Original Article

The First National Resident Survey Assessing the Greek Urology Residency Training Programs

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Abstract

Background and Objectives: This is the first national survey regarding Greek Urology residency programs. The main objective of this study is to assess the level of confidence and perception of Greek Urology residents regarding their educational program and detect areas that necessitate improvement. **Materials and Methods:** A 51-question survey was developed via an electronic platform and 87.5% of residents (91 out of 104) participated from March 2019 until May 2019. Fisher's exact test, Chi-square test, and Kruskal–Wallis test were used with statistical significance set at $P = 0.05$. **Results:** The median overall satisfaction from surgical training was 6/10, and was independent of working schedule, working in a University Department, postgraduate years or number of residents in clinic. Among diagnostic and therapeutic procedures, kidney-ureter-bladder ultrasound, cystoscopy, and double-J stent insertion were common for trainees. On the other hand, most residents have not performed any scrotal ultrasound or pressure-flow studies. About 70.4% of residents reported bureaucracy as a major issue. 80.2% have not performed any ESWL, while 58.2% of residents performed <10 ureteroscopies and only the last year trainees performed more than 10 TURBT and transurethral resection of prostate. Most of the participants mentioned to rarely perform basic steps in many open or laparoscopic urological procedures. Surprisingly, 59.3% of residents have not published any study in peer-reviewed journals. 44% rarely feel satisfied from their work and 59.3% sometimes suffer from burnout. **Conclusions:** Considering the results from this survey regulatory authorities should join forces to establish a structured curriculum of clinical, surgical, and research training in Urology across Europe.

Keywords: *Greek urology residency program, Greek urology training program, national resident survey, resident surveys*

Introduction

Urology residency is a competitive period for physicians, due to long working schedules and demands to master many different surgical fields. In Europe, recent studies revealed mediocre results regarding satisfaction of training in several European countries.[1-4] Meanwhile, as we already know, in Greece, there is no minimum surgical case log or specific training program, that needs to be accomplished to be appointed as urologist after succeeding in the residency board examinations. In consequence, the staff of Urology departments along with residents is responsible for the educational program under the supervision and advisory of each department's director.

Another main issue is the lack of feedback from the residents' point of view regarding the accredited training centers. The main objective of this study is to assess the level of confidence and perception of Greek Urology residents regarding their educational program and detect areas that necessitate improvement.

Materials and Methods

Ethics

The study was approved by the Ethics Committee of the National and Kapodistrian University of Athens, located in Athens, Greece. The study complied with the principles of the Declaration of Helsinki for the protection of human rights.

All participants were informed in detail for inclusion in the study and signed informed consent before participation.

Study design

Selection and description of participants

In Greece, the training program of urology residents consists of a 5-year period, with

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the 1st year devoted to learning General Surgery skills and the remaining 4 years to General Urology. In this study postgraduate years (PGY) 1–4 refers to the relevant year of the Urology training period. In addition, we decided to further include fellow Urologists in the survey, as they actively participate in Urology Departments' daily program.

Technical information

A 51-question survey was developed using the electronic platform www.free online surveys.com, according to the Checklist for Reporting Results of Internet Surveys.[5] The survey was sent initially via E-mail to all Greek Residents, who were members of HUA in March 2019, and the survey collector was operational between March 2019 and May 2019. The questions were in Greek language and the completion of the questionnaire was anonymous and voluntary. Several parameters of residents' training program were examined such as quality of surgical and theoretical training and subjects related to research involvement as well as trainees' quality of life. A committee of Greek Urology experts further reviewed the quality of the survey, which was evaluated for usability and functionality before further distribution.

Statistics

Categorical variables are described as proportions. Fisher's exact test and Chi-square test were used to compare categorical variables. Kruskal–Wallis test was conducted to determine if there were differences in the several areas describing the quality of education and potential predictive factors, such as belonging to a University Department, the proportion of bureaucracy to daily workload, the PGY, working hours per day, possession of an MSc or PhD and age group. Pairwise comparisons were performed whenever a statistical significance was detected, using Dunn's procedure. Statistical significance was set at $P = 0.05$. All analyses were performed with IBM SPSS Statistics 25.0 software (SPSS Inc., Chicago, IL, USA).

Results

Demographic characteristics

A total of 91 out of 104 (87.5%) Urology residents responded to the survey. Among them 28 (30.8%) were 25–30 years/old, 43 (47.3%) 30–35 years/old, 14 (15.4%) 35–40 years/old and 6 (6.6%) ≥40 years/old while 77 (84.6%) were men and 14 (15.4%) were women. Regarding the year of residency, 21 (23.1%) were PGY1, 19 (20.9%) PGY2, 18 (19.8%) PGY3 and the same rate were PGY4, while fellow urologists were 15 (16.5%), showing an equal distribution among categories. Among responders, 42 (46.2%) worked at a University Department and 49 (53.8%) to a Community Hospital. The questionnaire revealed that a proportion of 34.1% and 28.6% worked for 8–10 and 10–12 h daily, respectively, while 41 (45.1%) of the participants were obliged to undergo 6–8 24-h shifts monthly. Altogether, most residents surpass the limit of 50 h/week. Finally, bureaucracy seems to represent a major issue for daily practice since 64 (70.4%) report more than 50% of daily workload to be related to it.

Clinical workload

In Table 1, the number of diagnostic procedures per PGY is shown. Among them, cystoscopy and kidney-ureter-bladder ultrasound seem to be common procedures for residents, since most of the participants reported to perform more than 50. Concerning transrectal ultrasound (TRUS) the majority of residents responded to perform 11–50 except PGY4 and fellow Urologists who seem to be more experienced with more than 50 procedures. Similarly, trainees become more confident to perform TRUS-guided biopsy in the last years of residency programs, since PGY3–4 and fellow Urologists performed more than 50 cases in contrast to PGY2 and PGY1 with 11–50 and <10, respectively. Finally, most residents have not performed any scrotal ultrasound or pressure-flow studies, except PGY4 and fellow Urologists.

In Figures 1 and 2, the number of endourological procedures [Figure 1] and surgeries [Figure 2] performed or involved as a first assistant who completed some steps of the procedure, is graphically depicted. Double-J stent insertion is a common procedure done by residents since most of them have placed more than 11–50 stents. The 52.7% and 60.4% of the responders performed 1–10 varicocele and hydrocele corrections, respectively. The majority (80.2%) have not performed any ESWL, while 53 (58.2%) residents performed <10 ureteroscopies. Transurethral resection of bladder tumors (TURBT) was reported to be performed rarely by PGY1–2 residents, while PGY3–4 trainees performed more than 10 TURBTs in the majority of them (67% and 100%, respectively). Similarly, transurethral resection of prostate adenomas was rarely performed by PGY1–3 residents, in contrast with all PGY4 trainees who reported completing more than 10 cases. Finally, most residents mentioned to rarely perform basic steps of the following procedures more than 10 times: Percutaneous nephrolithotripsy (98.9%), open radical nephrectomy (86.9%), laparoscopic nephrectomy (98.9%),

Table 1: Diagnostic procedures

Procedure	0 (%)	1-10 (%)	11-50 (%)	51-100 (%)	>100 (%)
KUB ultrasound					
PGY1	0	5 (23.8)	8 (38.1)	3 (14.3)	5 (23.8)
PGY2	0	4 (21.1)	4 (21.1)	5 (26.3)	6 (31.6)
PGY3	0	5 (27.8)	5 (27.8)	5 (27.8)	3 (16.7)
PGY4	0	3 (16.7)	2 (11.1)	0	13 (72.2)
Fellow urologist	1 (6.7)	4 (26.7)	1 (6.7)	2 (13.3)	7 (46.7)
TRUS					
PGY1	4 (19)	7 (33.3)	9 (42.9)	1 (4.8)	0
PGY2	0	6 (31.6)	10 (52.6)	2 (10.5)	1 (5.3)
PGY3	1 (5.6)	6 (33.3)	8 (44.4)	3 (16.7)	0
PGY4	1 (5.6)	1 (5.6)	5 (27.8)	6 (33.3)	5 (27.8)
Fellow	1 (6.7)	2 (13.3)	4 (26.7)	4 (26.7)	4 (26.7)
Scrotal ultrasound					
PGY1	12 (57.1)	8 (38.1)	1 (4.8)	0	0
PGY2	11 (57.9)	5 (26.3)	2 (10.5)	0	1 (5.3)
PGY3	12 (66.7)	5 (27.8)	0	0	1 (5.6)
PGY4	10 (55.6)	3 (16.7)	3 (16.7)	0	2 (11.1)
Fellow urologist	6 (40)	5 (33.3)	2 (13.3)	1 (6.7)	1 (6.7)
Pressure-flow studies					
PGY1	12 (57.1)	7 (33.3)	2 (9.5)	0	0
PGY2	10 (52.6)	6 (31.6)	2 (10.5)	1 (5.3)	0
PGY3	10 (55.6)	5 (27.8)	1 (5.6)	1 (5.6)	1 (5.6)
PGY4	2 (11.1)	5 (27.8)	9 (50)	2 (11.1)	0
Fellow urologist	5 (33.3)	7 (46.7)	2 (13.3)	1 (6.7)	0
Cystoscopy					
PGY1	1 (4.8)	7 (33.3)	6 (28.6)	5 (23.8)	2 (9.5)
PGY2	0	1 (5.3)	10 (52.6)	5 (26.3)	3 (15.8)
PGY3	0	0	2 (11.1)	10 (55.6)	6 (33.3)
PGY4	0	0	3 (16.7)	1 (5.6)	14 (77.8)
Fellow urologist	1 (6.7)	0	1 (6.7)	2 (13.3)	11 (73.3)
TRUS guided prostate biopsy					
PGY1	8 (38.1)	9 (42.9)	4 (19)	0	0
PGY2	2 (10.5)	5 (26.3)	11 (57.9)	0	1 (5.3)
PGY3	1 (5.6)	2 (11.1)	6 (33.3)	9 (50)	0
PGY4	0	2 (11.1)	4 (22.2)	6 (33.3)	6 (33.3)
Fellow urologist	1 (6.7)	0	5 (33.3)	3 (20)	6 (40)

PGY: Postgraduate years, TRUS: Transrectal ultrasound, KUB: Kidney-ureter-bladder

open transvesical (Freyer's) prostatectomy (78.1%), and open radical prostatectomy (89%). The median overall satisfaction from surgical training is 6/10, which seems to be independent of working schedule, working in a University Department, PGY or number of residents in the clinic [Tables 2-5].

Research activity

Surprisingly, 54 (59.3%) of residents have not published any study in peer-reviewed journals, while as a reasonable consequence, the vast majority of them reported a very low level of confidence in leading a research project (75.8%) or writing a scientific manuscript (68.1%). The vast majority of participants (74.8%) reported no educational courses during residency programs or in the best case 1–2 monthly. Interestingly, working at a University Department didnot affect positively neither the confidence level for leading a project or writing a paper nor the number of publications or congresses attended, although these clinics seem to occupy more residents and for a significantly larger amount of time [$P < 0.001$, Table 3]. Moreover, the level of confidence and number of publications did not differ according to bureaucracy workload, PGY, working hours, possession of MSc/PhD, or age group [Tables 2-8].

Quality of life

Most residents who participated in the survey rated their QoL during residency as moderate (5/10) and most of them reported to rarely feel satisfied (44%). 46 residents (50.5%) stated that they rarely manage to meet family or friends due to heavy programs. Despite adequate hours of daily sleep of 6–7/day in 39.6% and 5–6/day in 36.3%, 54 of

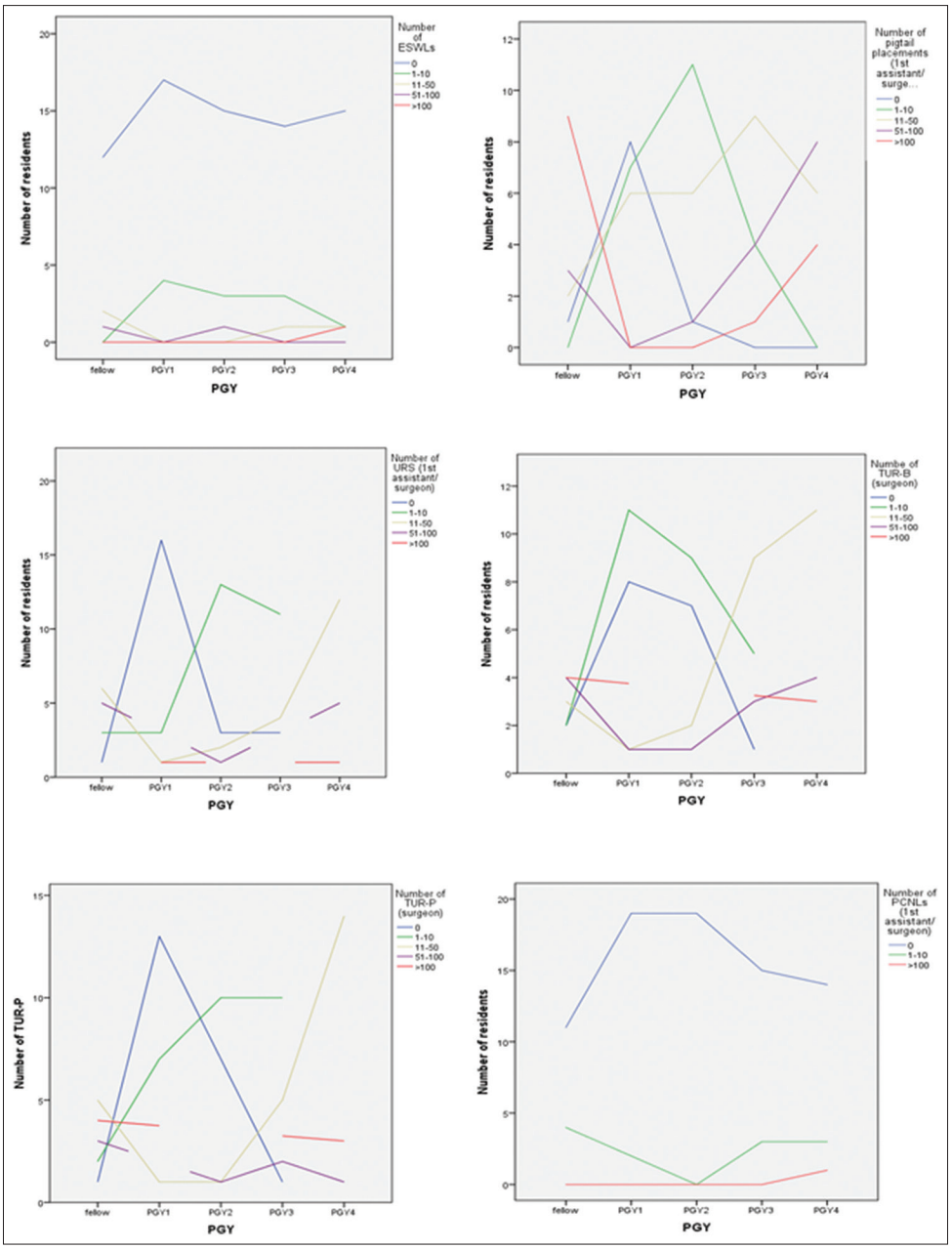

Figure 1: Number of endourological procedures

Table 2: Effect of working hours per day at urology residency in Greece

Variable	Median overall	6-8 h	8-10 h	10-12 h	>12 h	*P*
Number of responders	91	22	31	26	12	
How often do you feel you suffer from burnout	Sometimes	Sometimes	Sometimes	Sometimes	Often	0.028*
What is your confidence level for leading a research project	Very low	Very low	Very low	Very low	Very low	0.848
What is your confidence level for writing a scientific paper	Very low	Very low	Very low	Very low	Very low	0.760
Number of international publications	None	None	None	1-2	None	0.153
How often do you feel satisfied from your work	Sometimes	Sometimes	Rarely	Sometimes	Rarely	0.266
How satisfied are you from your training in surgery	6/10	7/10	6/10	6/10	5/10	0.168

