UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA VETERINÁRIA

PLACEMENT OF A SUBCUTANEOUS URETERAL BYPASS FOR THE TREATMENT OF URETERAL OBSTRUCTION IN CATS: A RETROSPECTIVE STUDY

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Resumo

Colocação de um *bypass* ureteral subcutâneo para o tratamento da obstrução ureteral em gatos: um estudo retrospetivo

A obstrução ureteral em gatos é uma condição multifatorial e potencialmente fatal com tendência crescente, sendo a causa mais comum a obstrução intraluminal secundária a ureterolitíase. A manifestação pode ser rápida ou insidiosa, e após o diagnóstico, a intervenção imediata é essencial para aliviar a pressão no bacinete renal e evitar uma redução da função renal e lesões renais irreversíveis. O diagnóstico é determinado com base na avaliação dos sinais clínicos, análises sanguíneas, particularmente as concentrações séricas da creatinina e BUN, e exames imagiológicas, tipicamente ultrassonografia e radiografia. Para o tratamento, a abordagem médica deve ser tentada por um curto período de tempo para estabilizar o paciente e procurar resolução. No caso de insucesso da terapêutica médica, a implantação de um *bypass* subcutâneo ureteral (SUB) surge como uma terapia promissorapelo seu potencial na resolução de obstruções ureterais que não teriam outra resolução.

O presente estudo, descreve os resultados e as complicações da colocação do dispositivo SUB em gatos, para o tratamento de obstruções ureterais, no Hospital Veterinário do Porto. Foram analisados de forma detalhada os registos médicos de 5 gatos com ureterolitíase obstrutiva, submetidos à colocação do dispositivo SUB. Os resultados indicam que este procedimento proporciona alívio imediato do bacinete renal, com consequente resolução da lesão renal aguda pós-renal desencadeada pela ureterolitíase obstrutiva. No entanto verificaram-se as seguintes complicações: infeção urinária por bactérias com resistência a múltiplos antibióticos, resultando na morte de dois pacientes. Outras complicações incluíram hipotermia, obstipação, anemia, hematúria e disúria.

Palavras-chave: Obstrução ureteral benigna, Gato, Ureterolitíase, Bypass ureteral subcutâneo, Complicações

Abstract

Placement of a subcutaneous ureteral bypass for the treatment of ureteral obstruction in cats: a retrospective study

Benign ureteral obstruction in cats is a multifactorial and life-threatening condition with an increasing tendency, with the most common cause being an intraluminal obstruction, secondary to ureterolithiasis. The manifestation can be rapid or insidious, and upon diagnosis, immediate intervention is essential to relieve the pressure on the renal pelvis and prevent a decline in renal function and irreversible renal lesions. The diagnosis is determined based on the evaluation of the clinical signs, blood analysis, particularly serum creatinine and BUN concentrations, and imaging modalities, typically ultrasonography and radiography. For treatment, medical management must be attempted for a short period of time in order to stabilize the patient and seek resolution. However, in case of failure of medical therapy, the implantation of a subcutaneous ureteral bypass emerges as a promising therapy due to its potential in resolving ureteral obstructions that would not have any resolution.

The present study describes the outcomes and complications of placing the SUB device in cats for the treatment of ureteral obstructions at the Veterinary Hospital of Porto. The medical records of 5 cats with obstructive ureterolithiasis undergoing SUB device placement were thoroughly analyzed. The results indicate that this procedure provides immediate relief of the renal pelvis, leading to the resolution of post-renal acute kidney injury triggered by obstructive ureterolithiasis. However, the following complications were observed: urinary tract infection caused by bacteria resistant to multiple antibiotics, resulting in the death of two patients. Other complications included hypothermia, constipation, anemia, hematuria, and dysuria.

Keywords: Benign ureteral obstruction, Cat, Ureterolithiasis, Subcutaneous ureteral bypass, Complications

Resumo alargado

Colocação de um *bypass* ureteral subcutâneo para o tratamento da obstrução ureteral em gatos: um estudo retrospetivo

A obstrução ureteral benigna é uma doença multifatorial e potencialmente fatal, com tendências crescentes em gatos. A obstrução ureteral pode manifestar-se rapidamente ou insidiosamente, e uma vez diagnosticada, é necessária uma intervenção urgente para descomprimir a pelve renal e prevenir a diminuição da função renal. O oxalato de cálcio é o tipo mais comum de ureterólitos, que não se dissolvem com o tratamento médico.

