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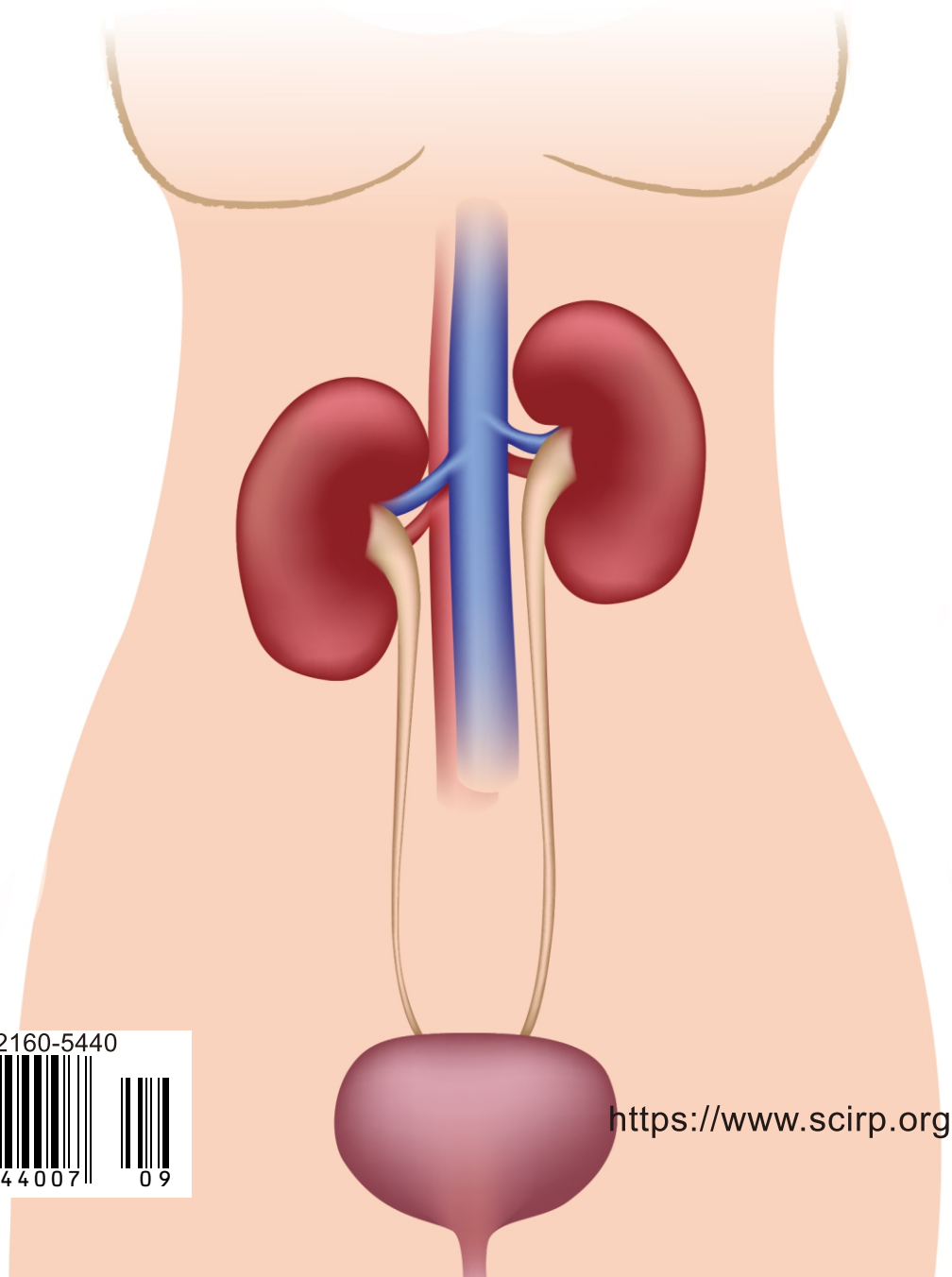

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Can Computerized Hounsfield Unit Estimation Be Used as Predictor for Ureteric Stone Localization by Fluoroscopy during Extra Corporal Shock Wave Lithotripsy and Ureteroscopy?

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Abstract

Current minimally invasive interventions for ureteric stones involve either ESWL or Ureteroscopy and stone localization is mandatory for successful treatment in both. **Objectives:** To avoid doing KUB radiograph before ESWL routinely by correlating the stone attenuation value on CT KUB with stone visualization at fluoroscopy. **Methods:** This is a prospective cross sectional hospital based, Multicentric study carried out on 1010 patients with ureteric stones in Sudan from August 2014 to March 2016. **Results:** Mean stone density in HU was 704.45 ± 300 (SD) ranging (81 - 1873) HU. All of the stones were localized using fluoroscopy and only 26.5% of them were not seen under fluoroscopy. I.V contrast was used mostly, and also mainly in the upper ureter. More than 80% of the application of contrast through the ureteric catheter was in the lower ureteric stones. 91.2% of patients with stone density ≤ 400 HU failed to appear at fluoroscopy and therefore 400 HU attenuation value can be used as a cut-off level to request doing KUB before ESWL and Ureteroscopy. **Conclusion:** the ureteric stones with density ≤400 HU the likelihood of being non-visualized at fluoroscopy is 91.2% therefore if the stone has ≤400 HU at CT KUB it is mandatory to do KUB before treatment above that it is most likely to be seen at fluoroscopy and no need to request KUB for them before ESWL or URS. 1) **Inclusion Criteria:** All patients diagnosed by CT scan to have ureteric stones for ESWL or Ureteroscopy. 2) **Exclusion Criteria:** Patients for whom treatment of ureteric stone by ESWL or ureteroscopy is not indicated like severe infection or poor kidney function where

nephrectomy is needed.

Keywords

Ureteric Stones, Hounsfield Unit, Attenuation, KUB, CT KUB,
Cut off Level, Visualization of Ureteric Stones, ESWL, Ureteroscopy

1. Introduction

Urinary calculus is the third most common urological problem after urinary tract infection and prostate disease with a lifetime prevalence of urolithiasis at 10% - 15% [1]. Ureteral stones may cause ureterohydronephrosis and acute pyelonephritis with pain and patients may need immediate and rapid medical intervention, the size, localization, and composition of the stone, the severity of the obstruction, symptoms and the anatomy of the urinary system are all involved in determining the proper treatment approach [2]. NCCT and IVU both reliably determine stone position [3] [4] [5]. This is important for ureteric calculi where location, along with stone size and obstruction are the main factors in deciding treatment [6].

Computed tomography (CT) has long replaced the plain abdominal radiograph as the gold standard in the diagnosis of urolithiasis [7]. It is now firmly recognized as the best imaging method for establishing the diagnosis of acute ureteric colic and is replacing intra-venous urography (IVU) at an increasing number of centers [8]. In computerized tomography (CT), the Hounsfield unit (HU) is used to assess tissue and body fluid density. In urinary system calculus, HU is useful in assessing the compactness of individual stones [9]. Previous studies conducted on this subject have demonstrated a reverse correlation between the HU and extracorporeal shock wave lithotripsy (ESWL) for stone breakability [10] [11]. In addition, it has been shown that the Hounsfield density (HD) value, obtained by dividing the HU value of the stone by its dimensions can determine the composition of the stones [12]. Advances in ureteroscope design and ongoing development in ESWL have resulted in a change in the balance in the use of these treatment modalities in the management of ureteric stones, ESWL is now the most widely used method of managing proximal ureteral calculi [13] [14]. Fluoroscopy is the only possible method used for ureteric stone localization during ESWL and Ureteroscopy, there are ureteric stones which are not seen under fluoroscopy during ESWL and Ureteroscopy and this is suggesting that, there's some ureteral stone with a HU estimation that can be correlated with a radio-opaque stone and can be sent to the shockwave lithotripsy or ureteroscopy right away, whereas others ureteral stones with a HU estimation that can correlate with a radiolucent stone which needs the injection of contrast medium for localization by fluoroscopy during ESWL and Ureteroscopy.

In this study, we try to use the CT sonogram attenuation value of a stone to

predict its appearance under fluoroscopy during ESWL and Ureteroscopy without the need for a preoperative KUB. And by that patient can avoid having to undergo a plain abdominal radiograph as routinely and can be well prepared for the possible use of contrast.

2. Objectives

To avoid doing KUB radiograph routinely by correlating the stone attenuation value on CT KUB with stone visualization at fluoroscopy.

3. Methodology

A prospective descriptive cross-sectional, hospital-based multicenter study of all patients with ureteric stones who undergoing ESWL or ureteroscopy from august 2014 to march 2016.

Patients' selection:

Inclusion criteria: All patients diagnosed by CT scan to have ureteric stones for ESWL or Ureteroscopy. Exclusion criteria: Patients with severe infection or poor kidney function when URS or ESWL are not indicated.

Sampling: statistician consultation for the quantity needed for proper representation of Sudanese patients with ureteric stones.

Methods of data collection: Standard structured forms were filled in an interview with the patients by the researcher.

Data management and analysis plan: The data has been fed to Statistical Package for Social Sciences (SPSS) version 17, Illinois-Chicago©.

Ethical consideration: Ethical approval was obtained from the council of Urology, the ethical committee of SMSB, and the Hospital directorate. Verbal consent was obtained from the patients.

4. Results

1010 patients were included in our study; the mean age was 37.6 years ranging from 1 - 90. Two third of the patients were males, and more than half of them came from the countryside. More than half of the stones were in the upper ureter, 26.1% were in the lower ureter, and only 20.7% were in the mid ureter. Pie chart in **Figure 1** shows the distribution of the stone site. Mean stone density in HU was 704.45 ± 300 (SD) with a minimum density of 81 HU and a maximum of 1873 HU.

93.3% of the patients had an X-ray-KUB film, of which most of the stones were visible 75%. All of the stones were localized using fluoroscopy and only 26.5% of them were not seen under fluoroscopy. Most of the stones (84.1%) were treated by ESWL. In correlation of the operator and the treatment plan using the Pearson Chi-square test, it was found that the bulk of cases was done by the registrars, 50.9% ESWL and 63.8% URS, and the rest were done by (residents) medical officers (MO) and consultants.

In correlation with the fate of the stone and the operator using the Pearson

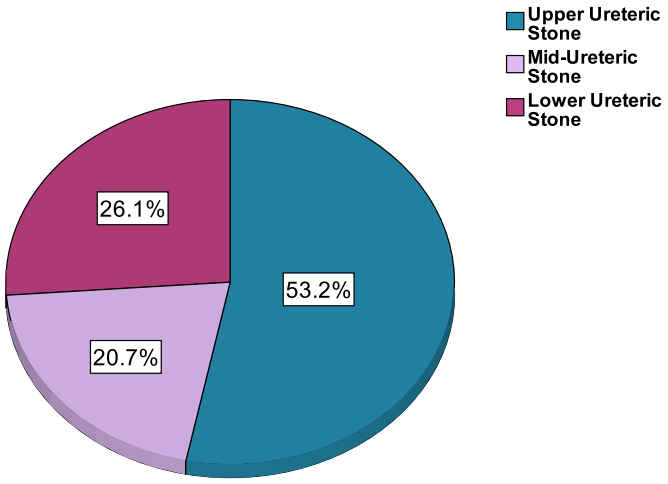

Figure 1. Pie chart shows the distribution of the stone site in percentages.

Chi-square test, it was found that the majority of nonvisible stones were operated by the registrars and most IV contrasts were used by them in 65.9% of cases. Failure of localization was in 20 cases 70% of them were among the registrar as an operator. *P* value was 0.001. The majority (65.7%) of nonvisible stones were localized using IV contrast injection. 13.8% localized by contrast injection through a ureteric catheter and 13.1% only by passages of a ureteric catheter. Failure of localization was in 7.5% of the cases and their procedure was postponed. See Table 1.

In correlation with the fate of the stone and the treatment plan (ESWL vs. URS), it was found that 12 (1%) of the patients had both of the procedures. On the other hand, (95%) of the failure rate was ESWL (19 patients). See Table 2.

Correlation using the Pearson Chi-square test between the site of the stone and the appearance under fluoroscopy signified that the majority of nonvisible stones were in the lower ureter 116 (43.3%), 32.1% were in the upper ureter, and 24.6% in the mid ureter. See Table 3. *P* value was 0.001.

The fate of the nonvisible stone has been further correlated with the site of the stone using the Pearson Chi-square test as clear in Table 4. I.V contrast was used mostly, and also mainly in the upper ureter. More than 80% of the application of contrast through the ureteric catheter was in the lower ureteric stones, and also the ureteric catheter. *P* value 0.001. 45% of failure of localization occurred in the lower ureter (9 cases). Density has been grouped in 400 HU apart, except the last group ranged from 800 to 1837. In correlation of the grouped densities with appearance under fluoroscopy using Pearson Chi-square test, densities up to 400 HU total numbers of patients were 181; stones that were not seen under fluoroscopy were 165 (91.2%).

On the other hand, the number of patients with a stone density of more than ranging from 400 - 800 HU was 448, and 99 (22.1%) were not seen and those with a stone density of more than 800 HU were 381, and only 1% of them not

Table 1. Shows the correlation fate of non-visible stones.

	IV contrast injection	Contrast injection through the ureteric catheter	Passage of Ureteric Catheter only	Postponed	Total
Non-Visible stones under Fluoroscopy	176	37	35	20	268
Percentage	65.7%	13.8%	13.1%	7.5%	100.0%

Table 2. Shows the correlation between the treatment plan and the fate of the nonvisible stone.

Non-Visible Stone	ESWL	URS	Total
IV contrast injection	176	0	176
	100.0%	0.0%	100.0%
Contrast injection through the ureteric catheter	1	36	37
	2.7%	97.3%	100.0%
Passage of Ureteric Catheter only	11	24	35
	31.4%	68.6%	100.0%
Failure of localization	19	1	20
	95.0%	5.0%	100.0%
Total	849	160	1010
	84.1%	15.8%	100.0%

Table 3. Shows the appearance of the stone under fluoroscopy in correlation to the site of the stone.

Visibility Under Fluoroscopy	Upper Ureteric Stone	Mid-Ureteric Stone	Lower Ureteric Stone	Total
Visible	451	143	148	742
	60.8%	19.3%	19.9%	100.0%
Non-Visible	86	66	116	268
	32.1%	24.6%	43.3%	100.0%
Total	537	209	264	1010
	53.2%	20.7%	26.1%	100.0%

seen under fluoroscopy. *P* value was 0.001

Correlation between the grouped densities and the treatment plan was done to assess the integrity of the decision made. >80% of the patients with densities less than 400 HU underwent ESWL when only 8.8% of them were seen under fluo

Table 4. Shows the fate of the nonvisible stone in correlation with the site of the stone.

Nonvisible stones	Upper Ureteric Stone	Mid-Ureteric Stone	Lower Ureteric Stone	
IV contrast injection	67 (38.1%)	52 (29.5%)	57 (32.4%)	176 (100%)
Contrast injection through the ureteric catheter	5 (13.5%)	2 (5.4%)	30 (81.1%)	37 (100%)
Passage of Ureteric Catheter only	8 (22.9%)	7 (20%)	20 (57.1%)	35 (100%)
Failed	6 (30%)	5 (25%)	9 (45%)	20 (100%)
Total	86 (53.2%)	66 (20.7%)	116 (26.1%)	268 (100%)

Table 5. Shows the relation between grouped densities and the fate of the stone.

		Categorized densities (HU)			
		<400	401 - 800	>800	Total
Visible Stone Fate of Non-Visible Stone	IV contrast injection	16	349	377	742
		8.8%	77.9%	99.0%	73.5%
		110	64	2	176
		60.8%	14.3%	0.5%	17.4%
	Contrast injection through the ureteric catheter	19	17	1	37
		10.5%	3.8%	0.3%	3.7%
	Passage of Ureteric Catheter only	20	14	1	35
		11.0%	3.1%	0.3%	3.5%
	Postponed	16	4	0	20
		8.8%	0.9%	0.0%	2.0%
	Total	181	448	381	1010
		100.0%	100.0%	100.0%	100.0%

roscopy.