*Groups 6-8 versus >12 h differed significantly (*P*=0.016)

the participants (59.3%) suffer from burnout sometimes. Level of satisfaction and burnout frequency does not seem to be affected by parameters such as bureaucracy workload, PGY, residency at a University Department, age and number of residents in the department [Tables 3,5-8]. On the other hand, working hours per day have a significant

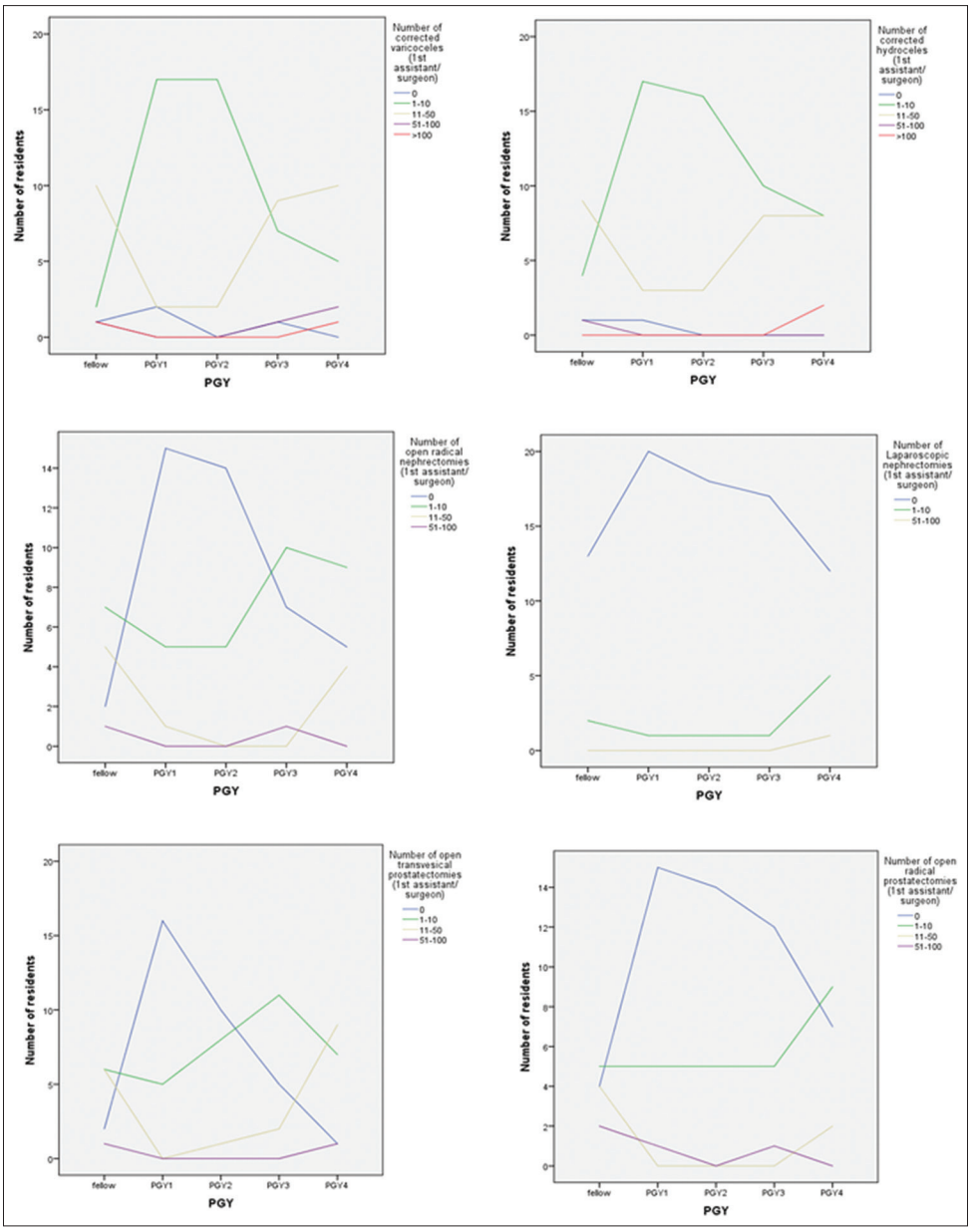

Figure 2: Number of surgeries

and negative impact, since residents who work >12 h daily, reported to suffer from burnout often [$P = 0.028$, Table 2].

Discussion

In Europe, in contrast with the US, residency programs vary significantly regarding organization and content, sometimes even across the same country.[6] Carrion *et al*. reported a 14% of satisfied last-year trainees coming from several European countries, regarding their surgical exposure.[4] This lack of training implicates a direct impact on confidence level to operate independently as shown by recent studies, where 38% of General Surgery residents do not feel confident after completing 5-year training program.[7] As a reasonable consequence, nearly 80% of European Urology Residents seek a future fellowship program.[4] Possible reasons for these findings are pressure to minimize operative time, increased working hours, and the high proportion of bureaucratic work, as well as lack of organized and structured curriculum of clinical and surgical education. Our study confirms this trend since most of Greek Urology Residents' level of satisfaction for their surgical education is moderate.

One of the most important tools that trainees should gain during their training is the ability to criticize before adopting new concepts. Research training time, besides providing the opportunity for critical thinking, will also render residents more competitive candidates for fellowship positions abroad and follow an academic, rather than private practice career.[8,9] Even though academic activity is commonly accepted as important part of residency

Table 3: Effect of being urology resident at a university clinic in Greece

Variable	Median overall	No university clinic	University clinic	*P*
Number of responders	91	49	42	
Number of residents	4-6	4-6	7-9	<0.001
Number of weekly educational courses in clinic (monthly)	1-2	1-2	1-2	0.342
What is your confidence level for leading a research project	Very low	Very low	Very low	0.815
What is your confidence level for writing a scientific paper	Very low	Very low	Very low	0.612
Number of international publications	None	None	1-2	0.163
Number of international urologic congresses attended last year	None	None	1-2	0.491
Do you use urology apps with your smartphone (nomograms, scores etc.)	-	52.3%	47.7%	0.642
How often do you feel satisfied from your work	Sometimes	Sometimes	Rarely	0.542
Hos satisfied are you from your training in surgery	6/10	7/10	6/10	0.029
Monthly days off clinic	None	None	None	0.227
How often do you feel you suffer from burnout	Sometimes	Sometimes	Often	0.120
Weekly hours devoted to urologic literature search/studying	1-5	1-5	1-5	0.208
Working hours per day	8-10	8-10	10-12	<0.001

Table 4: Effect of being a PhD or MSc candidate at urology residency in Greece

Variable	Median overall	No PhD or MSc	PhD or MSc	*P*
Number of responders	91	42	49	
What is your confidence level for leading a research project	Very low	Very low	Very low	0.591
What is your confidence level for writing a scientific paper	Very low	Very low	Very low	0.524
Number of international publications	None	None	None	0.143
Number of International Urologic Congresses attended last year	None	None	None	0.243
Do you use urology apps with your smartphone (nomograms, scores etc.)	-	41.5%	58.5%	0.163
Weekly hours devoted to urologic literature search/studying	1-5	1-5	1-5	0.080

Table 5: Effect of number of residents in clinic at urology residency in Greece

Variable	Median overall	1-3	4-6	7-9	≥10	*P*
Number of responders	91	21	28	28	14	
Working hours per day	8-10	8–10	8-10	10-12	10-12	<0.001*
Hos satisfied are you from your training in surgery	6/10	6/10	6/10	6/10	5/10	0.668
Monthly days off clinic	None	None	None	None	None	0.469
How often do you feel you suffer from burnout	Sometimes	Sometimes	Sometimes	Sometimes	Sometimes	0.368

*All groups differed significantly between them except groups 1-3 versus 4-6, 7-9 versus ≥10

training programs, many studies demonstrate low academic activity and scientific production among residents.[10,11] In Greece, academic scholarship is greatly underestimated, depicted by the fact that no Urology residency program offers a protected and dedicated block time for research involvement. Since according to our findings, confidence level to lead a research project or publish a scientific paper does not differ between University and Community Hospitals, there is the risk of future lack in physician-researchers and academicians in our field. Possible reasons to explain this phenomenon are the lack of funding, constricted time and absence of facilities, as well as the lack of research-oriented med-schools and minimal training during undergraduate years, which inevitably leads to an imbalance between academic career and private practice, forcing urologists to the second aim.[12] Bench differs from clinical research and needs more time and skills to be mastered during a limited block of training, thus clinical research skills such as data gathering, scientific, and grant writing and biostatistics should be highlighted at least initially.

Laparoscopic surgery is currently utilized worldwide, despite the dominance of robotic surgery in many centers. Since in most countries, there is a lack of robotic training simulators, residency programs should at least provide to young trainees the chance to expose themselves to basic laparoscopy via dry-lab training, a relatively inexpensive form of hands-on exercise. According to our findings, only 36.7% of community programs and 23.8% of University Departments offer a training box ($P = 0.183$), lying in alliance with findings across Europe.[4] In 2007, European Urology Residents Education Program was initiated, during which last year trainees accessed a laparoscopy course. Initially, during the first 2 years, only 4.2% passed the examination based on both time and quality criteria,[13] with an improved pass-rate of 55% overall have been reported

Table 6: Effect of Bureaucracy % during everyday practice at Urology Residency in Greece

Variable	Median Overall	10%	20%	30%	40%	50%	60%	70%	80%	90%	*P*-value
Number of responders 064	91	1	4	8	14	17	14	18	11	4	
What is your confidence level for leading a research project	Very Low	Moderate	Low	Very Low	Very Low	Very low	Very Low	Very Low	Very Low	Very Low	0.237
What is your confidence level for writing a scientific paper	Very Low	Moderate	Low	Low	Very Low	Very low	Very Low	Very Low	Very Low	Very Low	0.113
How often do you feel satisfied from your work	Sometimes	Sometimes	Sometimes	Sometimes	Sometimes	Rarely	Sometimes	Rarely	Rarely	Rarely	0.064
How often do you feel you suffer from burnout	Sometimes	Sometimes	Sometimes	Sometimes	Sometimes	Sometimes	Sometimes	Sometimes	Sometimes	Often	0.389
Working hours per day	8-10	8-10	8-10	8-10	8-10	8-10	10-12	8-10	10-12	8-10	0.542

Table 7: Effect of postgraduate year at urology residence in Greece

Variable	Median overall	Fellow	PGY1	PGY2	PGY3	PGY4	*P*
Number of responders	91	15	21	19	18	18	
What is your confidence level for leading a research project	Very low	Very low	Very low	Very low	Very low	Very low	0.164
What is your confidence level for writing a scientific paper	Very low	Very low	Very low	Very low	Very low	Very low	0.127
Number of international publications	None	None	None	None	None	1-2	0.128
How often do you feel satisfied from your work	Sometimes	Sometimes	Rarely	Rarely	Sometimes	Sometimes	0.560
How satisfied are you from your training in surgery	6/10	7/10	7/10	6/10	6/10	5/10	0.573
Number of international urologic congresses attended last year	None	None	None	None	None	1-2	0.196
How often do you feel you suffer from burnout	Sometimes	Rarely	Sometimes	Sometimes	Sometimes	Rarely	0.275
Weekly hours devoted to urologic literature search/ studying	1-5	1-5	1-5	1-5	1-5	1-5	0.450

PGY: Postgraduate year

Table 8: Effect of age group at urology residency in Greece

Variable	Median overall	25-30 years/old	30-35 years/old	35-40 years/old	≥40 years/old	*P*
Number of responders	91	28	43	14	6	
Number of international urologic congresses attended last year	None	None	None	None	None	0.348
Number of international publications	None	None	None	None	None	0.482
How often do you feel you suffer from burnout	Sometimes	Rarely	Sometimes	Sometimes	Often	0.198

by Somani *et al*. in 2019.[14] Higher rates of success were accompanied by more hours of training on box trainers and assisting in a larger number of laparoscopic operations.[14] Therefore, regulatory authorities across every European country should pay special attention and provide residency programs with the necessary equipment and tutors toward fulfilling this aim.

