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Original Articles

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- Positive surgical margins and bladder neck sparing during laparoscopic radical prostatectomy.
- Comparison of the results and complications for transrectal ultrasound guided versus transperineal mapping biopsy of the prostate.

Reviews

- Retrograde Intrarenal Surgery: Scopes, lasers and disposables (part 2)
- Usage and Dosage of Fosfomycin for NIH Category II Chronic Bacterial Prostatitis.

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Implementation of quality management systems in public health: The experience of the Department of Urology, University General Hospital of Heraklion, University of Crete, Medical School

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Abstract

Introduction-Objective: Assessing the quality of health service provision at a Department level is difficult and needs to be documented. Documentation is achieved by certification. In spite of the increasing trend for more specialized quality standards, ISO 9001:2015 is the most widespread one. The Directorate of the Department of Urology of the University General Hospital

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Implementation of quality management systems in public health: The experience of the Department of Urology, University General Hospital of Heraklion, University of Crete, Medical School.
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of Heraklion, in cooperation with the Hospital Administration proceeded to study/ install the quality management system (QMS) according to ISO 9001:2015 for the provision by the Department of Urology and its Special Units (Non-Invasive Urology-Lithotripsy & Cystoscopy-Urodynamics) of diagnostic, therapeutic and nursing services as well as for the production of scientific work, research activity and provision of educational services. The procedure was implemented in July 2017 through the Special Account for Research of the University of Crete; using funds from a specific program set up for the development of the Department of Urology. To the best of our knowledge, this is the first case of certification of a Urological Department in a Public Hospital in Greece. The purpose of this study is to present the initial experience/results from the implementation of a QMS according to ISO 9001:2015 at our Department.

Material and Methods: The procedure was initiated by providing medical-nursing and administrative staff with self-assessment questionnaires and special forms for problem-filling and improvement suggestions. All forms were filled in anonymously. All data gathered were processed by our quality management consultant. The results were presented to the parties involved in an open meeting at the Department and formed the basis for the QMS design. Through a 12-month strenuous workout with meetings about every 15 days, a QMS consisting of 14 procedures, two working instructions, 17 forms, and 13 administrative nursing protocols was set up. The system included 24 forms provided by the Ministry of Health and 29 clinical nursing protocols issued by the local Health Region. The staff was systematically trained in keeping them up and, with suggestions/ corrective actions the QMS was improved.

Results: Through patient satisfaction questionnaires, the Department was rated with 9.1/10 (reception/stay), 9.8/10 (medical follow up), 9.3/10 (nursing care) and 9.2/10 (general service). With the implementation of the QMS, quality indicators related to medical-nursing care (drop-fall rates, fever rates, admission severity-related mortality, etc.) are monitored. Through staff meetings the progress of indicators is presented and actions are being taken aiming at improvements. The operation of the Department has been parameterized and co-perception has been conquered. By implementing a QMS, future goals have also been set: a) Higher staff participation rate problems/suggestions for improvement recording, b) Monitoring achievement of research objectives through standardized procedures, c) Higher satisfaction score achievement, d) Certification according to EN 15224, in order to introduce the of clinical risk concept by adopting scientifically registered protocols in daily diagnostic/ therapeutic practice.

Conclusions: Certification of the QMS of a Urological Department in a Public Hospital is difficult but feasible. It can be successful despite organizational-technical difficulties/lack of resources. The benefits are many, such as enhancing organizational structure efficiency and improving communication within/outside the hospital.

INTRODUCTION

Key words
Health Care Sector; Quality Assurance, Health Care; Quality Indicators, Health Care; Quality Management Systems; Quality of Health Care

The Healthcare Sector (HCS) is particularly demanding and competitive; facing constantly the challenge of delivering better quality services; lowering costs; and optimizing adaptation to the modern era [1]. The need to implement a Quality Management System (QMS) in the HCS stems from the continuing increase of interest in the quality of health services by recipients, but also from the needs of employees in health services and of the society more generally [2]. Consequently, the continuing evolution of the HCS in developed countries has shifted the center of gravity of the scientific interest and research in the field of health systems; from the quantity and adequacy towards the quality of services [3]. Improving the quality of services in the HCS[1] is included among the priorities and orientations of health systems, while reforming efforts are under way in most developed countries worldwide. There is growing international interest towards the need to define-adopt specific standards[2], an action which is nowadays considered

1. *Professional activities and processes requiring specialized know-how and logistical resources so that healthcare needs of the citizen are met across the whole range of prevention, diagnosis, treatment and rehabilitation [1].*
2. *Documents including for continuous and repeated use rules, guidelines or characteristics of activities or their re-*

imperative, taking into account the sensitivity and the strong ethical/social HCS dimensions. Standardization[3] of the procedures and certification[4] of the hospitals is constantly evolving with many institutions nowadays voluntarily opting for addressing independent bodies to define and control their applied standards [4].

Despite the increasing trend of more specialized quality standards, ISO 9001:2015 is currently the most widespread globally. The Directorate of the Department of Urology of the University General Hospital of Heraklion, in cooperation with the Hospital Administration proceeded to study/install the QMS according to ISO 9001:2015 for the provision by the Department and its Special Units (Non-Invasive Urology-Lithotripsy & Cystoscopy-Urodynamics) of diagnostic, therapeutic and nursing services as well as for the production of scientific work, research activity and provision of educational services. The purpose of this study is to present the initial experience/results from the implementation of a QMS according to ISO 9001:2015 at our Department.

Material and Methods

The process of implementing the QMS required the initial recording of the existing operating status of the Department. The procedure was therefore initiated by providing medical-nursing and administrative staff with self-assessment questionnaires and special forms for problem-filling and improvement suggestions. All forms were filled in anonymously. All data gathered were processed by our quality management consultant. The results were presented to the parties involved in an open meeting at the Department and formed the basis for the QMS design. Through a 12-month strenuous workout with meetings about every 15 days, a QMS consisting of 14 procedures, two working instructions, 17 forms, and 13 administrative nursing protocols was set up. The system included 24 forms provided by the Ministry of Health and 29 clinical nursing protocols issued by the local Health Region. The staff was systematically trained in keeping them up and, with suggestions/corrective actions the QMS was improved.

In the summer of 2017, questionnaires were distributed to all patients in the Department to investigate the degree of satisfaction from the medical, nursing and administrative services. The patients were informed by the Department staff on the content of the questions and the confidential nature of the research, which aimed at improving the provided services. Completion of the questionnaire was anonymous and optional. If a patient was unable to complete it, this was possible to be done by the escort. The majority of the questions were closed-ended with five distinct grades (Likert Scale: Bad, Probably Bad, Neither Good nor Bad, Probably Good, Good) [5]. The questionnaire initially included questions about reception and hospital stay of patients, then asked to evaluate the care of the medical and nursing staff and finally about the general care received. The objective of the research was to investigate a) the degree of patient satisfaction by the quality of the health services provided at the Department and b) the benefits resulting from the implementation of the QMS.

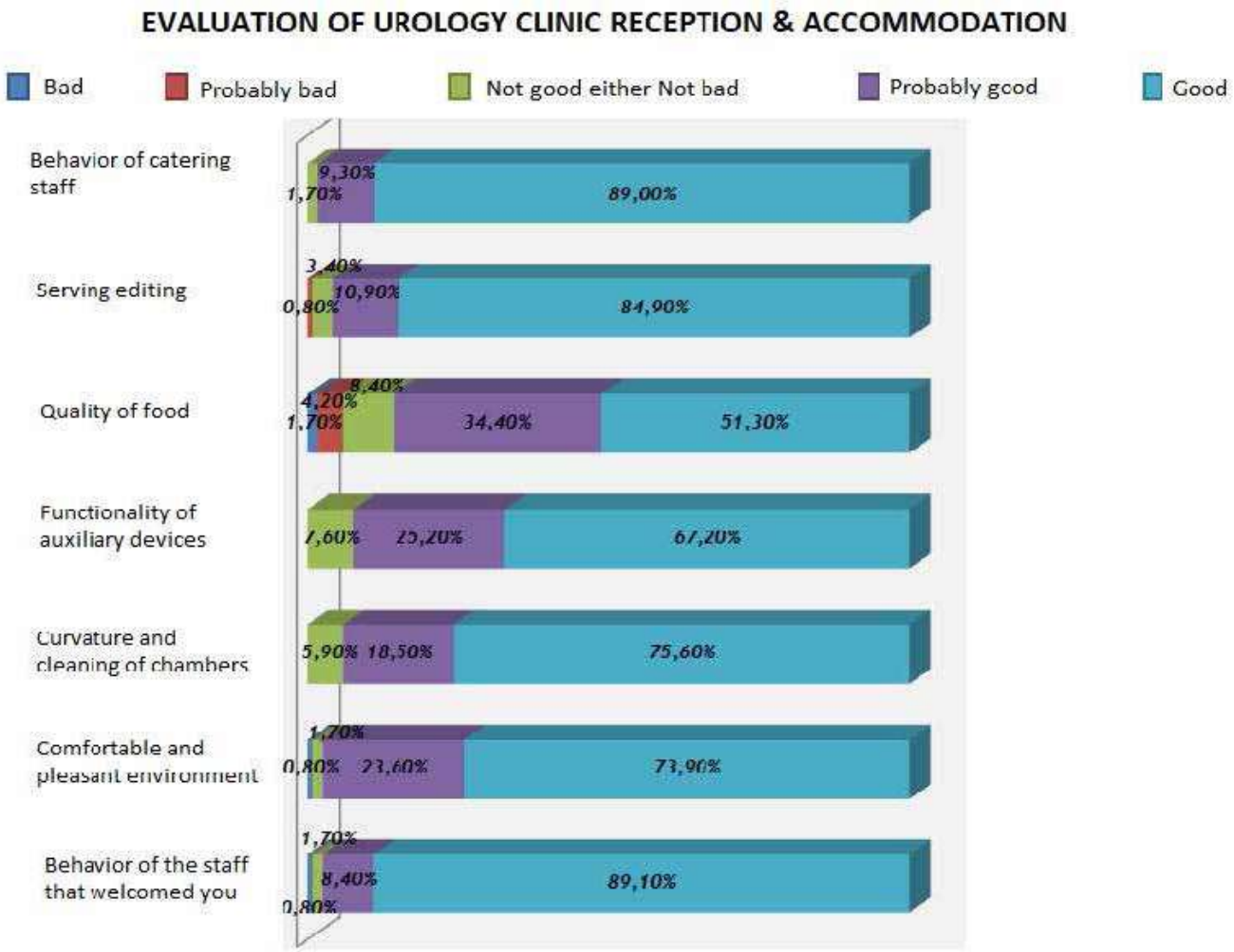
Results

A total of 119 subjects (93 men-26 women: 78.2% and 21.8%, respectively), with an average age of 60.4 years and an average hospitalization duration of 7.3 days, participated in the satisfaction survey. The Department scored a total of 9.1/10 (reception/stay), 9.8/10 (medical follow-up), 9.3/10 (nursing care) and 9.2/10 (general service). The majority of the participants stated that the welcoming staff behavior was "good" and "rather good" (89.1% and 8.4%, respectively). All responses to this category of questions scored similarly high, with the highest levels of satisfaction being observed with catering staff behavior (89.0%) (**Figure 1**). The next questionnaire section referred to medical care quality, focusing on the information and speed of service. In particular, regarding the adequacy of the information provided by the medical staff about the disease, 87.4% of respondents stated that it was "good" and 10.1% "probably good". Subsequently, 91.6% stated that the instructions given by doctors about treatment were "good" and 5.9% stated that they were "probably good". At similar levels was recorded the degree of satisfaction with waiting time, with "good" and "probably good" rates reaching 76.3% and 14.3%, respectively. The behavior of medical staff during the examination was rated as "good" by the vast majority of participants

sults that have been prepared by a recognized organization after consent to achieve the best possible degree of order in a given application framework [1].

3. *An activity that establishes provisions intended to be applied to address actual or potential problems to achieve the best possible degree of order within a given implementation framework [1].*
4. *Process by which a third party (certification body) provides written assurance that a product, process or service complies with the prescribed requirements [1].*

Figure 1



(87.4%) (**Figure 2**). The next questionnaire section referred to the quality of the services provided by the nursing staff. The majority were satisfied with the behavior of the nursing staff; rates reaching 90.6% and 4.2% for "good" and "probably good", respectively. Similarly, participants were highly satisfied with the adequacy of information receiving by the nursing staff about nursing care, with rates of 84.9% and 8.4% for "good" and "probably good", respectively. Regarding nursing care quality, 84.0% stated that it was "good" and 11.0% stated "probably good" (**Figure 3**). Last but not least, the level of satisfaction with general care of the personnel was also high (**Figure 4**).

With the implementation of the QMS, quality indicators related to medical-nursing care (drop-fall rates, fever rates, admission severity-related mortality, etc.) are monitored. The progress of indicators is presented at staff meetings and actions are discussed aiming at improvements. The operation of the Department has been parameterized and co-perception has been conquered. By implementing a QMS, future goals have also been set: a) Higher staff participation rate in problems/suggestions for improvement recording, b) Monitoring the achievement of research objectives through standardized procedures, c) Higher satisfaction score achievement, d) Certification according to EN 15224, in order to introduce the concept of clinical risk by adopting scientifically registered protocols in daily diagnostic/therapeutic practice.

Discussion

The implementation of a QMS in accordance with the International Standard ISO 9001:2015 secures standardization of the way an organization operates in order to continuously improve the quality of services. Consequently, efficiency/competitiveness increases, and at the same time client (patient) satisfaction increases

