor with a solid component that has intermediate or late contrast enhancement.

Treatment has been surgical due to the difficulty in differentiating these lesions from possible malignant tumors, for which these patients have undergone partial nephrectomy, radical nephrectomy, and there have even been some cases of radical nephroureterectomy due to suspicion of urothelial tumor. There are no predictive prognoses for these tumors and their histogenesis and clinical behavior require future studies.

Conclusions

MEST is a clinically uncommon entity that is considered a benign neoplastic group with good outcome, but its malignant transformation is possible. These tumors must be differentiated from other renal neoplasms given that they share certain clinical and radiologic characteristics. Their diagnosis should be contemplated in the presence of a cystic renal mass, especially in peri-menopausal women or patients with a history of hormone therapy. Further studies are required to determine the etiology, pathogenesis, and natural history of these lesions.

Ethical responsibilities

Protection of persons and animals. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that they have followed the protocols of their work center in relation to the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.
References


Financial disclosure

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Conflict of interest

The authors declare that there is no conflict of interest.

Figure 2  Tomographic scan of the abdomen and pelvis with intravenous contrast medium. Anterolateral cortical lesion with a solid component in its interior that takes up the contrast medium (Bosniak IV complex cyst).

Figure 3  At low magnification, a neoplastic lesion made up of a solid, cystic component can be observed.

Figure 4  The mesenchymal component is similar to ovarian stroma and is densely cellular with fusiform cells.

Figure 5  Immunostaining with smooth muscle actin that is expressed in cells with a stromal component.

Figure 6  Immunostaining for progesterone receptors that shows nuclear positivity.
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Figure 7  Estrogen receptors with nuclear positivity in fusiform cells.
CLINICAL CASE

Bladder melanoma: a case report and literature review


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KEYWORDS
Melanoma of the bladder; Genitourinary melanoma; Malignant non-urothelial neoplasia of the bladder

Abstract Melanoma of the bladder is a rare malignant neoplasia. Isolated primary cases have been reported, but the most common presentation is metastatic disease. The diagnosis of bladder melanoma is complicated and requires a thorough interdisciplinary study of the patient. In addition, there are no well-standardized histopathologic criteria confirming its primary site. Presented herein is the case of a 42-year-old man with bladder melanoma that manifested as suprapubic pain, dysuria, and weight loss. Both the clinical and histopathologic diagnoses were difficult and it was not possible to determine whether the lesion was a primary one, due to the advanced stage of presentation, as well as to the lack of complementary studies.

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PALABRAS CLAVES Melanoma en vejiga; Melanoma genitourinario; Neoplasia maligna no urotelial de vejiga

Resumen El melanoma en vejiga es una neoplasia maligna poco frecuente, se han reportado casos aislados como sitio primario y la presentación más común es la metastásica. El diagnóstico del melanoma en vejiga es complicado y requiere de un estudio exhaustivo interdisciplinario del paciente, además, no se encuentran bien estandarizados los criterios histopatológicos que confirmen su sitio primario. Se presenta el caso de un hombre de 42 años con melanoma en vejiga que inició con dolor suprapúbico, disuria y pérdida de peso. El diagnóstico resultó difícil, tanto clínico como histopatológico, y no fue posible identificar si se trató de una lesión primaria debido al estadio avanzado de presentación, así como a la falta de estudios complementarios.

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Introduction

Melanoma is a malignant neoplasia made up of melanocytes, which are cells that embryologically originate in the neural crest and then migrate to the skin, mucosa, and different anatomic sites.1-2 Melanoma is the third most common malignant neoplasia of the skin and typically presents as a pigmented asymmetric lesion with irregular edges, in the shape of a macule, papule, or nodule. However, it can present at sites other than the skin, such as the mucosa of the oral cavity, the anogenital mucosa, the meninges, the esophagus, and the eye.3 The bladder is a rare presentation site and in general it is secondary to metastasis originating in the skin.4-5 Thus, it requires a thorough analysis of the skin and ruling out of other organs of frequent presentation to determine whether melanoma originates in the bladder, and even so, in the majority of cases it is not possible to confirm primary origin.5

Case presentation

A 42-year-old man with an unremarkable past medical history presented with intense colicky suprapubic pain, dysuria, and a 10-kg weight loss in 4 months. Later, post-micturition dripping of blood, and nausea and vomiting were added. Physical examination revealed pain upon palpation of the hypogastrium, right inguinal adenomegaly, hydrocele, and preputial edema. Abdominal ultrasound reported no bladder lesions. A computerized axial tomography scan only showed bladder wall thickening. The patient underwent cystoscopy and bladder biopsy and the histopathologic study reported high-grade transitional cell carcinoma. Two months later, the patient developed an acute postrenal kidney lesion requiring kidney function support with hemodialysis. Laboratory studies reported leukocytes 9,800/μL, hemoglobin 9.6 g/dl, hematocrit 29.4%, platelets 361000/μL, creatinine 5.62 mg/dl, uric nitrogen 28 mg/dl, urea 59.92 mg/dl, and prostate-specific antigen 0.93 ng/ml.