Marchalik *et al*. detected a 40% rate of burnout, with the highest rates among Portuguese residents.[15] In this study, Greek residents reported feeling burnout sometimes, which was associated significantly with working >12 h/day. Dissatisfaction and unmet expectations from training are also major drives for burnout.[15] Potential solutions like structured mentorship during residency, access to health-care advisors and relaxing activities, along with improvements in the program structure may alleviate this problem and should be implemented in European Residency programs.[15]

This unprecedented COVID-19 pandemic has resulted in significant changes in urology residency programs worldwide, with a negative impact on matters such as surgical training and academic activities. A slowdown in the learning curve of urology residents is noticed, as many scheduled surgeries were postponed and congresses/courses were delayed or even cancelled.[16] In this era, the adoption of smart learning modalities in the form of webinars, podcasts, prerecorded sessions, and social media is fundamental tool for continuous training.[16] These educational and healthcare resources challenge urology residents to reinvent themselves during the pandemic, especially in the de-escalation phase.[17] Theoretical training could be approached via telemedicine and virtual courses offered by EAU and AUA, along with distant learning organized by the faculty of each Department.[18] Surgical training via laparoscopy boxes, along with watching video surgeries or courses for operative techniques could blunt the slow-down of the learning curve. Research activities are also limited due to prioritization given by institutional review boards to trials related to the management of COVID-19 patients.

The main strength of our study is that it is only assessing the quality of education of Greek Urology Residents. The great interest from the residents' part, is revealed by the high proportion of responders. As all surveys, this study suffers from the subjectivity of the responders. We did not perform a comparison between men and women trainees, due to the small number of women who completed the questionnaire.

Conclusions

This is the first national survey assessing Greek Urology residency programs. Based on the results, residency programs are marked by the low level of satisfaction mainly regarding surgical education, low confidence level for performing clinical research, and risk of burnout due to increased working hours. As these findings allies from studies coming from other European countries, regulatory authorities should join forces to establish a structured curriculum of clinical, surgical, and research training in Urology across Europe.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Comparison of Cancer Waiting Time Targets in Urology, Pre-COVID Era, and during the COVID Era – A Single-Center Experience

Abstract

Objectives: The objective of this study is to measure the impact of COVID-19 pandemic on treatment targets for urgent urology cases in our hospital and compare it with previous research publications. **Materials and Methods:** We retrospectively collected and analyzed data over 10 months for 2 consecutive years. The data were analyzed from April to October in 2019 and 2020. This includes all suspected cancer. We collected a total number of referrals, time to the first consultation, and time of first definitive treatment. **Results:** The total number of patients referred in 2019 pre-COVID was 478 as compared to 278 in the subsequent year at the time of the first wave of COVID-19 pandemic. A total number of 118 cancers were detected in 2019 which makes up 24.6% of the total patients referred. Forty-one patients received treatment >62 days. This is 41 (34.7%) of the cancers or 8.5% of the referrals. Similarly, 60 patients were detected with cancer in 2020 making up 22.2% of the total referrals. Nineteen patients received treatment >62 days. This equates to 31.6% of the cancers or 7% of the total referrals. **Conclusion:** During the COVID-19 pandemic peak, though we did see a slight improvement in the total number of patients breached for their targeted dates of cancer treatment, this is largely due to the significant reduction of around 44% in the total number of referrals. This data also strengthens other large studies for other cancers which show a significantly lower number of patients being referred for cancer diagnosis.

Keywords: *COVID-19, delayed treatment, urology cancers*

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Introduction

The year 2020 unified and divided the world with a single stroke, COVID-19 pandemic.

The whole world remained focused on COVID-19 pandemic and other issues were pushed deep down in the priority list. This raised concerns, especially in the medical world about the catastrophe that will unfold once the storm will settle. One paper raised concerns about the possibility of significant increase in the number of avoidable cancer deaths in England as a result of diagnostic delays due to the COVID-19 pandemic.[1]

We decided to look at the cancer management pre-COVID and during the first wave of COVID-19 pandemic in the department of urology within our trust. The idea is that it will not only give us a true picture of our services, but it will also help us design strategies for future, we also want to contribute to the world as more data means a better understanding for the future.

Materials and Methods

We collected referral data from the cancer pathway coordinators for a period between April–October in 2019 and the equivalent period in 2020 to get a direct comparison. The data for all the suspected cancer patients are stored within the TRUST website including patient's demographics, date of referral, date of patients are offered appointments, dates of consultations, and dates and types of investigations and treatments. This data from electronic health records were obtained for each patient to obtain the treatment start dates and calculate the time to treatment. The department deals with adults (16+ years old), and hence no pediatric urology evaluation is made. The data analysis was completed through an Excel sheet. We determined the total number of suspected cancer referrals, simply named under term 2 week wait urological referrals in April–October 2019 and compared it to April–October 2020 in our hospital. We also determine the time between referral to first seen for each patient in each year. The detailed evaluation also

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included the time between referral to first treatment for each patient. The investigation and treatment pathways were also looked at to cut down the delays.

Results

In 2019 preceding COVID-19 pandemic, our hospital received a total of 478 referrals on a suspected cancer pathway for urology. This number was for April–October. All these patients were offered outpatient appointments for the first consultation within 14 days. Thirty-six patients (7.5%) had their first outpatient clinic after 14 days from referral. This was due to the patient being unable to attend in the initially given time slot. In the subsequent year during the first wave of COVID-19 pandemic, we did see a sharp decline in the number of patients referred for suspected urology cancer. This number for 2020 for the same amount of time fell to 270 patients. This showed a 44% decrease in the total number of referrals. Twenty-five patients (9.2%) had their first outpatient clinic after 14 days from referral. This was again due to patient choice. In 2019, of the 478 referrals, 118 patients (25%) were found to have cancer. The main bulk of the cancers were related to the prostate followed by the bladder. The exact number and percentage of these are as follows:

- 74 Prostate (62%)
- 29 Bladder (24.5%)
- 8 Kidney (6.7%)
- 5 Testicle (4.23%)
- 2 Penile (1.6%) [Graph 1].

When we compared it to 270 referrals in 2020, results were not too different albeit less numerically. A total of 60 cancers were detected making it a total of 22.2%. Again, prostate cancer was the leading diagnosis with exact numbers and percentages as follows:

- 35 Prostate (58.3%)
- 23 Bladder (38.3%)
- 1 Upper tract transitional cell carcinoma (TCC) (1.66%)
- 1 Kidney (1.66%) [Graph 2].

The next important parameter we compared was the time from referral to first treatment. In 2019, 41 (34.7%) patients received treatment >62 days. All the other patients diagnosed with cancer had their treatment started within 62 days. The reasons of delay in the treatment are discussed later and a lot of improvement has been achieved since this study. The breakdown is as follows:

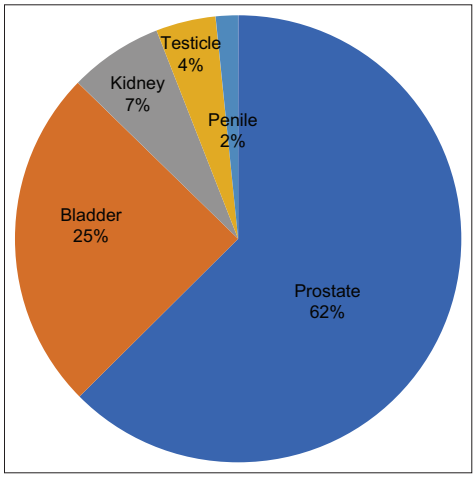
- Prostate = 31-Hormone therapy-4, Robotic-assisted radical prostatectomy (RALP)-12, Radiotherapy-10, Watchful waiting 5
- Bladder = 5– Transurethral resection of bladder tumor (TURBT) 5. All high-grade tumors but superficial require resection at 4-6 weeks, and hence unavoidable breach
- Penile = 2-Partial penectomy 1, Glansectemy 1
- Testicle = 1-Right orchidectemy. Awaited chemotherapy postsurgery [Graph 3].
- Kidney = 2 Laparoscopic nephrectomy 2.

In 2020, there were 19 (31.6%) patients who received treatment >62 days.

- Prostate = 14 Hormones and radiotherapy 9, RALP 4, and HIFU Trial 1
- Bladder = 3, TURBT 3
- Kidney = 1, Radical nephrectomy 1
- Upper tract TCC: 1 nephroureterectomy 1 [Graph 3].

We saw a sharp drop in the number of referrals to the urology department in the first wave of COVID-19 pandemic. There were 44% fewer referrals in 2020 than in 2019. This could be due to several factors but most importantly a fear of a visit to health-care service was the main palpable factor. When the performance is translated into timely management of cancers, we have seen an improvement in the percentage of patients receiving their treatment within target dates during the COVID-19 pandemic era. This is also demonstrated in Table 1. Table 1 shows head-to-head comparison of the 2 years and shows 3% less breaches in 2020. However, during COVID-19 pandemic, the urology department has to cope with a significantly low volume of patients (the routine or nonurgent cases which have not been discussed here were virtually nonexistent taking off further workload). It will be important to note that during COVID-19 pandemic, there was all sort of strains on health services including depleted staff (either off or relocated), less in patients beds available for most of the wards converted to COVID wards. Furthermore, for extra protective measures and social distancing with extra cleaning and hygiene, a lot of time and space was not available for direct patient care. This means that we had much less capacity to deal with patients. We can safely conclude that improvement in relative numbers for targeted treatment was solely due to a decrease in demand for services for cancer investigations and treatment. This argument is further strengthened from the figures below:

- For prostate cancer in 2019 - out of 13 patients referred for RALP, 12 breached the treatment date

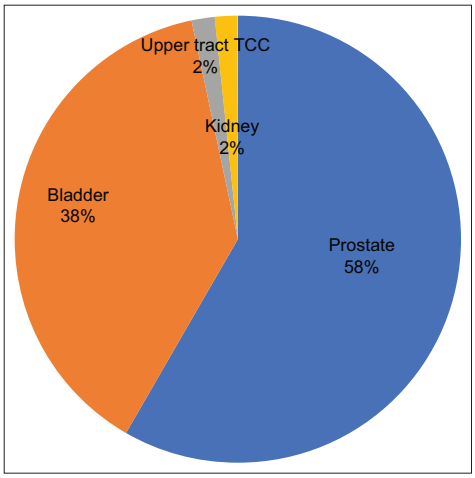


Graph 1: Percentage of cancers in 2019

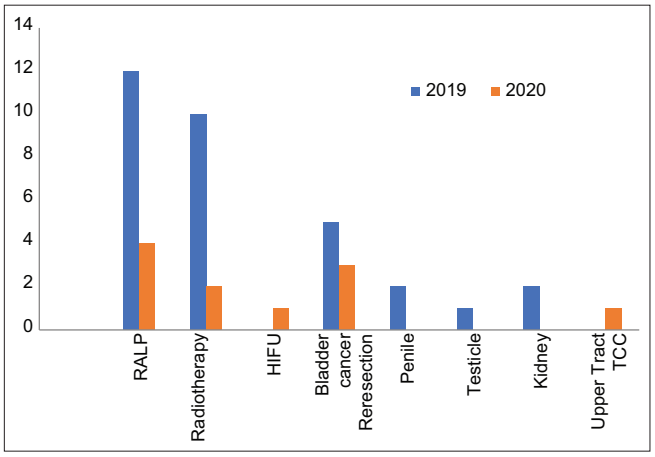
Table 1: Direct comparison of referrals and treatment targets in 2019 and 2020

	Year 2019	Year 2020	Percentage change
Total referrals	478	270	44 less referrals
Breach for first consultation (%)	36 (7.5)	25 (9.2)	1.7 more breaches
Total cancers (%)	118 (25)	60 (22)	3 less
Breach of target dates (%)	41 (34.7)	19 (31.6)	3 less breaches
Percentage breaches to total patients (%)	8.5	7	1.5 less breaches
Average breach time to treatment	3 months	3 months	N/A
Maximum breach time to treatment	7 months	7 months	N/A
Treatment type with maximum breach time	RALP	RALP	N/A

RALP: Robotic-assisted laparoscopic prostatectomy, N/A: Not applicable



Graph 2: Percentage of cancers 2020



Graph 3: Comparison of treatment breaches in 2019 and 2020

- For prostate cancer in 2020 - out of five patients referred for RALP, four breached the treatment date
- The average time for treatment in patients who breached the 62 days target both pre and during COVID time was the same. It was around 3 months with a maximum time of up to 7 months. The maximum delays were again noted for RALP patients.

This simply shows that there was no improvement in specific treatment target time for robotic-assisted laparoscopic prostatectomy or average target time for breach patients.

Discussion

The timeline of COVID-19 pandemic in the United Kingdom (UK) is as follows:

- The emergency of SARS-CoV-2– the first cases of unexplained pneumonia were noted in the city of Wuhan, China[2]
- The causative virus was rapidly isolated from patients and sequences with the results from China being shared and published in January 2020[2]
- Index case entered the UK on 23/01/20 from Hubei province in China[3]
- First death in the UK March 05[4]
- First lockdown March 23[5]
- First vaccine– December 8, 2020[6]

In the UK, the national health system follows very specific time guidelines for the management of cancer-related issues. These cancer waiting time standards are as follows:

National Cancer Waiting Times Monitoring Dataset Guidance– Version 11.0 September 2020.[7]

- Maximum 14 days from receipt of urgent referral for suspected cancer to first outpatient attendance
- Maximum 28 days from receipt of urgent referral for suspected cancer to the date the patient is informed of a diagnosis or ruled out of cancer
- Maximum 31 days until a decision to treat with first definitive treatment
- Maximum 62 days from urgent referral for suspected cancer to first treatment.