Using contrast increased the visibility up to 71%, and 8.8% of the patients with stone density up to 400 HU localization failed and the procedure was postponed, see Table 5. Pearson Chi-square test was used for both correlations and the *P* value was 0.001.

5. Discussion

More than 90% of urolithiasis cases are treated with SWL which is known to be the primary treatment modality for stones in the kidney and ureter [15].

The success of SWL depends on accurate stone localization proper fragmentation and complete clearance of fragments. Fluoroscopy is the only possible method used for ureteric stone localization during ESWL and Ureteroscopy, there are ureteric stones that are not seen under fluoroscopy during ESWL and Ure-

teroscopy although seen on CT KUB and we might need to postpone the procedure because of failure of localization. and this is suggesting that there is some ureteral stone with a HU estimation that can be correlated with a radio-opaque stone and can be sent for shockwave lithotripsy or ureteroscopy right away, whereas other ureteral stones with a HU estimation can be correlated with a radiolucent stone which needs the injection of contrast medium for localization by fluoroscopy during ESWL and Ureteroscopy or other methods of localization such as the passage of ureteric catheter up the ureter.

The demographic data from our study were comparable to the global picture of ureteric stone disease prevalence and incidence, with the peak incidence at the age range of 40 - 49 [16]. The 2:1 male-to-female ratio described in our study was similar to the previous study. The difference may be attributed to the protective effect of estrogen on stone formation in premenopausal women mainly before 45 years of age, due to enhanced renal calcium absorption and reduced bone resorption as the metabolic advantage [17]. Most of our patients came from the countryside.

The majority of nonvisible stones were in the lower ureter this is to illustrate that position of the stone had a great impact on the appearance of the stones under fluoroscopy which mimics other studies due to more osseous structures and other overlying soft-tissue densities that obscure the lower ureteric stones [17].

In this study all the stones were diagnosed by CT which is the best modality for diagnosing ureteric calculi would provide accurate information regarding stone presence and size, location, and adjacent anatomy so Patients suspected of having acute ureteral colic are best managed with a non-contrast helical CT scan [18]. Mean stone density in HU was 704.45 ± 300 (STD) with a minimum density of 81 HU and a maximum of 1873 HU. In computerized tomography (CT), the Hounsfield unit (HU) is used to assess tissue of body fluid density. According to these density measurements, the density of water is 0, the density of air is (−) 1000, the density of compact bone is (+) 1000, and the density of solid organs and soft tissues varies between 10 and 90 [9].

A set HU cut-off value with optimal sensitivity and specificity in predicting calculus' radiolucency or radio-opacity can change the clinical management of the urologists, and by that patients can avoid having to undergo a plain abdominal radiograph and can be well prepared for the possible use of contrast. This offers the advantage of avoiding additional radiation exposure, as well as time and cost, and minimizes the anxiety and discomfort of the patient regarding an additional diagnostic test. In our study the stone density has been grouped in 400 HU apart, except the last ranged from 800 to 1837. Roughly densities < 400 HU were 181; stones not seen under fluoroscopy were 165 (91.2%). On the other hand, the number of patients with stone density > 400 HU was 829 and those who were not seen under fluoroscopy were only 103 (12.4%). Stones with HU > 800 were visible in 99%. These findings were quite similar to the study done by

Huang et al. who described the CT attenuation-level HU and its predictive value on whether calculus is radio-opaque or radiolucent. In their study, multivariate analyses of the 84 CT scans that detected ureteral stones revealed that the significant predictor of visibility on KUB was the stone HU, All ureteric calculi with a density of > 800 HU were visible on KUB, while 17 (74%) of 23 calculi with the density < 200 HU were not visible on KUB so Ureteral calculi characteristics on UHCT are useful for predicting their visibility on KUB [19]. We found in our study that HU of < 400 is a cut level for doing preoperative KUB.

An earlier study found a threshold value of 498.5 HU in a CT sonogram was established as the optimal cut-off in determining whether calculus is radio-opaque or radiolucent and a HU below 498.5 identified the likeliness of the calculi to be radiolucent, and a HU above 498.5 [20]. Also, Michael et al. used the CT scout film and concluded that the cut-off value at which none can be seen on CT Scout, but can be identified on KUB X-ray was set at 630 HU, in the stones with an attenuation value equal to or higher than the set cut-off point is considered radiopaque and those with HU below the set cut-off point maybe considered radiolucent [17].

In this study, we have 17% of patients with stone density up to 400 HU. 8.8% appeared in x-ray KUB and under fluoroscopy; Correlation of the CT stonogram attenuation level with the stone composition has been studied extensively in recent literature. Patel *et al.* described that CT stonogram HU range of 879 ± 230 was mainly composed of calcium oxalate monohydrate, while HU range of 338 ± 145 was usually composed of uric acid stones [21]. Demirel et al. described a similar range of Hounsfield units for calcium oxalate stones (812 ± 135) and uric acid stones (413 ± 143) [22]. Stone size was omitted from our analysis which may have predictive value in stone appearance under fluoroscopy.

6. Conclusion

This study confirmed that in stones with density up to 400 HU, the likelihood that it will not appear on fluoroscopy is 91.2% which can be used as a cutoff level for doing KUB radiograph on patients presenting with ureteric stones and planned for treatment by ESWL or URS, and the patient presenting with a stone of a density more than 400 HU is deemed to be radio-opaque and there is no need to request KUB for them before ESWL or URS.

Recommendations

Operating ESWL machines with CT guided will be very valuable for localization, as shown by the visibility of all stones on CT KUB but not on fluoroscopy until then the CT value of 400 HU can be used for the prediction of visibility of stones at ESWL.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Randomized Clinical Study, Comparative of Parallel Groups, to Evaluate the Effectiveness of Three Preparations of Potassium Citrate in Producing an Increase in Urinary pH in Patients with a History of Kidney Stones

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Abstract

Background: A very strict control of urinary pH is recommended to maintain it between 5.5 and 6.2, preventing formation or recurrence of crystals. Kidney stones are a common problem, with a high rate of recurrence, not altered by the success of surgery. Medical treatment prevents recurrence. Potassium Citrate inhibits crystallization of calcium salts. It influences calculogenesis by increasing urinary citrates and alkalinizing the urine. **Purpose:** to evaluate the similarity in the effect of three K citrate products, K citrate reference product Urocit® 10 mEq, and K citrate from Laboratorios LETI S.A.V., 10 mEq and 15 mEq, on urinary pH. **Materials and Methods:** We carried out a prospective, randomized study of three parallel groups. We admitted female and male patients with history of kidney stones or evidence of lithiasis (grit, microlithiasis) in the renal echosonogram. Laboratory assessments: urine, 24-hour urine, urinary pH, Calcium, uric acid, Phosphorus, Sodium, protein and urinary creatinine at times: start, day 7, day 21, 30 of treatment. **Results:** all three products produced a slight increase in urinary pH in the simple urine test and 24-hour urine, with no differences between groups or their logarithmically transformed means and their CI95, which did not exceed the range between 80% and 125%. **Conclusions:** K Citrate, 10 mEq and 7.5 mEq, from Laboratorios LETI, S.A.V., at a dose of 30 mEq daily in patients with history of kidney stones are equivalent to the reference product Urocit®, in its effects on urinary pH in 24-hour urine, and in the simple urine test.

Keywords

Nephrolithiasis, Potassium Citrate, Urine pH, Pharmacodynamic Equivalence

1. Introduction

Kidney stones continue to be a very common problem. Its diagnosis and prevention have not decreased its frequency, with a high rate of recurrence that is not altered by the success of surgery. There is currently ample evidence that medical treatment does prevent recurrence, which is why pharmacological treatment has been returned.

Citrate has received great interest in the study and prevention of kidney stones, mainly due to its powerful inhibitory action on the crystallization of calcium salts, and is currently the best studied non-organic inhibitor. The recommended dose is 30 - 100 mEq/day, depending on the level of citraturia to be corrected. Doses greater than 30 mEq/day should be divided into 2 to 3 daily doses [1].

Renal lithiasis has an incidence of 10% in industrialized countries, it is three times more common in men, recurrence occurs in 40% to 50% in the first five years and recurrence intervals become shorter [2].

Citric acid is a tricarboxylic acid with a pK of 5.6; therefore, at physiological pH more than 90% is found as trivalent anion. Plasma citrate concentration is low, 0.14 mmol/l (2.4 mg/dl), varies between 0.05 and 0.3 mM and circulates largely in complexes with sodium (Na), calcium (Ca) and magnesium (Mg) and very little bound to large molecules, thus more than 90% of plasma citrate is freely filtered by the kidney [3]. Plasma citrate is endogenous, its main sources being bone and intermediate liver and muscle metabolism. Its plasmatic levels seem to be quite independent of the diet, because once the citrate from food is absorbed, it is rapidly metabolized in the liver. However, if an oral citrate load, for example, a citrate salt, is given, its plasma levels transiently increase [4]. At the intracellular level, it is a central component of the Krebs cycle, that is, it is an energy donor. Citrate is mainly used by two organs, liver and kidney [4]. At the urinary level, it is a powerful inhibitor of the crystallization of calcium oxalate salts (OxCa) and calcium phosphate (PCa); therefore, hypocitraturia is a risk factor for calcium stone formation [5] [6].

Citrate, primarily the divalent citrate species, binds to Ca^{2+} in the urine and forms a soluble salt, calcium citrate; on the other hand, by reducing Ca^{2+}, it manages to reduce urinary saturation with respect to OxCa (Calcium Oxalate) and PCa (Calcium Phosphate) [6] [7] and directly inhibits the crystallization of OxCa and PCa [4]. It has also been shown to inhibit spontaneous OxCa precipitation [7] and monosodium urate-induced OxCa nucleation [8].

It is a potent inhibitor of the aggregation of preformed OxCa crystals [9], especially the trivalent species. It binds to the surface of crystals and forms an Ox-

Ca-citrate complex, preventing crystal aggregation. The importance of this action lies in the fact that crystal aggregation plays a critical role in the process of stone formation.

Systemic, tubular, and intracellular pH is the factor that most affects citrate excretion; acidosis decreases its excretion while alkalosis increases it. Small decreases in tubular pH (7.4 to 7.2) significantly increase its tubular reabsorption.

The use of potassium citrate (K citrate) in the prophylaxis of kidney stones did not begin, however, until 1985, when the US Food and Drug Administration approved it under certain conditions [10].

The therapeutic effect of potassium citrate on calculogenesis is due to the increase in urinary citrates and its alkalinizing action. A second protective effect of citrate on calculogenesis is due to its inhibitory effect on the crystallization of calcium oxalates and phosphates, inhibiting nucleation. Spontaneous formation of these calcium salts and the heterogeneous nucleation of calcium oxalate on urates, delaying the agglomeration of existing calcium oxalate crystals and inhibiting the growth of calcium oxalate and calcium phosphate crystals. Finally, the third effect of citrate derives from the elevation of urinary pH, which increases the amount of dissociated uric acid and the formation of alkaline urates in the urine, preventing the formation of uric acid stones or redissolving those already formed; it also prevents the formation of uric acid crystals that could act as very effective heterogeneous nucleators of calcium oxalate [11] [12].

LETI Laboratories has developed a modified release formulation of K citrate in tablets of 10 and 7.5 mEq, which must be compared with the reference product Urocit® 10 mEq, approved in the country, to demonstrate that they are equivalent in their effect on the urinary pH.

Potassium Citrate 7.5 and 10 mEq, LP Tablets from LETI Laboratories, are prolonged-release products in the form of white, oblong-shaped, coated tablets. Its active ingredient is Tripotassium Citrate Monohydrate, which provides 7.5 or 10 mEq (respectively) required for the dose to be administered. The nature of the design is of the polymeric matrix type that generates, when hydrated, a gradual release of the active ingredient for up to 5 hours, providing the patient with the desired effect as urine alkalinizer in the treatment of Renal Lithiasis. The tabletsare covered by a polymer layer that guarantees easy swallowing of the tablet by the patient. [13].

Definitively, the desired benefit with the administration of potassium citrate in patients with kidney stones is to achieve an increase in urinary pH that produces a decrease in urinary calcium and its crystallization [11] [14] [15].

Taking into consideration that it is the increase in urinary pH that determines the final therapeutic action of the product, this study was carried out in order to compare three formulations of K citrate with modified release. The aim was to demonstrate equivalence in their effect on pH and, therefore, on their ability to reduce the production of kidney stones, comparing their ability to modify urinary pH in patients with a history of kidney stones.

1) Objectives: to evaluate the similarity in the effect of three potassium (K) citrate products, K citrate reference product Urocit™ 10 mEq, and K citrate from Laboratorios LETI S.A.V, 10 mEq and 15 mEq, on urinary pH.

2) Materials and methods: We conducted a prospective, randomized study of three parallel groups.

Inclusion criteria

1) Stone-forming patients.

2) Patients aged between 18 and 85 years.

3) Patients with a history of kidney stones.

4) Patients who present evidence of lithiasis (grit, microlithiasis) on the renal echosonogram.

5) Patients who have signed a written consent that they have been sufficiently informed about the study and that they agree to participate in it.

Exclusion criteria

1) Patients in treatment with drugs prohibited in this study: Macromolecules: Glycosaminoglycans: Citrate, Phytate, Tartrate. Amino acids: Aspartic, Glutamic, Alanine, Magnesium, Pyrophosphate, Trace elements.

2) High levels of potassium in the blood (hyperkalemia), the normal range is 3.7 to 5.2 mEq/L.

3) Patients with hypercalcemia (Normal values range from 8.5 to 10.2 mg/dL (2.13 to 2.55 millimole/L).

4) Urinary tract infection.

5) Patients with diarrheal syndrome.

6) Previous diagnosis of Addison's disease (adrenal gland).

7) Soft tissue injury or acute burn.

8) Diagnosis or history of peptic ulcer.

9) Dehydrated patients.

10) Patients taking a "potassium-sparing" diuretic such as amiloride (Midamor, Moduretic), or spironolactone (Aldactone, Aldactazide), triamterene (Dyrenium, Dyazide, Maxzide).

11) Creatinine > 1.5 mg/dL.

12) History of metabolic alkalosis or conditioning diseases of said pathology.

13) Patients receiving anticholinergic therapy.

14) Intestinal obstruction.

15) Treatment with: Angiotensin converting enzyme inhibitors, Angiotensin AT1 receptor antagonists, indomethacin, sodium bicarbonate or other preparations containing potassium and treatment with thiazides or allopurinol.

16) Uncontrolled arterial hypertension SBP ≥ 140 mmHg and DBP ≥ 90 mmHg.

17) Previous diagnosis of myocardial infarction within six months prior to the start of the study.

18) Previous diagnosis of cerebrovascular accident of any type within the six months before the start of the study.

19) Patients with a previous diagnosis of asthma or with COPD.

20) Cardiac arrhythmias of any kind as background, or identified in the research doctor's office through physical examination.

21) Acute dehydration.

22) Gastric emptying disorders.

23) Congestive heart failure > Grade I NYHA.

24) Presence or suspicion of pregnancy, ruled out, if suspected, by blood determination of the β fraction of human chorionic gonadotropin.

25) Breastfeeding patients.

26) Severe liver function disorders (liver enzymes 3 times above their normal value).

27) Previous diagnosis of peripheral arterial vascular disorders.

28) Patients taking birth control pills (patients of childbearing potential should avoid pregnancy by using a barrier method, intrauterine device, or being surgically sterilized).

29) Poorly controlled diabetes (basal blood glucose greater than 126 mg/dL or glycosylated HB greater than 7%). Diabetes care volume 40 Suppl 1 January 2017, Glycemic Targets pg S50.

30) History of alcohol abuse.

31) Drug abuse, defined as excessive, persistent, or sporadic use of drugs that is not consistent with or related to acceptable medical practice.