Cystoprostatectomy was performed and the intraoperative findings were peritoneal implants and enlarged pelvic lymph nodes.

The anatomopathologic study reported that the bladder and prostate were brown and of firm consistency and had irregular external surfaces with poorly defined edges; when cut, a diffuse, maximum 3 cm thickening of the bladder wall and a whitish nodular bladder mucosa were identified (fig. 1). Microscopic study revealed an ulcerated neoplasia made up of polygonal cell nests with abundant, clear cytoplasm, a pleomorphic vesicular central nucleus, a prominent

![Figure 1](image1.png) Surgical specimen. The cut bladder shows diffuse thickening of the wall and mucosa with a multinodular aspect.

![Figure 2](image2.png) a) Histopathology section shows transitional epithelium of the bladder and malignant neoplasia with a nodular pattern in the lamina propria and muscularis propria (x50). b) Malignant neoplasia with a solid and nodular pattern invading the muscularis propria layer of the bladder (x50). c) The neoplastic cells show great nuclear pleomorphism, prominent nucleolus, and mitosis (x400).
eosinophilic nucleolus and absence of pigment (fig. 2). The immunohistochemical study showed a neoplasia of melanocytic origin that was positive for melan-A, HMB45, and PS100 (fig. 3) and negative for CK7, CK20, and prostate-specific antigen. The final histopathologic diagnosis was malignant melanoma in the bladder and prostate and it could not be determined whether it was a primary tumor.

The patient died a few days after surgery.

Discussion

Primary melanoma of the genitourinary apparatus is extremely rare, representing approximately 0.2% of all melanomas, and the urethra and penis are its most common locations. Up to 2013, fewer than 20 cases of primary melanoma in the bladder have been reported in the literature and in all the cases, patient age ranges from 52 to 82 years. Involvement has been the same for men and women.

Clinically, the patients usually present with gross hematuria, dysuria, and symptoms related to metastasis. Our patient clinically presented with hematuria, dysuria, and weight loss.

A pigmented exophytic lesion can be seen through cystoscopy that varies from 1 to 8 cm and on occasion is diffuse, making detection difficult through imaging studies, as occurred in our case. Histologically these lesions present as tumor cell nests that can infiltrate transmurally. The neoplastic cells are polygonal or fusiform, with a pleomorphic nucleus, prominent nucleolus, and sometimes with the presence of melanin, atypical mitoses, and necrosis.

Diagnosis of bladder melanoma must be confirmed through immunohistochemical reactions. The antibodies that are positive for melanoma are S-100, HMB-45, and melan-A. The criteria for determining primary bladder melanoma are the absence of suspicious cutaneous lesions, ruling out the recurrence of melanoma in skin with the help of a Woods lamp, the absence of another primary visceral melanoma, and at the microscopic level, the infiltration pattern, added to the presence of atypical melanocytes in the tumor margins. Nevertheless, Tepeler et al. comment that not all the cases reported as primary bladder melanoma fit these criteria. It was not possible to determine whether our case was a primary or a metastatic lesion due to the lack of complementary studies and the advanced disease stage.

Radical cystectomy is the treatment for patients with primary melanoma of the bladder that offers high curative probabilities. In a review of case reports, this treatment enabled longer survival, with a mean of 10 months, compared with partial cystectomy, transurethral resection, and chemotherapy. However, outcome is poor and patients generally die within three years of diagnosis. Our patient was diagnosed in an advanced stage of the disease, which complicated our defining the primary presentation site and limited medical and surgical management.

Conclusions

Melanoma is frequent in the skin and mucosae, but other primary sites are not common. Cases in the genitourinary tract are extremely rare and largely metastatic. Clinical presentation is variable and therefore a thorough and interdisciplinary study of the patient is important and should include anatomopathologic study supported by a complete immunohistochemical panel to make a precise diagnosis.

Ethical responsibilities

Protection of persons and animals. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that no patient data appear in this article.

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References