Whereas "Definitive treatment" is defined as:

- "A treatment is an intervention intended to manage the patient's disease, condition, or injury and to avoid further intervention. It is a matter of clinical judgment in consultation with the patient"[7]
- "For cancer waits a first definitive treatment is defined as the start of the treatment aimed at removing or eradicating cancer completely or at reducing tumor bulk."[7]

What cannot be classified as the first treatment for urological cancers

- Surgical biopsy for diagnostic purposes, including transurethral resection of bladder tumor commonly called TURBT (unless the tumor is effectively removed by the procedure). *New Guidance from July 2020*[7]
- Palliative care for any patient who is fit for active treatment (unless they decline active treatment options and wish to have only palliative treatment)[7]
- Furthermore, it is worth noting that active monitoring is not counted as treatment. Time to active monitoring counts as– FDS (Faster Diagnosis Standard). If the final decision is another form of treatment other than active monitoring, the clock does not stop and they should have further treatment within 31 days.[7]

The COVID-19 pandemic stirred fear and panic among the general population and one study showed that almost half of people with potential cancer symptoms did not contact their GP during the first wave of the pandemic. They also found that 31% did not seek help after coughing up blood, 41% did not seek help for an unexplained lump or swelling, and 59% did not seek help after noticing changes to the appearance of a mole.[8] There are quite a few papers published discussing the effects of COVID-19 pandemic on other cancer-related issues such as disease progression,[9] and screening and treatment. A paper mentioned a significant reduction in the number of admissions for urological diseases in China.[10] A systematic review by Riera *et al*. concluded that *the* reduction of the COVID-19 burden unintentionally posed a major risk on cancer care worldwide.[11]

There is no doubt COVID-19 pandemic has changed the world in every aspect and health services are no exception. There is an urgent desire to look for other than traditional ways of providing service. Different healthy proposals are suggested.[12] These included measures such as:

1. Remote consultation services over the phone/video link within our trust
2. Furthermore, we radicalized the system by incorporating more help from our Allied health professionals including urology specialist nurses. They were more engaged in giving diagnoses to patients and proposing treatment plans after discussion with the respective consultants and in our specialist multidisciplinary team meeting
3. More and more services were brought back to our local hospital from regional centers such as transperineal prostate biopsies and were done under local anesthesia thus saving a lot of theater time
4. For low surgical risk patients, more and more preoperative assessment was done over the phone
5. Cancers were segregated and preference was given to cancer with more potential of harmful effect to patients (such as muscle invasive localized bladder cancers).

Conclusion

We can say that though COVID-19 pandemic has caused a lot of disruption to the medical services, at the same time, it has allowed us to rethink and improve our quality of services.

We recommend that more and more studies related to COVID-19 pandemic should be encouraged. These can include studies about patient's experience, staff experience, and management level experience including financial constraints. The more we know, the better it will be for future.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Peri-Operative Predictors of Postoperative Bleeding and Sepsis after Percutaneous Nephrolithotomy

Abstract

Introduction: Percutaneous nephrolithotomy (PCNL) is the most common minimal access method used for the management of large renal and pelvic stones. The two most common complications after PCNL are bleeding and sepsis. In this context, we did this study to find out perioperative predictors of postoperative bleeding and sepsis after PCNL. **Materials and Methods:** We conducted this study on 110 patients who came for PCNL at our institute from March 1, 2018 to August 31, 2019. Data were collected using a pro forma, and the same analyzed by appropriate statistical methods using the SPSS software. **Results:** The perioperative factors correlated to postoperative bleeding were stone size, density of stone, Guy's stone score, size of Amplatz sheath used, number of working tracts created, and duration of surgery. On regression analysis factors which were predictive of postoperative bleeding were size of Amplatz sheath and number of working tracts created. Peri-operative factors correlated with postoperative sepsis were body mass index of the patient, preoperative total count, density of stone, preoperative pyuria, preoperative positive urine culture, superior calyceal puncture, postoperative total leukocyte count, and postoperative fever within 24 h. The factors which were predictive of postoperative sepsis were preoperative pyuria, preoperative urine culture, superior calyceal puncture, and postoperative fever on regression analysis. **Conclusion:** This study shows perioperative predictors of postoperative bleeding and sepsis after PCNL. Out of 43.63% total complications, 20% were major and 23.63% minor complications.

Keywords: *Complications, percutaneous nephrolithotomy, peri-operative predictors*

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Introduction

Urinary tract is one among the most common organ system prone to have stones. Its surgical management which was previously done by open method is now being done by minimal access methods. Percutaneous nephrolithotomy (PCNL) is currently the most common minimal access method used for the management of large calyceal and renal pelvic stones. The safety and efficacy of PCNL have increased since the eighties when it was first introduced due to the refinement of technology, improved surgical instrumentation, and increasing experience.[1] PCNL can be performed through access into the upper, middle, or lower calyx of the kidney by either fluoroscopic or ultrasound guidance. Although there has been rapid evolution in sizes of nephroscope resulting in the development of mini PCNL, ultramini PCNL, and microperc and in using various energy sources like pneumatic lithotripters, ultrasonic devices and lasers to fragment stones, significant complications are seen in up to one quarter of PCNL patients who undergoes this surgery.[2,3]

Studying the factors which affect the complications of PCNL is important to reduce the rate of complications and to improve the quality of service.[4] The two most common complications after PCNL are bleeding requiring transfusion and sepsis. It is in this scenario we are doing this research at our institute to assess the perioperative predictors of postoperative bleeding and sepsis after PCNL.

Materials and Methods

This was a prospective study conducted in a tertiary care hospital in Kerala, India. The objective of the study was to find out perioperative predictors of postoperative bleeding and sepsis after PCNL in patients admitted for this procedure at our institute from March 1, 2018 to August 31, 2019. The inclusion criteria were all those patients admitted for PCNL who were willing to participate in the study and whose Karnofsky performance status was

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80 and above. The exclusion criteria were those admitted patients who were not willing to participate in the study and patients with Karnofsky performance status below 80.

According to a previous study conducted by Shakhawan H. A., Said *et al*. from department of Urology, Sulaymaniyah Surgical Teaching Hospital, Iraq; among 200 patients, 47.5% had different types of complications. Seventeen (8.5%) patients had bleeding which needed blood transfusions and 32 (16%) had bleeding which responded to bed rest and i.v crystalloids. Intraoperative perforations occurred in 32 (16%) and infective complications in 30 (15%) patients.[5] Using this information, sample size has been estimated to 106 using the formula $(Z\alpha)^2$ PQ/d^2, where Zα is 1.96 for 5% significance, *P* is 47.5 and Q is (100-P) which is 52.5, d is precision which is 20% of P. Taking into consideration, drop out cases in between study also, final sample size is 110. The study was started after getting institutional research and ethics committee approval. A detailed consent form for the willingness to participate in the study was obtained from patients.

Information about the patients who are participating in the study will be collected using a pro forma. Patients who fulfill inclusion criteria will be personally interviewed and data will be collected. These patients will undergo blood and urine investigations with ultrasonography of Kidney Ureter Bladder (KUB) and computerized tomography (CT) KUB stone protocol. The pro forma will contain details pertaining to age, sex, IP | OP number, relevant history, and body mass index. It contains preoperative variables such as hemoglobin, total white blood cell count, presence of pyuria, urine bacterial culture status, degree of hydronephrosis, stone size, stone density in Hounsfield units identified by CT scan, and stone complexity Guy's Stone Score (GSS) grade.[6] GSS comprises four grades: Grade I is solitary stone in mid/lower pole or solitary stone in the pelvis with simple anatomy; Grade II solitary stone in upper pole or multiple stones in a patient with simple anatomy or a solitary stone in a patient with abnormal anatomy; Grade III multiple stones in a patient with abnormal anatomy or stones in a calyceal diverticulum or partial staghorn calculus; Grade IV is staghorn calculus or any stone in a patient with spina bifida or spinal injury. Intraoperative variables in data collection are size of Amplatz sheath, intraoperative position of stone, site of puncture, number of tracts, and duration of surgery.

This procedure PCNL was done under general anesthesia. Prophylactic antibiotics were given according to the institutional protocol. After placing the patient in the lithotomy position, ureteric catheterization was done in retrograde manner with a 6 F ureteric catheter (Aster Medispro, Bangalore, India) using a rigid cystoscope (30° Karl Storz with 22 F outer sheath, Tuttlingen, Germany). Later, the patient was turned to prone position, and all pressure points were adequately padded. The target calyx was accessed under C-arm fluoroscopy (Shimadzu, Kyoto, Japan) guidance using 16 G initial puncture needle (Aster Medispro, Bangalore, India). The floppy tipped guidewire was then passed into the collecting system through the needle. A working tract was established using a serial metallic dilator system under fluoroscopy control and 28–32 F Amplatz sheath (Rusch Teleflex, Morrisville, USA) was placed over the dilated tract. Through Amplatz sheath, a nephroscope (20 degree R. Wolf with 24 F outer sheath, Illinois, USA) was then placed directly into the kidney. Fragmentation of stones was done using a pneumatic lithotripter (Status medical equipments, Satara, India). Forceps and irrigating fluid were used to remove stone fragments. At the end of the procedure, the ureteric catheter would be retained and the same removed next day if there were no complications. A nephrostomy tube (16 F) was placed in all patients and clamped for 8 h. A Per urethral 16 F Foley's catheter was also placed.

Those patients who underwent either blood transfusion or any adjuvant procedures such as angioembolization or surgery will be considered to have postoperative bleeding. Patients who have systemic inflammatory response syndrome (SIRS) with infection or suspected infection (Sepsis 2 criteria) after surgery will be considered in postoperative sepsis category.[7] SIRS means two or more of the following such as leukocytosis or leukopenia, hyperthermia or hypothermia, tachycardia, and tachyapnea. The data thus collected will be statistically analyzed to identify whether these perioperative predictive factors are significantly related to postoperative bleeding and sepsis.

Qualitative variables were summarized using percentages and quantitative variables using mean with standard deviation. Then, statistical analysis was done to identify peri-operative factors with correlation to postoperative bleeding and sepsis. Qualitative variables were tested by using Chi-square test and quantitative variables by Pearson's correlation analysis. Those peri operative factors either by Chi-square test or by Pearson's correlation analysis with $P < 0.05$ were considered significant. Later regression analysis was done to find out significant perioperative predictive factors for postoperative bleeding and sepsis. Perioperative factors with regression co-efficient whose *P* value is <0.05 at 95% confidence interval (CI) were considered predictive of complications. All statistical analysis was performed using the SPSS software (SPSS Inc. Released 2009. PASW statistics for windows, version 18.0 SPSS Inc., Chicago, Illinois, USA).

Results

In our study, 110 patients underwent PCNL in 18 months. Sex distribution of the study population is shown in Figure 1. The distribution of various preoperative variables is shown in Figures 2-4.

The total number of patients with complications (both minor and major) was 48 (43.63%). Out of these

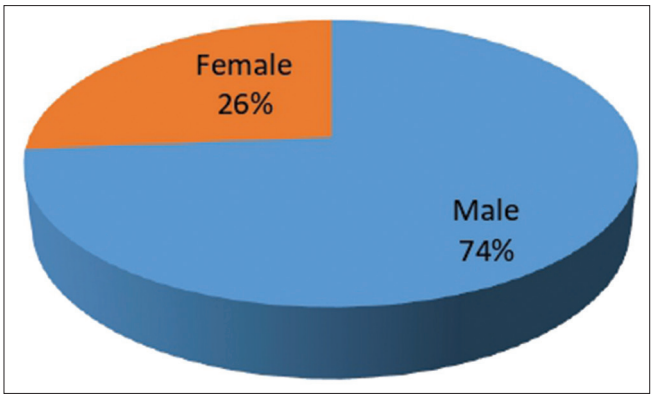

Figure 1: Sex distribution of study population (male = 81 patients and female = 29 patients)

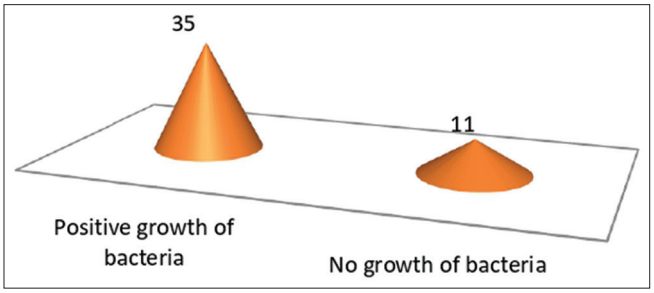

Figure 3: Distribution of preoperative urine culture result among patients with pyuria

26 (23.63%) patients had minor complications such as mild postoperative blood stain in urine (11 patients, 10%) and chest infections (15 patients, 13.64%) which were managed conservatively.

Twenty-two patients (20%) had severe complications such as postoperative bleeding which needed either blood transfusion or adjuvant procedures, sepsis, pulmonary edema, and pleural injury. We had 7 (6.36%) patients with postoperative bleeding which needed further treatment. Out of these seven patients, 4 (3.63%) cases were managed by blood transfusion, 2 (1.81%) cases by doing angioembolization by endovascular coiling and one case (0.90%) was managed by emergency open surgery with suturing of PCNL track in the kidney within 12 h of surgery.

Urinary sepsis was found in 12 patients (10.90%) which were managed by giving antibiotics according to urine culture and sensitivity. Eight patients had *E. coli* and 4 had Klebsiella bacteria isolated from their urine. In our study population, two (1.81%) patients had postoperative atelectasis which was managed conservatively. One (0.90%) patient developed pulmonary edema due to myocardial infarction within 24 h of surgery and died.