Figure 2

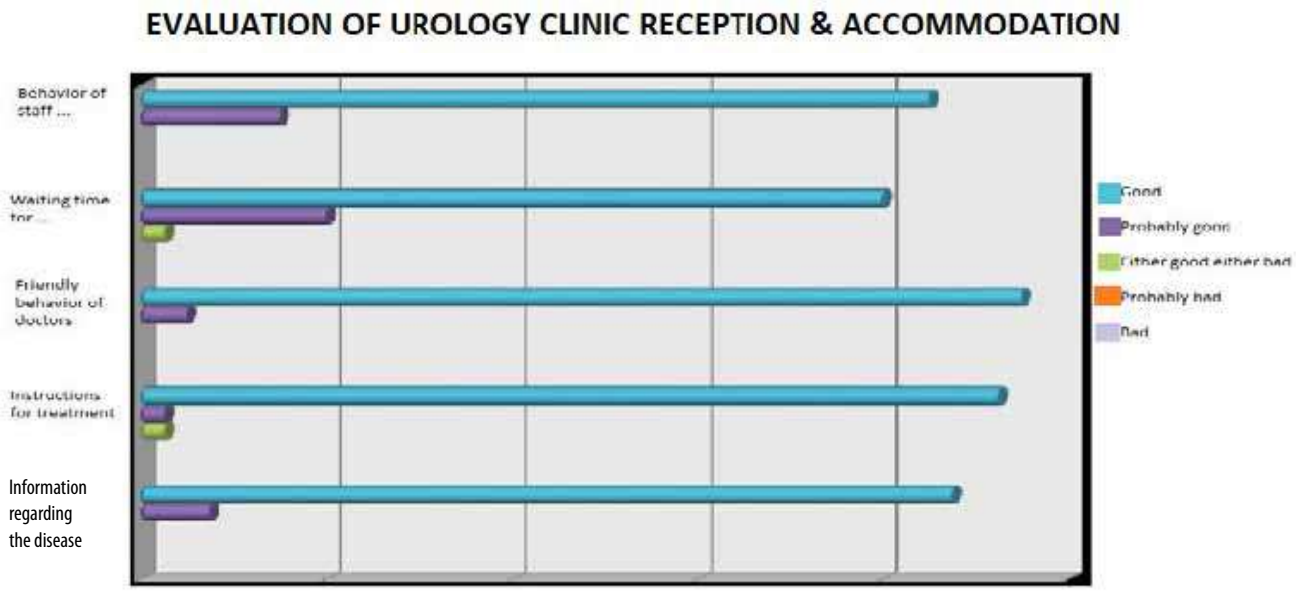
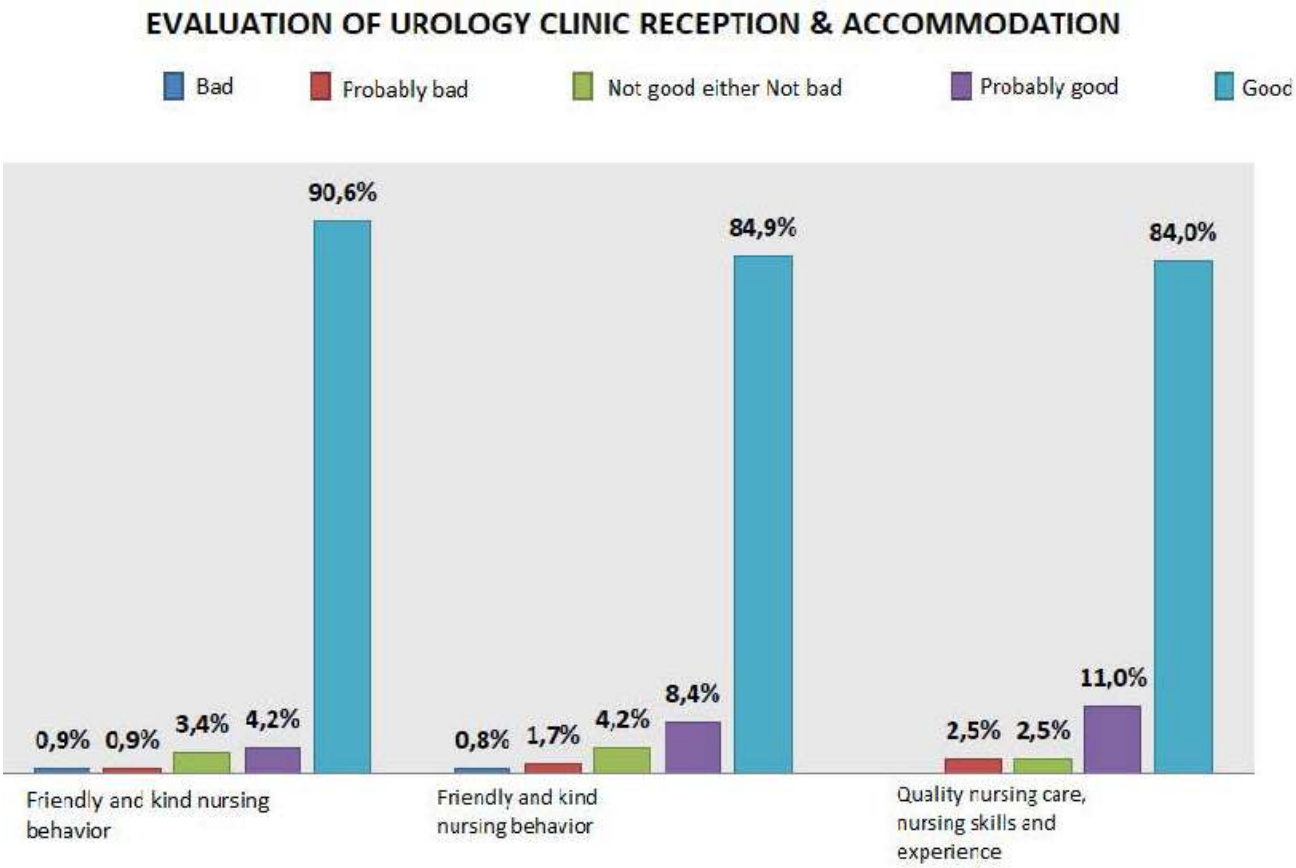
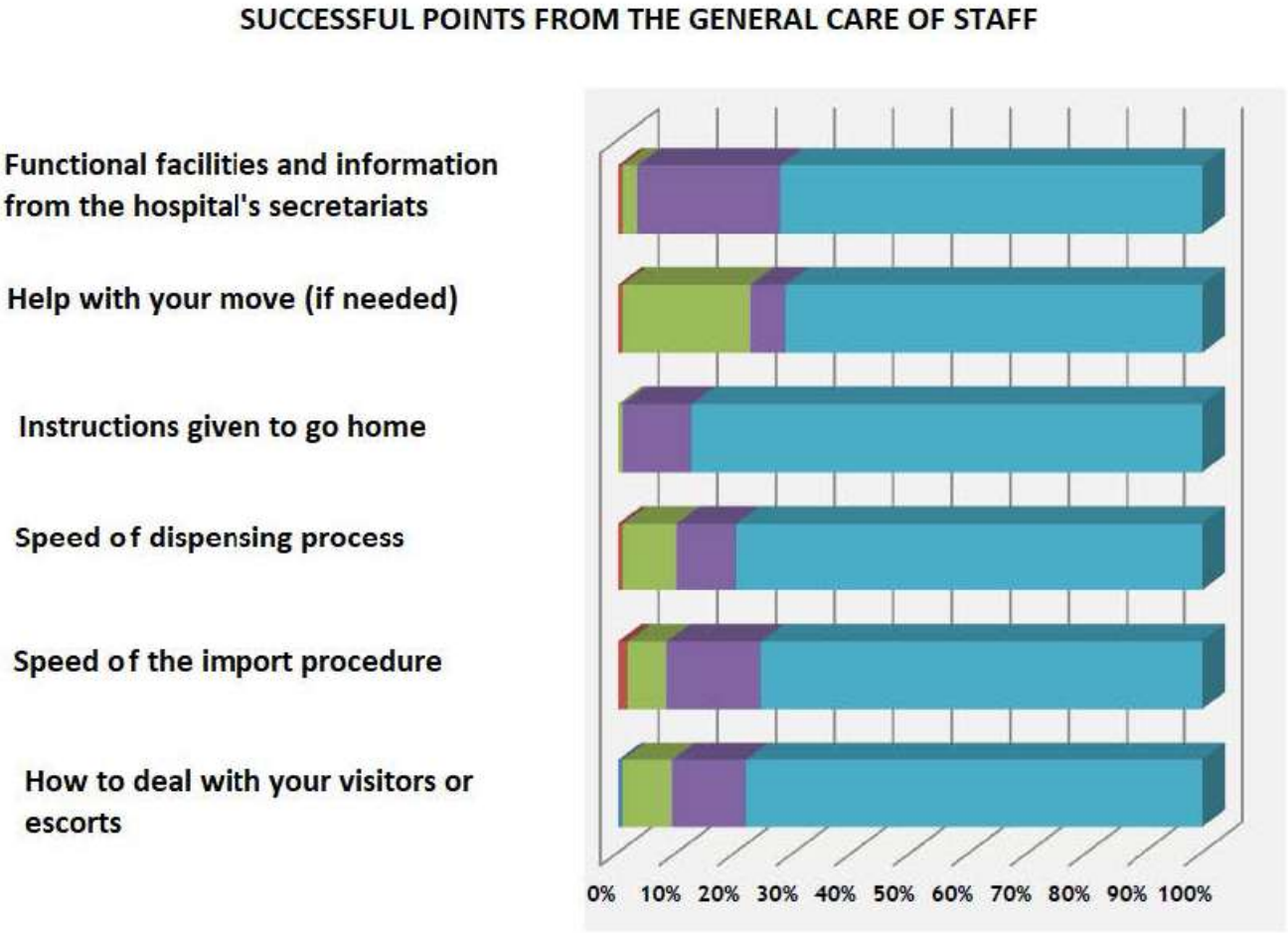


Figure 3



through improvement of the organization function [6, 7]. The implementation of specific structures aiming at controlling/improving the quality health service provided in the public sector is clearly lagging behind private sector not only in our country but also in most of the European Union countries, where systems for both

Figure 4



quality assurance and medical act control have been developed. The consequence of this situation is the perpetuation of inefficient practices, misuse of human resources and wastage of public money.

However, the high level of satisfaction and trust in the Greek HCS turns people in domestic public hospitals, with what this entails for the economy and the insurance funds of the country [8]. A research program conducted in two hospitals in Attiki (a specialized non-profit and a newly established public hospital) with the aim to present the results of the analysis of the application of "quality" to hospital services, and the use of indicators describing the quality of the hospital in satisfaction numbers, led to the conclusion that the satisfaction rate in both hospitals was high, especially in the non-profit one, where the QMS was used for a long period [9]. In both cases there appeared to be a relationship between the use of QMS and patient satisfaction. The overall conclusion is that the more familiar the staff with these systems becomes, the greater satisfaction is expressed by the patients [9].

Cost reduction and efficiency gains are usually seen as the first measurable positive results from implementation of QMSs in most health service providers, and thus their effectiveness is difficult to be challenged. However, the main challenge that needs to be addressed in order to ensure continuity and success of such an implementation is to achieve staff commitment to quality issues. A strategy that can bring about this result is the pursuit of staff participation in key positions on quality issues, creating thus a link between administration and medical-nursing staff [10].

Assessing the quality of health service provision at a Department level is difficult and needs to be documented. Documentation is achieved by certification. The procedure of certification in our case was implemented through the Special Account for Research (ELKE) of the University of Crete; using funds from a specific program

set up for the development of the Department of Urology. To the best of our knowledge this is the first case of certification of a Urological Department in a Public Hospital in Greece[5]. The implementation of the QMS satisfies the quality policy as defined by the Directorate of the Department and the Administration of the Hospital, ensuring the robustness of the quality of services provided.

The aim of the present work is to raise awareness about the implementation of an integrated-organized QMS at a Urological Department level of a Public Hospital for the first time, and to present the initial results of the analysis of the application of "quality" to hospital services; in particular the use of indicators describing the quality of a Department in patient satisfaction figures. This effort is undoubtedly based on the creation of a quality culture with an ultimate aim of improving the services provided and ensuring greatest possible clinical effectiveness in everyday practice. The implementation of a QMS in line with the international standard ISO 9001:2015 of a Urological Clinic of a Public Hospital is difficult but feasible.

Changes that have started to occur in the organizational structure and the operation of the Department by the implementation of a QMS may be summarized as follows:

- Establishment of a recorded organogram and patient flow diagrams.
- Definition and monitoring of quality indicators.
- Set up of patient/staff satisfaction studies through standardized questionnaires.
- Training of medical-nursing staff.
- Improved archiving, with a more direct access and updating of patient data.
- Intensification of clinical studies and promotion of science.
- Recording of intervention outcomes and statistical data export.
- Recording and maintenance of all the equipment in the Department.
- Detection, assessment and management of potential risks and opportunities.

Conclusions

The implementation of a QMS in public health is not easy and has many dimensions. However, it offers a competitive advantage, improving the efficiency and the effectiveness of healthcare providers by contributing to the improvement of the services provided. Certification of a Urological Department QMS in a Public Hospital is difficult but feasible. It can be successful despite organizational-technical difficulties and lack of resources. Benefits are multiple, such as enhancing organizational structure efficiency and improving communication within and outside the hospital.

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Conflicts of Interest: The authors declare no conflict of interest.

5. http://www.pagni.gr/myCode/ISO/CERT_PAGNI_OUROLOGIKI_9001_2015_2017.pdf.

Περίληψη

ΕΙΣΑΓΩΓΗ/ΣΚΟΠΟΣ: Η αξιολόγηση της ποιότητας παροχής υπηρεσιών υγείας σε επίπεδο Κλινικής είναι δύσκολη και οφείλει να είναι τεκμηριωμένη. Η τεκμηρίωση επιτυγχάνεται με την πιστοποίηση. Παρά την αυξανόμενη τάση έκδοσης πιο εξειδικευμένων προτύπων ποιότητας, το ISO 9001:2015 είναι το πλέον διαδεδομένο. Η Διεύθυνση της Κλινικής σε συνεργασία με τη Διοίκηση του Νοσοκομείου προχώρησε στη μελέτη/εγκατάσταση του συστήματος διαχείρισης ποιότητας σύμφωνα με το πρότυπο ISO 9001:2015 για παροχή διαγνωστικών, θεραπευτικών και νοσηλευτικών υπηρεσιών καθώς και για παραγωγή επιστημονικού έργου, ερευνητική δραστηριότητα και παροχή εκπαιδευτικών υπηρεσιών από την Κλινική και τις Ειδικές Μονάδες της (Μη Επεμβατικής Ουρολογίας-Λιθοθρυψίας & Κυστεοσκοπήσεων-Ουροδυναμικής). Η διαδικασία

Λέξεις ευρετηριασμού
Τομέας Παροχής Υπηρεσιών Υγείας, Διασφάλιση Ποιότητας Υπηρεσιών Υγείας, Δείκτες Ποιότητας Υπηρεσιών Υγείας, Διαχειριστικά Συστήματα Ποιότητας, Ποιότητα Υπηρεσιών Υγείας

υλοποιήθηκε (2017) μέσω Ειδικού Λογαριασμού Κονδυλίων Έρευνας του Πανεπιστημίου μας από συγκεκριμένο αναπτυξιακό πρόγραμμα της Κλινικής, αποτελεί δε πρώτη περίπτωση πιστοποίησης Ουρολογικής Κλινικής Δημόσιου Νοσοκομείου. Σκοπός της εργασίας είναι η παρουσίαση της εμπειρίας από την εφαρμογή του ISO 9001:2015 στην Κλινική μας.

ΥΛΙΚΟ & ΜΕΘΟΔΟΣ: Η διαδικασία ξεκίνησε με διάθεση στο ιατρο-νοσηλευτικό-διοικητικό προσωπικό εντύπου ανώνυμης αυτοαξιολόγησης/κατάθεσης προβλημάτων-προτάσεων βελτίωσης. Ακολούθησε επεξεργασία από τον σύμβουλό μας. Τα αποτελέσματα παρουσιάστηκαν σε ανοικτή συγκέντρωση αποτελώντας βάση σχεδιασμού του συστήματος ποιότητας. Μέσα από μία 12-μηνη πορεία επίπονης εργασίας με συναντήσεις ανά 15νθήμερο περίπου δομήσαμε ένα σύστημα ποιότητας που αποτελείται από 14 διαδικασίες, 2 οδηγίες εργασίας, 17 έντυπα, 13 διοικητικά νοσηλευτικά πρωτόκολλα. Στο σύστημα έχουν ενταχθεί 24 προβλεπόμενα από το Υπουργείο Υγείας έντυπα και 29 κλινικά νοσηλευτικά πρωτόκολλα που έχουν εκδοθεί από την ΥΠΕ. Το προσωπικό εκπαιδεύτηκε συστηματικά στη τήρηση τους και με υποδείξεις-παρατηρήσεις βοήθησε στη βελτίωση του συστήματος ποιότητας.

ΑΠΟΤΕΛΕΣΜΑΤΑ: Μέσα από ερωτηματολόγια ικανοποίησης ασθενών η Κλινική βαθμολογήθηκε με 9,1/10 (υποδοχή/διαμονή), 9,8/10 (ιατρική παρακολούθηση), 9,3/10 (νοσηλευτική φροντίδα) και 9,2/10 (γενική εξυπηρέτηση). Παρακολουθούνται δείκτες ποιότητας σχετιζόμενοι με την ιατρο-νοσηλευτική φροντίδα (ποσοστά πτώσεων-εμπυρέτων, σχετιζόμενη με τη βαρύτητα εισαγωγής θνητότητα κ.α.). Μέσα από συσκέψεις προσωπικού παρουσιάζεται η πρόοδος των δεικτών και αποφασίζονται ενέργειες με στόχο τη βελτίωση. Η λειτουργία της Κλινικής έχει παραμετροποιηθεί και έχει κατακτηθεί η συναντίληψη. Με την εφαρμογή πρότυπου ποιότητας τέθηκαν μελλοντικοί στόχοι: α) Συμμετοχή περισσότερου προσωπικού στην καταγραφή προβλημάτων/προτάσεων βελτίωσης, β) Παρακολούθηση επίτευξη ερευνητικών στόχων μέσω προβλεπόμενων διαδικασιών, γ) Επίτευξη υψηλότερης βαθμολογίας ικανοποίησης, δ) Πιστοποίηση με το πρότυπο EN 15224, ώστε να εισαχθεί στη λειτουργία η έννοια του κλινικού κινδύνου, υϊοθετώντας επιστημονικά καταχωρημένα πρωτόκολλα στη καθημερινή διαγνωστική/θεραπευτική πράξη.

ΣΥΜΠΕΡΑΣΜΑΤΑ: Η πιστοποίηση του συστήματος ποιότητας μιας Ουρολογικής Κλινικής Δημόσιου Νοσοκομείου είναι δύσκολη αλλά εφικτή. Μπορεί να στεφθεί με επιτυχία παρά τις οργανωτικές-τεχνικές δυσκολίες/έλλειψη πόρων. Τα οφέλη είναι πολλά όπως η ενίσχυση αποτελεσματικότητας οργανωτικής δομής-βελτίωση επικοινωνίας εντός/εκτός νοσοκομείου.

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ORIGINAL ARTICLE

Positive surgical margins and bladder neck sparing during laparoscopic radical prostatectomy

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Abstract

INTRODUCTION: The aim of the study is to evaluate the result of bladder neck sparing technique associated with positive surgical margins in patients operated with laparoscopic radical prostatectomy.

MATERIAL AND METHOD: We analyze data from 17 patients with localized PCa patients treated with laparoscopic radical prostatectomy while preserve the bladder neck. In all patients, an intra-operative biopsy was performed from the bladder neck while topographic histological findings, potential positive margins and urinary continence after 3.6 and 12 months were presented.

RESULTS: The mean age of the patients was 65.17 (range 56 to 70). The mean PSA was 6.14 ng/ml (range 3.2 to 10.1), and the most common Gleason Score was 6 (range 6 to 8). In all cases the biopsy from the bladder neck was negative. Sixteen men (94.1%) had clinical stage pT2 and 1 (5.9%) were pT3a. Positive surgical margins were found at the top of the prostate in only 1 case whereas 11, 13 and 15 patients were normalized at 3.6.12 months, respectively.

CONCLUSIONS: It seems in our patients, that the bladder neck sparing technique is not associated with the increase incidence of positive surgical margins and can also be performed safely to achieve better functional outcomes.

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Key words
laparoscopic radical prostatectomy, bladder neck sparing

INTRODUCTION

The first laparoscopic radical prostatectomy (LRP) was described by Schuessler however, it was established and developed as a technique by Guilleneau & Vallencien. The technique of extraperitoneal LRP was originally described by Raboy et al in 1997 and since then has been adopted by several centers as a method of choice for the treatment of prostatic cancer with minimal invasive therapies[1, 2, 3].

Nonetheless, urinary incontinence is a 'potential' complication of the operation since it is adversely affected by the mechanisms of continence[4, 5].

Bladder neck sparing (BNS) has reduced the likelihood of incontinence of the urine and contraction of the bladder neck. However, as a surgical manipulation it is controversial, as it increases the probability of positive surgical margins[6, 7, 8, 9].

The purpose of the study is to describe our technique, to analyze the first data and to present the initial impressions in the treatment of our patients.

MATERIAL AND METHOD

From February 2016 to January 2017, 17 patients with prostate cancer were treated laparoscopically. All patients were informed in detail and signed a written consent in accordance with the ethics and ethical rules of the institutions.

The operations were performed under general anesthesia, with extraperitoneal access. Three trocars of 5mm, one of 10mm and one of 12mm were used, while Ultracision scissors were used to dissect soft tissues. For the ligation of the Santorini plexus, a Vicryl suture or no suture was used in seven and ten cases respectively. During suturing the surgeon changed position with the cameraman.