All patients signed a written consent indicating that they had been sufficiently informed about the study and that they agreed to participate in it. The study was approved by an institutional ethics committee and by the National Regulatory Authority (approval JRPF-0307-2017).

The purpose of the study was explained to the patients. Upon accepting their participation, they signed the Informed Subject Consent and were randomly assigned to one of the three (3) groups. Two of the groups were instructed to receive potassium citrate at a dose of 10 mEq (one 10 mEq tablet) three times a day for 30 days; a third group was assigned to receive the Leti Potassium Citrate formulation (two 7.5 mEq tablets) twice daily for 30 days.

At the beginning and at the end, laboratory tests were performed (complete blood count, blood glucose, glycosylated hemoglobin, urea, creatinine, transaminases, triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, electrolytes, urine); at the times: start, day 7, day 21 and 30 of treatment, urine, 24-hour urine with determination of pH, Calcium, uric acid, Phosphorus, Sodium was performed. (Neither citrate nor oxalate could be determined because these reagents were not available in the country at the time of the study).

The formula used to calculate the size of the samples is based on the development presented by J. Fleiss[1] taking the pH data from the study: Reference values of urinary citrate and oxalate for inhabitants of the metropolitan area of Anzoátegui State, Venezuela, Interscience, vol. 26, No. 3, March, 2001, p. 122-125.

[1]Fleiss, J. The design and analysis of clinical experiments. Statistical methods for rates and proportions. John Wiley & Sons, 1986, p. 432.

According to the calculations, with 15 patients per group (3 groups) we could analyze the urinary pH and demonstrate a difference in pH of 10%.

2. Results

We admitted 47 patients in the study, of which only 46 entered the analysis because one patient violated protocol and was admitted with a urinary tract infection.

There were statistically significant differences (*) in the parameters: weight, height, body mass index and SBP, without clinical significance, as seen in Table 1.

Given that the only difference detected between the groups K Citrate Ref., 10 mEq and K Citrate TEST 10 mEq were observed on day 30 of treatment, the confidence intervals were analyzed to determine if the difference between the means included the intervals (Table 2).

Neither for the pH data, or its logarithmic transformation, the means or the confidence intervals are far from the established limits of Bioequivalence 80% - 125%: Mean: 105%, CI min: 102.1%, CI max 107, 8%.

The other variables measured in the simple urine test: glucose, ketones, proteins, leukocytes, cylinders or bacteria did not show significant changes. In some patients, the number of red blood cells was increased by the presence of menstruation.

Neither the means nor the CI are below 80% or above 125% (Table 3 and Table 4).

Table 1. Description of the evaluated population.

Parameter	Potassium citrate (Ref) 10 mEq	Potassium citrate (Test) 10 mEq	P between Ref. and Test (10 mEq)	Potassium citrate (Test) 15 mEq	P between Ref. and Test (15 mEq)
Age (years)	43.7 ± 15.3	36.6 ± 12.3	0.17	45.1 ± 12.9	0.79
Sex (f/m)	8/7	6/9		13/3	
Weight (kg)	65.4 ± 12.7	74.0 ± 13.5	0.08	73.06 ± 25.9	0.00*
Height (m)	1.62 ± 0.1	1.67 ± 0.1	0.11	1.63 ± 0.1	0.00*
BMI	24.8 ± 3.9	26.5 ± 4.3	0.24	25.48 ± 9.3	0.00*
SAP (mmHg)	118.1 ± 12.4	118.1 ± 10.4	1	117.5 ± 12.9	0.00*
DAP (mmHg)	73.9 ± 8.8	75.4 ± 6.7	0.6	73.1 ± 8.7	0.79
Evaluation of symptoms					
Pain	0	0		0	
Macroscopic hematuria	0	0		0	
Alterations in physical exam	0	0		0	

Table 2. pH in simple urine test.

Time	Potassium citrate (Ref) 10 mEq	Potassium citrate (Test) 10 mEq	P between Ref. and Test (10 mEq)	Potassium citrate (Test) 15 mEq	P between Ref. and Test (15 mEq)
Beginning	5.81 ± 0.6	5.18 ± 1.6	0.17	5.73 ± 0.5	0.69
Day 7	5.73 ± 0.7	5.66 ± 0.7	0.78	5.97 ± 0.6	0.37
Day 21	5.75 ± 0.5	5.74 ± 0.7	0.98	5.78 ± 0.8	0.90
Day 30	5.52 ± 0.5	6.01 ± 0.6	0.04*	5.8 ± 0.7	0.24

There was a statistically significant difference (*).

Table 3. 24-hour urine pH (Graph 1).

Time	Potassium citrate (Ref) 10 mEq	Potassium citrate (Test) 10 mEq	P between Ref. and Test (10 mEq)	Potassium citrate (Test) 15 mEq	P between Ref. and Test (15 mEq)
Beginning	5.94 ± 0.5	5.88 ± 0.4	0.70	5.79 ± 0.4	0.34
Day 7	5.93 ± 0.6	5.94 ± 0.3	0.96	6.13 ± 0.5	0.32
Day 21	6.10 ± 0.5	5.86 ± 0.9	0.38	5.97 ± 0.8	0.61
Day 30	6.08 ± 0.6	6.16 ± 0.2	0.69	5.83 ± 0.6	0.31

Table 4. Equivalence analysis of the main variable pH of 24-hour urine. Comparison between K CitrateUrocit™ vs K Citrate TEST 10 mEq (logarithmically transformed data to ensure normality).

Time	Minimum IC 95 (%)	Mean (%)	Maximum IC 95 (%)
Beginning	97.85	99.48	101.12
Day 7	98.81	100.23	101.65
Day 21	93.52	97.39	101.27
Day 30	99.86	100.84	101.83

Neither the means nor the CI are below 80% or above 125% for the pH values in 24-h urine, in any of the periods evaluated (Table 5).

There were not statistical differences in other 24-hour urine parameters (Table 6).

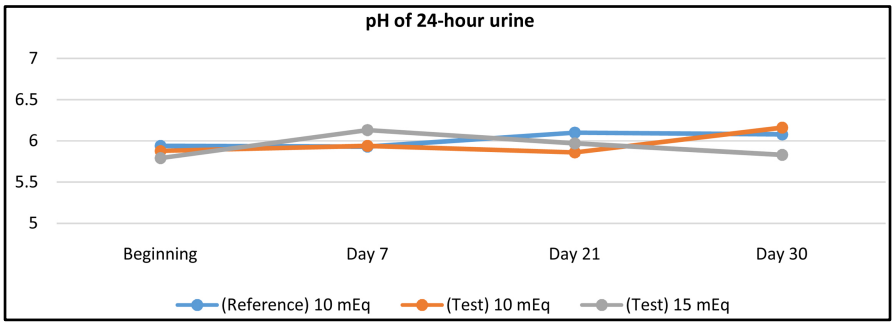
No adverse effects were reported in any group. In laboratory tests, one patient in the Urocit® brand K Citrate group presented elevated transaminases at the end of the study, without other alterations.

3. Discussion

Urolithiasis is common in developed countries, with a prevalence of 10%, and is

Table 5. Equivalence analysis of the main variable pH of 24-hour urine. Comparison between K Citrate Urocit™ vs K Citrate TEST 15 mEq (logarithmically transformed data to ensure normality).

Time	Minimum IC 95 (%)	Mean (%)	Maximum IC 95 (%)
Beginning	96.78	98.54	100.29
Day 7	99.69	101.99	104.30
Day 21	94.71	98.37	102.02
Day 30	90.82	95.83	100.83



Graph 1. Evolution of the means in the pH values of 24-hour urine.

associated with an increased risk of subsequent loss of renal function and cardiovascular disease [16]. The recurrence rate after the first stone episode is up to 40% in the first 5 years and 75% after 20 years [17]. The management of recurrent lithiasis requires knowledge of the risk factors in patients who form stones.

Hypercalciuria and hypocitraturia are the most important risk factors for stone formation, followed by hyperoxaluria and hyperuricosuria [18].

In a retrospective study, 503 patients who received potassium citrate for a median duration of 41 months (range, 6-168). They evaluated the changes in urinary profile: the changes observed werean increased urinary pH (5.90 to 6.46, $p < 0.0001$) and increased urinary citrate (470 to 700 mg daily, $p < 0.0001$) 6 months after the start of therapy.

These patients had a significant decrease in stone formation rate after initiation of potassium citrate from 1.89 to 0.46 stones per year ($p < 0.0001$), a remission rate of 68%, and a decreased 93% in stone formation rate. These changes in profiles kept up to 14 years after starting treatment. The results obtained by this study confirmed the long-term efficacy of potassium citrate therapy in patients with recurrent nephrolithiasis [19].

A review of a database on metabolic renal stone formation in a tertiary care academic hospital was carried out in order to assess the effect of potassium citrate on calcium excretion.

Patients with a history of calcium oxalate nephrolithiasis and hypocitraturia were identified who had received potassium citrate therapy for a minimum of 3 months.

Table 6. Other 24-hour urine parameters.

Time	Potassium citrate (Ref) 10 mEq	Potassium citrate (Test) 10 mEq	P between Ref. and Test (10 mEq)	Potassium citrate (Test) 15 mEq	P between Ref. and Test (15 mEq)
Urinary volume in 24 hours (mL)					
Beginning	2120.67 ± 1022.0	2157.27 ± 1091.9	0.93	2357.50 ± 1125.0	0.54
Day 7	2085.00 ± 1032.1	1904.80 ± 1139.4	0.66	2590.91 ± 1105.7	0.26
Day 21	2207.69 ± 1154.5	1868.21 ± 1043.0	0.43	2665.00 ± 1142.6	0.31
Day 30	1810.0 ± 532.8	1499.00 ± 705.7	0.22	2715.45 ± 1026.0	0.02*
Calcium (50 - 150 mg/24hr)					
Beginning	44.78 ± 22.1	104.61 ± 89.3	0.02*	147.31 ± 99.6	0.00*
Day 7	99.37 ± 190.1	90.86 ± 87.9	0.88	109.83 ± 70.0	0.85
Day 21	80.68 ± 64.7	65.78 ± 53.8	0.52	172.05 ± 118.9	0.02*
Day 30	59.77 ± 45.8	86.57 ± 60.3	0.22	158.16 ± 94.0	0.00*
Sodium (27 - 287 mEq/24hr)					
Beginning	104.2 ± 38.2	99.73 ± 35.2	0.74	90.89 ± 29.7	0.29
Day 7	87.14 ± 23.4	94.08 ± 43.7	0.60	90.45 ± 24.3	0.73
Day 21	119.00 ± 30.4	92.44 ± 35.1	0.04	94.57 ± 20.4	0.02*
Day 30	100.6 ± 21.8	93.61 ± 36.7	0.56	107.09 ± 31.2	0.58
Creatinine(500 - 2000 mg/24hr)					
Beginning	1144.9 ± 1233.2	687.0 ± 308.6	0.18	851.01 ± 304.2	0.15
Day 7	782.01 ± 274.3	708.93 ± 296.2	0.50	783.84 ± 378.1	0.60
Day 21	892.48 ± 418.1	686.69 ± 422.0	0.21	865.16 ± 297.87	0.22
Day 30	723.32 ± 315.2	775.92 ± 473.5	0.74	830.91 ± 211.4	0.71
Phosphorus (380 - 1300 mg/24hr)					
Beginning	1228.00 ± 2020.8	759.53 ± 410.3	0.39	525.00 ± 270.8	0.20
Day 7	642.86 ± 277.9	736.48 ± 400.7	0.47	548.18 ± 506.1	0.59
Day 21	651.67 ± 380.7	613.19 ± 422.7	0.81	500.71 ± 273.5	0.27
Day 30	527.00 ± 247.8	555.79 ± 346.0	0.81	466.36 ± 129.9	0.50
Protein (0 - 300 mg/24hr)					
Beginning	196.27 ± 84.9	216.72 ± 115.0	0.58	153.81 ± 59.4	0.12
Day 7	225.07 ± 125.4	284.15 ± 210.3	0.49	172.27 ± 71.9	0.2
Day 21	239.54 ± 84.3	199.79 ± 89.5	0.25	139.29 ± 49.9	<0.001*
Day 30	223.00 ± 75.1	167.13 ± 67.9	0.07	148.73 ± 38.6	0.01*
Uric acid (250 - 750 mg/24hr)					
Beginning	496.23 ± 154.1			521.72 ± 317.0	0.79
Day 7	461.94 ± 201.4	649.63 ± 572.9	0.30	640.66 ± 652.6	0.40
Day 21	474.19 ± 199.5	573.94 ± 432.4	0.49	447.24 ± 178.4	0.72
Day 30	390.00 ± 168.5	462.09 ± 323.1	0.52	367.44 ± 228.6	0.79

There was a statistically significant difference (*).

The composition of the urine was analyzed, prior to the initiation of potassium citrate therapy and after 3 months of therapy. Patients received 30 - 60 mEq potassium citrate by mouth daily. Inclusion criterion was a change in urine potassium of 20 mEq/day or greater, which suggests compliance with potassium citrate therapy.

Twenty-two patients were evaluated. Mean pre-treatment 24-h urine values were as follows: citrate 280.0 mg/day, potassium 58.7 mEq/day, calcium 216.0 mg/day, pH 5.87. Potassium citrate therapy was associated with statistically significant changes in each of these parameters-citrate increased to 548.4 mg/day ($p < 0.0001$), potassium increased to 94.1 mEq/day ($p < 0.0001$), calcium decreased to 156.5 mg/day ($p = 0.04$), pH increased to 6.47 ($p = 0.001$). Urine sodium excretion was not different pre- and post-therapy (175 mEq/day pre-therapy versus 201 mEq/day post-therapy, p = NS). Urinary calcium excretion decreased by a mean of 60 mg/day on potassium citrate therapy-a nearly 30 % decrease in urine calcium excretion. These data lend support to the hypothesis that alkali therapy reduces urine calcium excretion [20].

In another study evaluating the therapeutic role of potassium citrate in the treatment of renal stones, 56 patients (Mean age = 43.7 ± 10.8) from June 2018 to December 2018 with a total of 86 renal stones enrolled in the study and treated with potassium citrate (10 mEq tablets, three times a day). Moreover, the patients were recommended to reduce sodium intake as well as oxalate-rich foods, have at least 2 liters of water per day and normalize calcium intake. Finally, they were assessed 8 weeks after the treatment initiation, while in those whose stones remained, the assessments were repeated for another 8 weeks. 42 and 25 stones were completely dissolved at the first and second visit, respectively. Compared to the baseline parameters, the mean size of stones in the largest diameter decreased significantly from 5.13 to 1.96 mm and 5.13 to 0.79 mm (p-value < 0.001) at the first and second visit, respectively [21].

Potassium citrate supplementation in patients with a history of kidney stones in Switzerland resulted in a beneficial change in urinary risk profile, particularly increasing anti-lithogenic factors. Fasting glucose, HbA1c, cholesterol levels, and BMI were not affected by potassium citrate therapy after 3 months, suggesting that potassium citrate is safe and not associated with adverse effects, nor metabolic side effects. Finally, 1.25(OH)2 D3 levels were not associated with urinary citrate excretion [22].

In this study, carried out in order to compare the effect of potassium citrate on urinary pH of two new presentations from Laboratorios Leti, S.A.V. against the effect of the innovative drug, we found similar results to previous studies with a slight increase in urinary pH, with no difference between the groups compared

The results of our study show that the variation in urinary pH obtained with the two test products is equivalent to that obtained with the reference product, both in the pH of the simple urine tests, and for the urine samples of 24 hours.

According to all that has been explained, and to the results obtained, no differences are found between the test drugs and the reference drug, and they can be used in the same way for their ability to prevent the formation of kidney stones in people with this predisposition to their formation.

4. Conclusion

Based on the results obtained, and the statistical analyzes performed on the data set collected for the pharmacodynamic equivalence study, it can be concluded that the test formulations K Citrate 10 mEq and K Citrate 7.5 mEq, test products, from Laboratories LETI, S.A.V., administered in doses of 30 mEq daily in patients with a history of kidney stones, are equivalent to the reference product K citrate Urocit® in their effects on urinary pH in 24-hour urine, and in the simple urine test.