When Pearson's correlation co-efficient analysis was done after analyzing results, perioperative factors correlated to postoperative bleeding [Table 1] were stone size (P = 0.0433), density of stone (P = 0.0131),

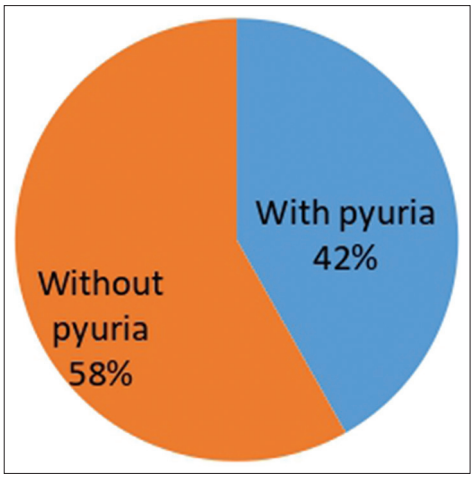

Figure 2: Distribution of preoperative pyuria among patients. (without pyuria = 64 patients, with pyuria = 46 patients)

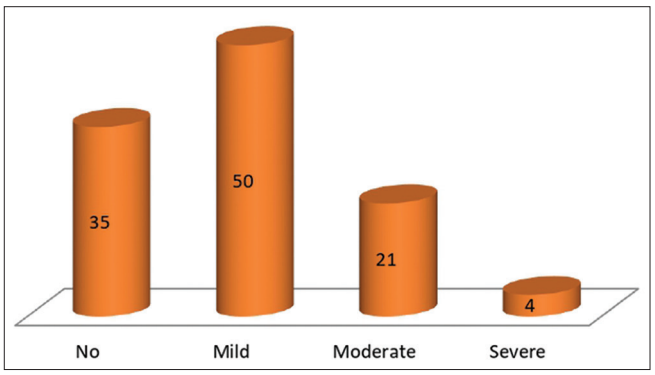

Figure 4: Degree of hydronephrosis by ultrasonography

Table 1: Correlation analysis of variables for postoperative bleeding

Peri operative factor	Pearson's (*r*)	*P*	Significant
Age	−0.0734	0.4460	No
BMI	−0.0432	0.6540	No
Preoperative hemoglobin	−0.0017	0.9859	No
Preoperative total leukocyte count	−0.0951	0.3230	No
Preoperative blood urea	−0.1658	0.0834	No
Preoperative serum creatinine	−0.1051	0.2745	No
Degree of hydronephrosis	0.0908	0.3454	No
Stone size	0.193	0.0433	Yes
Density of stone	0.2357	0.0131	Yes
GSS	0.2388	0.0119	Yes
Size of Amplatz sheath	0.3576	0.0001	Yes
Number of working tracts	0.3786	<0.001	Yes
Duration of surgery	0.3417	<0.001	Yes

BMI: Body mass index, GSS: Guy's stone score

GSS (P = 0.0119), size of Amplatz sheath used (P = 0.0001), number of working tracts created (P < 0.001), and duration of surgery (P < 0.001). When regression analysis [Table 2] was done, those factors which were predictive of postoperative bleeding were size

Table 2: Regression analysis showing predictive factors of postoperative bleeding

Peri operative factor	Regression co efficient	CI (%)	Significance	Predictor
Age	0.001	95	0.996	No
Sex	0.003	95	0.979	No
BMI	−0.091	95	0.364	No
Patients with diabetes mellitus	−0.162	95	0.134	No
Patients with hypertension	0.17	95	0.882	No
Patients with a history of previous ipsilateral renal surgery	0.15	95	0.087	No
Preoperative hemoglobin	−0.036	95	0.793	No
Preoperative total leukocyte count	−0.001	95	0.995	No
Preoperative blood urea	−0.082	95	0.527	No
Preoperative serum creatinine	−0.028	95	0.852	No
Patients on antiplatelets drugs	0.115	95	0.064	No
Patients with pyuria	0.180	95	0.213	No
Patients with positive urine culture	−0.172	95	0.246	No
Degree of hydronephrosis	−0.005	95	0.959	No
Stone size	−0.023	95	0.855	No
Density of stone	−0.103	95	0.321	No
GSS	−0.082	95	0.571	No
Side of surgery	−0.034	95	0.714	No
Size of Amplatz sheath	−0.255	95	0.010	Yes
Position of stone intraoperatively	−0.040	95	0.735	No
Site of puncture	−0.060	95	0.550	No
Number of working tracts	−0.300	95	0.002	Yes
Duration of surgery	−0.076	95	0.596	No

BMI: Body mass index, GSS: Guy's stone score, CI: Confidence interval

of Amplatz sheath (95% CI, $P = 0.010$) and number of working tracts (95% CI, $P = 0.002$) created only.

For postoperative sepsis [Tables 3 and 4], factors correlated were body mass index of patient ($P = 0.0036$), preoperative total count ($P = 0.0043$), density of stone ($P = 0.0412$), preoperative pyuria ($P < 0.001$), preoperative positive urine culture ($P < 0.001$), superior calyceal puncture ($P = 0.012$), postoperative total leucocyte count at 24 h of surgery ($P < 0.0001$) and postoperative fever within 24 h ($P < 0.0001$). When regression analysis was done [Table 5], those factors which were predictive of postoperative sepsis were preoperative pyuria (95% CI, $P = 0.032$), preoperative urine culture (95% CI, $P = 0.030$), superior calyceal puncture (95% CI, $P = 0.002$), and postoperative fever (95% CI, $P = 0.001$).

Table 3: Correlation analysis of quantitative variables for postoperative sepsis

Peri operative factor	Pearson's (*r*)	*P*	Significant
Age	−0.005	0.9586	No
BMI	0.2752	0.0036	Yes
Preoperative hemoglobin	−0.0671	0.4861	No
Preoperative total leukocyte count	0.2709	0.0043	Yes
Preoperative blood urea	0.1191	0.2156	No
Preoperative serum creatinine	0.1381	0.1505	No
Degree of hydronephrosis	0.0236	0.8114	No
Stone size	0.0289	0.7715	No
Density of stone	0.1958	0.0412	Yes
GSS	0.0315	0.7478	No
Size of Amplatz sheath	0.125	0.1826	No
Number of working tracts	−0.0586	0.5472	No
Duration of surgery	0.0659	0.4998	No
Postoperative hemoglobin	0.0471	0.6258	No
Postoperative leucocyte count	0.736	<0.0001	Yes
Postoperative fever	0.9526	<0.0001	Yes

BMI: Body mass index, GSS: Guy's stone score

Discussion

According to review of literature done in this particular topic from PubMed, Embase, and science direct database, total complication rate varies between 28% and 49.8%. In our study, total complication rate (including major and minor) was 43.63%. Rate of major complication in literature was between 7% and 17.8%. Our major complication rate was 20% like postoperative bleeding which needed either blood transfusion or adjuvant procedures, sepsis, pulmonary edema, and pleural injury. We had 23.63% of minor complications. Here in the literature, the rate of minor complications varied between 18.8% and 28.3%.

In a study by Olvera-Posada D *et al*. which was a series of 2318 patients, blood transfusion rate was 1.4%.[8] Blood transfusion rate in our study was 3.63%. After reviewing various other studies, blood transfusion rate varies between 1% and 10%. Among our study population, 1.81% was the rate of angioembolization. According to a study by Arora A M, *et al*., 0.51% of patients who

underwent PCNL at their institute required embolization to control bleeding.[9]

According to the literature, predictive factors of postoperative bleeding which needed either blood transfusion or adjuvant procedures were number of tracts dilated, stone type, diabetes, preoperative hemoglobin level, duration of surgery, degree of hydronephrosis, and diabetes. In our study, perioperative factors correlated to postoperative bleeding were stone size ($P = 0.0433$), density of stone ($P = 0.0131$), GSS ($P = 0.0119$), size of Amplatz sheath used ($P = 0.0001$), number of working tracts created ($P < 0.001$), and duration of surgery ($P < 0.001$). Those factors which were predictive of postoperative bleeding were size of Amplatz sheath (95% CI, $P = 0.010$) and number of working tracts created (95% CI, $P = 0.002$) only.

Table 4: Correlation analysis of qualitative variables for postoperative sepsis

Peri operative factor	χ^2	*P*	Significant
Sex	0.013	0.910	No
Patients with diabetes mellitus	0.863	0.353	No
Patients with hypertension	0.337	0.562	No
History of ipsilateral previous renal surgery	1.056	0.304	No
Patients on antiplatelets drugs	0.216	0.642	No
Patients with pyuria	18.740	<0.001	Yes
Patients with positive urine culture	22.239	<0.001	Yes
Side of surgery	0.021	0.884	No
Position of stone intraoperatively	6.403	0.380	No
Site of puncture	6.277	0.012	Yes

Out of 110 patients, 10.90% patients had urinary sepsis, and on literature review, it can vary between 6.2% and 28.9%. According to a study of 241 cases by Liu J, *et al*., urosepsis occurred in 17% of patients after PCNL. Based on multivariate logistic regression analysis, the independent risk factors associated with postoperative urosepsis included preoperative leukocyte elevation (OR = 3.973, $P = 0.005$), positive urine nitrite (odds ratio [OR] = 3.697, $P = 0.010$), and positive urine culture (OR = 3.562, $P = 0.002$).[10] In a study by Rivera M, *et al*. 16% had infectious complications. Eleven patients (5%) with urinary tract infection/pyelonephritis, 21 patients (9%) with SIRS and 2 (0.9%) with sepsis. There were no significant differences between those with and without infectious complication with regard to age, gender, stone size, presence of diabetes, or procedure duration. Those with infectious complication were more likely to have a positive intraoperative stone culture ($P = 0.01$), struvite stone composition ($P < 0.01$), staghorn calculi ($P < 0.001$), and multiple stones ($P = 0.02$).[11] Another study by Zhu L, *et al*. preoperative urinary tract infection (OR = 4.38, 95% CI:

Table 5: Regression analysis showing predictive factors of postoperative sepsis

Perioperative factor	Regression coefficient	CI (%)	Significance	Predictor
Age	−0.049	95	0.193	No
Sex	0.013	95	0.757	No
BMI	0.021	95	0.515	No
Patients with diabetes mellitus	−0.042	95	0.221	No
Patients with hypertension	−0.002	95	0.963	No
Patients with history of previous ipsilateral renal surgery	−0.010	95	0.744	No
Preoperative hemoglobin	0.049	95	0.344	No
Preoperative total leukocyte count	−0.034	95	0.315	No
Preoperative blood urea	0.026	95	0.530	No
Preoperative serum creatinine	−0.038	95	0.423	No
Patients on antiplatelets drugs	0.004	95	0.907	No
Patients with pyuria	0.099	95	0.032	Yes
Patients with positive urine culture	−0.104	95	0.030	Yes
Degree of hydronephrosis	−0.021	95	0.521	No
Stone size	0.038	95	0.359	No
Density of stone	0.021	95	0.531	No
GSS	0.036	95	0.436	No
Side of surgery	−0.014	95	0.634	No
Size of Amplatz sheath	−0.086	95	0.119	Yes
Position of stone intraoperatively	0.007	95	0.848	No
Site of puncture	0.107	95	0.002	Yes
Number of working tracts	0.025	95	0.430	No
Duration of surgery	−0.044	95	0.339	No
Postoperative hemoglobin	−0.69	95	0.122	No
Postoperative total leukocyte count	−0.038	95	0.483	No
Postoperative fever	0.913	95	0.001	Yes

BMI: Body mass index, GSS: Guy's stone score, CI: Confidence interval

1.15–9.53), multiple access (OR = 5.31, 95% CI: 1.23–10.75), diabetes (OR = 4.97, 95% CI: 1.37–9.86), length of operation ≥60 min (OR = 5.67, 95% CI: 2.24–13.42), estimated blood loss in PCNL ≥500 mL (OR = 2.78, 95% CI: 2.32–3.61) were the independent risk factors associated with postoperative infection.[12]

In our study factors related to sepsis were body mass index of patient (P = 0.0036), preoperative total count (P = 0.0043), density of stone (P = 0.0412), preoperative pyuria ($P < 0.001$), preoperative positive urine culture ($P < 0.001$), superior calyceal puncture ($P = 0.012$), postoperative total leukocyte count ($P < 0.0001$) and postoperative fever within 24 h ($P < 0.0001$). When regression analysis was done, those factors which were predictive of postoperative sepsis were preoperative pyuria (95% CI, $P = 0.032$), preoperative urine culture (95% CI, P = 0.030), superior calyceal puncture (95% CI, $P = 0.002$), and postoperative fever (95% CI, $P = 0.001$).

Conclusion

This study conducted at our institute shows perioperative predictors of postoperative bleeding and sepsis after PCNL. In this study, perioperative factors correlated to postoperative bleeding were stone size, density of stone, GSS, size of Amplatz sheath used, number of working tracts created, and duration of surgery, but those which were predictive of postoperative bleeding were size of Amplatz sheath and number of working tracts created only.

Perioperative risk factors correlated with sepsis were body mass index of patient, preoperative total count, density of stone, preoperative pyuria, preoperative positive urine culture, superior calyceal puncture, postoperative total leukocyte count, and postoperative fever within 24 h but only preoperative pyuria, preoperative urine culture, superior calyceal puncture, and postoperative fever were found to be predictive of postoperative sepsis.

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Conflicts of interest

There are no conflicts of interest.

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Review Article

Urinary Stones: Medical Dissolution and Monitoring

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Abstract

Surgical management is the cornerstone of urolithiasis treatment, but since prevention is better than treatment, we need to explore other measures for treating and especially for monitoring patients before recurrence. Several laboratory studies have performed testing of experimental treatments to reduce kidney stone formation and cellular damage and showed encouraging results. A few prospective and randomized studies proved the efficacy and safety of oral chemolysis for radiolucent stones. The purpose of this review is to present the most recent data regarding dissolution therapy and ways of monitoring stone patients.

Keywords: *Chemolysis, follow-up, medical dissolution therapy, nephrolithiasis*

Introduction

The cornerstone of urolithiasis management in most clinical settings is the surgical removal of stone burden even though it is well documented that prevention is better than treatment. Certain metabolic abnormalities are associated with a higher occurrence of stone diseases, such as hyperoxaluria, hypercalciuria, and hyperuricosuria. Medical dissolution therapy along with preventive measures is available, but long-term adherence is difficult, and efficacy is not well-proven. Although guidelines on urolithiasis management are available for many years, there is no standard pathway for follow-up of stone patients (primary and recurring), therefore the main goal of our paper is to establish a well-documented algorithm.[1] The aim of this review is to summarize the latest advances in medical dissolution therapy for stone disease and monitoring of this condition.