The time of the interventions was determined from the initial incision until the placement of the last suture. All patients were hydrated and mobilized on the 1st postoperative day, drainage was removed after 72 hours, and postoperative pain was treated with simple painkillers (paracetamol).

Clinical and pathological data, intraoperative and postoperative parameters, complications, and hospitalization time were recorded prospectively.

TECHNIQUE

All the procedures were performed by one surgeon, following the same surgical technique without any tutor presence: a 1.5 to 2 cm long subumbilical incision introduced spacemaker trocar for Retzious space, through which about 300 ml of air is introduced to prepare pneumo-Retzius. Then 4 trocars are placed under direct vision in circular array (fan array – **image 1**).

The use of the ultrasound scissors facilitates the preparation of the tissues near bladder neck and the cross section of the anterior wall of the urethra is performed by simultaneously pulling back the bladder from the assistant (**image 2**).

Image 1. *The fan array trocar placement*

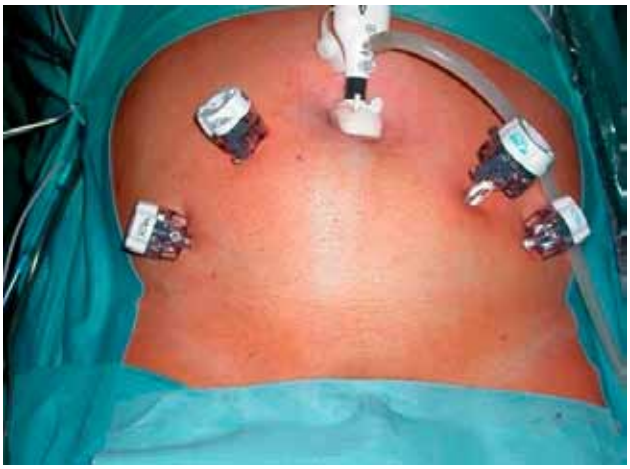


Image 2. *Bladder neck sparing procedure*

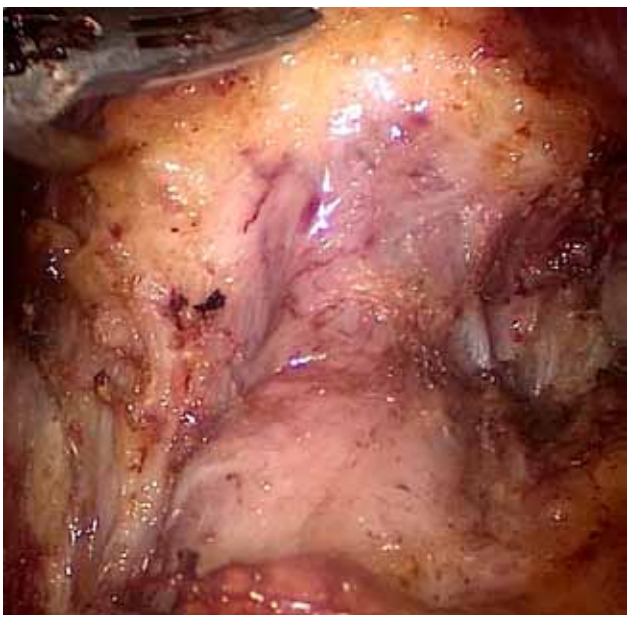


Image 3. *Prostate traction with Carter – Thommanson instrument*

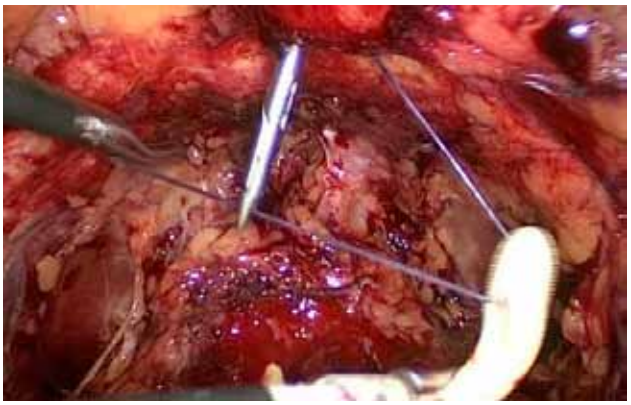


Image 4. *Preparation of the seminal duct and seminal vesicles*

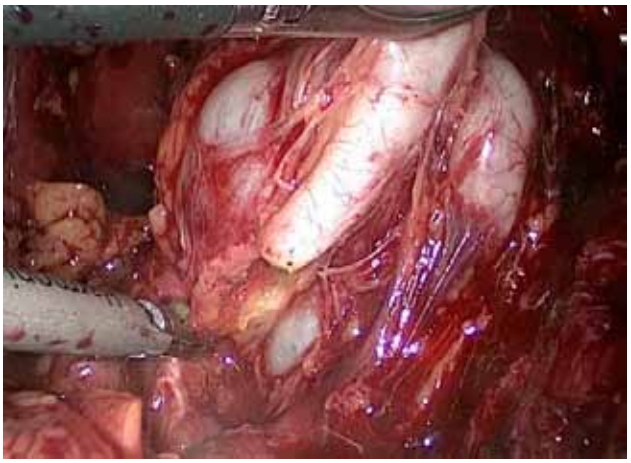


Image 5. *Membranous urethra preservation*

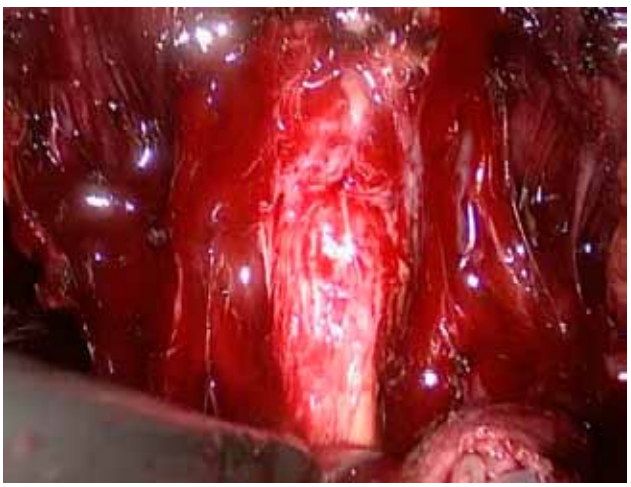
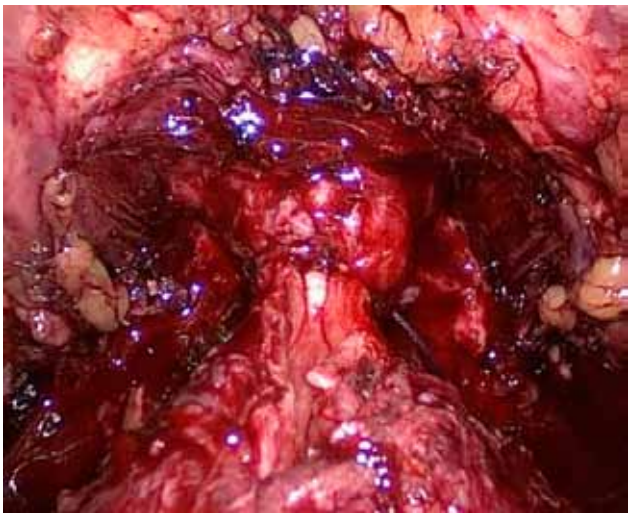


Image 6. *Urethrovesical anastomosis*



The posterior wall of the urethra intersected 'into' the prostate, after the prostate has been raised by the Carter-Thommanson tool (**image 3**), while the preparation of the seminal duct and seminal vesicles is done with gentle pulling upwards (**image 4**).

The preparation of prostatic pedicles - neurovascular bundles (when necessary) is usually done by placing 10mm metal clips and gently pulling the bundles outward by the assistant.

At the apex, the (anterior - posterior) wall of the urethra was cutting with cold knife with simultaneous posterior traction of the prostate in order to maintain as long as possible the membrane urethra and therefore, to preserve the secondary continence mechanism (**image 5**).

Anastomosis was performed by placing 3, 4, 5 or 6 interrupted Vicryl 2-0 sutures with a 5/8 needle in 1, 10, 4 and 2 patients respectively (**image 6**).

RESULTS

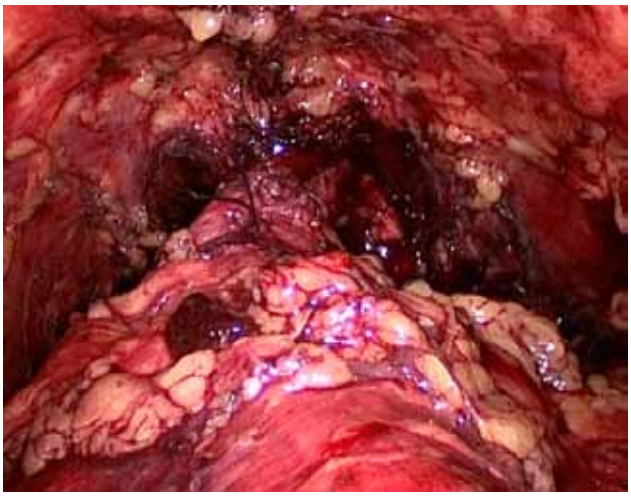
Over a period of 11 months, 17 patients underwent a laparoscopic radical prostatectomy due to localized prostate cancer. The average age of the patients was 65.17 years old (range 56-70), the mean PSA was 6.14 ng/ml (range 3.2 to 10.1ng/ml), and the most common Gleason Score was 6 (range 6-8) (**Table 1**).

In all cases the intraoperative biopsy of the bladder neck was negative. Average surgery time was 4 hours and 38 minutes (range 190-320 minutes). In 3 cases LRP was converted into open surgery, one because of a technical problem located in the gas filter while the

Table 1 *Patients characteristics*

Parameter	Value	Average
Age	**56-70 years**	**65.17**
PSA value	**3.2ng/ml -10.1ng/ml**	**6.14**
Gleason score		**6**
6	13 patients	
7	3 patients	
8	1 patients	

Image 7. *Final result*



others were converted at the time of urethrocystic anastomosis because of hemorrhage.

In one patient, the epigastric vessels were injured during trocar insertion, where was identified and directly ligated, in another patient the peritoneum was opened from the entrance of the trocar # 5 (surgery continued) and no patient needed a blood transfusion.

Significant post-operative complication occurred in a patient (which was the cause of long hospital staying) due to accidental violent removal of the urinary catheter in the 3rd post OP day. Overall, the average hospital stay was 5.2 days. Pathological examination revealed sixteen men (94.1%) of pT2 and 1 (5.9%) of pT3a. Positive surgical margin were found at the top of the prostate in only 1 case, whereas 11, 13 and 15 patients were continent at 3, 6 and 12 months respectively (**Table 2**).

DISCUSSION

Various surgical techniques have been developed to improve radical prostatectomy, in order to maintain important anatomical structures including neurovascular pedicles and bladder neck which, however, jeopardize the disease prognosis. [8, 9, 10, 11, 12]

In the literature, the postoperative urinary incontinence presented with a wide range of rates during LRP and/or RARP ranging from 2.5-87%, depending on the author's definition of incontinence[11, 13].

The bladder neck sparing technique has begun –20 years ago– initially in open surgery and has developed as well by minimally invasive procedures since as it is easy and reproducible surgical manipulation in order to achieved a cancer free status while avoiding complications: urinary incontinence, anastomotic stenosis, etc[6, 8, 9, 14].

In a same direction, Azuma et al suggests the BNS among six other key points for rapid restoration of incontinence in patients after LRP. The rest are: minimal distal incision of the endopelvic fascia; (2) preservation of the bladder neck; (3) bilateral nerve-sparing surgery; (4) preservation of the puboprostatic ligament and its refixation to the anterior aspect of the bladder neck (bladder neck sling suspension); (5) preservation of the posterior (membranous) urethra; (6) suturing of the posterior aspect of the rhabdosphincter, the remaining portion of the Denonvilliers fascia, and the bladder neck (restoration of the Denonvilliers fascia)[15].

Similarly, Stolzenburg et al. agree that the BNS technique is closely linked to the rapid restoration of urinary continence in patients who underwent LRP[16].

On the other hand, Selli et al suggest that keeping the neck does not play a role in urinary continence but is important in rapid recovery and hence in improving quality of life (QoL)[7].

Maintaining the bladder neck involves a potential risk of positive surgical margins due to limited bladder neck excision leading to a possible residual disease[8, 9].

Several studies in the past mentioned the existence of positive surgical margins in RP with rates ranging

Table 2 *Patients data*

	Age	Duration of the surgery procedure (min)	Number of sutures at the anastomosis	Perioperative complications	Post-operative complications	Days of hospitalization	TNM staging	Catheter removal (postoperative day)
1	68	320	3	SUBCUTANEOUS EMPHYSEMA	N	4	T2	8TH
2	62	280	4	N	N	4	T2	8TH
3	65	290	6	CONVERSION TO OPEN SURGERY	N	5	T2	8TH
4	70	250	4	N	N	4	T2	7TH
5	72	260	5	N	N	4	T2	7TH
6	56	220	6	CONVERSION TO OPEN SURGERY	N	4	T2	10TH
7	59	210	4	N	N	4	T2	7TH
8	69	230	5	CONVERSION TO OPEN SURGERY	N	4	T2	14TH
9	60	220	4	N	CATHETER TRACTION	23	T2	22ND
10	68	200	4	N	N	4	T2	7TH
11	68	240	4	EPIGASTRIC VESSELS INJURY	N	4	T2	14TH
12	70	230	4	N	N	4	T2	12TH
13	66	190	4	N	N	4	T2	10TH
14	63	225	4	N	N	4	T2	7TH
15	60	220	4	N	N	4	T3	12TH
16	64	250	5	PERITONEAL INJURY	N	4	T2	7TH
17	66	240	5	N	N	4	T2	7TH

from 16.6% to 39.4%. Their conclusions are unclear and there are many reports suggesting the BNS as a safe oncologically technique –since in most of the cases, extraprostatic extension is located topographically at other sites of the gland– but with some limitations[8, 9, 17]:

Thus, Markovic et al and Terakawa et al suggests that BNS technique should not take place in higher than pT3 stages because it is associated with increased percentages of positive surgical margins reaching up to 71%[18, 19].

In contrast, Gomez et al analyzed 676 prostatectomies and revealed positive surgical margins for the bladder neck area at only 4.3%[6].

Bianco et al, in a study of 555 patients, suggests that the BNS does not increase the percentage of positive surgical margins in the anatomical area and does not reduce the survival of free disease[20].

In addition, LRP or RARP studies reveal lower rates of positive surgical margins with values ranging from 4.3 to 14.7% attributable to early diagnosis and best surgical technique[21, 22, 23].

In this article we present the experience of two district urological clinics by showing this technique in a small number of patients for evaluation without further comparison.

In general, we suggest that in our social health system status and current surgical practice, LRP can be a first-choice procedure of particular importance and its implementation is more than ever necessary, as it is a link to the application of future technologies[24].

CONCLUSIONS

Bladder neck-sparing technique is not associated with the positive surgical margins and is a safe oncologically technique in specific cancer stages, while can be performed without any particular difficulty in achieving better functional outcomes and rapid recovery.

Περίληψη

ΕΙΣΑΓΩΓΗ: Ο σκοπός της μελέτης είναι να εκτιμηθεί το αποτέλεσμα της διατήρησης του αυχένα της κύστης με τα θετικά χειρουργικά όρια σε ασθενείς μετά λαπαροσκοπική ριζική προστατεκτομή.

ΥΛΙΚΟ και ΜΕΘΟΔΟΣ: Αναλύουμε δεδομένα 17 ασθενών δυο κλινικών με εντοπισμένο Ca προστάτη που αντιμετωπίστηκαν με λαπαροσκοπική ριζική προστατεκτομή διατηρώντας τον αυχένα της κύστης. Σε όλους τους ασθενείς διενεργήθηκε βιοψία από τον αυχένα ενώ παρουσιάζονται τοπογραφικά τα ιστολογικά ευρήματα, τα πιθανά θετικά όρια και η εγκράτεια των ούρων μετά 3,6 και 12 μήνες.

ΑΠΟΤΕΛΕΣΜΑΤΑ: Η μέση ηλικία των ασθενών ήταν 65,17 (εύρος 56 έως 70). Η μέση τιμή PSA ήταν 6,14 ng/ml (εύρος 3,2 έως 10,1), και το συχνότερο Gleason Score ήταν 6 (εύρος 6 έως 8). Σε όλες τις περιπτώσεις που έγινε διεγχειρητική βιοψία στον αυχένα της κύστης ήταν αρνητική. Δεκαέξι άνδρες (94,1%) είχαν κλινικό στάδιο pT2 και 1 (5,9%) ήταν σταδίου pT3a. Θετικά χειρουργικά όρια βρέθηκαν στην κορυφή του προστάτη μόνο σε 1 περίπτωση ενώ 11, 13 και 15 ασθενείς ήταν εγκρατείς στους 3,6,12 μήνες αντίστοιχα.

ΣΥΜΠΕΡΑΣΜΑΤΑ: Στην σειρά των ασθενών μας φαίνεται ότι η bladder neck sparing τεχνική δεν συνδέεται με την εμφάνιση των θετικών ορίων ενώ παράλληλα μπορεί να πραγματοποιηθεί με ασφάλεια για την επίτευξη καλύτερων λειτουργικών αποτελεσμάτων.

Λέξεις ευρετηριασμού

Λαπαροσκοπική ριζική προστατεκτομή, διατήρηση αυχένα ουροδόχου κύστης

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ORIGINAL ARTICLE

Comparison of the results and complications for transrectal ultrasound guided versus transperineal mapping biopsy of the prostate

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Abstract

Introduction: To compare the biopsy results and complication rates in men undergoing TRUS- guided vs. transperineal mapping biopsy (TPMB) of the prostate.