Support

Laboratorios Leti, S.A.V.

Conflicts of Interest

Dr. Eloy González and Dr. Tellez Mendez reveal no conflict of interest. Dr. Maria González Yibirín and Dr. David Rincón Matute work at Laboratorios Leti S.A.V.

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Pyeloplasty According to Küss-Anderson-Hynes: Results and Complications at the Urology-Andrology Department of the Sino-Guinean Friendship Hospital

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Abstract

Objective: Evaluate pyeloplasty according to Küss-Anderson-Hynes at the urology-andrology department of the Sino-Guinean Friendship Hospital. **Patient and Method:** This is a 3-year prospective descriptive study from January 1, 2018 to December 31, 2020. It focused on a sample of 21 patients, who had undergone pyeloplasty according to Küss-Anderson-Hynes. **Results:** The averages age of the patients was 24.24 years. Lumbar pain was the main reason for consultation in 71.43% of cases. pyeloplasty according to Küss-Anderson-Hynes alone was performed in 76.20% of cases. It was associated with lower pole vessel uncrossing in 14.29% of cases and in 9.52% of cases with pyelolithotomy. The main Postoperative complications consisted of surgical site infections (23.81%) and fistula of the pyelo-ureteral junction (9.52%). The result of the pyeloplasty evaluated after three years, was qualified as good in 13 patients (86.67%), conversely the result was declared bad in 2 patients or 13.33%. During the follow-up period, postoperatively, we had lost sight of 6 patients. **Conclusion:** Pyeloplasty according to Küss-Anderson-Hynes in addition to its excellent results reported by the literature was the only therapeutic alternative performed during this study. However, its indications are considerably reduced with the advancement of laparoscopy.

Keywords

Pyeloplasty, Küss-Anderson-Hynes, Parietal Suppuration

1. Introduction

Pyeloplasty is a surgical technique that consists of resection of the narrowed pyelo-ureteral zone followed by a pyelo-ureteral anastomosis [1].

The management of ureteropelvic junction syndrome has evolved considerably over the past 20 years. Before the era of obstetric ultrasound, the diagnosis was made after symptoms. Nowadays in developed countries, systematic antenatal screening has modified the clinical profile of this pathology.

Added to this is the management of pyelo-ureteral junction syndrome by so-called minimally invasive techniques with multiple advantages.

In developing countries, however, the clinical manifestations still remain the circumstances of discovery of the syndrome of the pyelo-ureteral junction.

In 2008 Savoie P H and col. [2] in France concluded that pyeloplasty by resection anastomosis is the reference treatment for stenosis of the ureteropelvic junction.

- In Senegal Diao B *et al*. [3] concluded that the success rate of open pyeloplasty according to Anderson-Hynes was over 90%.
- In Burkina Faso, Kirakoya B *et al*. [4] affirmed that pyeloplasty according to Küss-Anderson-Hynes remained the reference technique with excellent results: 90% to 95%.
- In Guinea, little previous study has been done on the subject.

The evaluation of this technique in the management of the anomaly of the pyelo-ureteral junction through its results and complications in the urology-andrology department of the Sino-Guinean Friendship Hospital constituted the aim of this study.

2. Patients and Method

Our descriptive-type prospective study spanned a period of 3 years from January 1, 2018 to December 31, 2020.

Were included in this study, all patients who underwent open pyeloplasty with a complete medical file.

Were not included in this study:

- All patients admitted for abnormality of the ureteral pyelojunction who did not undergo open pyeloplasty;
- All patients who underwent open pyeloplasty outside the study period.

The parameters studied were clinical and therapeutic.

3. Results

The average age of our patients was 24.24 years with a sex ratio of 1.33. Lumbar pain was the main reason for consultation in 71.43% of cases. Lombotomy was the most used approach with 15 cases or 71.43%. (**Figures 1-3** and **Table 1**)

4. Discussion

Described in the literature as the most frequent obstructive uropathy of the

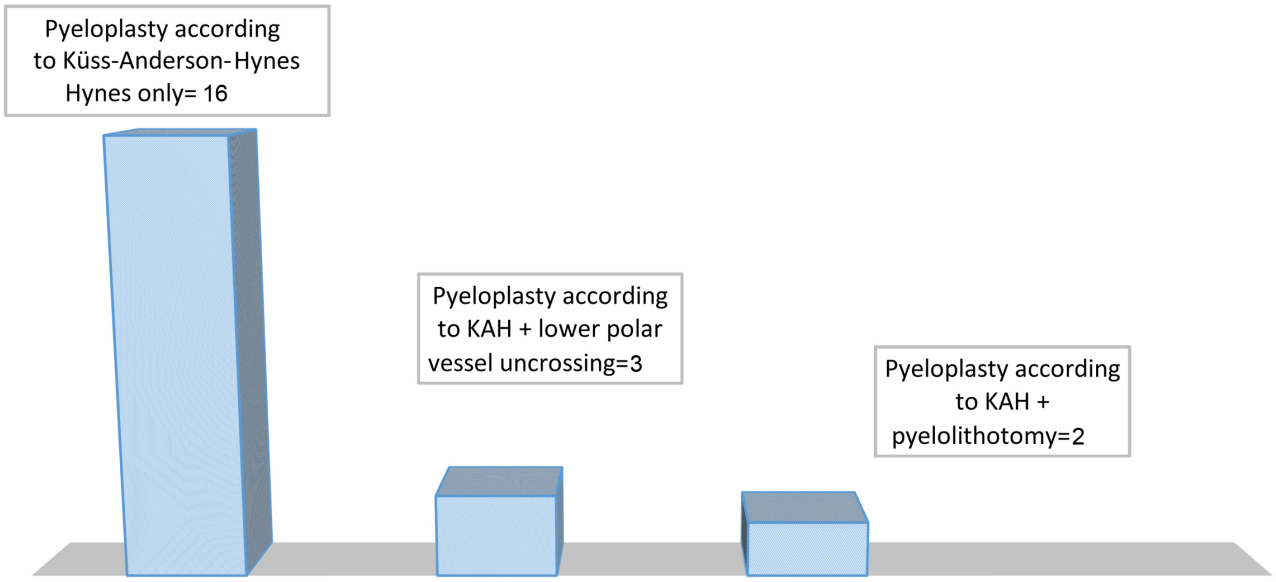

Figure 1. Distribution of patients by surgical procedure.

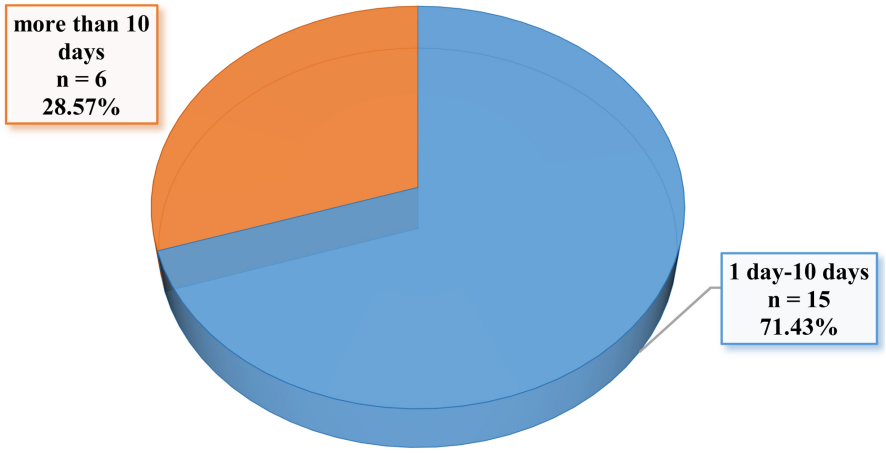

Figure 2. Distribution of patients by length of stay.

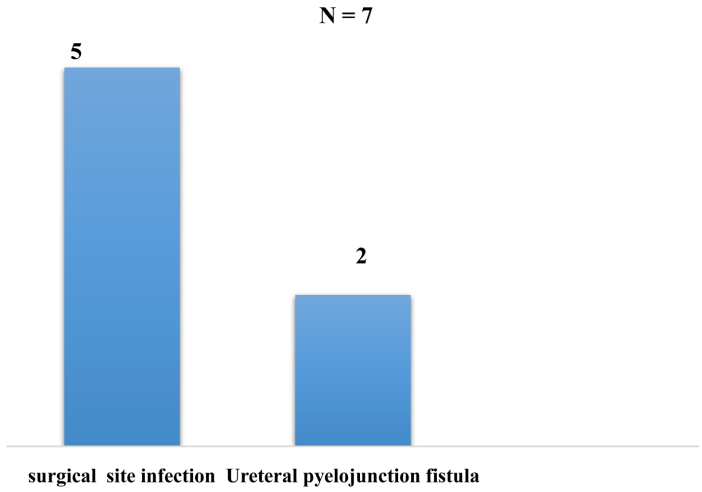

Figure 3. Distribution of patients according to postoperative complications.

Table 1. Distribution of patients according to treatment results and follow-up.

Decline in months	Results	Effective	%
12	**Good**	**21**	**100**
	Bad	0	0
36	Good	13	86.67
	Bad	2	13.33

Text 1: After a follow-up of 36 months, we lost sight of six patients.

upper urinary tract [5] [6], the anomaly of the pyelo-ureteral junction manifests itself at any age from intrauterine life to adulthood in passing through the neonatal period [6].

The most affected age group in our study is that of 21 - 30 years with extremes of 1 year and 50 years. The average age was 24.24 ± 20 years. Diao B *et al*. [7] reported a mean patient age of 26.3 ± 16.7 years (2.5 - 60 years), whereas Kirakoya B *et al*. [6] reported a mean age of 31.3 years (extremes of 10 years and 60 years). In fact, these different results are superimposable. Moreover, in our series, the majority of patients are aged greater than or equal to twenty-one years (21 years), again reflecting in our context, the notorious insufficiency of ultrasound in the monitoring of pregnancies for earlier diagnosis and management. This makes clinical manifestations such as lumbar pain (71.43% of cases) the main circumstances of discovery of the disease in our study.

Other authors [8] [9] also reported low back pain as the main reason for consultation in their study. These results corroborate with the data of the literature making the painful symptomatology, the dominant clinical element in the abnormalities of the ureteral pyelojunction. Since the advent of antenatal ultrasound in developed countries, the discovery of the anomaly of the pyelo-ureteral junction on painful warning signs has become considerably reduced. However, they are far from having disappeared, especially in most countries of the 1/3 world [8], as our study attests.

Classically in open surgery, the approach initially described for the management of of the anomaly of the pyelo-ureteral junction is lumbotomy [10]. This route has the advantage of relative simplicity and "urological habit" [7].

Pyeloplasty according to Küss-Anderson-Hynes, as described in the literature, makes it possible to treat the anomaly of the pyelo-ureteral junction either in isolation, or by associating the uncrossing of a lower polar vessel or the ablation of a possible calculation pyelic [11]. All patients in our series benefited from pyeloplasty according to Küss-Anderson-Hynes isolation in 76.20% of cases, associated with uncrossing of the inferior polar vessel in 14.29% of cases and pyelolihotomy in 9.52% cases. Our study can be superimposed on that of Kirakoya B *et al*. in Burkina Faso [9]. Nowadays, the management of ureteral pyelojunction syndrome is marked by the development of so-called minimally invasive techniques such as laparoscopic pyeloplasty and endopyelotomy with multiple advantages and similar functional results [7]. Access to the kidney by open surgery,

in particular according to the Küss-Anderson-Hynes technique, although via the retroperitoneal route, does not protect against intraoperative complications. They are rarely severe but can reach 20% of cases [11]. In our series, there were 3 of them, consisting of peritoneal rupture, 2 cases immediately repaired and one case of controlled compartment hemorrhage, which did not require blood transfusion.

Diao B et col. [3] reported one case of peritoneal breach and two cases of pleural breach as the only intraoperative incidents immediately repaired.

Early complications related to pyeloplasty according to Küss-Anderson-Hynes in the management of PJPU have become rare [9]. According to Diao B *et al.* [3], the early surgical complications of open pyeloplasty are essentially urinary leakage at the level of the ureteropyelic anastomosis, urinoma and surgical site infections which fall within the scope of infectious complications. These complications can occur during both open and laparoscopic pyeloplasty. Our series includes seven, including five surgical site infections, a ureteropyelic fistula manifesting as urine leakage and a urinoma.

Carpentier X *et al.* [11] reported anastomotic leaks responsible for urinoma (0.3%). Diao B and col [3] found in their study, 3 cases (10%) of uro-haematoma and 3 cases (10%) of parietal suppuration. In Burkina Faso, kirakoya B *et al.* [9] noted two early complications: urinary leakage and parietal suppuration.

The management of the complications in our series consisted of appropriate antibiotic therapy, double J catheterization and drainage, respectively. These results with converging tendencies confirm the data of the literature on the merits of this technique [10] [12] [13] [14].

However, pyeloplasty according to Küss-Anderson-Hynes causes significant postoperative pain, prolonged convalescence and non-aesthetic scarring, as well as limited access in certain categories of obese patients [11].

The majority of our patients had an average length of stay of 10 days (70% of cases). Kirakoya B *et al.* found an average length of stay of 14 days, while Diao B *et al.* reported a mean hospital stay of 10.4 ± 5.1 days (5 - 25 days).

These different average durations of hospitalization are similar to the average durations reported in the literature (10 to 12 days) [11]. One of the great advantages of laparoscopic surgery is to shorten the hospital stay to an average of three to five days [1] [2] [15].

Admittedly, laparoscopic pyeloplasty has the disadvantage of being much more expensive, but the shortening of the duration of hospitalization and the rapid resumption of activity could compensate for this cost factor [3] [7] [16] [17].

Küss-Anderson-Hynes type pyeloplasty is the technique for treating anomalies of the pyelo-ureteral junction for which we have the greatest experience. Its effectiveness is durable for more than 10 years in the series of the literature [11] [18] [19]. In our study, after a follow-up of 36 months, we noted a good result in thirteen patients (86.67%) by the disappearance of the pain and a passage of the product of contrast at the level of the junction with a clear opacification of the

ureter under pyelic, witness of the lifting of the obstacle.

And conversely the result was declared bad in two patients (13.33%). Diao B and col. [3] noted a mean follow-up of 28 ± 13.7 months (13 - 48 months). Six patients (20%) had complications. Our result is lower than that of Diao B *et al*.

Our Study has some limitations:

1) The non-respect of appointments;

2) the impossibility of carrying out check-ups;

3) the instability of the patients were among other obstacles to the realization of this study.

5. Conclusions

The anomaly of the pyelo-ureteral junction is the most frequent malformative uropathy [5] [6] affecting more men than women. If the antenatal diagnosis of this condition is possible in developed countries with the contribution of ultrasound, it is still late in our conditions based mainly on clinical manifestations such as low back pain.

Open surgery according to Küss-Anderson-Hynes was the only therapeutic method that was practiced in this study. Surgical site infections and ureteropyelic fistulas were the postoperative complications recorded in this study. However, we noted a good result in 86.67% of cases. Nowadays, the indications for open pyeloplasty are considerably reduced with the advancement of laparoscopy.

Conflict of Interest Statement

The authors declare that there is no conflict of interest with any financial organization or corporation or individual that can inappropriately influence this work.