Materials and Methods

A literature search in Medline was conducted between 2019 and 2021, to identify all relevant titles to stone medical dissolution therapy. Our search algorithm consisted of the terms: Urolithiasis, medical dissolution therapy, potassium citrate, sodium bicarbonate, alkalizing agents. Reference lists of included articles were also searched for any relevant studies. Abstract/full-text screening was performed independently by two authors (L. T., A. S.) and disagreements were resolved on consensus.

Results

Urine pH and metabolic composition alterations are some of the main contributing factors in the formation and establishment of stone disease. Acidic pH can lead to crystallization of CaOx monohydrate and injury of renal cells while alkaline pH facilitates the formation of CaOx dehydrate, which is considered less pathogenic.[2] Potassium citrate is an alkalizing agent which goal is to increase urinary pH and citrate levels while reducing stone formation in patients with CaOx or urate stones with hypocitraturia, but long-term patient compliance is difficult due to gastrointestinal adverse events. It is also not advised for patients at risk for hyperkalemia or renal failure. Boydston *et al.*[3] examined whether sodium bicarbonate and potassium bicarbonate are effective as alkalizing agents, compared to potassium citrate and concluded that both agents increase urinary citrate, pH and CaP supernaturation, while CaOx supernaturation was reduced only with potassium citrate. Patients taking sodium/potassium bicarbonate showed a greater 3-month adherence of nearly 70% versus 58% with potassium citrate with lesser cost.[3] Medullary sponge kidney (MSK) is often complicated by nephrolithiasis,

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which affects quality of life in these patients. Cicerello *et al*.[4] report a clinically significant increase of urinary pH in patients with MSK and normal urine composition which was accompanied by a decreased need for invasive procedures during the follow-up of these patients. To study this context, Doizi *et al*.,[5] designed a randomized controlled trial (RCT) where patients with CaP stones and no hypercalciuria were administered potassium citrate or citric acid, which offers the citrates but is not accompanied by increase in urinary pH. The authors reported no significant increase in urinary citrate, pH, or ammonium with no difference in CaP crystal growth or saturation, between citric acid and placebo.[5]

Dietary advice are simple and applicable measures for stone recurrence prevention and there are present in nearly all urological guidelines worldwide. Citrate is a known stone formation inhibitor since it binds to calcium ions and prevents high urinary concentrations. Cheng *et al*.[6] tested two types of lemonade (diet and regular), which is a natural source of citrates, in patients with kidney stones, in a randomized trial. Patients in both groups showed increased urine output with no changes in urinary composition, except citrate which increased in diet and decreased in regular group.[6] Superannuation of CaOx decreased in diet group at an excess of nearly 800 calories daily for regular lemonade.[6] At a similar manner, Sromicki and Hess[7] evaluated the efficacy of simple dietary tips (increased fluid intake, limited consumption of oxalate and concurrent intake of calcium up to 1200 mg/day, limited intake of meat/poultry and sufficient amounts of fruits/vegetables) and reported increased urinary volume and calcium concentration, while urinary oxalate/urate and CaOx supernaturation were decreased by 21.5%.

Uric acid stones account for nearly 10% of stone composition and the main contributing factor for their formation is acidic urinary pH. The increased rates of obesity, metabolic syndrome, and its components like diabetes mellitus are believed to further increase the occurrence of this type of stone.[8] The European Association of Urology Guidelines suggest oral chemolysis for uric acid stone management, but the level of existing evidence is low.[9] Elbaset *et al*.[10] designed a RCT to compare efficacy of oral dissolution therapy with oral potassium citrate and ultrasound-guided safe working load or combination, for the management of radiolucent stones 1–2.5 cm and detected a better stone free rate and stone volume reduction in group receiving both treatments during a 3-month follow-up.[10] Gridley *et al*.[11] assessed efficacy of potassium citrate with or without allopurinol in renal urate stones and reported that 67% had complete response, 33% partial response with a median reduction of 68% in stone burden, while only 13% of patients underwent an axillary surgical intervention during a 3-month follow-up.[11] Similarly, Salem *et al*.[12] report a response rate of 65%, while Tsaturyan *et al*.[13] found a complete response at 61% of patients with a 22.1% requiring a surgical procedure during the 3-month period of follow-up.

Another trial evaluated the role of febuxostat 40 mg or 80 mg versus the standard treatment of allopurinol 300 mg for urate stones and detected that greater stone size reduction of serum uric acid level, occurred to the group of febuxostat 80 mg with a similar safety profile.[14] Theobromine exhibits a suspensory effect on uric acid crystal aggregation, therefore Hernandez *et al*.[15] designed a RCT to compare citrate versus citrate combined with theobromine for the treatment of urate or CaOx monohydrate/urate stones and found no statistically significant differences in clinical efficacy.[15] Finally, Elsawy *et al*.[16] found a stone free rate of 53.2% at 3 and 83% at 6 months. Despite a reported response rate of 53%–83% for oral chemolysis in urate stones, it is important to identify predictors of this response. Lower stone density,[12,13,16] smaller stone size,[12,13] and initial clinical response with higher urine pH at 3 months,[16] seem to independently predict success, while presenting did not offer additional information at regression analysis.

Traditional herbs are currently used in many countries and are considered complementary to modern medicine. Several studies have demonstrated the potential role of different plant extracts to stone disease management.[17-19] Plyllanthus niruri combined with B6 and magnesium, led to a stone-free rate (SFR) of 25% at 3 months[17] whereas patients who received black seeds (Nigella sativa L.) and suffered from stones 5–6.9 mm were most likely to experience stone expulsion or stone burden reduction compared to placebo.[18]

Since recurrence rates are high in urolithiasis, monitoring of patients is very important. Castiglione *et al*.,[20] assessed whether dephosphorylated and uncarboxylated Matrix-Gla-protein (dpucMGP) could predict recurrence at 5 years and concluded that it is not predictive of either stone formation or recurrence.[20] Lee *et al*.[21] tried to identify patient characteristics that led to the completion of a 24-h urine test and concluded that increasing age, family history of nephrolithiasis and renal colic as initial presentation increased the likelihood, while public insurance and neurogenic bladder led to a decreased proportion.[21] Yang *et al*.,[22] assessed the efficacy of kidney injury test on a spot urine sample for detection of nephrolithiasis and detected a higher score in patients with stones compared to healthy controls with a 95% accuracy, while obstructive disease led to an even higher score.

Conclusions

During the last years, major advances have been made in medical treatment of stone disease, which showed encouraging results for new molecules in stone era (tolvaptan, a-La, herbs) and enhanced the strength of evidence for older practices, like oral dissolution therapy

for uric acid stones. However, these should be further tested in larger-scale trials, before incorporating them into clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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Review Article

Renal Infarction: A Nonurologic Disease Mimicking a Urologic Emergency Event

Abstract

Renal infarction is a rare vascular disease describing the obstruction of the renal artery or its branches from blood clots formed in the vascular system of the patient. The correct diagnosis may prove to be a challenging procedure considering that the disease may mimic the symptomatology of urinary lithiasis or other urologic emergencies. A discussion of the diagnostic dilemmas, imaging modalities, treatment options, and prognosis of the disease, based on the more recent findings, is presented in this review.

Keywords: *Artery, infarction, kidney, renal*

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Introduction

Renal infarction (RI) describes the obstruction of the renal artery or its branches from blood clots formed in the vascular system of the patient.[1] It is a rare vascular disease, with an incidence as low as 0.004% to 0.007% of the diagnoses on admissions to the emergency department.[2] Surprisingly, in a study of 14,411 autopsies published in 1940, the incidence of RI was 1.4%.[1,2]

RI has traditionally been associated with heart diseases, such as atrial fibrillation or valve disorders, as well as with blood and vascular diseases, leading to hypercoagulative conditions. Considering that the kidney comprises end arteries with minimal overlapping of blood supply, it is estimated that 90 min of ischemia can lead to irreversible damage to the renal parenchyma.[3,4]

Clinical suspicion for this condition is usually low, given the fact that the disease can mimic acute pyelonephritis, renal colic, or other urinary diseases, thus engaging the urologist in the diagnostic process and treatment. The appropriate treatment is also poor defined, and different therapies have historically been applied. Various therapeutic schemes have been reported in the literature with various results in terms of preservation of renal function and survival rates.[1-10]

Herein, a brief narrative review of RI syndrome is attempted from the urologist's standpoint, and an overview of the diagnostic, therapeutic, and prognostic factors is provided.

Materials and Methods

MEDLINE/PubMed database was reviewed, using the terms renal, kidney, artery, and infarction. All abstracts were screened by the two authors of this manuscript, and relevant articles were identified. Emphasis was given in the more recent advances in the diagnosis and treatment of the disease. Case reports and retrospective case series were the main studies included in this review.

Etiology and predisposing factors

Several factors are involved with RI such as arterial hypertension, hyperlipidemia, atrial fibrillation, congestive heart failure, coronary artery disease, mitral valve disease, and cerebrovascular disease.[9-11] Of great importance is the deficiency of protein S and C and the past medical history of an embolic event.[4,8,12] Occasionally, RI has been associated with renal trauma.[4,13] In some patients, predisposing factors for the disease cannot be identified, and RI is characterized as idiopathic. The rate of idiopathic RI may be as high as 60%.[6] Recently, COVID-19 virus has been implicated in the development of thromboembolic events including the renal artery as well as the renal vein.[14,15]

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Symptoms signs and laboratory tests

Pain was the most common presenting symptom, located primarily in the lumbar area with detection rates ranging from 32% to 100%, followed by abdominal pain, nausea, vomiting, and fever. Hematuria and proteinuria are also common findings among patients with RI. During the first hours after pain onset, serum biochemistry and urinary studies indicative of tissue or cellular damage (e.g., serum lactate dehydrogenase (LDH) increase, hematuria, or proteinuria) may be absent; therefore, early diagnosis only from the features of the pain cannot be established.[9]

The median time from the onset of pain till the admission to the emergency department has been reported to be 10 h.[9] A median of 8 more hours till the diagnosis of RI was required corresponding to a median overall delay of 18 h.[9] Bolderman *et al*. reported a 6-h delay in idiopathic (noncardiogenic) population representing a significant improvement compared to older studies.

However, patients usually visited a physician, only after a median of 15 h from the onset of symptoms.[6] Doctors and patients should be aware and cautious about the possibility for RI to be developed. Patients with high-risk history should be instructed to visit the emergency departments, as soon as possible and physicians to promptly evaluate this group of patients with the proper panel of tests.

This panel of tests, apart from the urinalysis or dipstick, should also include total blood count and biochemical examinations including renal biochemistry and nonspecific indexes of tissue damage. However, in other reports the mean or median values of these tests were persistently moderately elevated across all case series.[5] On the contrary, very high levels of LDH have also been persistently published in the literature. Although it is a nonspecific for RI, these very high values could be an alarming finding. In most of the series of Table 1, the serum LDH was above the threshold of 1000 IU/L, while for most laboratories, the upper normal limit is approximately 280 IU/L.

AST/SGOT was also moderately elevated, but the indexes of renal function and particularly of serum creatinine levels were surprisingly almost normal. Similarly, the mean or median estimated glomerular filtration rare was normal ranging from 64 to 76 mL/min/1.73 m^2.[2,5]

Differential diagnosis and imaging modalities

RI is mainly misdiagnosed as renal colic in up to 20% of the cases, followed by acute pyelonephritis and/or urinary tract infection in up to 16% of the patients, obstruction of the mesentery artery in 16% of patients, and biliary tract disorders in 5% of the cases.[7] The disease may also be confused with acute myocardial infarction, congestive heart failure, and acute abdomen disorder. Other researchers have reported that RI can be misdiagnosed as renal colic up to 57%.[10,12]

Therefore, the urologist may be actively involved in the management of RI. High index of suspicious is required to avoid any delays in the correct diagnosis and foremost, a prompt and appropriate management to be offered to these patients. For these reasons, apart from the careful medical history taking and the physical examination of all the systems, targeted imaging tests requested.