Materials and Methods: 379 men, of which 271 (71.5%) had a prior TRUS-guided biopsy, had TPMB performed through template with biopsies taken at 5 mm intervals. TRUS had a median of 12 cores (range 6-26) sampled while the TPMB group had 51.5 (range16-151).

Results: Median age and PSA were 65 years (range 34-86) and 5.5 ng/ml (range 0.02-118). Of the 271 men with prior TRUS biopsies, 89 (32.8%) had prostate cancer (Gleason score 6 in 76.1%). In contrast, 240/379 (63.3%) were diagnosed with prostate cancer by TPMB with a median of 5.0 cores positive (range 1-37) for Gleason score 6 in 11 4 (47.5%), 7 in 102 (42.5%) and 8-10 in 24 (10%). Of the 182 negative TRUS biopsies. 121 (66.5%) were positive by TPMB of which 62 (51.2%) were Gleason score $\geq$ 7. 11/271 (4.1%) of the men who had TRUS biopsy developed urinary tract infection compared to 3/379 (0.79%) of those with mapping biopsy. No men developed retention after TRUS biopsy while 30/379 (7.9%) did following TPMB. Older

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age (p = 0.010) and larger prostate volume (PV) (p = 0.016) were associated with urinary retention. Men older than 65 years had 12.8% vs. 3.9% (OR 3.7, 95% CI 1.6-8.4, p = 0.001) and PV > 42 cc had 13.4% vs. 2.7% (OR 5.7, 95% CI 2.1-15.1) retention incidence.

Conclusion: Prostate cancer is diagnosed in twice as many men with TPMB v. TRUS biopsy and detects cancer in two thirds of men with a negative TRUS biopsy. TPMB is rarely associated with infection but more commonly with urinary retention.

Key words
prostate cancer, transrectal ultrasound guided biopsy, transperineal mapping biopsy, biopsy results, complications

Introduction

There are over 3.4 million prostate biopsies performed worldwide per year with more than 95% by transrectal ultrasound (TRUS) guidance [1]. Due to its relatively low cancer detection rate of between 35% and 48%, many of the newly diagnosed 174,650 men in U.S.A. in 2019 may in fact be underdiagnosed and thus treated incorrectly due to inaccurate risk stratification [2].The standard systematic 12-core TRUS-guided biopsy remains the most common procedure for newly diagnosed prostate cancer with only a minority (less than 5%) performed by the transperineal mapping biopsy route (TPMB) [3]. After TRUS biopsy was first introduced and popularized by Hodge and Stamey as a 6-core technique, the number of specimens increased to 12 with lateral directed biopsies improving the diagnostic yield [4-7]. Various investigators have sought to improve its accuracy by sampling 20 of more sites but most urologists have maintained the 12-core TRUS biopsy approach as the standard of care [3, 8]. Despite these changes, serious problems remain with the TRUS approach. Thirty percent of biopsies need repeating because of false negatives and as many as 50% of cases may be mischaracterized with respect to grade [9]. A TRUS biopsy Gleason score of 6 is upgraded in 30-40% of men undergoing radical prostatectomy (RP) contributing to unnecessary overtreatment such as RP or radiation in 40% [10, 11]. In those electing active surveillance, 45% were switched to definitive therapy within 5 years because of tumor progression or patient concern (e.g. PSA anxiety) that may suggest an incorrect staging in some cases after primary standard systematic biopsy [12]. Finally, an increasing incidence of post-procedure infection and sepsis is of great concern for clinicians and patients [13].

In order to improve the diagnostic accuracy of prostate biopsy, some urologists have switched to the TPMB procedure, either as the confirmatory biopsy after a diagnosis of low risk disease, after a negative TRUS biopsies or in some cases as the primary biopsy [14]. The TPMB has been shown to more closely represent to disease found at RP and has improved risk stratification [15, 16]. While the advantages of TPMB have been well documented, it is associated with a different morbidity profile than TRUS biopsy [17]. Herein we compare the biopsy results and morbidity in men who underwent TPMB with or without a previous TRUS biopsy from two institutions with extensive experience in both procedures. We also identified strategies and predictive factors to reduce morbidity for both procedures.

Materials and Methods

TRUS biopsy and TPMB data of 379 men including 173 from Hygeia Hospital (HH), Athens, Greece and 206 from University of Colorado Hospital (UCH), Colorado, U.S.A. were entered into a combined database. Data reporting was approved by the institutional review boards. 271/379 (71.5%) had previous TRUS-guided biopsy prior to TPMB and 108 had TPMB as the initial biopsy. There was a median of 1.0 prior TRUS biopsy procedure performed (range 1-7) prior to having the TPMB, which included 15.2% with more than 2 biopsies. All TRUS procedures were performed with either an 18 or 16G coaxial biopsy device with a 17-20 mm core bed. Patients with a positive TRUS biopsy (n = 89) underwent TPMB for intra-prostatic staging prior to focal therapy consideration.

The TPMB was performed by one surgeon at each institution under anesthesia through a brachytherapy template with biopsies taken at 5 mm intervals [18]. Multiple in-line samples (up to 3) were taken if prostate length exceeded 2 cm. The pathologic evaluation of prostatic cores was performed by experienced uropathologists in both institutions. The TRUS and the TPMB patients were given fluoroquinolone prophylaxis (Ciprofloxacin) prior to and for a short time after the

Table 1 *Results for transperineal mapping biopsy (TPMB) by PSA, PSAD and Gleason score for ≤ 5 positive cores or more*

Variable	≤ 5 positive cores	> 5 cores	P value
PSA (ng/mL)	5.7 (95%CI 4.9-6.5)	8.6 (95%CI 6.2-11)	0.014
PSAD	0.15 (95%CI 0.12-0.17)	2.4 (95%CI 0.17-0.31)	0.008
Gleason score			
6	83 (72.8%)	31 (27.2%)	
7	40 (39.2%)	62 (60.8%)	
8-10	7 (29.2%)	17 (40.8%)	< 0.001

procedures. A urinary catheter was placed at the time of the mapping biopsy which was removed either in the recovery room (HH) or the next day (maximum 48 hours at UCH). If the patient failed a voiding trial in the recovery room or after removal in the clinic, he was sent home with a catheter and the patient was considered to have urinary retention. Patients presenting with post biopsy urinary symptoms or fever and who had a positive culture were classified as infected.

Statistical analysis. Associations between PSA, PSAD and core number were compared to the cancer detection rate (CDR) and the detection of clinically significant cancers (Gleason score > 6). Urinary infection and retention were compared for TRUS and TPMB with age, core number, prostate volume (PV), and prior TRUS-guided biopsy number (number of cores and procedures) by ANOVA and chi-square. Multiple significant associations were compared by linear regression. Statistical analysis was performed using SPSS v.20.

RESULTS

The median age, PSA and PSAD and PV were 64.4 years (range 34-86), 5.5 ng/ml (range 0.02-118), 0.159 (range 0.001-3.58) and 41.6 cc (range 9-178), respectively. Men with prior TRUS had a median of 12 cores sampled (range 6-26) and 89 (32.8%) were positive with 67 (76.1%) Gleason 6 prostate cancer.

A median of 51.5 (range 16-151) cores were removed during TPMB with a biopsy density of 1.4 cores/cc. 240/379 (63.3%) were diagnosed with prostate cancer. There was a median of 5 (range 1-37) positive cores of which 114 (47.5%) were Gleason score 6, 102 (42.5%) 7 and 24 (10%) 8-10. Pre-biopsy PSA was not associated with a positive TPMB (p = 0.46) while PSAD was, 0.12 (95%CI 0.11-0.13) and 0.18 (95%CI 0.15-0.22) for negative versus positive biopsy (p = 0.004). PSAD was 0.14 (95%CI 0.12-0.16) for Gleason score 6, 0.23 (95%CI 0.16-0.31) for Gleason score 7 and 0.24 (95%CI 0.16-0.33) for Gleason scores 8-10 (p = 0.017). A higher PSA (p = 0.014), PSAD (p = 0.008) and Gleason score (p < 0.001) were associated with more than 5 positive cores (**table 1**). Of the 182 negative TRUS biopsies. 121 (66.5%) were positive by TPMB of which 62 (51.2%) were Gleason score ≥ 7. 41.9% of these men also had small volume disease (≤ 5 positive cores).

11/271 (4.1%) of the men who had TRUS biopsy developed urinary tract infections compared to 3/379 (0.79%) of those with mapping biopsy. Age (p = 0.251), the number of TRUS biopsy procedures (p = 0.692) and PV (p = 0.081) were not associated with TRUS infections. Men with infection had a mean of 19.3 TRUS cores vs. 12.7 in those without infection (p < 0.001). Infection was 14.8% in men with 13 or more cores vs. 2.9% in those with 12 or less (OR 5.8, 95% CI 1.6-21.2, p = 0.003). In contrast, none of these factors were associated with infection following TPMB.

No men developed retention after TRUS biopsy while 30/379 (7.9%) did following TPMB. Retention was 12/206 (5.8%) from UCH and 18/173 (10.4%) from HH (p = 0.100) (**Table 2**). Older age, larger PV and higher core number were associated with urinary retention. Linear regression revealed age (p = 0.010) and PV (p = 0.016) as significant predictive factors, while the number of cores removed and the institution where biopsy was performed were not significant. Retention was 12.8% in men > 65 years vs. 3.9% for the younger men (OR 3.7, 95% CI 1.6-8.4, p = 0.001). Those with prostate volume greater than 42 cc (median size) had 13.4% vs. 2.7% retention incidence for men with smaller prostates (OR 5.7, 95% CI 2.1-15.1). There was no difference in retention incidence for men with PV ≤ 42 cc (p = 0.582) or larger (p = 0.731) between the 2 institutions. Two men (0.5%) required hospitalization for gross hematuria.

Table 2 *Association with mean age, prostate size and number of TMPB cores in men with urinary retention from UCH, Hygeia Hospital and in the combined group*

Variable	Age (years)	Prostate size (cc)	# Cores
UCH			
retention	69.3	48.2	68
no retention	62.6	38.9	66.9
P value	0.003	0.054	0.009
Hygea			
retention	69.4	72.2	53.8
no retention	65.8	54.5	44.4
P value	0.079	< 0.001	0.003
Total			
retention	69.4	64.4	67.2
no retention	64.0	45.9	56.7
P value	< 0.001	< 0.001	0.023

Discussion

There are only a few studies in of the literature that demonstrate the role of TPMB for improved diagnosis and almost all of them include a significant rate of tumor upgrading from conventional serial TRUS biopsies which vary from 13 to 45% [19, 20]. The current study demonstrated 66.5% of men with a prior negative TRUS biopsy had prostate cancer when a TPMB was performed and the majority had clinically significant disease. In addition, 41.9% had small volume disease ($\leq$ 5 positive cores). Physicians should recognize that an MRI ordered in men with a clinical suspicion for prostate cancer who have a negative TRUS may not be reliable in excluding clinically significant cancer in 40% of men. This study also demonstrated that a higher PSAD is strongly associated with more aggressive disease and that a man with PSAD of $\leq$ 0.14 is more likely to have Gleason score=6 disease. Some have advocated that men with a negative MRI and a PSAD < 0.15 could be spared a subsequent TRUS biopsy [21]. However, the data from this investigation identified 51 (40.5%) of the men with high grade disease who also had a PSAD $\leq$ 0.14.

While the complications associated with TRUS biopsy are well recognized the infection rate is on the rise reflecting an increasing prevalence multidrug-resistant gram negative bacteria [22]. Nam et al. conducted a population based study of 75,190 men who underwent a TRUS biopsy and found the 30-day hospital admission rate increased from 1.0% in 1996 to 4.1% in 2005 (p <0.0001) with the majority for infection related reasons [23]. The European Randomized Study of Screening for Prostate Cancer (ERSPC) included 10,474 men undergoing TRUS guided prostate biopsy from 1993 to 2011 and demonstrated a febrile infection rate of 4.2% and a hospital readmission rate of 0.8%, 81% of them were of infection origin [24]. According to a meta-analysis of the literature based on 7,000 records, the occurrence of serious complications after TRUS guided biopsy requiring hospital admission primarily due the infection ranged from 0.5% to 6.9% depending upon the antimicrobial prophylactic regimen [25].

While many studies in the literature have not demonstrated an increased risk of urinary tract infections (UTI) after different saturation techniques, our data suggested that men with more than 12 cores TRUS biopsy may be at an additional increased risk for infection [26-30]. For instance, the infection rate was 6 times higher in cohort of patients with 13 or more cores than in those who had standard 12 cores (median core number). Simsir et al. also demonstrated an increased risk of infection with a greater number of sampled biopsy cores [31]. It may be prudent in the current era of fusion biopsy, where physicians perform 2-4 target cores as well as 12 systematic biopsies for urologists to be aware of the possible increased infection risk and may want to take additional prophylactic measures [32].

The TMPB approach was introduced to better characterize the type, amount, and spatial distribution of cancer inside the prostate. Many studies have docu-

Table 3 *Acute urinary retention after TRUS and TPMB procedures*

TPMB % (Number)	
Pepe et al. [39]	6.7 (3,000)
Grummet et al.[36]	0 (1,194)
Vyas[6]	1.1 (634)
Suzuki et al.[27]	0 (539)
Muthuveloe et al. [38]	12.5 (200)
Mai et al. [30]	1.9 (3,007)
Present study	7.9 (379)
TRUS-guided % (Number)	
Loeb et al (ERSPC)[24]	0.8 (10,474)
Nam et al.[23]	1.4 (75,190)
Womble et al. (MUSIC)[40]	0.56 (4,087)
Wagenlehner FM et al.(GPIU)[41]	3.1 (521)
Marino et al.[42]	2.4 (455)
Chiang et al. [37]	2.1 (1,875)
Present study	0 (265)

mented both an increase in cancer detection rate and precise spatial cancer distribution after TPMB as a primary biopsy or as a confirmatory biopsy in men on active surveillance [33-35]. The incidence of clinically significant UTI is significantly lower (from 0.1% to 0.7%) when comparing TPMBs to TRUS guided biopsies [13]. This is predominantly due to the fact that, unlike transrectal approach, there is no needle passage through rectal fecal flora. Grummet et al. performed a review of 16 series of TPMB with a total of 6,609 patients and noted that only five men were admitted to hospital for sepsis, for an overall rate of just 0.076% [36]. Other studies also reflect negligible rates of sepsis, which are 40 to 70 times lower than those currently reported for TRUS guided biopsy [24,30, 37].

The most serious complication reported after TPMB is acute urinary retention (AUR), affecting up to 12.5 % of the cases [26, 27, 30, 36, 38, 39]. This is significantly greater than the risk of AUR with TRUS guided biopsies, which in a systematic review was reported from 0 to 3.1% [23, 4, 37, 40-42]. The higher risk of retention from TPMB is a consequence of intra-prostatic swelling and bleeding from the increased number of biopsies. This is similar to what is often seen following prostate brachytherapy where an average of 30 needles are inserted to deliver the radioactive sources [43]. AUR following TPMB is mainly managed conservatively, with most patients responding to a trial without a catheter within a few days post-procedure. Muthuveloe et al. also found that the use of a single dose of tamsulosin 0.4 mg at the time of template biopsy significantly reduced the rate of AUR to 5.3% with a relative risk of developing retention without tamsulosin of 2.5x [38].

A large study by Pepe et al. reported complication rates in 3000 patients who underwent 12 vs. 18 vs. 24 core template transperineal biopsies [39]. They showed that the risk of AUR increased from 4.1% to 7.1% and 11.1% respectively, suggesting that the number of cores taken has a direct correlation with the rate of AUR. In the current study while the number cores taken was also significantly associated with retention, however, in the regression analysis only PV and age remained significant. Even though we did not find retention in our TRUS population Shen et al. in a systematic review and meta-analysis of all randomized and case-control trials comparing TRUS to TPMB biopsy found similar rates in both groups [44] (**Table 3**). The discrepancies in retention rates in TPMB is most likely related to how the procedure is performed. When the biopsy index is greater than 1 core/cc of PV (which increases the number of punctures for larger prostates) AUR will increase. Buskirk et al. showed that there was a correlation between gland size and the likelihood of going into AUR following template biopsies [45]. Subjects with a gland size of <50 mL exhibited an AUR rate of 4%, whereas those with a gland size of >50 mL had an AUR rate of

20% (p = 0.039). Our data suggested the threshold for prostate volume to predict AUR is 42 cc (AUR in 2.7 % vs.13.4% for larger glands).

Conclusion

TPMB diagnoses more clinically significant disease than TRUS biopsy. It should be considered the diagnostic approach of choice in men with a negative TRUS biopsy who harbor a clinical suspicion of prostate cancer. UTI are 5.4 times more common in TRUS guided biopsy compared to TPMB. In addition, the risk of infection in 5.8 times greater in men undergoing TRUS guided biopsy when more than 12 cores are taken, which is common with MRI targeted biopsy procedures. Additional prophylactic measures should be considered in men undergoing more than 12 TRUS guided biopsy cores. In the present study TPMB was rarely associated with infection (0.78%) but more commonly with urinary retention (7.9%). Urinary retention was associated with older age and larger prostates. Men older than 65 and with PV greater than 42 cc are at 4-5 times greater risk. Consideration should be given to discharge these men with urinary catheters following the procedure.