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Long-Term Management of Post-Transplant Ureteral Stricture with Surgical Reconstruction: A Case Series and Literature Review

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Abstract

Introduction: Ureteral stricture is the most common complication after kidney transplant and is largely responsible for graft dysfunction. Surgical intervention is the definitive treatment if conservative management with stenting and percutaneous nephrostomy tube placement fails and has been shown to have comparable long-term survival rates and limited post-operative complications. Methods: This is a single-center retrospective study following seven patients who received a kidney or a kidney and pancreas transplant between August 2012 and January 2021. These patients underwent surgical ureteral reconstruction after failed conservative management of a ureteral stricture. The reconstruction procedures performed were native ureter to transplanted kidney ureteropyelostomy, native bladder to transplanted renal pelvis vesicopyelostomy, non-transecting side-to-side ureteroneocystostomy, and a Boari flap creation. Data collected from electronic medical records included recipient age, gender, delayed post-transplant complications, ureteral reconstruction technique, and post-reconstruction outcomes. Renal ultrasound (RUS), renogram, nephrostogram, serum creatinine (Cr), and graft biopsy were used to assess for severity of hydronephrosis, ureteral stricture, and graft dysfunction. Serum Cr and RUS were used to assess renal function after the ureteral reconstruction. Results: Six out of seven cases resulted in reduced or resolved hydronephrosis and preserved graft function without future nephrostomy or ureteral stenting. One case required immediate revision due to persistent obstruction, and this patient had concomitant rejection leading to intrarenal stricture requiring ureterocalycostomy. Conclusions: Formal ureteral reconstruction is the definitive treatment for many cases of ureteral strictures after

transplant. The surgical technique chosen for these procedures must consider the physical and functional state of the bladder, ureter, and kidney. Our series outlines multiple surgical approaches that should be considered early in the management of post-transplant ureteral strictures to limit graft dysfunction.

Keywords

Ureteral Stricture, Ureteral Reconstruction, Post-Transplant Complications

1. Introduction

Ureteral complications after kidney transplant are responsible for many cases of graft dysfunction that require multiple interventions and possible graft loss. Ureteral stricture, the most common type of ureteral complication, has been reported to occur in 0.6% [1] - 10.5% [2] of patients after receiving a kidney transplant. These complications have been associated with the use of older donors and the presence of post-transplant delayed graft function [3]. Therefore, with the increased use of elderly and marginal donors as well as increased cold ischemia time (CIT) expected with the new organ distribution algorithms, one should expect this complication to be observed with increased frequency. Initial management of ureteral stricture consists of stenting and/or placing a percutaneous nephrostomy tube (PCN) to divert the urine, but this is not ideal for long-term management. Ureteral dilation may be attempted for shorter strictures, but this often results in recurrence of the stricture. The preferred management for distal strictures has been ureteroneocystostomy. Occasionally, the bladder is not suitable for this procedure, or the stricture is too proximal. Thus, other surgical interventions may be required, such as native ureter to transplant kidney ureteropyelostomy, transplant ureter to native ureter ureteroureterostomy, Boari flap creation, etc., and are selected on a case-by-case basis. These surgical interventions have been shown to have comparable long-term survival rates [4] and limited post-operative complications [5], suggesting that surgical reconstruction is the most effective method for long-term management and that it should be considered early in the treatment course to limit graft dysfunction. We report a case series of seven patients who received surgical intervention due to ureteral stricture recurrence after failed initial conservative management.

2. Methods

This is a retrospective study performed at the University of Texas Medical Branch in Galveston, Texas following seven patients who received a kidney or a kidney and pancreas transplant between August 2012 and January 2021. All patients who underwent surgical ureteral reconstruction at this institution due to the development of a post-transplant ureteral stricture during this time period were included in this study. All seven had hypertension (HTN), and four had

diabetes mellitus type 1 (DMI) or type 2 (DMII). Five patients received tacrolimus and mycophenolic acid (MPA) for immunosuppression maintenance, one received belatacept and MPA, and one received belatacept, MPA, and prednisone. The reconstruction procedures consisted of native ureter to transplanted kidney ureteropyelostomy, native bladder to transplanted renal pelvis vesicopyelostomy, non-transecting side-to-side ureteroneocystostomy, and a Boari flap creation. Data collection was from electronic medical records and consisted of recipient age, gender, delayed post-transplant complications, ureteral reconstruction technique, and post-reconstruction outcomes. Renal ultrasound (RUS), renogram, nephrostogram, serum creatinine (Cr), and graft biopsy were used to assess for severity of hydronephrosis, ureteral stricture, and graft dysfunction. Serum Cr and RUS were also used to assess renal function after the ureteral reconstruction. All procedures were performed with an intraperitoneal approach to avoid dissecting dense pericapsular adhesions and adhesions near the vascular anastomoses, therefore reducing the risk of vascular complications and hemorrhage. Moreover, when utilized, the native ureter on the same side of the graft was always stented preoperatively via cystoscopy, and intraoperative ultrasound (US) was used to identify the transplanted renal pelvis and vascular structures during the surgical dissection prior to reconstruction. All ureteral reconstructions were performed by a surgical team consisting of a transplant surgeon and a urologist at the same institution between November 2012 and March 2021.

3. Cases: Ureteropyelostomy

3.1. Case 1

A 69-year-old female patient with a medical history of DMII, HTN, and recurrent urinary tract infections (UTIs) underwent a cadaveric renal transplant in September 2015 for end stage renal disease (ESRD) secondary to DMII. Her immunosuppressive therapy consisted of tacrolimus and MPA. The ureteral stent was removed three weeks later. The patient had multiple admissions throughout the next three months due to acute kidney injury (AKI) and recurrent UTIs. RUSs and renal biopsies throughout this period showed mild to moderate hydronephrosis of the transplanted kidney and capillaritis, glomerulitis, and thrombotic microangiopathy (TMA), suggestive of mild calcineurin inhibitor (CNI) toxicity.

She was hospitalized three months after the transplant with a Cr of 4.06, and a subsequent nephrostogram showed complete occlusion of the mid-ureter. Due to this occlusion, a balloon ureteroplasty was performed, and a double-J ureteric stent was placed. A nephrostogram taken after stent placement showed free passage of contrast through the stented ureter and into the bladder. Her Cr decreased to 2.97, and she was discharged home.

The PCN and stent were removed three weeks after her discharge, and she was hospitalized three weeks later for AKI. RUS showed stable moderate hydronephrosis of the transplanted kidney (**Figure 1**), and a PCN and stent were

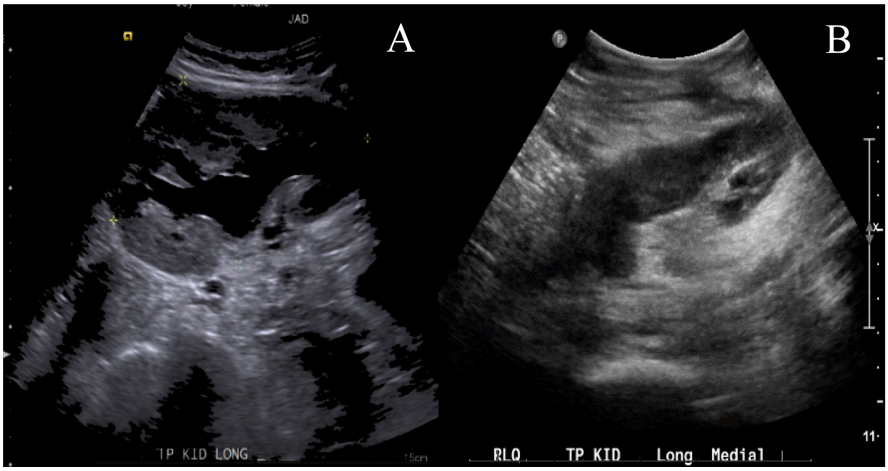

Figure 1. Case 1: RUS before ureteral reconstruction (A) showing stable moderate hydronephrosis and after (B) showing improvement in hydronephrosis.

placed. Subsequent nephrostogram showed free flow of contrast into the urinary bladder through the ureteral stent and the PCN was removed. She was discharged home with a Cr of 2.2.

Five months later, she underwent a right stent exchange. A retrograde pyelogram was performed and showed no filling defects or hydronephrosis of the right native ureter, but the transplanted ureteral orifice showed a stricture preventing the drainage of contrast solution over 20 minutes. The next month, she underwent ureteropyelostomy of the right native ureter to the pelvic transplanted kidney. During this procedure, an intraoperative US was performed to aid in identifying the transplanted ureter. There were no complications, and she was discharged home with a Cr of 1.70.

The ureteral stent was removed two months after the ureteropyelostomy. The patient's most recent RUS taken five months after this reconstruction (**Figure 1**) showed improvement in hydronephrosis. Her kidney allograft function has been consistent since surgery with Cr values remaining around 1.5.

3.2. Case 2

A 30-year-old male patient with a medical history of DMI, HTN, and metabolic bone disease underwent a cadaveric kidney and pancreas transplant in February 2017. His immunosuppressive therapy consisted of tacrolimus and MPA. The ureteral stent was removed three weeks later. He was admitted to the hospital multiple times within the next eight months due to various infections and leukopenia; however, his kidney function remained stable throughout.

He was hospitalized for fever and pancreatitis nine months post-transplant, during which a RUS showed moderate hydronephrosis of the transplanted kidney and renal biopsy showed acute T-cell-mediated rejection, BANFF 1A, for which he was started on thymoglobulin. He had a rise in Cr to 5.37 and was taken to the operating room (OR) for cystoscopy with plans for retrograde pyelogram and possible ureteral dilation. There were unsuccessful attempts via re-

trograde cannulation of the transplanted ureteral orifice to perform a retrograde pyelogram, and, therefore, a PCN was placed. A month into this admission, the patient underwent an internalization of the PCN to a double J stent. His Cr decreased to 1.34, and he was discharged home.

Within the next four months, he was hospitalized multiple times for recurrent UTIs and AKI. He continued to have obstructive uropathy despite Foley catheterization and PCN placement. Additionally, RUS continued to show mild-moderate hydronephrosis and perirenal fluid collection over this period. A month after this last admission, a nephrostogram was performed and showed no passage of contrast past the UPJ, suggesting worsening stricture. The patient was hospitalized the next day for a rise in Cr to 3.86. RUS showed mild hydronephrosis of the transplanted kidney (**Figure 2**), so he underwent a PCN tube exchange and was discharged home the next day with a Cr of 3.72.

Two months after the PCN exchange, he underwent cystoscopy, stent placement into the native ureter, and an exploratory laparotomy with native ureter to transplanted kidney ureteropyelostomy. Nephrostrogram taken on post-operative day one revealed contrast within the renal collecting system with no contrast passing into the ureter, indicating that the ureteropyelostomy was unsuccessful most likely due to the stricture involving the UPJ and renal pelvis. He then went back to the OR for cystoscopy and retrograde pyelogram with revision ureterocalycostomy of the native ureter to the transplanted renal calyx. The PCN tube was removed a few days later, and he was discharged home with a Cr of 4.86.

His Cr values remained in the 4s for the next several months due to chronic rejection. Throughout the next six months, he continued to have elevated Cr > 4 but no hydronephrosis of the transplanted kidney (**Figure 2**). The patient was listed as "active" on the transplant list in UNOS 6 months after his reconstruction, and the ureteral stent was removed within the next few days. His Cr values have remained between 4 - 6 since being listed in UNOS.

3.3. Case 3

A 70-year-old male patient with a medical history of DMII and HTN underwent

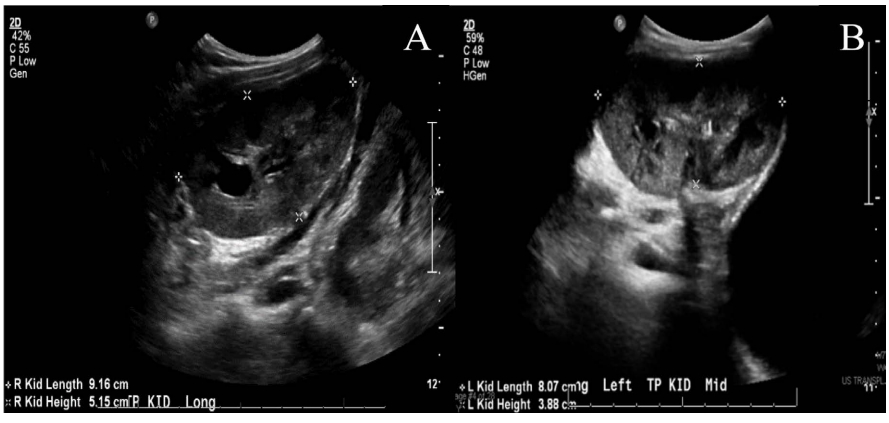

Figure 2. Case 2: RUS before ureteral reconstruction (A) showing mild hydronephrosis and after (B) showing resolved hydronephrosis.

a cadaveric kidney transplant in March 2017 for ESRD secondary to DMII and HTN. His immunosuppressive therapy consisted of tacrolimus and MPA. The ureteral stent was removed one month later. The patient's allograft function had remained stable for the following twelve months.

Within eighteen months post-transplant, he was admitted two times for AKI. During the second admission, RUS showed hydronephrosis of the transplanted kidney, so a PCN tube was placed and then exchanged for a nephroureteral catheter. Nephrostogram showed a high-grade stricture at the UPJ. A renal scan taken the next week showed normal perfusion and adequate excretion with a T1/2 of 14 minutes with the nephroureteral catheter still in place. A week later, cystoscopy showed no prostatic obstruction, the nephroureteral stent was still in place, and his post-void residual was 57cc. The nephroureteral stent was accidentally pulled out three days later and subsequently replaced with a PCN.

During the next twelve months, the patient was admitted multiple times for recurrent UTIs and AKI. Two nephrostograms taken during this time showed UPJ obstruction and ureteral narrowing. CT scans and RUSs continued to show mild-moderate hydronephrosis (Figure 3).

Within thirty months post-transplant, the patient underwent ureteropyelostomy of the right native ureter to the renal pelvis of the transplanted kidney. A ureteral stent was also placed, and the PCN was removed. There were no post-operative complications, and the patient was discharged home with a Cr of 1.96. RUS taken two weeks later with the ureteral stent in place showed resolved hydronephrosis (Figure 3). The ureteral stent was removed one month after the reconstruction. Cr taken five months later was 1.92 and has been stable since this procedure.

3.4. Case 4

A 55-year-old male patient with a medical history of HTN, DMII, HLD, benign prostatic hyperplasia, and CKD underwent a cadaveric kidney and pancreas

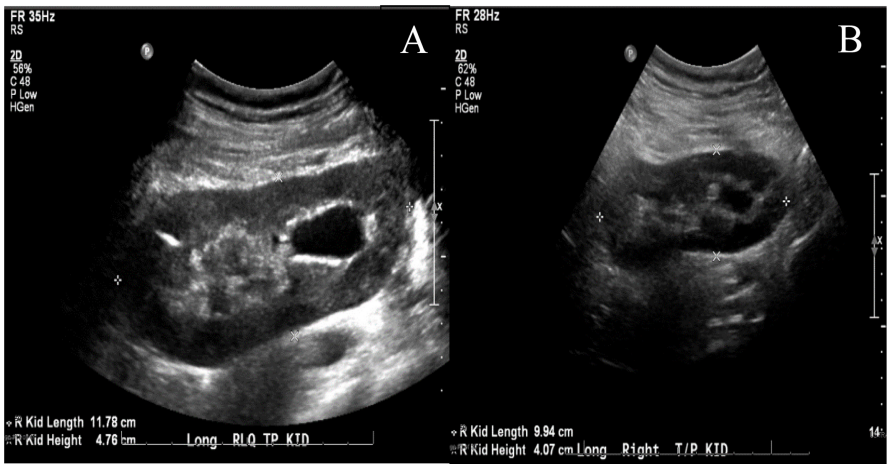

Figure 3. Case 3: RUS before ureteral reconstruction (A) showing mild-moderate hydronephrosis and after (B) showing resolved hydronephrosis.

transplant in April 2017. His immunosuppressive therapy consisted of tacrolimus and MPA. He was discharged home with a Cr of 2.11. Cystoscopy with stent removal was performed six weeks after the transplant. Within the next three months, he was admitted multiple times for intra-abdominal abscess, small bowel obstruction, and enterocutaneous fistula, but his kidney function remained stable throughout this time, and repeat RUSs showed no hydronephrosis.