The ultrasographic examination of the affected the kidney may be initially performed as a mean for early detection of the renal pathology. It may reveal renal lithiasis as a causative factor of the lumbar or abdominal pain or hydronephrosis. Ultrasograpy may also detect malignancies of the parenchyma or the collecting system causing hematuria. In patients presenting with RI, the findings of ultrasography are expected to be unremarkable. Doppler mode, however, performed by an experienced radiologist may define the impairment blood perfusion of the renal unit.[3] With the use of Doppler ultrasound mode the detection rate of RI throughout the literature ranges from 11% to 56%.[7,16]

Renal isotope scan is another imaging modality used for the diagnosis of RI. Correct diagnosis has been reported to be as high as 97%.[16] However, nuclear laboratory facilities are not always available on 24-h basis. Moreover, lack of perfusion cannot determine the etiology of a filling defect; this finding may be related not only with RI but also with disorders such as renal scarring, simple or complicated parenchymal cysts, or pyelonephritis.[7]

CT is nowadays an excellent modality for the diagnosis of urolithiasis in patients with renal colic. Imaging with or without iv contrast may also be used to determine other etiologies of acute pain such as gastrointestinal tract rupture, biliary tract disorders, and vascular diseases such as aneurysms, appendicitis, or other causes of acute abdomen syndrome. It can also reveal the presence of abdominal malignancies and determine the extent and the etiology of hydronephrosis. In RI cases, though, nonenhanced imaging usually fails to demonstrate the etiology of the pain. In the patients with inconclusive results in non-enhanced CT imaging, the administration of contrast agent could be performed. Apart from the confirmation of the diagnosis of RI, other challenging vascular disorders such as thromboembolism of the superior mesentery artery might be excluded as well.[7,8]

The typical findings of enhanced CT imaging comprise one or multiple wedge-shaped filling defects of the renal parenchyma or global hypoattenuation of the affected renal unit, compared with the healthy one. Infarcts involving >50% of the renal tissue are considered global. Smaller single or multiples lesions (<50% of the renal unit) are classified as focal or multifocal, respectively.[17]

Enhanced computed tomography (CT) scan is associated with high percentages of detection rate, being reported as

Table 1: An overview of the clinical manifestations of renal infarction as derived from the most recent studies

	Oh *et al*., 2016[5]	Yun 2015[1]	Bourgaul *et al*., 2013[2]	Hazanov *et al*., 2004[7]	Korzets *et al*., 2002[8]
Age (years), mean (median)	60.0 (range: 17-97)	61 (range 29-89)	52.9 (SD±16.6)	69.5 (SD±12.6)	67.4 (SD±21.1)
Pain lumbar	50	100	48.9	32	91
Pain abdominal	53		50.9	68	
Nausia	16.9	4	27.6		
Vomiting	13		20.2	43	27.3
Fever	10.3	45	20.2	41	45.5
WBC cells/μl (mean) (me dian), (range) (IQR)	11,100 (range: 1500-19,500)	12,900 (SD±4700)	11,000 (IQR 8100-13,480)		12,988 (SD±3841)
Urea (mg/dl)	14.0 (range: 4.8-58.2)				40.4 (SD±32.8)
Creatinine mg/dl	0.95 (range: 0.35-5.60)	1.2 (SD±0.5)	1.26 (IQR±0.98-1.67)		1.4 (SD±0.7)
LDH (IU/L)	656 (152-7660)	1096.6 (SD±735.2)	660 (IQR: 380-1417)	1100.2±984.6	1570 (SD±703)
AST/SGO T		60.1 (SD±48.7)		99.8±195.1	
Hematuria	31.7	40	48.3	54	
Proteinuria	12.1	53		45	
Pyuria		21			
Delay in diagnosis			5.4 days (SD±6.5)	>24 h (79.5%)	64 h (24-144)

In this table, the most comprehensive publications are presented. ANR: Above normal range, SD: Standard deviation, IQR: Interquartile range, WBC: White blood cell, LDH: Lactate dehydrogenase, AST: Aspartate aminotransferase, SGOT: Serum glutamic oxalacetic transaminase

high as 97.3%[5,7] Due to the advantages of CT scan over other imaging modalities, its noninvasive nature, the rapid execution, and the capability of examining the whole body, it should be performed as early as possible should RI is suspected.[9]

Digital subtraction renal arteriography is also a highly sensitive examination with detection rates approaching 100%. It is characterized by great invasiveness[3] and therefore is related with a higher risk of complications. In older series, particularly when CT tomographs were ill available, it was the diagnostic procedure of choice, but in contemporary series, arteriography has lost much of its popularity and is performed in selected cases only.[2,4,7] Nevertheless, arteriography may be associated with the delivery of thrombolytic agent directly on the obstructing clot as a measure for achieving recanalization of the artery.[3]

Treatment and Outcome

As mentioned previously, interventional procedures were more frequently performed in the past. Lessman *et al*. in 1978, apart from the administration of warfarin and heparine, performed embolectomy or nephrectomy in 17.6% of the cases. Nearly 23.5% of the patients died in less than a month from the diagnosis, primarily due to cardiovascular disorders. Therefore, the authors recommended aggressive treatment only in cases with bilateral RI.[10]

Recent studies reveal a shift of the management strategies toward less invasive procedures. As shown in Table 2, thrombolysis with arterial infusion of thrombolytic agents such as streptokinase, urokinase, or tissue plasminogen activator (tPA) is performed in <20% of the cases. More invasive strategies such as arterial bypass or nephrectomy are occasionally implemented too. The availability of the new generation oral and intravenous agents, such as coumarin derivatives, low-molecular-weight heparin, aspirin, and antiplatelet agents received either as monotherapy or in combination, is nowadays the preferred treatments with a reasonable risk of complications.[1,5,7,8]

In one of the largest multicenter series originating from France, the treatment of choice was mainly based on noninterventional procedures. Albeit arteriography was performed in one out of three of the patients, concomitant thrombolytic procedures (intra-arterial urokinase infusion, thromboaspiration, and renal artery stenting) were implicated in only 5% of the participants. In these patients, warfarin or coumarin derivatives with or without antiplatelet agents were the preferred treatment. With this therapeutic strategy, a mortality rate of <1% was achieved.[2]

Optimal results have been reported by Bolderman *et al*. in the subgroup of patients without any history of previous cardiovascular events (idiopathic subgroup comprising the 59% of the total group). With the use of combination of antithrombotic and antiplatelet drugs and without the use of any invasive therapy, renal function was preserved and no deaths were occurred. In this subgroup, RI could be attributed only to smoking and arterial hypertention. On the contrary, those with diabetes mellitus, coronary artery infarction, atrial fibrillation, previous thromboembolic event, and/or cardiovascular family history (41% of the total group) experienced worse outcomes with a mortality rate of 18.2%.[6]

Table 2: Overview of the treatment and outcome of renal infarction in the more recent case series

Treatment	Oh *et al*., 2016[5]	Yun 2015[1]	Bourgaul *et al*., 2013[2]	Hazanov *et al*., 2004[7]	Korzets *et al*., 2002[8]
Heparin unfractionated (%)	81	0			36.4
LMW heparine (%)		0			
Warfarin (%)	78.2	100	38.3		18.2
Coumarin derivatives (%)					
Antiplatelet (%)	37.2		35.1	6.8	
No treatment (%)	7.5	0		6.8	
Thrombolysis	4.5	0	5.3	15.9	9.1
Streptokinase/urokinase/tissue plasminogen activator arterial infusion (%)					
Other interventions angioplasty, bypass, nephrectomy (%)		0		2.2	
ESRD (%)	2.1	9% in 1 year 18% in 3 years	6.3	8	10
Mortality (%)	5	23.4 of any cause	0% (<1 months) 1% total	11 (<1 months)	0

In this table, the most comprehensive publications are presented. LMW: Low molecular weight, KI: Kidney injury, ESRD: End-stage renal disease

The rate of diagnosis of acute renal injury following RI ranges from 10.9% to 18%. As it is shown in Table 2, the short-term incidence of ESRD was <10%, whereas the midterm rate was almost 20%.[5-7] Regarding the robust end point of mortality rate, a minimum of 0% up to a maximum of 23.4% is encountered.[5] This maximum value, however, is related with death of any cause after a long-term follow-up.[1] In most of the recent series, the mortality rate is <11% during the 1st year of follow-up.[3,5-8]

Outcome

The ideal treatment of patients with RI is yet to be determined. Intravenous heparin, oral warfarin, with or without rivaroxaban have been examined in respect to the mortality rate and have been compared with a nontreatment group. The treatment scheme exerted a protective role, considering that those who received anticoagulant therapy experienced a 92% improved survival compared to the nontreatment arm (hazard ratio 0.08, 95% confidence interval: 0.02–0.34).[18] Similar studies regarding the possible protective role of thrombolytic agents or surgical interventions has not been performed so far.

Apart from the oral anticoagulants, the outcome of patients with RI may be influenced by the duration of ischemia. The classical teaching supports that, after 90 min of complete normothermic occlusion of the artery, irreversible damage of the renal parenchyma is expected. However, in none of the series, any of the patients has been treated as early as in 90 min from the ischemia onset. In one study, a delay of more than 24 h was recorded in 80% of the patients, whereas in two other studies, the median delay in diagnosis was between 64 h and 5.4 days. However, despite this delay, the morbidity and mortality rates were both acceptable, ranging from 6.3%–10% for end-stage renal disease requiring hemodialysis and from 0% to 11% for 1-month post event mortality [Table 2].[2,7,8]

It seems that other factors also determine the outcome. According to an observational study by Gasparini *et al*., the extent and degree of renal artery occlusion may be an important factor for the preservation of renal function. Surprisingly, in this study, renal function was salvaged in 17% of the patients, when the duration of ischemia was <10 h, whereas for longer ischemia time, the preservation of renal function was over 66%. An explanation for this finding may be that a collateral flow may be developed in the kidney, bridging the renal artery branches with others from the inferior adrenal, ureteral, and capsular arteries.[4,12]

The long-term outcome of RI is still under investigation. Based on 47 patients with a mean age of 61 years, 19% of the patients experienced recurrent thromboembolic events outside the renal vasculature. Dialysis-free survival rate was approximately 64% at 5 years, after long-term anticoagulation oral therapy. Deaths were related with over vascular disorders including myocardial infarction, congestive heart failure, cerebral infarction, superior mesenteric artery embolism, and gastric cancer. It is assumed that RI is a systematic disease affecting all the cardiovascular system and caution should be undertaken toward avoiding new vascular events. Therefore, these patients should be referred to a physician specialist for vascular diseases (e.g., a vascular surgeon).[1]

This review study represents a nonsystematic evaluation of retrospective single-arm case series. Included studies are based on a limited number of participants, nonstandardized diagnostic procedures, and treatment is based on the preferences of the responsible physicians. Caution should be exercised during comparison of the end points of different studies in respect to renal function preservation, complications rates, and cause of death. Prospective randomized trials have not been conducted so far, and the presented results and recommendations broadly reflect

experts' opinions. All the aforementioned should be considered as limitations of this review.

Conclusion

Lumbar and/or abdominal pain and hematuria may be the misleading symptoms in patients with RI, leading to the involvement of the urologist in the management of this disease. Investigation for acute RI should be implemented in patients with relevant history and an inconclusive initial diagnostic workup is inconclusive. High-risk patients should be informed about this rare condition, and the importance of prompt admission to the emergency department. A group of trained physicians should be involved in the management of these patients including a specialist in internal medicine, an interventional radiologist, a vascular surgeon, and perhaps urologist, nephrologist, and intensive care unit specialist. A good cooperation of this multimodal medical team is of utmost importance for avoiding unnecessary diagnostic and therapeutic delays and for the administration of prompt treatment.

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Conflicts of interest

There are no conflicts of interest.

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Recurrence of Primary Hydrocele 1 Month after Hydrocelectomy in a 35-Year-Old Patient

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Abstract

A hydrocele is a painless enlargement of the scrotum resulting from an irregular accumulation of serous fluid between the parietal and the visceral layers of the tunica vaginalis which surrounds the testis To treat hydrocele various modalities are used, the gold standard of which being open hydrocelectomy. Hydroceles can sometimes be recurrent. Rarely, in these cases, an underlying pathological condition such as hypoproteinemia, filarial infection, pelvic cavity malignancy, or a concurrent inguinal hernia is found during investigation. This paper describes a rare case of hydrocele recurrence immediately after open hydrocelectomy. The presence of intact tunical anatomy of the scrotum found during revision hydrocelectomy in our case raised questions concerning the extent of the previous excision and as such recurrence should be attributed to the uninverted remaining tunical sack.

Keywords: *Hydrocele, hydrocelectomy, recurrence*

Introduction

A hydrocele is a painless enlargement of the scrotum resulting from an irregular accumulation of serous fluid between the parietal and the visceral layers of the tunica vaginalis which surrounds the testis. It is estimated to affect 1% of all adult men and can be divided into primary (or idiopathic) and secondary hydrocele.[1,2] The etiology of primary hydrocele is considered to be an imbalance between secretion of fluid inside the tunica vaginalis of the testis and its absorption through lymphatic channels secondary hydrocele can result from trauma, infection, or even neoplasms (e.g. rhabdomyosarcoma, mesothelioma, adenocarcinoma, and neuroblastoma). The vast majority of hydroceles are primary and a particular etiology can rarely be identified.[2,3] Although most hydroceles are of little clinical significance requiring conservative management, some cases of large hydroceles can cause esthetic problems or even become symptomatic causing awkwardness or pain during walking and will require treatment.[4-6] Transillumination of scrotum during the clinical examination can facilitate differential diagnosis of hydrocele from other causes of scrotal swelling. Nevertheless, the gold standard diagnostic modality is the scrotal ultrasound setting the diagnosis in the vast majority of cases. To treat hydrocele various modalities are used, the gold standard of which being open hydrocelectomy. Less invasive alternatives such as aspiration and/or sclerotherapy have also been proposed. The less invasive nature of these modalities, resulting in less complications and morbidity has attracted renewed interest.[7] Finally, hydroceles can sometimes be recurrent. Rarely, in these cases, underlying pathological conditions such as hypoproteinemia, filarial infection, or pelvic cavity malignancy are found during investigation. A concurrent inguinal hernia should also be excluded from the study.[3] In this paper, a case of hydrocele recurrence immediately after open hydrocelectomy will be described.

Case Report

A 35-year-old man presented to our department complaining for a painless enlargement of his right scrotum. The patient reports that he had been subjected to ipsilateral hydrocelectomy 2 months before for a large hydrocele present since 2 years back. Postoperatively, the patient reported an uneventful period with his scrotum regaining normal appearance within the

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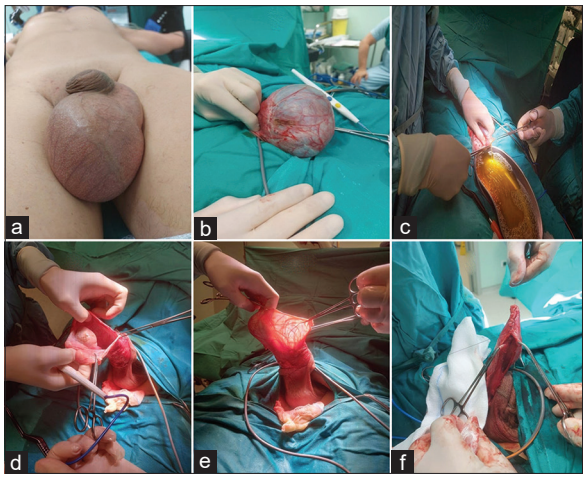

Figure 1: Revision of the hydrocelectomy performed in our department. (a) Preoperative appearance of recurrent hydrocele (b) operative picture before opening the visceral layer of tunica vaginalis (c) evacuated liquid (d) tunical sack after fluid evacuation (e) tunical excision using transillumination to avoid injury of scrotal contents (f) eversion of tunica vaginalis behind the testis

first 2 weeks after surgery. Then, his scrotum started dilating again reaching the initial size of preoperative dilation within a month time after surgery. The clinical and ultrasonic evaluation revealed the presence of a big recurrent unilateral hydrocele with no other clinical pathology such as a concurrent inguinal hernia. The patient had no other comorbidities and underwent a hydrocelectomy revision with the excision of excessive tunica vaginalis and eversion behind the testis. Despite the previous surgery, the testicular tunics looked relative intact during surgery, calling into question the extent of the previous excision. The hydrocele's liquid was sent for bacterial culture, parasitological examination, malignant cytology, and acid-fast bacilli staining. The whole lesion was sent to a pathologist after its excision. No pathology or malignancy was found in both surgical specimen and hydrocele fluid. Three months after the revision of the hydrocelectomy, the patient remained asymptomatic with no evidence of recurrent hydrocele formation [Figure 1].