Περίληψη

Παγκοσμίως πάνω από 3.4 εκατομμύρια βιοψίες εκτελούνται ανά έτος, με την κλασική καθοδηγούμενη από διορθικό υπέρηχο τεχνική 12 λήψεων να αποτελεί την πιο συχνή μέθοδο βιοψίας των ασθενών που διαγιγνώσκονται για πρώτη φορά με καρκίνο στον προστάτη. Αντιθέτως, η διαπερινεϊκή βιοψία χαρτογράφησης του αδένα (ΔΒΠ) εφαρμόζεται στη μειονότητα των ασθενών, σε ποσοστό δηλαδή μικρότερο του 5%. Η διορθική μέθοδος όμως έχει χαμηλό ποσοστό επιτυχίας στην ανίχνευση του προστατικού καρκίνου (35% - 48%), με αποτέλεσμα την υποσταδιοποίηση των ασθενών με αρχική διάγνωση της νόσου και ενδεχομένως την εσφαλμένη θεραπεία καθώς οι ασθενείς δεν κατατάσσονται σωστά στο ανάλογο στάδιο επικινδυνότητας. Η ΔΒΠ είναι μία τεχνική που έρχεται να προσφέρει μεγαλύτερη ακρίβεια στην εκτίμηση της ιστολογίας του αδένα, ενώ ταυτόχρονα βελτιώνει την ανίχνευση σε ασθενείς που είχαν υποβληθεί στο παρελθόν σε αρνητική διορθική βιοψία.

Το 32.8% των ασθενών (89/271) έλαβαν μέρος στη μελέτη έχοντας ήδη διαγνωστεί με καρκίνο προστάτη μέσω διορθικής βιοψίας και ο βαθμός Gleason τους ήταν 6 σε ποσοστό 76.1%. Αντιθέτως, το 63.3% (240/379) των ασθενών που διαγνώστηκαν με καρκίνο προστάτη από τη ΔΒΠ είχαν κατά μέσο όρο 5 θετικά δείγματα (1-37) και ο βαθμός Gleason τους ήταν 6 σε 114 (47.5%), 7 σε 102 (42.5%) και 8-10 σε 24 (10%) ασθενείς. Από τους 182 ασθενείς με αρνητική προηγηθείσα διορθική βιοψία, οι 121 (66.5%) είχαν θετική ΔΒΠ και 62 (51.2%) εξ αυτών με βαθμό Gleason > 7. Οι 11/271 (4.1%) εμφάνισαν λοίμωξη της ουροφόρου οδού μετά από διορθική βιοψία, σε αντίθεση με 3/379 (0.79%) μετά από ΔΒΠ. Επίσχεση ούρων δεν εμφάνισε κανένας ασθενής που υποβλήθηκε σε διορθική βιοψία ενώ 30/379 (7.9%) ασθενείς εμφάνισαν επίσχεση μετά από ΔΒΠ. Η ΔΒΠ διπλασιάζει τη διάγνωση του καρκίνου του προστάτη σε σχέση με τη διορθική και ανιχνεύει καρκίνο προστάτη στα 2/3 των ασθενών που στο παρελθόν είχαν υποβληθεί σε αρνητική διορθική βιοψία.

Λέξεις ευρετηριασμού

Καρκίνος Προστάτη, Βιοψία προστάτη με διορθικό υπέρηχο, Διαπερινεϊκή βιοψία χαρτογράφησης, Αποτελέσματα βιοψίας προστάτη, Επιπλοκές βιοψίας προστάτη

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REVIEW

Retrograde Intrarenal Surgery: Scopes, lasers and disposables (part 2)

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Abstract

Flexible instrumentation is the mainstay of minimal invasive stone surgery and this led to the invention of smaller and safer instruments which performed remarkable good to a variety of procedures. Further developments like digital technology and single use ureteroscopes which along with similar technological advances in lasers and disposables transformed flexible surgery in a tool of paramount importance in the intrarenal surgery of various clinical entities. This is the second part of our review of the literature concerning the advances in the field of disposables for retrograde intrarenal surgery.

Key words
flexible, ureteroscope, intrarenal surgery, lasers

Laser fibers

Laser fiber is one of the essential components for the success of stone surgery. Most of commercially available fibers have significant performance differences with no single fibre considered as ideal for every situation[1,2]. Generally speaking, surgeons prefer smaller diameter fibers for performing retrograde intrarenal surgery and this fact gives a considerable advantage to the thulium laser that require smaller fibers to operate[3]. Currently many different manufacturers, produce a wide variety of fibers, each one with its unique characteristics. One of these characteristics, is the tip of the fiber and especially the ball shaped tip, which theoretically provide an advantage due to its reduced insertion force to a completely deflected ureteroscope with minimal or no damage[4]. Unfortunately, these fibers are limited by their cost and especially by their

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Table 3 *Holmium YAG: laser vs Thulium fibre laser*

Characteristics	Holmium YAG laser	Thulium fibre laser
Wavelength	2100	1940
Peak power	NA	500W
Pulse Rate	Up to 80 Hz	Up to 2000 Hz
Fibre	Silica	Silica
Fibre diameter	>200μm	>150μm
Energy	0.2-6 J	0.2-6 J
Weight	245kg	35kg

NA: Not available

quick deterioration with no significant ablation difference when compared to the standard fibers[4-7]. All fibers, are subject to damage due to contact with the hard surface of stones, burning of the tip, and bending of the scope irrelevant to their type. The abovementioned damage depends to laser characteristics (high energy, short pulse length etc.)[8-9]. As for the common practice of stripping the tip of the fiber in order to increase stone fragmentation efficiency of laser lithotripsy, recent data are quite revealing: coated fibers outperform stripped ones in terms of safety and efficiency[10-12].

Laser technology is progressing, and so laser delivery system technology must follow. There are many novel fibre-optic delivery systems that are developed or currently under development in order to meet the needs especially for the new emerging market of fibre lasers **(Table 3)**. In one type of fiber, the goal was to reduce as much as possible the disintegration of the tip that is one major drawback of the fibre laser. The idea was to produce a reverse tapered tip which is far more robust and provides a safer approach in terms of disintegration and burn out of it during an operation[13]. A different type of fiber, the miniaturized spherical tip fiber, enables a minimum insertion damage and in the same time can theoretically increase the distance that the laser beam requires for an effective lithotripsy[14]. Finally, many other designs, some of the them still experimental, focusing on the same goals, are currently being developed such as muzzle brake tip fiber, detachable tips etc[15, 16]. Each one holds its distinct characteristics that may help intracorporeal lithotripsy evolve in a very exciting future.

Ureteral Access Sheaths

With the development of flexible ureteroscopes and the emerging capabilities of retrograde intrarenal surgery, many issues arise, issues that required a solution: easy reintroducing of the scope, continuous irrigation, intrarenal pressure, risk of trauma to the surround tissues etc. A new disposable should be developed in order to deal effectively with all these difficulties. This novel device was first introduced by Takayasu and Aso as a "guide tube"[17] and has since then evolved to today's popular ureteral access sheath (UAS). Many of its distinct characteristics provide benefits that ultimately aid in the success of a retrograde intrarenal surgery. One of these, and possibly the most well studied, is the size. UAS come in various diameters and it is presented as two numbers the first representing the inner and the second the outer diameter. The first one varies from 9.5-14 F whereas the second from 11.5 to 18F. The selection of the appropriate diameter will be acquired taking into account patients characteristics as well as the size of the available ureteroscope since a few of them can fit in the smallest UAS currently available. The same applies also to the length of the instrument. A recent study reported the 12/14 Fr to be the more frequently used UAS both for fitting the available scopes and reducing ureteral injuries[18]. The available UAS are presented in **Table 4**. The second most important aspect of UAS use is the facilitation of smooth passage. This mainly depends except from surgeon's capabilities, on the coating of the UAS and the distinct shape of it. There are several improvements that different manufacturers implement in their products like adding new materials and coils that theoretically can reduce kinking during introducing of the sheath. Nevertheless, the direct compare between these products in the literature yields only contradictory results. In an in vitro study, no difference between the selected UAS was found in terms of friction force whereas kinking force was found to be significantly lower with the BARD and significantly higher with the Olympus UAS[19]. On the other hand a systematic evaluation of several UAS reported a better resistance in

Table 4 *Commercially available ureteral access sheaths*

	Name	Inner Diameter	Outer Diameter	Length
Applied Medical	Forte	12-16	16-18	20-28-35-45-55
Bard	Proxis	10-12	12-14	25-35-45
Boston Scientific	Navigator and Navigator HD	11-13	13-15	28-36-46
Coloplast	Retrace	10-12	12-14	35-45
Cook	Flexor, Flexor Parallelm Flexor dual lumen	9.5-14	11.5-16	13-20-28-35-45-55
Olympus	UroPass	10-13	12-15	24-38-46-54
Rocamed	Bi-Flex and BI- Flex Evo	10-12	12-14	35-45

buckling and kinking for the Cook Flexor and better resistance in kinking for the Applied Forte XE compared to the other UAS tested[20]. When these two were compared in a prospective randomized study, the Flexor sheath was found to be advantageous in terms of ease of placement ($p = 0.001$), ease of instrument passage ($p = 0.001$) and ease of stone extraction ($p = 0.023$)[21]. In addition, when Cook Flexor and Boston Navigator HD were compared for the ureteral damage they can potentially result, no statistically significant differences were reported by the authors[22].

As always, the use of an instrument, like UAS, has its own advantages and disadvantages. The practical advantages of the UAS, that have already been stressed before, are well documented in the literature[23]. The drawbacks though remain significant and must be pointed out. The first and major debate about UAS use is ureteral wall injury risk[24] and stricture formation that this injury may result. There are controversial data published in the literature concerning this important issue. A recent prospective study reports a 45.6% ureteral wall injury rate after insertion of UAS with a 13.3% of severe injury involving smooth muscle layers[25]. On the other hand, prospective data from all over the world (from CROES database), implementing more than 2200 patients, comparing UAS use vs no UAS use, found no difference in terms of bleeding and infection complications but also they didn't found any favorable outcomes in terms of stone free rates[26]. In the latter conclusion, about SFR, seems to agree most of the body of the literature[27,28] but the same for the former conclusion about stricture formation[29].

Other devices

The disposable that possibly remains one of the most necessary equipment in RIRS is the guidewire. They provide access to different parts of the urinary tract whereas they serve as a guide to pass several other equipment (stents, sheaths etc). Their diameter ranges from 0.018 to 0.038 inch and 145 to 280 cm respectively[30]. Their composition consists of an inner core and an outer covering which can facilitate an easy passage through urinary system structures. They type of the coating (PTFE or hydrophilic polymer) can be different for the tip and the body, differences that can by used according to the step of the procedure. Stiff wires are commonly utilized as guides for sheaths and catheters whereas hydrophilic polymer coated wires are excellent for maneuvering inside difficult urinary anatomy spots. In our point of view there is no ideal wire for all steps of retrograde intrarenal surgery. Nevertheless, the authors of a relatively recent study, compared in term of baseline characteristics 5 of the most commonly available wires. They found Amplatz SuperStiff wire has the stiffer shaft when compared to Sensor and U-Nite, whereas Boston Scientific wires had the lesser stiff tips compared to the Bard Guidewires[31]. Another most recent study, has evaluated the safety profile of the available hybrid guidewires. The comparison was between Sensor™ (Boston Scientific), Solo™ Plus (Bard), UltraTrack (Olympus), Rio Tracer™ (Rocamed), and Motion™ (Cook). Authors conclude that Solo Plus and UltraTrack had the safest profile demonstrating the greatest perforation force[32].

The second category of disposables that have managed to gain their position in contemporary RIRS is retrieval devices. Baskets are composed of wires of nitinol or still and are commonly used for stone retrieval and displacement and most recently for tumor biopsy. Their size ranges from 1.3 to 3.2 F. Nitinol baskets have more probably won the contest due to their flexibility, kinking resistance and tipless design[33]. Some of the unique characteristics of basket technology are extremely useful in everyday clinical practice. Escape

Stone basket (Microvasive/Boston Scientific) transforms from 4 wires to 2 wires, assisting in freeing stones that may have been entrapped during lithotripsy; same goal (releasing entrapped stones) but different mechanism, from the Dimension basket (Bard Urology) turning a specific wheel on the handle[34]. Comparing tipless and helical baskets in an in vitro ureteral model, revealed no statistical significant difference between the two groups whereas the Cook N- CIrcle was the most efficient from the ones tested[35]. Except baskets, another useful tool for stone extraction is graspers. There have been studies evaluating the efficacy and safety profile between different available graspers[36] but in our point of view the most important compare is between baskets and graspers. The latter was the objective of a ex vivo study utilizing different baskets and graspers in different models. Two prong graspers was the most efficient for stone removal in the single ureteral model, impacted stones were cleared faster with the graspers, steinstrasse was managed more efficiently with the helical basket and finally the parachute basket and the three prong grasper demonstrated the highest risk of mucosal damage. The results suggest that there is no ideal instrument for every case[37].

Other instruments that are not usually in the first list of an endourology surgeon, but it could potentially influence the outcomes of the procedures are endoscopic valves and irrigation devices and also ureteral dilating balloons. Irrigation devices are categorized as passive (pressure bag) and active (pump) depending of the way they deliver fluids[38]. Even though these instruments are under estimated, stone migration and clear field are two basic components for a successful endoscopic operation. A recent study evaluates two irrigation systems: single action pumping system (SAP, Boston Scientific) and Pathfinder Plus (PP, Utah Medical products) and in the same time a comparison was conducted between four different endoscopic valves. The results revealed that each device has its advantages and their use must be adjusted to surgeon´s preferences and according to each surgery[39]. Finally, despite the fact that balloon dilation of the ureter is a practice relatively controversial, there are data that suggest that it yields low failure rates, low complications rates and especially low ureteral stricture rates and so it can be safely performed in difficult ureters but after careful consideration[40-41].

Conclusions

Recent and continuous innovations and technological advances in the field of instrumentation and auxiliary equipment has improved our capabilities of management of many urological pathologies with only endoscopic manipulation. Minimal invasive surgery of the upper urinary tract is here to stay.

Περίληψη

Τα εύκαμπτα εργαλεία είναι ο βασικός πυλώνας της ελάχιστης επεμβατικής χειρουργικής του νεφρού και αυτό οδήγησε στην εφεύρεση μικρότερων και ασφαλέστερων οργάνων, τα οποία παρουσίασαν αξιοσημείωτα καλά αποτελέσματα σε μια ποικιλία ουρολογικών παθήσεων του νεφρού. Περαιτέρω εξελίξεις στην τεχνολογία των ινών λέιζερ αλλά και των αναλώσιμων, μεταμόρφωσαν την εύκαμπτη ουρητηροσκόπηση σε ένα εργαλείο πρωταρχικής σημασίας στην ενδονεφρική χειρουργική, διαφόρων ουρολογικών νεφρικών παθήσεων. Το παρόν αποτελεί το δεύτερο μέρος της ανασκόπησης της βιβλιογραφίας σχετικά με τις εξελίξεις στον τομέα των ουρητηροσκοπίων και των λέιζερ για την παλίνδρομη ενδονεφρική χειρουργική.

Λέξεις ευρετηριασμού
εύκαμπτο, ουρητηροσκόπιο, ενδονεφρική χειρουργική, λέιζερ

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REVIEW

Usage and Dosage of Fosfomycin for NIH Category II Chronic Bacterial Prostatitis

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Abstract

Chronic bacterial prostatitis (CBP, NIH category II) is a difficult-to-eradicate, recurring, chronic infection of the prostate, often characterized by disabling symptoms, significantly reducing the quality of life of patients. Fluoroquinolones have been for many years first-line agents for treatment of this condition. However, mounting pathogen resistance trends (especially in Mediterranean countries like Greece and Italy) are progressively restricting the usage of fluoroquinolones for treating many Gram-positive or Gram-negative infections in the urological field, and clinicians are increasingly treating bacterial prostatitis by empirically administering agents which have not been adequately tested in the frame of clinical trials.

In recent years, reports on the efficacy of the bactericidal antibiotic fosfomycin on CBP have been published. Most articles published so far are case reports, and only few case series or cohort studies are available. The aim of this article is to review the information published so far concerning the usage and dosage of fosfomycin for treatment of chronic bacterial prostatitis.

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Introduction

Chronic bacterial prostatitis (CBP, NIH category II) is a recurring, difficult-to-eradicate, chronic infection of the prostate, characterized by pain in the pelvic region, irritative and/or obstructive symptoms, sexual dysfunction and a considerable reduction of the quality of life. Recent meta-analysis data suggest that chronic prostatitis may be a risk factor for prostate cancer (1,2). Hence, aggressive therapeutic intervention is warranted to decrease such hazard and to improve the quality of life of sufferers.

Key words
prostate, prostatitis, chronic bcaterial prostatitis, fosfomycin, Fluoroquinolones

Fluoroquinolones have been for many years the mainstay treatment for CBP (3). However, mounting resistance trends -especially in Mediterranean countries like Greece and Italy- are progressively restricting the usage of such agents for treating Gram-positive or Gram-negative infections, both in the prostate and in the upper/lower urinary tract.

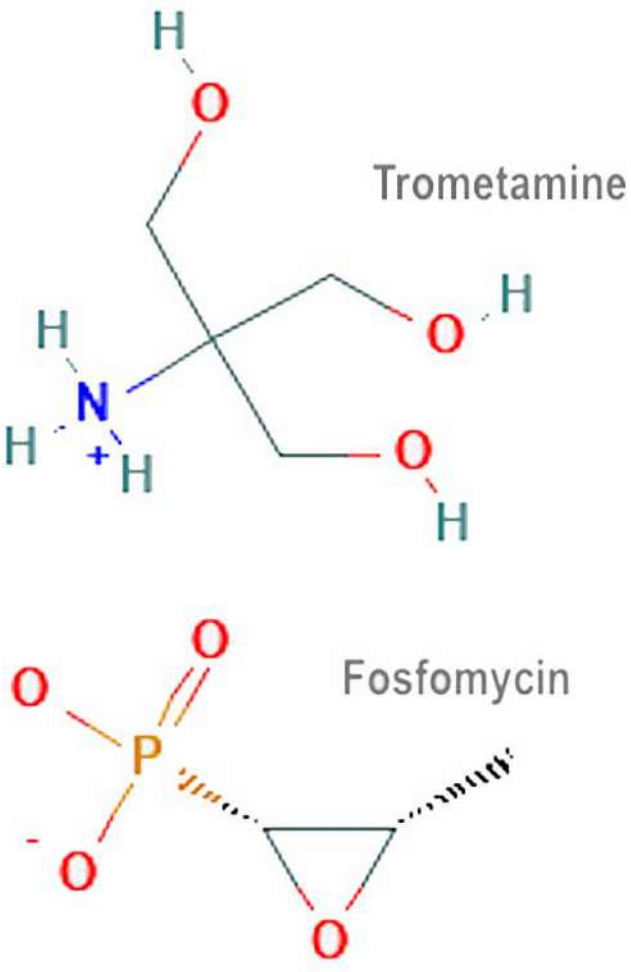
In such a worrisome scenario, clinicians are often compelled to treat CBP patients by empirically administering alternative agents which have not been adequately tested in the frame of clinical trials.