A CT taken three months after this last admission showed mild hydronephrosis and hydroureter. Subsequent RUS showed hydronephrosis of the transplanted kidney, and a renal biopsy taken three days later showed diffuse interstitial edema consistent with obstruction.

The patient was admitted two additional times within the next two months for AKI. During the first hospitalization, nephrostogram showed a high grade mid-ureteral stricture and RUS showed moderate hydronephrosis that was resolved with PCN placement. His Cr decreased to 1.56, and he was discharged home. A few weeks later, he underwent balloon dilation and anterograde stent placement. RUS taken a week after showed mild hydronephrosis, and he was admitted within the same month with a Cr of 2.29. Renal Mag3 scan showed normal perfusion and a T1/2 of 30. The ureteral stent was exchanged, and a retrograde pyelogram showed UPJ and proximal ureteral stenosis. RUS taken after the PCN exchange showed no hydronephrosis. He was discharged home with a Cr of 2.85.

He received a PCN tube placement a week later with a Cr of 2.91. Nephrostogram showed mid ureteral stenosis and confirmed the stent placement (**Figure 4**), and RUS showed no hydronephrosis. Approximately one-year post-transplant, he underwent ureteral reconstruction consisting of a left native ureter to transplant kidney ureteropyelostomy. Pelvic US taken two days later showed no hydronephrosis and confirmed correct stent placement (**Figure 4**).

There were no post-operative complications, and he was discharged home with a Cr of 3.45. Cystoscopy with stent removal was performed one month after the reconstruction. Cr taken five weeks later was 2.5 and has been stable since

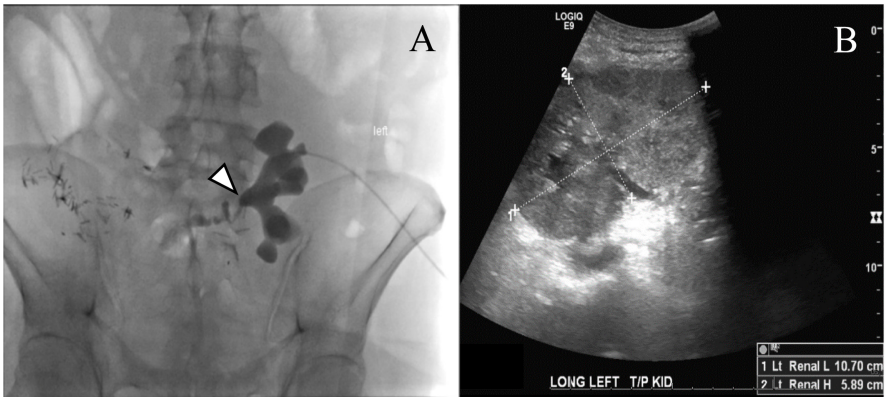

Figure 4. Case 4: (A) Antegrade nephrostogram demonstrating stenosis at ureteropelvic junction (arrowhead) and tortuous transplant ureter before ureteral reconstruction and (B) RUS showing resolved hydronephrosis after reconstruction.

this procedure.

4. Case: Vesicopyelostomy

Case 5

A 62-year-old female patient with a medical history of HTN underwent a cadaveric kidney transplant in February 2016 for ESRD secondary to focal segmental glomerulosclerosis (FSGS). Her immunosuppressive therapy consisted of tacrolimus and MPA. The ureteral stent was removed two months later. Within the next three months, she had multiple admissions for AKI. RUS showed mild hydronephrosis of the transplanted kidney, and renal biopsy showed TMA likely secondary to CNI toxicity. Kidney imaging with renogram performed during this time revealed decreased and delayed perfusion of the transplanted kidney and mild hydronephrosis with a stricture at the ureteropelvic junction (UPJ).

Within five months post-transplant, her Cr increased to 5.8, and a retrograde pyelogram revealed hydronephrosis and a stricture now at the vesicoureteral anastomosis. She then underwent cystoscopy, ureteral dilation, and stent placement with no complications.

The stent was removed five months later, and the patient was hospitalized the next week for AKI. Kidney imaging with renogram and RUS showed moderate hydronephrosis (**Figure 5**) of the transplanted kidney with delayed excretion, likely representing recurrent obstruction at the level of the transplantedureteral vesical junction (UVJ). She underwent cystoscopy and ureteral stent placement. She was discharged home with a Cr of 4.01.

Two months later, the patient underwent a reconstruction consisting of native bladder to transplanted renal pelvis vesicopyelostomy with ureteral stent placement. The procedure had no complications, and she was discharged home with a Cr of 1.33.

The ureteral stent was removed the next month, and a subsequent RUS showed resolved hydronephrosis with only mild residual pelviectasis (**Figure 5**).

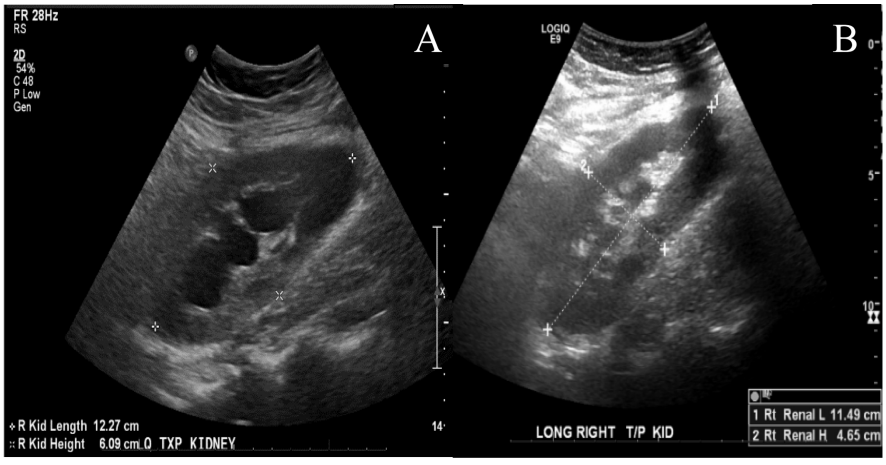

Figure 5. Case 5: RUS before ureteral reconstruction (A) showing moderate hydronephrosis and after (B) showing resolved hydronephrosis.

Her kidney allograft function has been stable since surgery with Cr values remaining around 1.3.

5. Case: Boari Flap

Case 6

A 36-year-old male patient with a medical history of HTN underwent a cadaveric kidney transplant in August 2012 for ESRD secondary to FSGS. His hospital course was complicated by post-operative bleeding, which was ultimately controlled by a blood transfusion and a percutaneous drain. His immunosuppressive therapy consisted of tacrolimus and MPA. Stent removal was scheduled for late August; however, cystourethroscopy showed significant edema at the anastomotic site, and the stent was not removed due to concern for obstruction of the transplanted ureteral orifice by local inflammation. He was admitted that day for pain around the drain and perinephric hematoma. He was discharged home a few days later with a Cr of 1.10.

The stent was removed three weeks after the patient's discharge. He was hospitalized three times within the next two months for AKI. RUS continued to show worsening hydronephrosis of the transplanted kidney. A PCN was placed during the third admission, and a subsequent nephrostogram showed UVJ stricture and anastomotic leak while a RUS showed resolved hydronephrosis. His Cr was stabilized to 1.43, and the patient was discharged home.

He was admitted two weeks later for a ureteral stricture and Cr of 1.62. During this admission and three months post-transplant, Boari flap creation between the transplanted ureter proximal to the stricture and the bladder was performed and a ureteral stent was placed. His Cr was stabilized to 1.3, and the patient was discharged home.

Cystogram performed 5 weeks after the procedure revealed no leak, and the ureteral stent was subsequently removed. RUS performed two months later showed mild but decreased hydronephrosis. Cr has been stable around 1 since the reconstruction.

6. Case: Ureteroneocystostomy

Case 7

A 69-year-old male patient with a medical history of HTN, peripheral artery disease, and previous kidney transplant in 1991 underwent a cadaveric kidney transplant in January 2021 for ESRD secondary to HTN. His immunosuppressive therapy consisted of belatacept, MPA, and prednisone. He was found to have acute tubular necrosis on post-operative day five and continued to have delayed graft function necessitating three sessions of hemodialysis postoperatively. He was discharged home with a Cr of 6.31, and his Foley catheter and JP drain were removed one week later.

Cystoscopy with stent removal was performed three weeks after the transplant, and the patient was admitted to the hospital one week later due to UTI

associated with bacteremia. RUS showed stable moderate hydronephrosis of the left transplant kidney and dilation of the proximal transplant ureter (Figure 6). Cr increased to 8.42 from a baseline of 5. Anterograde nephrostogram showed a severe distal ureteric stricture near the anastomosis. A PCN was placed, which was unable to be converted to a percutaneous nephroureteral stent due to complete obstruction of the ureteral anastomosis.

He underwent ureteral reconstruction consisting of a non-transecting side-to-side ureteroneocystostomy with stent placement within nine weeks after the initial transplant procedure. There were no immediate postoperative complications, and he was discharged home with a Foley catheter, JP drain, intact PCN, and Cr of 1.84. RUS took four days after discharge showed mild hydronephrosis of the transplanted kidney, which was decreased from previous imaging (Figure 6).

The Foley catheter was removed one week after the procedure, and he was hospitalized two days later for increased output from the JP drain. Fluid Cr was suggestive of urine leak. Nephrostogram showed no hydronephrosis or definite leak. The Foley catheter was replaced and the PCN was continued. He was discharged home with a Cr of 1.96. Nephrostogram performed three weeks later showed no leak, and the PCN, JP drain, and Foley catheter were removed. Cystourethroscopy with ureteral stent removal was performed one month after the reconstruction. RUS taken within three months of the reconstruction showed minimal hydronephrosis of the transplanted kidney, and the patient's Cr has remained stable around 2.1 since the procedure.

7. Results

The results of this case series are summarized in Table 1.

Among these seven patients, two of them are female, and five of them are male. The age range of the patients when they received the ureteral reconstruction was 28 - 69, with the average age being 53.1. The range of time between transplant and ureteral reconstruction for these patients was 2.1 - 30.1 months, with the average being 12.7 months.

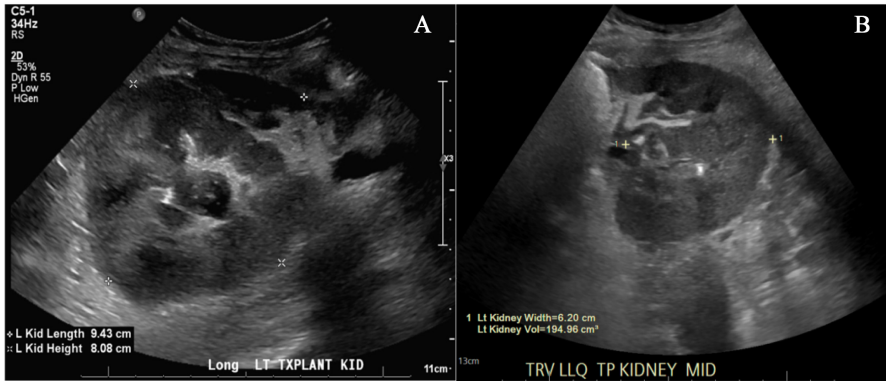

Figure 6. Case 7: RUS before ureteral reconstruction (A) showing stable moderate hydronephrosis and after (B) showing minimal hydronephrosis.

Table 1. Outcomes for the seven Ureteral reconstructions.

Patient #	Stricture Location	Procedure Performed	Outcomes
1	Mid-ureter	R native ureter to transplanted kidney ureteropyelostomy	Mild, but reduced hydronephrosis
2	UPJ	1. L native ureter to transplanted kidney ureteropyelostomy	1. Failed
3	UPJ	2. Revision ureterocalycostomy	2. Resolved hydronephrosis but developed chronic rejection
		R native ureter to transplanted kidney ureteropyelostomy	Resolved hydronephrosis
4	Mid-ureter	L native ureter to transplanted kidney ureteropyelostomy	Resolved hydronephrosis
5	UVJ	Transplanted ureter to bladder vesicopyelostomy	Resolved hydronephrosis
6	UVJ	Boari flap creation	Mild, but reduced hydronephrosis
7	Distal ureter near anastomosis	non-transecting side to side ureteroneocystostomy	Minimal, but reduced hydronephrosis

For all patients, ureteral stricture was suspected due to hydronephrosis and AKI, and later confirmed by nephrostogram or retrograde pyelogram. Two patients presented with a high grade mid ureteral stricture and two with a high-grade occlusion of the UPJ, all requiring ureteropyelostomy for correction. Three patients presented with a stricture at the ureterovesical anastomosis, one requiring a Boari flap, one a vesicopyelostomy, and the last a non-transecting side-to-side ureteroneocystostomy. Six out of the seven reconstructions were initially successful, with one requiring immediate revision due to persistent obstruction. This patient had concomitant rejection leading to intrarenal stricture requiring ureterocalycostomy. One reconstruction was complicated by anastomotic leak, which resolved with conservative management. Hydronephrosis was either reduced or completely resolved as shown by US in six out of the seven patients and these six patients had stabilization of kidney function post-operatively without any additional need for nephrostomy or ureteral stenting. Additionally, renal function in these patients has been preserved since their reconstruction. Unfortunately, renal function continued to decline in one patient most likely due to chronic graft rejection. Despite the successful correction of his obstruction, this patient was placed back on the transplant list in UNOS.

8. Discussion

The primary post-surgical complication rate for kidney transplant is estimated to be 7.1%, with ureteral strictures making up more than 50% of these complica-

tions [6]. Around 90% of early strictures (<3 months after surgery) are due to ureteral ischemia, while other notable causes include external compression from a hematoma or lymphocele as well as technical error. Additionally, late strictures (>3 months after surgery) are predominantly due to ischemic fibrosis, acute rejection, or vasoconstriction causing reduced blood flow as a side effect of immunosuppressants [7]. Risk factors for ureteral stenosis and strictures include donor and recipient age, number of arteries >2, prolonged warm ischemia time, and the presence of post-transplant delayed graft function [3] [8]. Although primary prevention of ureteral strictures is difficult, high-risk patients should undergo consistent monitoring to diagnose and treat this complication as soon as possible [8]. First-line treatment typically involves placement of a PCN, as was done in our seven patients, as well as dilation and stent placement. If these treatments fail, formal reconstruction is indicated. The specific procedure performed depends on many factors, including the length of available ureter, stricture length and location, bladder capacity, and surgeon discretion.

Our patients are complex, with many of them having a history of prior transplant, kidney-pancreas combined transplant, and many co-morbidities, likely contributing to stricture recurrence observed throughout their hospital course. Initial management consisted of stenting and/or PCN placement, while some patients also required ureteral dilation. However, every patient continued to have stricture recurrence post-dilation, independent of stricture location, resulting in multiple hospital readmissions for AKI. For many patients, allograft function was likely affected by recurrent infections and multiple co-morbidities, and no treatment given prior to the ureteral reconstruction was effective in stabilizing and preserving kidney function. Conservative management with dilation failed in all these cases and likely led to a prolonged course containing additional procedures with PCNs and stents, additional admissions, and potential loss of graft function.

Although there is significantly more data involving ureteroureterostomy and ureteroneocystostomy, our case series, as well as the current literature, reports comparable outcomes between these procedures and newer, less common ones, such as ureteropyelostomy and vesicopyelostomy (**Table 2**). Thus, our case series exemplifies potential surgical options that may be utilized when the condition of the ureter or bladder makes ureteroureterostomy and ureteroneocystostomy impractical. For example, Salomon et al. reported a case series in which distal ureteral strictures in nine out of ten patients were corrected with pyeloureterostomy with no evidence of recurrence at two-year follow-ups [9]. Additionally, pyelovesicostomy has been shown to be advantageous when the native ureter is too ischemic or fibrotic for reconstruction [10]. Our study, although small, further supports the use of these surgical procedures on a case-by-case basis. It is advisable to opt for surgical reconstruction early and to use an intraperitoneal approach to minimize graft and anastomotic injury. Performing the reconstruction early also offers the advantage of working with a slightly dilated

Table 2. Comparison of procedures and outcomes between the present study and the current literature.