Discussion

Several different techniques have been described for the definite treatment of hydrocele including open surgery as well as less invasive options such as aspiration and sclerotherapy. Less invasive methods demonstrate less morbidity than surgery at the cost of a higher recurrence rate and less long-term patient's satisfaction. Concerning sclerotherapy, numerous chemical substances have been documented in the literature including tetracycline, sodium tetradecyl sulfate, polidocanol, fibrin glue, phenol, OK-432, ethanolamine oleate, antazoline, rifampicin, and talc. All these sclerosing agents cause adherence of the walls of the sac, limiting the production of fluid.[7]

Regarding the surgical treatment of hydrocele, the three most common corrective surgical techniques are the Jaboulay procedure (eversion of sac followed by sewing the edges together behind testicle), conventional hydrocelectomy (excision of sac with oversewing of edges), and Lord's procedure (drainage of hydrocele fluid with plication of the parietal layer of tunica vaginalis). The difference between the Lord's procedure with hydrocelectomy and the Jaboulay procedure is that minimal dissection between the layers of Dartos and tunica vaginalis takes place, avoiding the release of the hydrocele sac outside of the scrotum. Tsai *et al*. compared the recurrence rates and the postoperative complications between these three different techniques. They observed no difference in recurrence rates between them. However, Lord's repair was associated with the lowest overall rates of complications and of postoperative hematoma, establishing Lord's repair as an effective and safe choice in treating hydroceles.[8]

Recurrence of hydrocele after surgical correction such as in the case presented in this article is generally rare. Any recurrence of hydrocele after therapeutic interventions should raise suspicions for underlying medical conditions such as hypoproteinemia, filarial infection, pelvic cavity malignancy, or concurrent inguinal hernia. In our case, no underlying cause was found despite thorough investigation. The presence of intact tunical anatomy of the scrotum found during revision hydrocelectomy in our case raised questions concerning the extent of the previous excision and as such recurrence should be attributed to the uninverted remaining tunical sack.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

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Case Report

Bilateral Synchronous Testicular Mass from Testicular Adrenal Rest Tumors, in a Patient with Congenital Adrenal Hyperplasia, or Testicular Leydig Cell Tumors? Dilemma for Bilateral Orchiectomy or Not

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Abstract

Congenital adrenal hyperplasia (CAH) refers to a group of autonomic disorders due to enzyme deficiency for the biosynthesis of steroid hormones. These disorders entail an increase in ACTH levels and as followed by adrenal hyperplasia. CAH is categorized into two types, classic and non-classic. In the common type we have a deficiency of 21-hydroxylase observed in a prevalence of 1 per 5000 per 145,000 births. We have insufficient aldosterone and cortisol production and as a result, elevated plasma ACTH levels, with subsequent disorders that this entails, depending on the level of deficiency. Testicular adrenal rest tumor (TART) develops from isletsectopic adrenal tissue within the gonads, directly affected by ACTH overproductions a complication of CAH, with a prevalence ranging from 27% to 47%. These are benign tumors that are recognized as palpable masses. A biopsy of these tumors is recommended as well as their surgical removal, so as to rule out malignancy.In this case report we present a case of bilateral synchronous TART tumor in association with medullolipoma in a patient with CAH. The dilemma arises regarding the decision of bilateral orchiectomy.

Keywords: *Bilateral synchronous testicular mass, congenital adrenal hyperplasia, testicular adrenal rest tumor, testicular Leydig cell tumors*

Introduction

Congenital adrenal hyperplasia (CAH) refers to a group of autosomal recessive disorders due to enzyme deficiency in the biosynthesis of adrenal steroids. These cause elevated adrenocotropic hormone (ACTH) levels and adrenocortical hyperplasia.[1] CAH may be divided into two basic types, the classic and the nonclassic one. The most common cause is 21-hydroxylase deficiency with an incidence 1/5.000–145.000 births, which blocks in the production of aldosterone and cortisol, leads to high plasma ACTH, causing virilizing syndrome, cortisol deficiency, and variable salt-wasting syndrome, depending on the extension of enzyme defect.

Testicular adrenal rest tumors (TARTs) develop from islands of ectopic adrenal tissue within gonads, stimulated by ACTH hypersecretation, as the compilation of CAH, with a prevalence ranging from 27% to 47%.[2] They are benign tumors presenting as palpable mass. Tissue biopsy is recommended and surgical removal may be performed to exclude a malignant neoplasm.

We report a case of bilateral synchronous TART associated with myelolipoma in a CAH patient and the dilemma of bilateral orchiectomy or not.

Case Report

A 34-year-old male who was known to have the CAH classic salt-wasting type diagnosed since birth was being treated insufficiently with fludrocortisone and hydrocortisone. He presented to the urology clinic with synchronous bilateral testicular masses and mild orchialgia in the right testis. He mentioned precocious development of secondary sexual characteristics at an early age and short stature.

Table 1 presents the laboratory tests of the patient. He underwent an Ultrasound study and an Abdomen – Thorax computerized Tomography.

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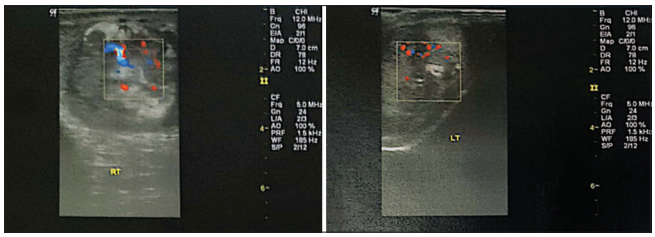

Figure 1: Right and left testis ultrasonography

Figure 2: Abdomen and pelvic computed tomography

Table 1: Laboratory Tests

Tumor markers	Fluid Serum	Normal value	Unit of measure
CEA	1.80	≤5	ng/mL
AFP	1.88	≤0.89-8.78	ng/mL
CA-125	9.00	≤35	U/mL
CA-15.3	16.60	≤31.3	U/mL
CA-19.9	10.95	≤37	U/mL
T.PSA	0.50	≤4	ng/mL

CEA: Carcinoembryonic antigen, CA125: Carbohydrate antigen 125, CA 15-3: Cancer antigen 15-3, CA19-9: Carbohydrate antigen 19-9, T.PSA: Total prostatic antigen

Ultrasound

Testicular parenchymal abnormality of ultrasound imaging with excessive blood supply. The right testis appeared to be larger than normal, with inhomogeneity of the whole parenchyma. The upper pole of the left testis also appeared inhomogeneity [Figure 1].

Abdomen-thorax computerized tomography

The right testis appeared to be lobar with increased contrast mediaabsorption. Furthermore, the left testis had some similar suspicious imaging characteristics. Mesenteric or retroperitoneal lymph nodes were not detected. The rest of the abdomen organs appeared to be normal [Figure 2].

Furthermore, computed tomography of the thorax had not revealed any metastatic masses.

Considering the possibility of malignant testicular neoplasm, the patient underwent right testicular biopsy and left orchiectomy. Macroscopically, the specimen (brown, firm mass) from the right testis measured 2.2 cm × 1 cm × 1 cm. with no evidence of necrosis or hemorragia. The left testis was oval with prominent vessels in the surface, measured 5.8 cm × 3.5 cm × 3 cm, with a segment of spermatic cord 9 cm long. The cut surface revealed a well-circumscribed 4.3 cm lesion, pale tan fleshy with areas of hemorrhage. No tumor was noted in the epididymis or spermatic cord.

Microscopic examination of the first material showed sheets or nests of large round and polygonal cells with abundant eosinophilic granular cytoplasm and round central nuclei, with rare gigantic hyperchromatic figures, separated by bands of fibrous tissue. The cells contained golden brown pigment consistent with lipochrome. No Reinke's crystals were identified. No testicular parenchyma was present.

The left testicular lesion comprised sheets or nests of cells histologically similar to the described ones of the right testicular biopsy. It must be mentioned that the cellular population were separated by myeloid and erythroid precursor cells in different stages of maturation with numerous scattered megakaryocytes admixed with apidocytes.

Immunohistochemical analyses were performed: positive staining for Melan A, inhibin, CD56, and negative staining of AR, PLAP, CD30, AFP, and HCG. The Ki67 index was low.

Based on the findings, a diagnosis of bilateral TART associated with myelolipoma was established.

Discussion

TART is a rare benign tumor in the testis that occurs secondary in patients with CAH. CAH is a group of autosomal recessive disorders related to enzyme deficiencies in the adrenal steroidogenesis pathway, which leads to impaired corticosteroid biosynthesis. Mutation of the steroid-hydroxylase gene (CYP21A2) located at chromosome 6p21 is responsible for 95% of the CAH cases.[3]

CAH has two major forms depending on the extension of the enzyme defect: Classic form, which includes salt wasting and simple virilizing and nonclassic, which is the mild form of disease.[3,4] In over 90%, the deficient enzyme is 21-hydroxylase.[5] The level of ACTH driven by negative feedback regulation increases and leads to hypertrophy of the adrenal glands.[5,6]

During embryonic adrenogonadal development, abnormal adrenal cells end up within the testis. Such cells are reported to exist in the testis of 15% healthy neonates.[1,6] These cells lead to the development of TART because of high ACTH levels, particularly in those of inadequate long hormone control stimulating their proliferation,[7] gonadal dysfunction, and infertility.[6,8] As far as the relationship of ACTH level and TARTS's size is concerned, some studies reported that TART cells have ACTH receptors while other studies suggested the involvement of other growth-promoting factors.[6]

The reported prevalence of TARTs in patients with CAH ranges from 27% to 47%. These lesions are typically

located within the rete testis and are bilateral, synchronous, nodular, and multiple. Lesions are palpable and/or ultrasound detectable.

Histopathologically, TARTs resemble adrenocortical tissue, with large polygonal cells with abundant granular eosinophilic cytoplasm arranged in strands, cords or lobules, containing lipochrome pigment.[9] The mitotic activity is low. Reinke crystals are absent. The adjacent testicular parenchyma is atrophic with reduced or absent spermatogenesis.[8] Immunohistochemically, TART shows diffuse and strong positivity for CD56, focal or diffuse reactivity for synaptophysin and negative reactivity for the androgen receptor and inhibin.[3]

TART should be suspected not only in CAH patients but also in all men with potentially high ACTH levels (Cushing syndrome, Addison's disease, adrenalectomy).[5] In some cases, doctors misdiagnose them as malignancies. It is necessary to discriminate TART from Leydig cell tumors (LCT) because they are closely related and share morphological characteristics. TARTs have benign behavior, being removed only after severe orchialgia or testicular parenchymal damage from large tumors. LCTs are less commonly bilateral (3%) and nonresponsive to corticosteroid therapy, with the presence of Reinke crystals. 10% of them are malignant.[3] LCT displays negative reactivity for CD56 and synaptophysin but positive reactivity for the androgen receptor.

Medical management is preferred since TARTs are potentially reversible by the reduction in plasma ACTH level after sufficient steroid therapy.[5,9]

Myelolipoma is an uncommon benign neoplasm of the adrenal gland, composed of apidose tissue and benign hematopoietic elements.[3] The hematopoietic elements contain myeloid, erythroid, and megakaryocytic lineages showing normal maturation. Rarely, foci of metaplastic ossification may be observed, and areas of infarction, hemorrhage, or thrombosis can occur. Myelolipomas are usually incidental findings, accounting for up to 9% of adrenal incidentalomas. They are asymptomatic and vary considerably in size, but some are quite large, causing compressive symptoms. They may also occur in other extra-adrenal sites.

The origin of adrenal myelolipoma is not clear. It has been suggested the differentiation of ectopic hematopoietic stem cells or cells of the mesenchyme of ectopic adrenal tissue.[10]

Myelolipomas have been reported in patients with CAH, supporting the role of hormonal stimuli in their formation.[11] The majority is localized in the adrenal gland, but there are references of myelolipomas in other locations, such as testis.[12] Specifically, the finding of testicular myelolipoma-associated TARTs, as in our case, suggests that other intrinsic factors related to the presence of adrenal cortical (like) cells play a role in the formation of myelolipoma. There is an association between ACTH excess[11] and the development of adrenal myelolipoma, but the direct causal link remains to be established. The prevalence of myelolipomas in CAH is 7.4%.[3]

The knowledge of the histological and immunohistochemical features of TART, in association with the patient's history, may allow preservation of fertility and avoidance of unnecessary surgical procedures in the case of testicular tumors. Testicular imaging is necessary to monitor males with CAH and should initially be performed in early adolescence.

Ultrasound is recommended as an imaging modal choice in detecting and monitoring these lesions. While computed tomography may be useful for some individuals who require extremely accurate preoperative assessment.

Imaging findings are nonspecific and difficult to differentiate from malignancy. Histologically, TART may look similar to Leydig cell hyperplasia, causing a diagnostic dilemma in these cases and leading to unnecessary surgery.

It is necessary to distinguish TART tumors from LCT because they are closely related and share morphological features. TARTs have good behavior, they are removed only after severe orchial pain or testicular damage to the parenchyma.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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