Fosfomycin (**Figure 1**), discovered in 1969, is a bactericidal antibiotic produced by various strains of *Streptomyces*, which acts as an inhibitor of the first step of the synthesis of the bacterial cell wall. Fosfomycin inactivates the enzyme UDP-N-acetylglucosamine enolpyruvyltransferase, involved in the biosynthesis of the peptidoglycan precursor UDP N-acetylmuramic acid (4). Fosfomycin has a broad spectrum of activity against the most common causative agents of CBP, namely *Enterococcus* faecalis (irrespective of vancomycin resistance), *Escherichia coli*, *Proteus mirabilis, Klebsiella pneumoniae* and other enteric bacteria (4). Fosfomycin has a half-life of 5.7 hours, an oral bioavailability of 37% when combined with the proton acceptor tromethamine, a high volume of distribution (2 L/kg), and is excreted unchanged in the urine by 60% (reviewed in: 5). According to preliminary data, an once-daily 3-gram dose of fosfomycin achieves plasma concentrations of about 6 μg/mL, and a 6-gram daily dose achieves plasma levels of ~12 μg/mL or higher) (6).

Little is known about the distribution of fosfomycin to different prostatic tissue components (e.g., ducts, interstitial spaces, etc.). It has been reported that a 3-gram dose of fosfomycin can achieve a prostate concentration up to 6.5 μg/g, and that levels above 4 μg/g are maintained for about 17 hours post-dosing (7). Due to the presence of confounding factors like for example circulating blood within the gland, intracellular drug accumulation etc., the assessment of whole-tissue concentrations is not an optimal strategy for assessing the distribution of a drug in the prostate; future kinetic studies will give a better insight about the concentrations of fosfomycin in prostatic ducts and prostatic fluid.

Pharmacokinetic and pharmacodynamic studies performed in rodent models of CBP demonstrated that fosfomycin is rapidly distributed

Figure 1. *Chemical structure of Fosfomycin-trometamol (source: National Center for Biotechnology Information. PubChem Database. Fosfomycin tromethamine, CID = 54331, 20)*



to the plasma and to the prostate. In the same model, a 7-day or 14-day administration of fosfomycin at the dose of 270 mg/kg slightly but significantly decreased the E. coli burden in rat ventral prostates. Interestingly, a concomitant significant reduction of PSA and of inflammatory Interleukin-6, Interleukin-8 and TNF was shown to occur at the same time points (8).

In recent years, the efficacy of fosfomycin therapy for CBP has been investigated. Most articles published so far are case reports, though few case series and cohort studies have recently appeared. Up to this time the administration of fosfomycin for CBP has been empirical, no official recommendation has been formulated and a variety of dosage protocols have been experimented. In 2018, Zhanel and coworkers reviewed the evidence contained in 4 articles concerning fosfomycin therapy for CBP caused by MDR-*E. coli* (9). However, other data, including one cohort study, have been recently published.

The aim of the present review is to examine the available evidence concerning fosfomycin (alone or in combination with other antibacterial agents), and *to attempt a first evaluation of possible dosing regimens for NIH category II Chronic Bacterial Prostatitis caused by any prostatic pathogen.* A simple PubMed search strategy {(fosfomycin [Title/abstract)] AND (prostatitis [Title/Abstract])} retrieved 29 records. National literature handsearching retrieved one record (congress abstract). Twenty-two records were excluded after full-text screening (17 focusing on prophylaxis related to surgical procedures on the prostate, one letter to the editor lacking clinical data, one review article, one case report describing administration of a single dose of fosfomycin after an ertapenem regimen to resolve a mixed prostatitis/pyelonephritis condition, one report of two acute/sub-acute cases), and 8 articles were finally included in this review.

Cohort studies and case series

1. Demonchy and coworkers recruited prospectively 23 patients showing acute (N = 9) and chronic (n = 14) bacterial prostatitis caused by extended-spectrum beta-lactamase-producing *Enterobacteriaceae* (10). Patients were treated with intravenous cefoxitin for about 6 weeks (median daily dose: 2-8 g, depending on patients' charatceristics), combined with fosfomycin (12 g/day) during the first 5 days of therapy. Notably, all strains were resistant or intermediate to cefotaxime or cefepime. Pathogen eradication rates were 57% at 3 months and 47% at 6 months, though clinical cure rates were higher (83% at 3 months and 77% at 6 months). Unfortunately, these data refer to the whole patient population, including acute and chronic cases. However, the authors state that there was no difference in clinical cure rates between acute and chronic cases. However, a similar statement was not made with respect to bacteriological eradication.

2. Los-arcos et al. report a series of fifteen cases of CBP, treated with single-agent oral fosfomycin. Fluoroquinolones were contra-indicated for various reasons, including previous therapy failure, adverse effects or drug resistance (11). The causative agents were *E. coli* in 14 cases (including 4 ESBL producers and 1 AmpC producer) and *Klebsiella oxytoca* in one case. Patients received fosfomycin trometamole at the dose of 3 grams "every 48 to 72 hours" for 6 weeks. The follow-up period was extended up to one year. Microbiological eradication, defined as negative cultures assessed at 1 month and 6 months after the completion of treatment (11), was recorded in 9/15 (60%) and 8/15 (53%) cases, respectively. The authors of this retrospective study suggest that the partial success of fosfomycin therapy can be explained by the fact that some isolates could have had MICs above 4 mg/L, and that fosfomycin shows optimal bactericidal activity at acidic pH, whereas most causative pathogens of CBP are known to generate an alkaline milieu.

3. The Hellenic members of our research group performed a retrospective analysis of 12 cases affected by CBP caused by MDR Gram-negative pathogens, showing failure of conventional treatment mainly due to fluoroquinolone resistance. Fosfomycin was administered orally at a dose of 3 g/day for up to 15 days. Ten days after termination of treatment the patients were subjected to the Meares-Stamey test and/or to sperm culture, and microbiological eradication was assessed in 6/12 patients (50%) (12).

4. Recently, Karaiskos and coworkers published the results of a well-designed prospective noncomparative study including 44 cases of CBP whose causative pathogens were resistant to commonly administered antibacterial agents (33/44 to fluoroquinolones, 24/37 to co-trimoxazole, 26/44 MDR phenotype, 10/44 ESBL-positive)(13). Interestingly, in this study fosfomycin was tested against a broad spectrum of pathogens, including various *Enterobacteriaceae* (*E. coli, Klebsiella, Proteus mirabilis*), *Pseudomonas aeruginosa* and *Enterococcus faecalis.*

The history of each patient was well documented,

and the MICs for fosfomycin were calculated. The authors divided patients in two main dosage groups, depending on the presence of frank prostatic calcifications, which are reputed to be sanctuaries of sessile pathogens. Patients with evidence of calcifications (n = 19) were treated for 12 weeks, whereas in patients without sign of calcifications the therapy course was shorter (6 weeks, n=25). After a first week of treatment with 3 grams once-daily oral fosfomycin, patients were switched to a dosage of 3 grams every 48 hours, likely to avoid the worsening of gastrointestinal disturbances. Alfa-adrenoceptor blockers were co-administered in 18 cases showing obstructive symptoms.

Microbiological eradication was achieved in 38/44 (86%) patients at the end of therapy and in 34/44 patients (77%) at the 6-month follow-up time point. Clinical cure (disappearance of all symptoms) was assessed in 37/44 (84%) patients at the end of therapy and in 35/44 cases (80%) after 6 months. The most common adverse effect was diarrhea (8/44 patients, 18%), which was attenuated by increasing the dosing intervals to 72 hours, without affecting the cure rates of infection.

In their article, the authors provide a diagnostic-therapeutic algorithm for CBP, including the fosfomycin treatment option, together with fluoroquinolones and co-trimoxazole (13).

Case reports

1A. 53-year old patient presented with repeated flare-ups of CBP. The Gram-negative *Raultella planticola* (*Enterobacteriaceae*) was repeatedly isolated and prostate calcifications (PCAL) were documented (14). Since the patient was allergic to fluoroquinolones, oral *fosflmycin* (3g q48h) was administered for 3 months. By month 2, dysurya resolved and the patient remained symptom-free for an off-therapy follow-up period of 3 months. Repeated cultures also remained negative (14).

2. Metallo-beta-lactamase-expressing *Pseudomonas aeruginosa* (bla_{VIM-2}) was isolated from a HIV-positive 46-year old patient, previously hospitalized in Saudi Arabia for an abdominal abscess (15). The pathogen was multi-drug resistant (fluoroquinolones, beta-lactams, aminoglycosides and others), and a combination of aztreonam (6g/day) and fosfomycin (12g/day) was administered for 21 days. The pathogen was eradicated and subsequent cultures remained negative. Importantly, fosfomycin and aztreonam were found to exert a synergistic effect on *P. aeruginosa* (15).

3.A. 53-year old patient, allergic to beta-lactams, was referred for chronic prostatitis caused by extended-spectrum beta-lactamase (ESBL)-expressing *E. coli*, resistant to doxycycline and quinolones, but susceptible to ampicillin/sulbactam, carbapenems, aminoglycosides and nitrofuratoin (5). Nitrofurantoin (100 mg, twice-daily for a month) failed to eradicate the pathogen, possibly due to poor prostate penetration. A first course of low-dose fosfomycin (3 g q72h for 1 month) failed to permanently eradicate the pathogen. The fosfomycin dose was increased (6 g q72h for 1 month), but therapy failed too. The patient underwent TURP for his BPH, with the secondary intent of removing most of his prostate calcifications. After surgery, his *E. coli* CBP relapsed, and he was treated with oral fosfomycin (3 g q72h) plus doxycycline (100 mg twice-daily). According to the study report, after 2 weeks, "urine cultures became negative, and he has since remained free of infection" (5).

4. A similar case was reported by Almeida and coworkers (16). A 51-year old man presented with numerous episodes of ESBL-*E. coli* prostatitis and UTIs, repeatedly relapsing due to failure of a large variety of therapy regimens (ciprofloxacin, 500 mg/day for 2 weeks, prulifloxacin, 600 mg/day for 3 weeks, intravenous ertapenem, 1 g/day for 25, 69 and 85 days [sic], ciprofloxacin 500 mg/day for 2 weeks, cefixime, 400 mg/day for 2 weeks, co-trimoxazole, dose unknown, for 2 weeks). The patient underwent TURP for his BPH and in the attempt to remove prostate calcifications, which were believed to be the sanctuary for the causative pathogen. Following TURP surgery the patient remained symptomatic, but a pathogen was not isolated. Subsequently, a one-year regimen of fosfomycin was designed as follows: 3 g/day for 15 days, followed by 3 g q48h for 3 months, followed by 3 g/week for 9 months. After 10 days the patient developed diarrhea, and a switch to the lower dosing level (3 g q48h) was anticipated. No recurrence was reported up to 9 months off-therapy (16).

Conclusions

Table 1 summarizes the main clinical data contained in the 8 articles included in this review.

Safety

Diarrhea and other gastrointestinal disturbances were the most common side effects reported by several authors who administered long-term fosfomycin therapy for CBP. In summary:

Table 1 *Synopsis of the CBP case reports, case series and cohort studies reviewed in this paper*

Number of patients (age)	Pathogen(s) detected	Previous therapy	Therapy rationale	Fosfomycin (FOS) therapy	Eradication (Yes/No, or %) at end of therapy	Follow-up data/ relapse	Adverse effect(s), remediation	Additional remarks	Reference
1 (53)	Raoultella planticol	Various antibacterial agents	Anaphylaxis to ciprofloxacin	FOS, 3 g q48h for 3 months	Yes	Symptom-free at 3 months	Not specified	Dysuria resolved by month 2	Gian and Cunha [14]
1 (46)	P. aeruginosa (bla_{VIM-2})	Not specified	Resistance to beta-lactams, fluoroquinolones, aminoglycosides	FOS (12 g/day) plus aztreonam (6 g/day) for 21 days (synergic combination)	Yes	"all subsequent cultures were sterile"	Not specified	Likely a catheter-caused nosocomial infection; HIV-positive patient	Guerin et al. [15]
1 (53)	ESBL-E. coli	FOS 3 g q72h, followed by FOS 6 g q 72h	Resistance to fluoroquinolones	FOS (3 g q72h) plus doxycyclne (100+100 mg/day) and microbiological assessment after 2 weeks	Yes	"has since remained free of infection"	Not specified	Subjected to TURP to remove BPH and calcifications	Cunha et al. [5]
1 (51)	ESBL-E. coli	Various regimens (prulifloxacin, intravenous ertapenem, ciprofloxacin, cefixime, co-trimoxazole)	Fluoroquinolone therapy ineffective	FOS, 3 g/day for 15 days, switched to 3 g q48h for 3 months, switched to 3 g/ week for 9 months	Yes	No recurrence for at least 9 months off-therapy	At day 10 diarrhea, dosing interval increased to 3 g q48h	Subjected to TURP to remove BPH and calcifications	Almeida et al. [16]
23 (median: 74)	Beta-lactamase-producing Enterobacteriaceae (E. coli, n=11; K. pneumoniae, n = 10; K. oxytoca, n = 2)	Not specified	Resistance to fluoroquinolones and co-trimoxazole	Intravenous cefoxitin, 2-8 g/day according to weight and kidney function for 3 weeks (acute cases) or 6 weeks (chronic cases), plus FOS, intravenous (12 g/day: 4g q8h, 4-h infusion), only during "the first 5 days of therapy	Assessed during follow-up	Eradication: 57% at 3 months and 47% at 6 months	No adverse effects reported during the entire study	//	Demonchy et al. [10]
15 (median: 54)	E. coli n=14 (including 4 ESBL producers and 1 AmpC producer); Klebsiella oxytoca (n = 1)	Not specified	Failure of long-term conventional therapy, fluoroquinolones and co-trimoxazole contra-indicated due to resistance, failure or side effects.	FOS, 3 grams "every 48 to 72 hours" for 6 weeks	9/15 (60%)	8/15 (53%) at 6 months	"there were no gastrointestinal side effects or allergic reactions"	One patient received a 7-day course of ertapenem before initiation of fosfomycin therapy	Los Arcos et al. [11]
12	MDR Gram-negative pathogens	Fluoroquinolones	failure of conventional treatment mainly due to fluoroquinolone resistance	FOS (3 g/day) for up to 15 days	6/12 (50%)	Not specified	No adverse effects reported during the entire study	//	Makris et al. [12]
44 (median: 54)	Enterobacteriaceae (E. coli, Klebsiella spp., Proteus mirabilis), Pseudomonas aeruginosa and Enterococcus faecalis.	Various protocols	Resistance to commonly administered antibacterial agents (33/44 to fluoroquinolones, 24/37 to co-trimoxazole, 26/44 MDR phenotype, 10/44 ESBL-positive)	FOS, 3 g/day for 7 days, switched to 3 g q48 hours, for 6 weeks (no calcifications, n = 25) or 12 weeks (presence of calcifications, n = 19)	38/44 (86%)	34/44 (77%) at 6 months	diarrhea (8/44 patients, 18%), dosing interval increased to 72 hours	Alfa-adrenergic blockers co-administered in 18/44 pts (41%); 100% eradication in patients switched to 3g q72h to control diarrhea.	Karaiskos et al. [13]

- Protocols starting with administration of 3 grams fosfomycin every 48 hours do not seem to evoke diarrhea (5, 11, 14).
- Daily administration of doses of 3 grams (31,16) or 6 grams (reported in two acute cases, 6) fosfomycin may cause diarrhea after 5-10 days of therapy. Notably, diarrheal pathogens were never isolated in these cases. When dosing intervals are increased (from q24h to q48/72h), diarrhea may subside (13, 16).

Efficacy

- The Karaiskos study reports high eradication rates of causative pathogens at the end of therapy and at follow-up (86%-77%, respectively)(13). Eradication rates ascertained in the frame of case series are lower, but may be strongly selection-biased (Makris et al., 50%; Demonchy et al., 57%-47%; Los-arcos et al., 60-53%) (10, 11, 12).
- A MIC of 4 ug/ml has been indicated by Los-Arcos et al. as maximum susceptibility threshold for initiating fosfomycin therapy (11).
- Fosfomycin as single agent has been administered for the duration of 6 or 12 weeks in several studies (11, 13, 14, 16). In cases not complicated by the presence of calcifications, a 6-week protocol seems to be sufficient to eradicate most causative pathogens. Notably, in the presence of prostatic calcifications, therapy may be extended up to 12 weeks (3 g q 48h), as suggested by the Karaiskos group (13).
- Transurethral resection of the prostate (TURP) was probably beneficial for the resolution of CBP in two difficult cases, which were complicated by prostate calcifications. Possibly, reduction of the calcified areas of the gland may have decreased the biofilm load in those patients, thus facilitating the fosfomycin-induced eradication of residual pathogens (5, 16).
- We do not find once-weekly administration of fosfomycin for several months (16) a recommendable option, especially because very-low-dose strategies are more prone to evoke pathogen resistance.
- Combination with aztreonam was shown to be synergic against *P. aeruginosa* prostatitis as shown in the Guerin et al. case report (15). Several studies have demonstrated that fosfomycin-fluoroquinolone combinations show synergistic bactericidal activity against established biofilms of *P. aeruginosa*, even when concentrations at which each drug independently produced no detectable decrease of sessile cells (17,18,19). Since CBP is generally reputed to be a biofilm disease, clinical studies are urgently required to confirm the efficacy of such combination in CBP patients.