Author	Number of Patients	Procedures Performed	Complications
Gurkan *et al.* [5]	75	41 ureteroureterostomy, 34 ureteroneocystostomy (Lich-Gregoir technique)	3 recurrent strictures and 2 hematuria in ureteroureterostomy group, 3 vesicoureteral reflux and 1 stent migration in ureteroneocystostomy group
Pike *et al.* [4]	41	Ureteroureterostomy	2 hematuria, 3 ureteral strictures
Riediger *et al.* [11]	16	16 ureteropyelostomy	2 early surgical complications, repaired with Boari flap
Helfand *et al.* [10]	13	6 transplant ureteral re-implant, 1 ureteroureterostomy, 5 pyelovesicostomy, 1 Boari flap creation	Recurrent stricture in 1 ureteral re-implant, 1 Boari flap creation, 1 pyelovesicostomy managed with either chronic stent exchange or balloon dilation
Yang *et al.* [12]	7	2 ureteroureterostomies, 5 pyeloureterostomy	1 ureteroureterostomy developed chronic rejection
Present Study	7	4 ureteropyelostomy, 1 vesicopyelostomy, 1 Boari flap creation, 1 ureteroneocystostomy	1 ureteropyelostomy required revision ureterocalycostomy and developed chronic rejection

renal pelvis that can facilitate easier identification and dissection when performing a ureteropyelostomy. It is also advisable to perform a kidney biopsy intraoperatively at the time of reconstruction to identify and, subsequently, correct other renal graft pathology.

The major limitations of this study are the small sample size and the limited number casesinvolving the various types of ureteral reconstruction. Additionally, there were too few patients to compare the effectiveness and outcomes of each specific type of ureteral reconstruction. Lastly, this study was performed at one institution and needs external validation to assess generalizability. More research needs to be done to sufficiently compare the complication and success rates of these interventions to establish a recommended standardized approach for surgical reconstruction. This is particularly important because with the progressively increased use of marginal donors and longer cold ischemia time, ureteral strictures may be seen with an increased frequency in the future.

9. Conclusion

Ureteral stricture is a common complication of kidney transplantation, for which formal reconstruction is the definitive treatment in many cases. These surgical techniques must be chosen on a case-by-case basis, considering both the physical and functional state of the bladder, ureter, and kidney. Our series outlines a few of the potential surgical approaches that may be performed to treat ureteral strictures, with all resulting in resolved hydronephrosis.

Consent to Publish

Informed consent was obtained from all patients for publication.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Urological Endoscopy: Results of the First 15 Months, in Kara (Togo)

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Abstract

Background: The urology department of the Teaching Hospital of Kara is the 2nd urology department in Togo, Kara being a semi-urban town located 400 km from Lomé the capital. While for a long time only open surgery was used, the acquisition of urological endoscopic equipment in February 2021, has revolutionized the urological management of patients. Objective: Report the results of the first 15 months of urological endoscopy practice at the Kara Teaching Hospital, identify the particularities, announce the prospects. Patients and Methods. This was a retrospective and descriptive study, which took place in the urology department of the Kara Teaching Hospital, from February 2021 to April 2022, *i.e.* a period of 15 months. The register of operative reports and patient records were used for data collection. The following parameters were studied: age, sex, diagnosis, indication, diagnostic or therapeutic nature of the procedure, and results. EPI INFO 7.2.4.0 software was used for data analysis. Results: A total of 102 urological procedures (endoscopic and non-endoscopic) were performed during the study period; of the 102 interventions, 62 were endoscopic urological interventions, *i.e.*, 60.7% of the interventions. The average age of patients treated was 55.5 years (±16.4) with extremes ranging from 28 to 87 years. Men accounted for 84% of patients treated. Prostatic hypertrophy was the most common urological pathology in our study, requiring endoscopic intervention in 40% of cases. Transurethral resection of the prostate was the most performed endoscopic procedure in our study with 43.5% of cases. The various endoscopic interventions resulted in success in 96.7% of cases. Conclusion: Urology nowadays cannot be done without endoscopy. At the Kara Teaching Hospital, the results are already promising after less than 24 months of endoscopic practice

in urology. Advocacy must be made to political decision-makers, so that the situation is even better, for the good of both urologists and patients.

Keywords

Urological Endoscopy, Results, Kara, Togo

1. Introduction

The advent of endoscopic techniques has revolutionized the management of urological pathologies, both diagnostically and therapeutically in the world. In our sub-Saharan countries, urological pathologies were treated by open surgery, for a very long time, with high morbidity and mortality and postoperative hospital stay [1]. While hospitals in African capitals are equipped with endoscopic equipment in order to offer the population better care [2] [3], hospitals in other distant cities often lag behind. In Kara, a semi-urban town, located 400 km north of Lomé, the capital of Togo, the urology department of the Kara teaching Hospital was equipped with endoscopic equipment at the beginning of 2021. Before this date, urological pathologies were treated only by open surgery, with high morbidity [1]; endoscopic techniques had never been used. The aim of our study was to report the results of the first 15 months of urological endoscopy practice at the Kara Teaching Hospital.

2. Patients and Methods

This was a retrospective and descriptive study, which took place in the urology department of the Kara Teaching Hospital, from February 2021 to April 2022, *i.e.* a period of 15 months. The register of operative reports and patient records were used for data collection, including any patient who underwent an endoscopic urological intervention in the urology department of kara teaching hospital, and whose file was usable. The following parameters were studied: age, sex, diagnosis, indication, diagnostic or therapeutic nature of the procedure, and results.

Data processing was done by Word, Excel and the EPI Info statistical software.

3. Results

A total of 102 urological procedures (endoscopic and non-endoscopic) were performed during the study period; of the 102 interventions, 62 were endoscopic urological interventions, *i.e.* 60.7% of the interventions. The average age of operated was 55.5 years (±16.4) with extremes ranging from 28 to 87 years. **Figure 1** shows the number of endoscopic procedures performed per year. **Figure 2** shows the distribution of operated patients according to sex. In our study, 40.3% of endoscopic interventions had been performed for prostatic hypertrophy, followed by interventions for the removal of ureteral endoprostheses in 17.7% of cases..

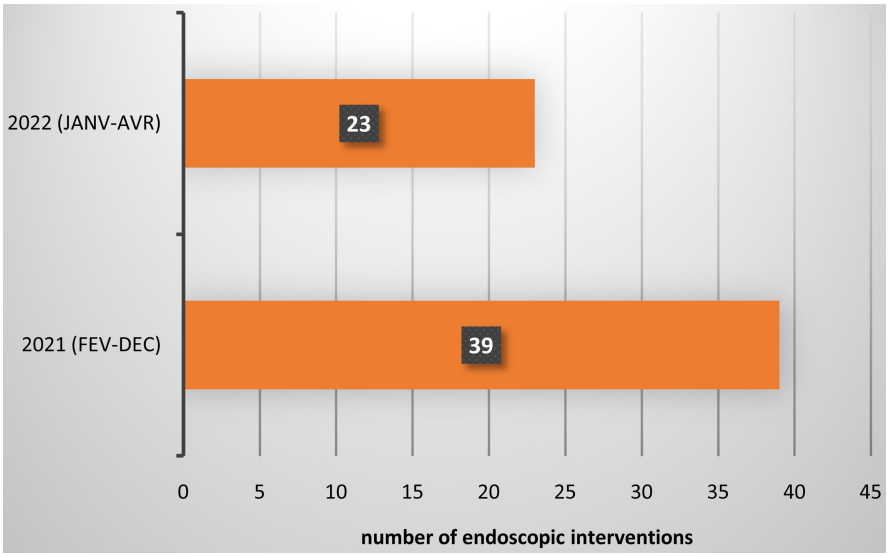

Figure 1. Distribution of endoscopic procedures by year.

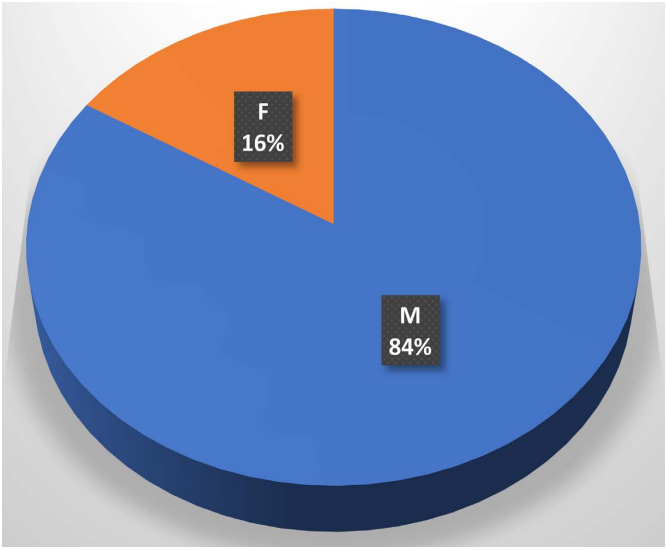

Figure 2. Distribution of patients according to sex. F: Feminine; M: Male.

Bladder tumours, and ureteral stones come next, with 9.6% of cases each. Table 1 shows the various pathologies diagnosed and which required endoscopic urologic intervention. TURP is the most used endoscopic intervention in our study with 43.5% of cases followed by the removal of JJ probes in 17.4% of cases. Table 2 shows the various indications requiring endoscopic intervention. The endoscopic intervention was performed for diagnostic purposes in 17.4% (11) of cases, and for therapeutic purposes in 82.2% (51) of cases. The various endoscopic interventions resulted in success in 96.7% of cases. About the patients with whom we had failures, it was about two patients who had a lumbar lithiasis, and in whom we had proposed a ureteroscopy. During their treatment, the stone moved up into the kidney; not having a flexible ureteroscope, we had just put in place a JJ probe.

Table 1. Pathologies requiring endoscopic intervention.

Diagnostic	Frequency	Percent
Ureterohydronephrosis by tumor compression	1	1.6
Cystitis	2	3.2
presence of ureteral endoprosthesis	11	17.7
Hématuria	1	1.6
Prostatic hypertrophy	25	40.3
Prostatic hypertrophy + Inguinal hernia	1	1.6
Prostatic Hypertrophy + Urethral Stenosis	2	3.2
Ureteral lithiasis	6	9.6
Acute retention of urine byclots	1	1.6
Urethral stricture	4	6.4
Bladder tumor	6	9.6
Ureterocele	1	1.6
Total	62	100

Table 2. Indications requiring an endoscopic intervention.

Indications	Fréquence	Pourcentage
JJ catheter removal	11	17.4
Endoscopic decaillotage + hemostasis	1	1.6
Bilateral JJ catheter ascent	3	4.8
Ureterocele resection	1	1.6
TURP	27	43.5
TURBT	4	6.4
Urethrotomy	3	4.8
Urethrotomy + TURP	1	1.6
Urethrotomy + TURP + Hydrocele	1	1.6
Rigidureteroscopy	4	6.4
Urethrocystoscopy	6	9.6
Total	62	100

4. Discussion

Endoscopy in urology consists of using minimally invasive techniques to explore and treat certain pathologies of the urinary system using optical equipment called an endoscope [2]. Endoscopic procedures are the most performed procedures in urology in the West, with a rate of around 80% [4] [5]. In our sub-Saharan countries, this rate barely exceeds 50% [6] [7] [8]. Difficulties, especially financial, would prevent the acquisition of adequate equipment for carry-

ing out endoscopic interventions. However, at home in Kara, nearly 60% of our interventions were endoscopic in 15 months of endoscopic practice. This difference with our sub-Saharan colleagues could be explained by the fact that the urology department of the Kara Teaching Hospital had endoscopic equipment from the outset, allowing not only diagnostic exploration, but also the therapeutic management of pathologies. many hospitals in black Africa, when acquiring their endoscopic equipment, only had what was necessary for endoscopic exploration (urethrocystoscopy, removal of the JJ probe, etc.). It was only afterwards that equipment was acquired to perform prostate or bladder resections, or even equipment to allow the management of urinary stones by rigid or flexible ureteroscopy [9].

We note in our study that transurethral resection of the prostate (TURP), was the most performed endoscopic intervention in 43.5% of cases. TURP is considered the gold standard in the surgical management of benign prostatic hyperplasia, with a significant reduction in morbidity and mortality and postoperative stay [10] [11]. Halidou in Niger had found at 0.96% in 2022 [2], and Kambou, 8% in 2006 in Burkina Faso [12]. We note that the figures differ depending on the year and the country. Halidou had noticed in his study that few hospitals had a resector; which explained the low performance rate of TURP; as for Kambou, its figures dating from 2006, it is very likely that the rate of realization of TURP is higher today. Prostatic pathology, being also the most encountered in a urology department, it is easy to see that TURP is the most performed intervention in our study. This rate would be even higher in our study if the available resection material allowed TURP to be performed for more than one hour. This constraint forces us to choose only patients whose prostate volume did not exceed 60 to 80 cc for TURP. Patients with a larger prostate volume benefited from a prostatic adenomectomy via the upper route. In the future, we plan to acquire equipment allowing prostatic resection for more than an hour.

Rigid ureteroscopy, for the management of ureteral stones, represented 6.4% of our endoscopic procedures. Preferred to open surgery, it has the advantage of considerably reducing the length of hospital stay. The rate of realization of this endoscopic technique is low in our study, because the diagnosis of ureteral stones is not often made in the department. It should also be noted that some patients treated for renal lithiasis had undergone open surgery, since we do not yet have a flexible ureteroscope. We agree with Niang [13] that the routine practice of ureteroscopy in sub-Saharan Africa remains a challenge for African urologists. When we know that the type of diet plays an important role in the occurrence of urolithiasis on the one hand, and that our diet is more and more modeled on the Western model on the other hand, it is inevitable that we will be increasingly faced with cases of urinary lithiasis. We must therefore fight to have the complete equipment necessary for the management of urolithiasis by endoscopic route.

The success rate of our endoscopic procedures was 96.7%. Halidou had also found a success rate of around 100% [2]. These figures prove that, despite the

recent nature of the acquisition of endoscopic equipment, in our African health structures, there are already urologists trained in its use; most acquired this skill during their specialization in certain countries of the sub-region, where urological endoscopy is already highly developed; or during internships in Western hospitals. It would be a shame if, after having acquired such skills, often at the cost of many sacrifices, to lose them for lack of an adequate technical platform; It is therefore urgent that, on the political level, the necessary is done, in order to remedy this situation, which does not help either the urologist who will lose his skills, nor the population who will not benefit from the best care.

5. Conclusion

Urology nowadays cannot be done without endoscopy. At the Kara Teaching Hospital, the results are already promising after less than 24 months of endoscopic practice in urology, with a technology platform that was still incomplete until then. The financial cost of acquiring such equipment prevents many sub-Saharan urologists from being comfortable in their daily desire to give the best possible care to their patients. Advocacy must be made for political decision-makers, so that the situation improves, for the good of both urologists and patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Renal Function in Patients Undergoing Nephrectomies for Benign and Malignant Causes: An Expected Outcome

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Abstract

Objective: to assess the evolution of serum creatinine in patients undergoing radical nephrectomy (malignant) or total (benign), to identify risk factors connected with an unfavorable renal function outcome. **Material and Methods:** observational, transversal and retrospective study, through analysis of records and lab exams of 146 patients undergoing nephrectomy from January 2015 to December 2018. **Results:** Statistically significant difference was found between etiology and patients' age (p-value < 0.001). Mean age of patients with malignant etiology (59.4 years) was significantly higher than the mean age of patients with benign etiology (47.3 years). As for the surgical technique, 49 had video-laparoscopic (VLP) nephrectomy. The main causes of nephrectomy were renal cancer (52%) and lithiasis (35.6%). Most patients had a fairly uneventful postoperative course (65%). There was a statistically significant difference between etiology and creatinine levels, with a significantly lower creatinine median in the patients with malignant etiology as compared to benign etiology in the preoperative period. **Conclusion:** This study shows that a large number of young patients undergo nephrectomy, many times avoidable; within a benign disease context with an increased risk of developing renal failure. Greater attention from the public service is required to tackle such chronic condition and its complications.

Keywords

Nephrectomy, Kidney Function, Chronic Kidney Disease, Health Plans and Programs

1. Introduction

Nephrectomy is indicated, mainly, within the benign diseases context, such as

non-functional kidney, urinary stones, infection and trauma (total or simple nephrectomy) [1] and malignant ones, in the cases of large tumors (radical nephrectomy) [1] [2]. The procedure, regardless of etiology, is associated with adverse perioperative and long term events.

Acute renal injury is a frequent complication following nephrectomy that may lead to the development of chronic renal disease (CRD) and further comorbidities [3] [4]. Strict follow-up of such patients is strongly recommended [5] [6].

In the literature, it is quite clear that preoperative renal dysfunction, old age, male gender and associated morbidities (DM, SAH, obesity) are a few of the risk factors connected with the occurrence of CRD following nephrectomy [1] [3] [7]. However, scarce is the data comparing whether the type of nephrectomy (radical vs. total) is associated with the development of CRD and related morbidity.

The total nephrectomy has been performed in younger patients within a chronic disease context and it may be considered a public health issue [8]. Formation of lithiasis occurs through a multifactorial and complex process, often leading to higher kidney function rates and comorbidities as compared to patients with renal tumors.

Based on analysis of patient records in a public service in the state of São Paulo, the aim of this paper was to assess the evolution of serum creatinine in patients undergoing radical or total nephrectomy, also identifying the factors connected with an unfavorable kidney function outcome.

2. Material and Methods

This is an observational, transversal and retrospective study that analyses the records and lab tests of patients undergoing radical or total unilateral nephrectomy from January 2015 through December 2018 approved by Institutional Review Board of the Santa Marcelina Hospital under number 1.014.385. The study included patients aged over 14 years, regardless of gender or ethnic, undergoing total or radical nephrectomy by an open or video-laparoscopic surgical approach.

The study data were captured through the electronic surgical records system, starting from the surgery name "nephrectomy—total and radical", thus informing the date of the procedure and the name of all patients who had had the surgery for later analysis of the entire record, collecting: age, cause of surgery, comorbidities and vices. Also analyzed were urea and creatinine serum lab tests: preoperative, immediate surgical postoperative, recent (3 months following surgery) and late (1 year after surgery). Information on the tumor size, surgical technique (video-laparoscopic or open) and postoperative complications (Clavien-Dindo) was also collected.

Patients with previous terminal renal failure, patients undergoing a living donor procedure for transplantation or partial nephrectomy were excluded. Those who missed outpatient follow-up during the first year after surgery were ex-

cluded as well.

The data analysis process began with a descriptive exploration of databases, including the distribution of variables frequencies and calculation of parameters as mean, standard deviation, median and interquartile range.

For comparison of etiology groups (benign and malignant), the Qui-square test or Fisher's exact test was used for qualitative variables; and T tests or Mann-Whitney test for quantitative variables. For comparison between the levels of urea and creatinine measured at different moments, within each group, Friedman's test was used, having Wilcoxon's test with Bonferroni's correction as *post hoc*.

As computer support we used IBM SPSS 26 (IBM corp., 2019) and Microsoft Excel 365® Software. All tests carried out took into consideration a two-tailed 0.05 α significance and a 95% confidence interval (CI).

3. Results

One hundred and forty-six (146) patients were assessed, irrespective of gender or ethnics, with average age of 59.4 ± 11.5 years for patients with a malignant disease and of 47.3 ± 14.1 for those with a benign disease (Table 1). Among the patients, approximately 51% were hypertensive, 25% diabetic, 10% had some degree of chronic renal failure, 21% smokers and 2% with a previous AMI (Table 2).

Table 1. Presentation of the study variables comprising the quantitative descriptive analysis of patients and nephrectomy surgeries performed.

Variables		Etiology			
		Benign		Malignant	
		Mean (±DP)	Median (P25 - P75)	Mean (±DP)	Median (P25 - P75)
Patient age* (years)		47.3 (±14)	48 (36 - 53)	59.4 (±11)	61 (53 - 67)
Urea	**Pre**	45 (±33)	31 (26 - 56)	37 (±17)	32 (26 - 42)
	POI	51 (±39)	36 (26 - 53)	47(±23)	45 (33 - 54)
	POT	54 (±40)	37 (30 - 57)	49.6 (±23)	44 (33 - 61)
	1 year	54 (±41)	41 (31 - 62)	49.7 (±26)	42 (35 - 56)
Creatinine	**Pre****	2.2 (±3.2)	1.07 (0.9 - 2)	1.15 (±0.9)	0.98 (0.7 - 1.3)
	POI	2.5 (±3.2)	1.2 (0.98 - 2)	1.6 (±0.94)	1.45 (1 - 1.9)
	POT	2.4 (±3.2)	1.16 (0.9 - 1.8)	1.5 (±0.9)	1.35 (1.07 - 1.6)
	1 year	2.3 (±2.8)	1.2 (0.9 - 1.9)	1.5 (±1.4)	1.22 (1 - 1.6)
Hospitalization (days)		4.8 (±6.7)	3 (3 - 4)	4 (±1.9)	3 (3 - 4)
Cancer Size		-	-	7.54 (±4)	7 (4.7 - 1)

*p-value < 0.001; **p-value = 0.1.

Table 2. Distribution of the study variables frequency, comprising qualitative descriptive analysis of patients and nephrectomy surgeries performed.

Variables	Etiology				Total (n = 146)	
	Benign (n = 69)		Malignant (n = 77)			
	N	%	n	%	n	%
Surgery						
Open	40	66.7	34	44.2	74	50.7
VLP	29	33.3	43	55.8	72	49.3
Laterality						
Right	27	39.13	38	49.35	65	44.52
Left	42	60.87	39	50.65	81	55.48
VLP Approach						
Retro	3	10.34	3	6.98	6	8.33
Trans	26	89.66	40	93.02	66	91.67
Cause						
Angiomyolipoma	1	1.45	-	-	1	0.68
Endometrioma	1	1.45	-	-	1	0.68
UPJ Stenosis	6	8.70	-	-	6	4.11
Lithiasis	52	75.36	-	-	52	35.62
Pyelonephritis	1	1.45	-	-	1	0.68
Vesicoureteral Reflux	1	1.45	-	-	1	0.68
Polycystic Kidney	4	5.80	-	-	4	2.74
Tuberculosis	1	1.45	-	-	1	0.68
Other	2	2.90	-	-	2	1.37
Renal cancer	-	-	76	98.70	76	52.05
Retroperitoneal Tumor	-	-	1	1.30	1	0.68
Age (years)						
20 - 30	8	11.59	1	1.30	9	6.16
31 - 40	17	24.64	5	6.49	22	15.07
41 - 50	19	27.54	10	12.99	29	19.86
51 - 60	11	15.94	22	28.57	33	22.60
61 - 70	10	14.49	28	36.36	38	26.03
71 - 80	3	4.35	10	12.99	13	8.90
>80	1	1.45	1	1.30	2	1.37
Comorbidities						
SAH	29	42.03	45	58.44	74	50.68
	40	57.97	32	41.56	72	49.32

Continued

DM	11	15.94	26	33.77	37	25.34
	58	84.06	51	66.23	109	74.66
CRD	11	15.94	4	5.19	15	10.27
	58	84.06	73	94.81	131	89.73
Smoking	9	13.04	22	28.57	31	21.23
	60	86.96	55	71.43	115	78.77
AMI	1	1.45	2	2.60	3	2.05
	68	98.55	75	97.40	143	97.95
Clavien-Dindo						
0	46	66.67	49	63.64	95	65.07
I	10	14.49	18	23.38	28	19.18
II	4	5.80	6	7.79	10	6.85
IIIa	1	1.45	0	0.00	1	0.68
IIIb	4	5.80	2	2.60	6	4.11
IVa	2	2.90	2	2.60	4	2.74
IVb	1	1.45	0	0.00	1	0.68
V	1	1.45	0	0.00	1	0.68

In regard to the surgical technique, about 49% had undergone video-laparoscopic nephrectomy, mostly through a transabdominal approach (91.7%), and 50.7% through an open approach. The left side was the main side approached in 44.5% of the patients. When analyzing the main etiologies, the main causes of nephrectomy were renal cancer (52%) and lithiasis (35.6%), the latter being the principal cause among the benign diseases (Table 2).

Most patients had no complications that would change the normal postoperative course (65%), and as few as 13 patients (8.9%) had severe complications (Clavien-Dindo III-IV), with death as adverse outcome for just one patient who underwent total open nephrectomy for a benign disease (Table 2).

A statistically significant difference was found between etiology and patient's age (p-value < 0.001). Mean age of patients with a malignant etiology (59.4 years and 95% CI [56.79 - 62.02]) is significantly higher than the mean age of patients with benign etiology (47.3 years and 95% CI [43.93 - 50.71]) (Table 1).

There was no statistically significant difference between etiology and urea levels, at any of the moments measured (Pre: p-value = 0.508; POI: p-value = 0.111; POT: p-value = 0.198; 1 year: p-value = 0.616). However, when each group was separately compared, in the benign etiology group, the median for urea levels at pre moment was significantly lower than at the "1 year" moment. Whereas in the malignant etiology group, the median for urea levels at pre moment was significantly lower as compared to POI, POT and 1 year (Table 3).

A statistically significant difference was found between etiology and creatinine

Table 3. Statistical analysis by groups separately, to verify the difference between urea and creatinine levels among the moments measured.

		Etiology	
		Benign	**Malignant**
		p-value	**p-value**
Urea	Pre × POI	0.187	<0.001*
	Pre × POT	0.010	<0.001*
	Pre × 1 year	0.001*	<0.001*
	POI × POT	0.073	0.039
	POI × 1 year	0.066	0.753
	POT × 1 year	0.474	0.502
Creatinine	Pre × POI	**0.002***	<0.001*
	Pre × POT	**0.172**	<0.001*
	Pre × 1 year	**0.031**	<0.001*
	POI × POT	**0.165**	0.032
	POI × 1 year	**0.300**	<0.001*
	POT × 1 year	**0.287**	0.013

*p-value considered significant by Bonferroni's correction (<0.008).

Table 4. Distribution of comorbidities according to the etiologic group (benign vs. malignant).

		Etiology – n (%)		Total (100%)
		Benign	**Malignant**	
SAH	**No**	40 (55.6)	32 (44.4)	72
	Yes	29 (39.2)	45 (60.8)	74
DM*	**No**	58 (53.2)	51 (46.8)	109
	Yes	11 (29.7)	26 (70.3)	37
CRD	**No**	58 (44.3)	73 (55.7)	131
	Yes	11 (73.3)	4 (26.7)	15
Smoking**	**No**	60 (52.2)	55 (47.8)	115
	Yes	9 (29)	22 (71)	31
AMI	**No**	68 (47.6)	75 (52.4)	143
	Yes	1 (33.3)	2 (66.7)	3

*p-value = 0.021. **p-value = 0.026.

levels at Pre moment; *i.e.*, at Pre moment, the median for the creatinine levels in the patients with a malignant etiology is significantly lower than creatinine levels median in the patients of benign etiology (Table 1).

In the analysis of groups individually, we noticed that in the benign etiology

group, the median for creatinine levels at Pre moment was significantly lower as compared to POI moment. Whereas in the malignant etiology group, the median for creatinine levels at Pre moment was significantly lower as compared to moments POI, POT and 1 year (Table 3).

When combining the etiologic groups (benign vs. malignant) and the comorbidities, a statistically significant difference was found only in regard to Diabetes Mellitus and smoking. The proportion of patients with DM of malignant etiology (70%) is significantly higher than the proportion of patients with DM of benign etiology (29.7%). And the proportion of smoking patients with malignant etiology (71%) is significantly higher than the proportion of smoking patients with benign etiology (29%) (Table 4).

4. Discussion

Our study showed mean age of patients with malignant etiology (59.4 years) and benign etiology (47.3 years) patients with a malignant etiology is significantly lower than creatinine levels median in the patients of benign etiology.

Most studies compare nephrectomy for renal tumor (radical) and nephrectomy in renal donors. However, this study carries an analysis between nephrectomies for malignant and benign causes, assessing evolution of the renal function and associated factors.

In this study, it is noticed that patients undergoing unilateral nephrectomy, irrespective of etiology, present higher levels of serum creatinine in the immediate postoperative period as compared to preoperative values. Such information, matches Garofalo *et al*. [4] findings, showing almost 50% of patients developing to acute renal injury in the immediate postoperative period, usually associated with aggravation of progressive renal function.

Development of CRD following a curative renal surgery is known to be associated with an increased risk of cardiovascular events, hospitalization and death [3] [4]. Regardless of the etiology, any loss of nephrons involves a risk of renal dysfunction [9]. In the literature, it is pointed that about 40% of patients undergoing unilateral nephrectomy will develop a progressive chronic renal disease, the main reason being adaptation of the contralateral kidney with hyperfiltration and hyperplasia of the nephrons, known as compensatory renal hypertrophy. At first and to a certain extension, this process keeps the glomerular filtration rate (GFR) stable, however causing structural changes such as glomerulosclerosis and tubular atrophy, evolving to an increased loss of nephrons and permanent renal injury [1] [4].

Lithiasis disease is the most common cause among the benign diseases that require nephrectomy secondary to the development of complications, 75% of cases as shown in our study. Chronic pain, recurrent urinary infections and hypertension are counted among indications for nephrectomy in such patients [10] [11] [12] [13].

Despite the benign character, nephrectomy for urolithiasis, especially through

the laparoscopic approach, is most likely said to be more challenging than radical nephrectomies, on account of intense inflammatory reaction, demanding procedures that are time consuming, complex, and of greater surgical trauma. Many times, the need for conversion to an open surgery is unavoidable [11]. In this study, we demonstrate the viability of a laparoscopic procedure in approximately half the cases connected with benign diseases, with a favorable outcome in all cases through such technique. We had but one death, precisely of a patient who underwent total open nephrectomy, within a benign disease context, evidencing all the technical difficulty in such cases.

The paper has a few limitations, such as retrospective analysis based on patients treated in a single referential center, and a small sample size. A further limitation is connected with underestimation of the glomerular filtration rate as mathematical formulae are not used to better assess the renal function, taking into account other parameters, besides serum creatinine.

In this series, the mean age was significantly smaller in the patients undergoing nephrectomy for benign disease (47.3 ± 14), as compared to a malignant one (59.4 ± 11), with an increased risk, along the time, of developing to a chronic renal disease, even requiring a renal substitution therapy (dialysis or renal transplantation). Such condition can be considered a public health issue to be tackled, due to the significantly higher government costs for patients with a chronic renal disease. Implementation of policies focusing on health promotion is important, as well as tracking risk factors at the primary care level, emphasizing prevention and early treatment.

5. Conclusion

This study shows that a large number of young patients undergo nephrectomy within a benign disease context, many times avoidable, with an increased risk of evolving to renal failure. More attention to the public service is important to tackle this chronic condition and its complications.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

DM = Diabetes mellitus
SAH = systemic arterial hypertension
AMI = acute myocardium infarct
Pre = preoperative
POI = immediate postoperative
POD = delayed
VLP = video-laparoscopic
UPJ = ureteropelvic junction
GFR = glomerular filtration rate

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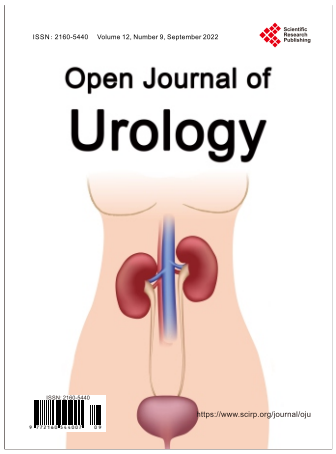

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