In summary, we believe that a "switch protocol" similar to the one suggested by Karaiskos et al. (3 g/day for 7-10 days, switched to 3 g q48h for 6 weeks)(13) can address at the same time (i) the need for a "full-dosage hit", at least at the start of treatment, and (ii) the necessity to prevent/control diarrhea for the subsequent weeks of therapy. Based on their evaluation of 4 reports focusing on MDR-*E. coli*, Zhanel and coworkers also seem to recommend this specific dosage (9).

In conclusion, in an era of mounting fluoroquinolone resistance and in the absence of newly developed antibacterial agents targeting Gram-negative enteric pathogens, fosfomycin may become an interesting, last-resource option for treatment of CBP. Hopefully, the high eradication rates reported by the Karaiskos group (13) will be confirmed in the next future by other groups in the frame of comparative prospective studies.

Today, the armamentarium in the hands of urologists for treatment of urinary tract and genital infections is very limited. Strict limitation of antibiotic usage, education of patients to therapy compliance and severe antibiotic stewardship measures are urgently warranted, especially in Mediterranean countries, to prevent chronic prostatic infections from becoming virtually untreatable.

Περίληψη

Η χρόνια βακτηριακή προστατίτιδα (κατηγορία II, CBP/NIH) είναι μια συχνά υποτροπιάζουσα και ενίοτε δύσκολα εξαλειφόμενη χρόνια λοίμωξη του προστάτη, που χαρακτηρίζεται από επίμονα συμπτώματα τα οποία μειώνουν σημαντικά την ποιότητα ζωής των ασθενών. Οι φθοριοκινολόνες έχουν από πολλά χρόνια καθιερωθεί ως παράγοντες πρώτης γραμμής για τη θεραπεία αυτής της κατάστασης, ωστόσο, οι τάσεις αντοχής των κυριότερων παθογόνων (ιδίως στις Μεσογειακές χώρες όπως η Ελλάδα και η Ιταλία) βαίνουν προοδευτικά αυξανόμενες περιορίζοντας τη χρήση των φθοριοκινολονών στη θεραπεία λοιμώξεων από ορισμένα Gram-θετικά και Gram-αρνητικά βακτήρια. Επιπλέον οι κλινικοί γιατροί θεραπεύουν όλο και περισσότερο την βακτηριακή προστατίτιδα με την εμπειρική χορήγηση παραγόντων που δεν έχουν δοκιμαστεί επαρκώς στο πλαίσιο κλινικών δοκιμών. Τα τελευταία χρόνια έχουν δημοσιευθεί αναφορές σχετικά με την αποτελεσματικότητα του βακτηριοκτόνου αντιβιοτικού φωσφομυκίνης στην χρόνια βακτηριακή προστατίτιδα. Τα περισσότερα άρθρα που έχουν δημοσιευτεί μέχρι στιγμής αφορούν κυρίως αναφορές περιπτώσεων και υπάρχουν μόνο λίγες μελέτες κοόρτης. Ο σκοπός αυτού του άρθρου είναι να επανεξετάσει τις πληροφορίες που δημοσιεύθηκαν μέχρι τώρα σχετικά με τη χρήση και τη δοσολογία της φωσφομυκίνης για τη θεραπεία της χρόνιας βακτηριακής προστατίτιδας.

Λέξεις ευρετηριασμού

προστάτης, προστατίτιδα, χρόνια βακτηριακή προστατίτιδα, φωσφομυκίνη, φθοροκινολόνες

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CASE REPORT

Potassium Para-aminobenzoate (Potaba) induced DRESS syndrome. A case report

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Abstract

Potassium Para-aminobenzoate (Potaba) is an antifibrotic agent indicated for use in the treatment of early stage Peyronie's disease. It exerts a protective effect by stabilizing the curvature, reducing the plaque size and improving pain perception. It is considered relatively safe with no significant side effects reported other than gastrointestinal irritation. In this paper, we report a case of DRESS syndrome associated with Potaba administration. Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a drug related allergic reaction with systemic manifestations and a significant mortality rate of up to 10%. It is a delayed type IVb hypersensitivity reaction characterised by fever, skin rash, lymphadenopathy, haematological abnormalities and multiple internal organ involvement such as the heart, kidneys, liver, pancreas and lungs. To the best of our knowledge, this is the second case of Potaba induced DRESS syndrome. The patient was managed conservatively and had fully recovered within 9 weeks after the discontinuation of the causative drug. Timely diagnosis of the condition is of paramount importance to avoid multiple organ damage since there is no disease specific treatment so far and supportive therapy with discontinuation of the triggering agent is the indicated response.

Introduction

Peyronie's disease (PD) is a connective tissue disorder of unknown aetiology characterized by the formation of a fibrotic lesion or plaque in the tunica albuginea, which leads to penile deformity and subsequently erectile dysfunction. It runs in a two phase fashion beginning as an initial acute inflammatory process with pain being the predominant symptom and continues with the calcifying or fibrotic

Key words
DRESS, Potaba

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phase which results in the formation of a hard plaque and culminates to disease stabilization. Patients in the early stage usually present with pain at the erect and flaccid state, a palpable nodule or plaque and a curvature during erection. At this stage conservative treatment is indicated and Potassium Para-aminobenzoate (Potaba) is an option that may result in a reduction in penile plaque size, mitigation of penile pain and penile curvature stabilization. Although no serious adverse events have been related to this specific treatment (mainly nausea, anorexia, pruritus, anxiety, confusion), one case report links Potaba to DRESS syndrome. Herein, we present an additional case of a 45-year old man with PD who developed DRESS syndrome six weeks after onset of Potaba treatment.

Case presentation

A 45 year old male presented to the andrology outpatient clinic reporting a 9 month history of penile deformity affecting his sexual life. His past medical history was unremarkable. He was not on any medication and did not report any allergies. He was also a avid runner, exercising 4-5 times a week and was otherwise fit and well. He was happy with his sexual life prior to the onset of the curvature and despite his developing condition he could still achieve and maintain a normal, although painful, erection.

Physical examination revealed a hard palpable nodule on the dorsum of the shaft below the coronal sulcus. During erection the distal penis was deflected dorsally, assuming a 45-degree angle as seen on a photo taken by himself (**image 1**). His disease appeared to be of early stage with fluctuating shaft angulation, painful erection and no calcifications. Once the diagnosis of Peyronie's disease was established he was commenced on Potaba 9 gr daily and penile vacuum pump stretching daily.

Six weeks after the initiation of the treatment he developed fever and a generalized, itching, morbilliform rash which gradually went diffuse covering his trunk and upper extremities (**image 2**).

The patient attended the emergency department and physical examination revealed a diffuse erythema covering the trunk, upper and lower extremities equaling to more than 50% of his BSA. He also had cervical lymphadenopathy and symptoms of jaundice.His laboratory tests were significant for peripheral eosinophilia and liver damage (more than 10fold increase of his LFTs) as seen in **Table 1**.

Image 1. *Presentation of penile deformity at diagnosis*

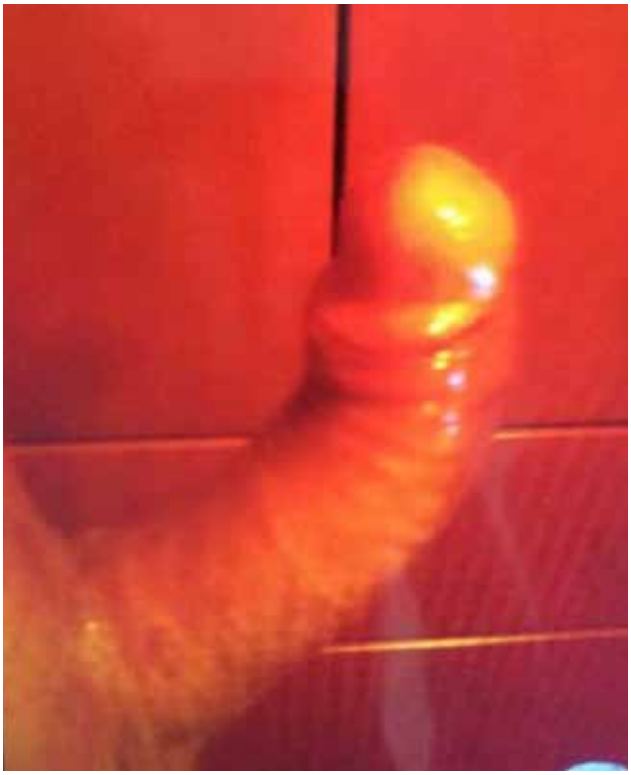

Image 2. *Skin rash*

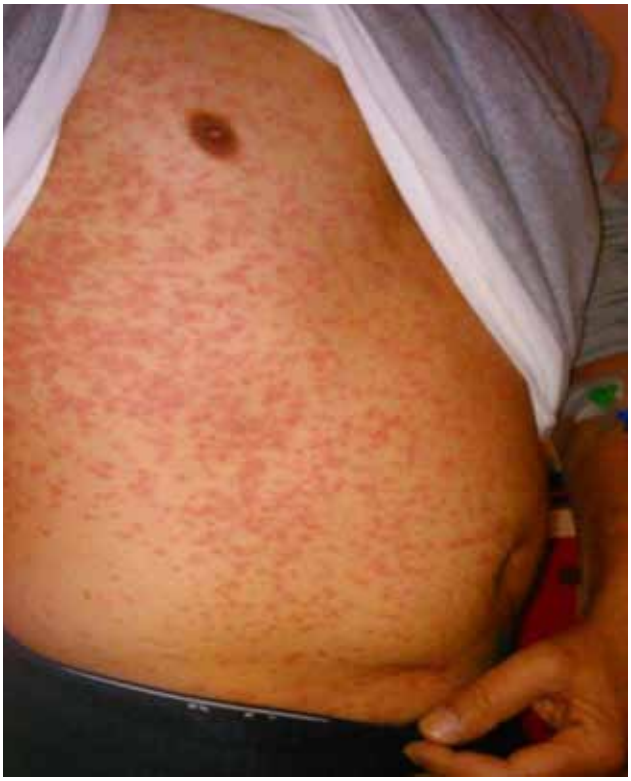

Table 1 Laboratory Tests at presentation

WBC	11.500 K/μl	4.0-11.0
EOS	24%	0.0-7.0
SGOT	17.0 U/L	5.0-34.0
SGPT	1339.0 U/L	0.0-55.0
γ-GT	241.0 U/L	12.0-64.0
LDH	594 U/L	125-220
TBIL	11.5 mg/dL	0.2-1.2
BIL	8.9 mg/dL	0.0-0.5
Ferritin	810.7 ng/mL	25.0-377.0
CRP	3.6 mg/dL	< 0.5

Table 2 Registry of severe cutaneous adverse reaction criteria for diagnosis of drug rash and eosinophilia with systemic symptoms

1. Hospitalization*
2. Reaction suspected to be drug-related*
3. vAcute rash*
4. Fever > 38°C +
5. Enlarged lymph nodes at a minimum of 2 sites +
6. Involvement of at least 1 internal organ +
7. Blood count abnormalities + Lymphocytes above or below normal limits Eosinophilis above the laboratory limits Platelets below the laboratory limits
* Necessary criteria are required for making the diagnosis + Three out of four criteria are required

Serologic screening for Hep A, B, C, CMV and EBV were negative.He underwent a U/S and a CT scan of abdomen with no signs of biliary obstruction. Based on the RegiSCAR criteria (**Table 2**) and taking into consideration the patient's unremarkable medical the diagnosis of drug induced hypersensitivity reaction with visceral involvement was established in the absence of other pathology. In the absence of any other medication his allergic reaction was attributed to Potaba.

The causative drug (POTABA) was immediate discontinued and high dose corticosteroids were administered along with adequate hydration. He responded promptly to the management and his symptoms (pruritus, fever, jaundice) started improving within 5 days on corticosteroids. His LFTs returned to normal levels on day 18 and he was discharged from the hospital on day 20 with scheduled regular follow up visits for physical examination and blood tests. Four weeks after discontinuation of POTABA he had completely recovered.

Discussion

Cutaneous reactions to medication are quite common and in most cases they are of mild to moderate severity. Drug induced reaction with eosinophilia and systemic symptoms (DRESS syndrome) on the contrary, is a life-threatening reaction which can cause multiorgan failure. Clinical findings include eosinophilia, lymphadenopathy in up to 75% of cases, fever and a cutaneous rash that might progress to exfoliating dermatitis. The most commonly affected organ is the liver and permanent liver damage necessitating transplantation has been described [1]. The syndrome has a latency period of up to 6 weeks from the first exposure to the allergen and its incidence ranges from 1 in 1000 to 1 in 10000[2]. The mortality rate is almost 10% and therefore early identification and prompt management is of paramount importance[3].

The pathophysiology of DRESS syndrome is not fully understood but immune responses including T-cell acti-

vation, reactivation of human herpes virus 6 and 7, CMV and EBV are believed to be involved and triggered by certain medications. That is why DRESS syndrome is also referred as a drug induced hypersensitivity syndrome. Another causative factor incriminated is a defect in the detoxification pathway of various medications that leads to accumulation of toxic metabolic intermediates.

Recently, RegiSCAR (Registry of Severe Cutaneous Adverse Reaction group) suggested criteria in an effort to standardize the diagnosis and set an algorithm aiming for timely identification and response. Patients must fulfil three main criteria and three out of four as seen in **Table 2**.

Although DRESS syndrome is a rare entity, many drugs have been associated with it, including carbamazepime, captopril, phenobarbital, vancomycin, phenytoin, allopurinol, sulfonamides and NSAIDs just to mention a few [4]. On the contrary, there is only one other reference in the literature linking potassium para-aminobenzoate (Potaba) to DRESS[5]. Our patient represents the second identified case and he was managed timely accomplishing an uneventful, complete recovery 6 weeks after the initial diagnosis and the discontinuation of the culprit drug. Although the use of steroids in this setting is argued[6, 7], he was successfully treated conservatively with high doses of corticosteroids, antipyretics and hydration. Regarding his PD, it was stabilized after 6 months and he underwent surgical plication one year later.

Conclusion

DRESS syndrome is exceedingly rare in urological practice and can prove to be fatal if not recognized and treated promptly. The reported association to Potaba aims to raise awareness around this medication taking into consideration its nature, since it is administered for long periods of up to 12 months. The urologist needs to be alert for signs of allergies and to be in touch with the patient through regular visits as not to miss any adverse events. Every reported case maters and adds to the growing body of evidence.

Περίληψη

Το Potaba αποτελεί μια από τις θεραπευτικές επιλογές για την αντιμετώπιση του αρχικού σταδίου της νόσου Peyronie. Έχει αποδειχθεί ότι σταθεροποιεί η νόσο και μειώνει τον πόνο που παρατηρείται στο στάδιο αυτό, χωρίς όμως να μεταβάλλει θεαματικά το μέγεθος της πλάκας. Θεωρείται σχετικά ασφαλές σκεύασμα με κύριες παρενέργειες τις γαστρεντερικές διαταραχές. Παρακάτω παρουσιάζουμε την περίπτωση ασθενούς που έλαβε potaba για νόσο peyronie και εμφάνισε μια πολύ σπάνια και δυνητικά θανατηφόρο αλλεργική αντίδραση. Αυτή εκδηλώνεται συστημικα και χαρακτηρίζεται ως σύνδρομο καθώς επηρεάζει πολλαπλά ζωτικά όργανα στο σώμα και μπορεί επιφέρει μόνιμη ανεπάρκεια αυτών, ακόμη και το θάνατο στο 10% των .περιπτώσεων. Είναι γνωστή ως σύνδρομο DRESS (Drug reaction with eosinophilia and systemic symptoms) και ακρογωνιαίος λίθος στην αντιμετώπιση του είναι καταρχάς η έγκαιρη αναγνώριση του και διακοπή του ενόχου φαρμάκου.

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DRESS, Potaba

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Technique

Extended pelvic lymph node dissection during extraperitoneal laparoscopic or robotic assisted radical prostatectomy

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Abstract

Objective: Extraperitoneal access in endoscopic (laparoscopicic or robotic assisted) radical prostatectomy is a standard approach in the management of prostatic cancer with well-established advantages over transperitoneal access. Still, traditionally, extraperitoneal endoscopic radical prostatectomy (EERP) has been associated with an inability to offer an extended pelvic lymph node dissection (PLND). The former is due to the fact that in the extraperitoneal space, peritoneal folding covers the majority of common iliac vessels and as a result in extraperitoneal PLND, lymph nodes (LNs) located above the bifurcation of common iliac vessels cannot be dissected. We herein present a simple and easy technique to offer an extended PLND during EERP.

Methods: After a conventional extraperitoneal PLND, a peritoneal fenestration cranially to extrernal iliac vessels is performed bilaterally exposing the common iliac vessels.

Results: Upon peritoneal fenestration, PLND can be continued in a standard fashion as in transperitoneal approach until the uppermost limit of the extended PLND template which is the ureteral crossing over common iliac vessels. Following LN dissection, both peritoneal fenestrations are left open at both sides, as this approach has been found to decrease the incidence of postoperative lymphocele formation.

Conclusions: Peritoneal fenestration over common iliac vessels during extraperitoneal PLND is an easy approach that allows surgeon to reach the uppermost limit of extended PLND template. The latter peritoneal dissection is not time consuming and is expected to decrease the morbidity of the operation reducing the incidence of postoperative lymphocele formation.

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Introduction

Extraperitoneal access in endoscopic (laparoscopicic or robotic assisted) radical prostatectomy is a standard approach in the management of prostatic cancer with well established advantages over transperitoneal access. Among them faster access to the prostate without the need of peritoneal incision, lack of peritoneal adhesions after a previous operation requiring dissection and lack of intestines protruding into operating field during prostatectomy are the most prominent [1]. Still, extraperitoneal approach has a significant drawback when a concomitant pelvic lymph node dissection (PLND) is required. In extraperitoneal PLND, lymph nodes located above the bifurcation of common iliac vessels cannot be dissected as peritoneal folding in the extraperitoneal space covers the majority of common iliac vesssels (**Figure 1**). As a result, extraperitoneal endoscopic radical prostatectomy (EERP) traditionally has been associated with the inability to offer an extended PLND [1,2]. In this article we document our technique to offer an extended PLND during EERP.

Key words
extraperitoneal; pelvic lymph node dissection; radical prostatectomy; prostate cancer

Step by step approach

Step 1: A modified PLND is performed at both sides including excision of the LNs located medially to the external iliac artery, laterally and caudally to the internal iliac artery including the obturator fossa. At this point, extraperitoneal PLND has no access to lymph nodes located above the bifurcation of common iliac vessels due to the peritoneal folding (**Figure 1**). As a result an extended extraperitoneal PLND cannot be performed without fenestration of the peritoneum.

Step 2: Using a 30 degree endoscope a peritoneal fenestration cranially to extrernal iliac vessels is performed exposing the common iliac vessels (**Figure 2**). Care should be taken to recognize and dissect potential

Figure 1. *Extraperitoneal view of peritoneal folding overlapping common iliac vessels*

Figure 2. *Fenestration of the peritoneum in the right and left side above the bifurcation of common iliac vessels*

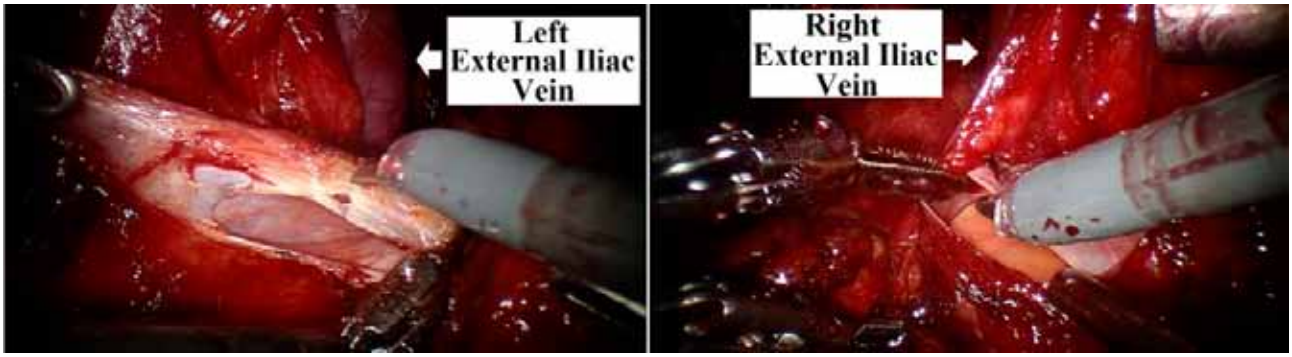


Figure 3. *Intraperitoneal adhesions located near to the site of incision (not the same case with figures1,2,4). Care should be taken to avoid bowel injury during peritoneal opening*

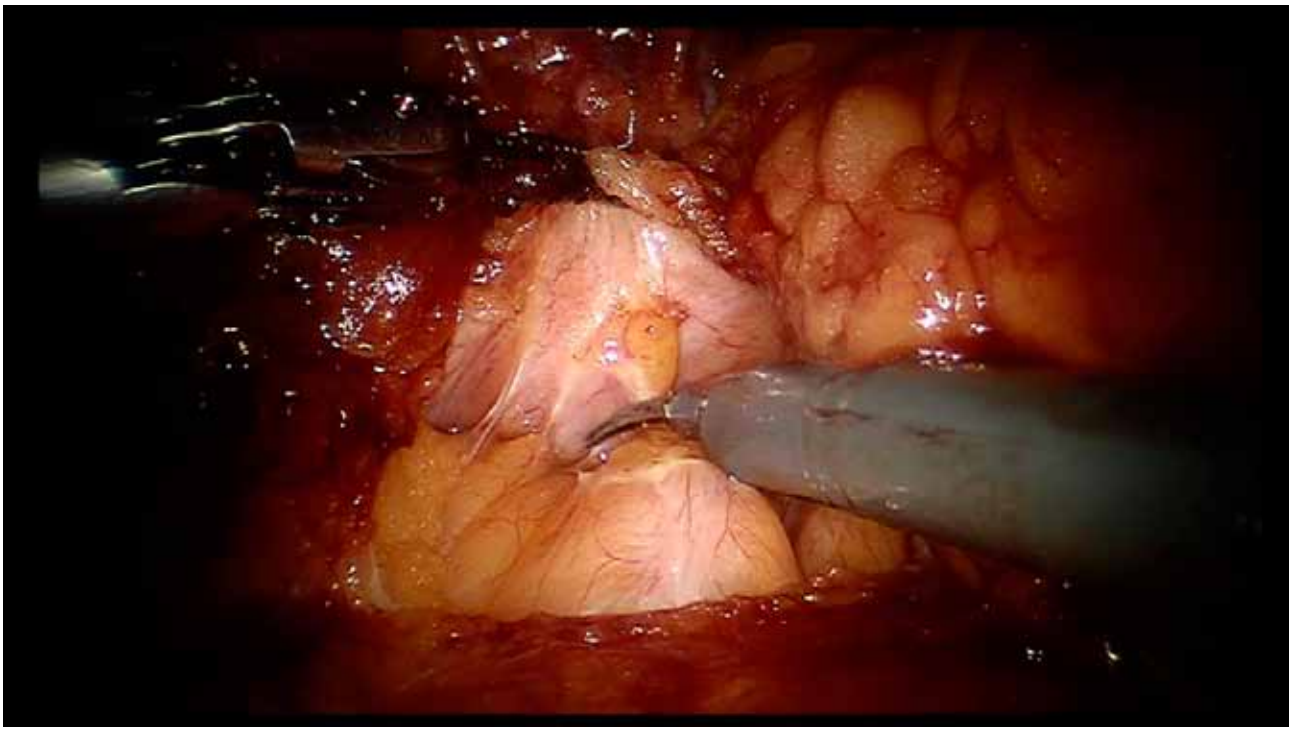
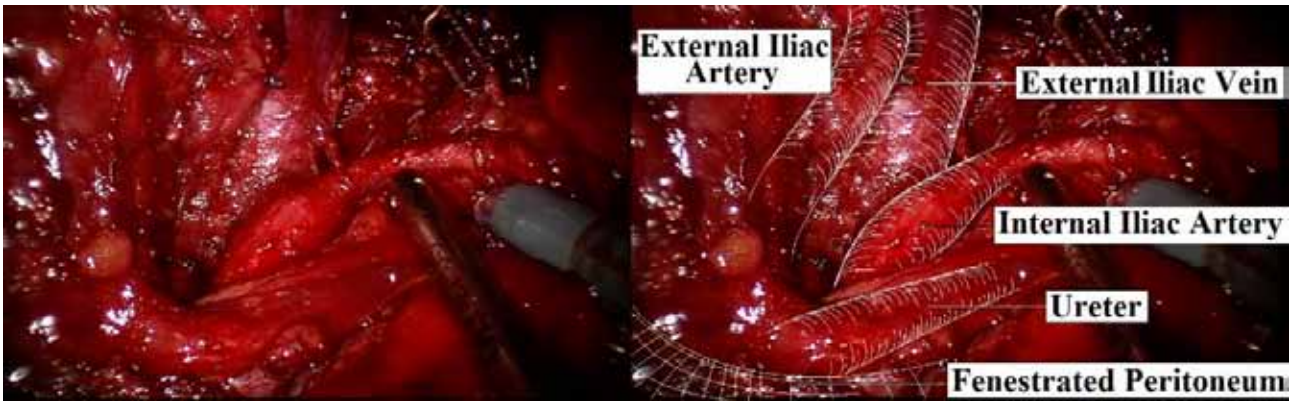


Figure 4. *Upon peritoneal fenestration, an easy access to lymph nodes located up to the crossing of the ureter over common iliac vessels is possible*



intrabdominal adhesions of bowel with the particular peritoneal segment in order to avoid bowel injury (**Figure 3**).

Step 4: PLND can be continued in a standard fashion as in a conventional transperitoneal approach until the uppermost limit of the extended PLND template which is the ureteral crossing over common iliac vessels (**Figure 4**).

Step 5: After lymhadenectomy, peritoneal opening to the extraperitoneal space is left open at both sides as peritoneal fenestration following extraperitoneal PLND has been shown to decrease the incidence of postoperative lymphocele formation [3].

Conclusions

Peritoneal fenestration over common iliac vessels during extraperitoneal PLND is an easy approach that al-

lows surgeon to reach the uppermost limit of extended PLND template. The latter peritoneal dissection is not time consuming and is not expected to increase the morbidity of the operation. In contrast it is expected to decrease the incidence of postoperative lymphocele formation

Περίληψη

Σκοπός: Η εξωπεριτοναϊκή πρόσβαση κατά την διενέργεια ενδοσκοπικής (λαπαροσκοπικής ή ρομποτικά υποβοηθούμενης) ριζικής προστατεκτομής αποτελεί μια καλά τεκμηριωμένη πρακτική με σημαντικά περιεγχειρητικά οφέλη για τον ασθενή έναντι της διαπεριτοναϊκής πρόσβασης. Εντούτοις, παραδοσιακά η εξωπεριτοναϊκή πρόσβαση έχει συνδεθεί με την αδυναμία να προσφερθεί εκτενής πυελικός λεμφαδενικός καθαρισμός καθώς η ανάσπαση του περιτοναίου πάνω στα κοινά λαγόνια αγγεία αποτρέπει την πρόσβαση στις ανώτερες λεμφαδενικές ομάδες. Στην παρούσα εργασία παρουσιάζουμε την τεχνική μας κατά την οποία μπορεί να προσφερθεί εκτεταμένος λεμφαδενικός καθαρισμός κατά την διενέργεια ριζικής προστατεκτομής με εξωπεριτοναϊκή πρόσβαση.

Μέθοδος: Μετά την ολοκλήρωση περιορισμένου πυελικού λεμφαδενικού καθαρισμού εξωπεριτοναϊκά, ο περιτοναϊκός σάκος που υπερκαλύπτει τα κοινά λαγόνια αγγεία διανοίγεται προσφέροντας πρόσβαση στις ανώτερες λεμφαδενικές ομάδες.

Αποτελέσματα: Κατόπιν της διάνοιξης του περιτοναίου ο λεμφαδενικός καθαρισμός μπορεί να επεκταθεί στο πεδίο της εκτεταμένης λεμφαδενεκτομής και να φτάσει μέχρι τη διασταύρωση του ουρητήρα με την κοινό λαγόνιο. Μετά το πέρας του λεμφαδενικού καθαρισμού τα δύο περιτοναϊκά ανοίγματα αφήνονται ανοιχτά καθώς ο χειρισμός αυτός έχει δειχθεί να περιορίζει σημαντικά τη δημιουργία μετεγχειρητικών λεμφοκηλών.

Συμπεράσματα: Συμπερασματικά, η περιτοναϊκή διάνοιξη στο ύψος των κοινών λαγόνιων αγγείων είναι ένας απλός χειρουργικός χειρισμός που επιτρέπει στην εξωπεριτοναϊκή πρόσβαση να προσφέρει εκτεταμένο πυελικό λεμφαδενικό καθαρισμό. Ο χειρισμός αυτός είναι τεχνικά εύκολος, δεν είναι χρονοβόρος και παράλληλα μειώνει την μετεγχειρητική επίπτωση λεμφοκήλης.

Λέξεις ευρετηριασμού

εξωπεριτοναικός, πυελικός λεμφαδενικός καθαρισμός, ριζική προστατεκτομή, καρκίνος προστάτη

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NOTES

NOTES

NOTES

Η Astellas είναι αφοσιωμένη στο να μετατρέπει την επιστημονική καινοτομία σε ιατρικές λύσεις που αποφέρουν αξία και ελπίδα στους ασθενείς παγκοσμίως.

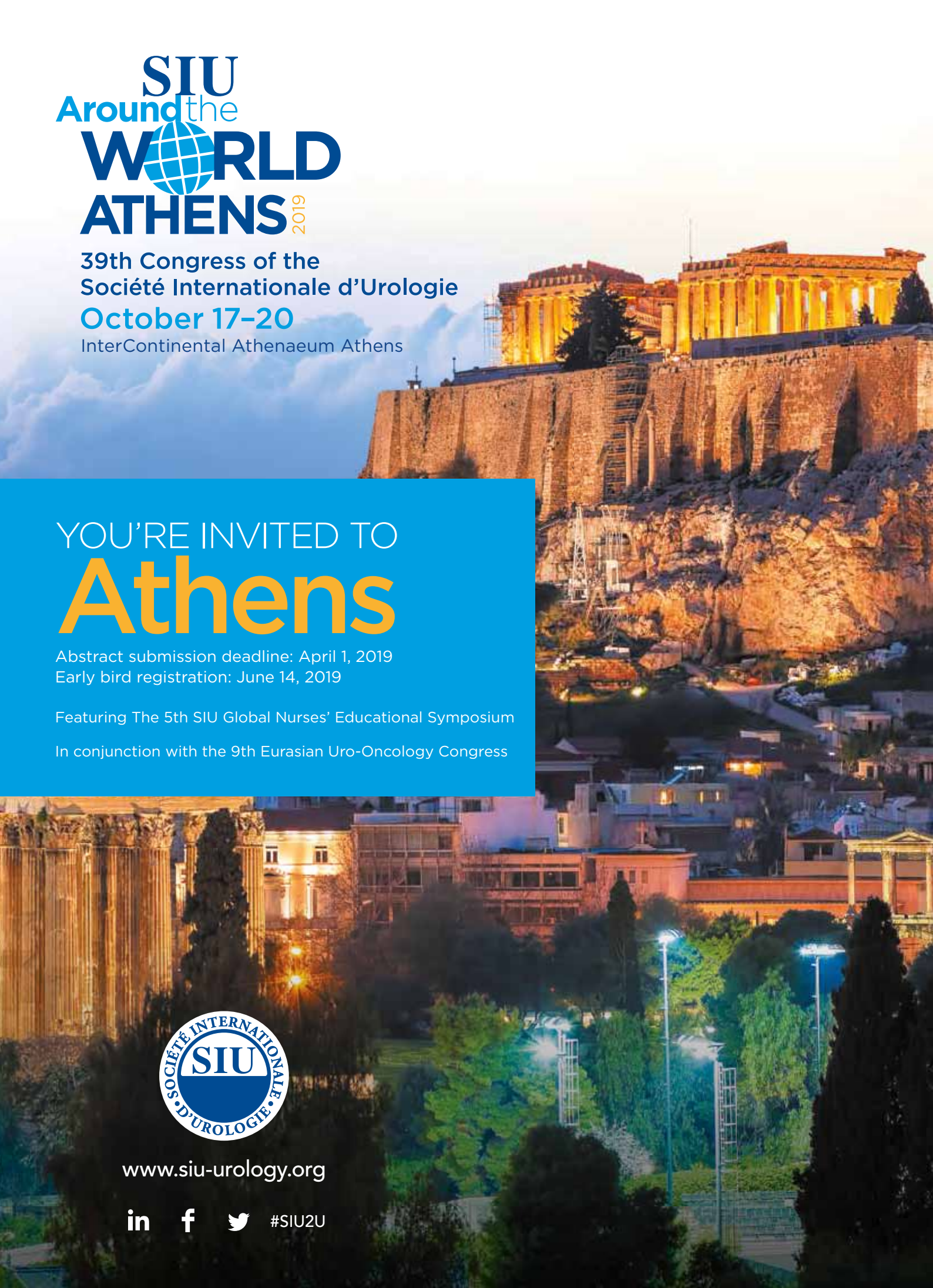
Κάθε μέρα εργαζόμαστε ώστε να καλύψουμε ανικανοποίητες ιατρικές ανάγκες εστιάζοντας πρωτίστως στις θεραπευτικές κατηγορίες της ογκολογίας, της ουρολογίας, των λοιμώξεων και της μεταμόσχευσης εξελίσσοντας παράλληλα νέες θεραπευτικές κατηγορίες και αξιοποιώντας νέες τεχνολογίες έρευνας. Παραμένουμε αφιερωμένοι στο να ικανοποιούμε τις ανάγκες των ασθενών και η υποστήριξή μας προς αυτούς δεν θα πάψει ποτέ να υφίσταται.

Μέσω της αφοσίωσής μας να προσφέρουμε στους ασθενείς ελπίδα για ένα λαμπρότερο μέλλον, επιδιώκουμε να ηγηθούμε στις θεραπευτικές κατηγορίες που εξειδικευόμαστε, εστιάζοντας στις κατηγορίες όπου υπάρχουν ιατρικές ανάγκες που παραμένουν ανικανοποίητες. Μέσω της καινοτομίας, θα συνεχίσουμε να αναγνωρίζουμε και να αναπτύσσουμε νέους τρόπους για να καλυτερεύσουμε την υγεία των ασθενών.

Στην Astellas, εστιάζουμε στο να κάνουμε πραγματικότητα το *αλλάζοντας το αύριο.*

astellas

astellas.gr



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