Várias abordagens têm sido documentadas para o maneio da obstrução ureteral. O tratamento médico demonstrou baixas taxas de sucesso, destacando a necessidade de haver intervenção cirúrgica com alguma frequência. As técnicas cirúrgicas tradicionais são invasivas e associadas a uma alta morbilidade, levando a um interesse crescente em explorar novas opções de intervenção. A colocação de stents ureterais é relatada como uma abordagem eficaz para o tratamento da obstrução ureteral. No entanto, está associada a um maior risco de complicações a longo prazo e a sua colocação é tecnicamente desafiante. Em certos casos, a colocação de stents ureterais é mesmo contraindicada, como por exemplo na presença de estenoses ureterais ou em pacientes imunocomprometidos. Para além disso, devido às menores dimensões dos ureteres dos gatos, para alguns pacientes a colocação de stents ureterais não é viável.

A implantação do bypass ureteral subcutâneo (SUB) tem sido descrita como um tratamento alternativo exequível para qualquer tipo de obstruções ureterais benignas. Consiste na colocação de um cateter de nefrostomia e um cateter de cistostomia que estão conectados a um portal que se encontra no espaço subcutâneo. Tal proporciona uma descompressão imediata do bacinete renal e permite que a urina seja transportada do rim diretamente para a bexiga, evitando a passagem pelo ureter. Comparativamente aos stents ureterais e aos procedimentos cirúrgicos tradicionais, a colocação do dispositivo SUB é considerada um tratamento com melhores resultados para a obstrução ureteral, pois os tempos cirúrgicos são mais curtos, as taxas de complicações mais baixas e tem resultados mais promissores. Para além disso, é um implante que permite que haja uma manutenção através de lavagens periódicas, proporcionando uma solução a longo prazo para as obstruções ureterais. No entanto, os seus resultados dependem bastante da experiência do cirurgião nessa técnica, existindo uma curva de aprendizagem.

O trabalho apresentado nesta dissertação, é um estudo retrospetivo que descreve os resultados e as complicações da colocação do dispositivo SUB em gatos, para o tratamento de obstruções ureterais, no Hospital Veterinário do Porto entre os anos de 2021 e 2023. Foram analisados de forma detalhada os registos médicos de 5 gatos com ureterolitíase obstrutiva,

submetidos à colocação do dispositivo SUB. Para diagnóstico, todos os pacientes foram submetidos, para além de terem uma historia clínica o mais detalhada possível, as análises sanguíneas (hemograma, concentrações séricas de ureia e creatinina, concentrações séricas de sódio e potássio), análises laboratoriais à urina (urinálise tipo I, urinálise tipo II e urocultura com teste de sensibilidade a antibióticos), ultrassonografia abdominal e a urografia intra-cirúrgica previamente. Pré-cirurgicamente, foram também submetidos inicialmente ao tratamento médico durante pelo menos 24 horas. Este consistia na administração de fluidoterapia endovenosa, maneio da dor com buprenorfina e administração de outros fármacos de acordo com as necessidades de cada paciente (anti-inflamatórios, antieméticos e inibidores da bomba de protões). Aqueles cuja urocultura estava positiva, iniciaram antibioterapia pelo menos 48h antes da cirurgia. Nenhum destes pacientes respondeu ao tratamento médico, pelo que avançaram para a cirurgia de colocação do SUB. Um dos pacientes já tinha sido submetido à colocação de um stent dois anos antes, que obstruiu devido a um nefrólito que progrediu para o ureter. Foram colocadas duas versões do dispositivo: SUB 2.0 e SUB 3.0, sob anestesia geral e fluoroscopia. O sistema SUB 3.0, mais recente, diferencia-se do SUB 2.0 por apresentar um terceiro cateter que permite conectar os cateteres de nefrotomia e de cistotomia à porta, que se encontra no espaço subcutâneo. Na versão anterior os cateteres de nefrostomia e de cistotomia ligavam-se diretamente ao portal. Um dos locais mais comuns para os cateteres vincarem é na saída para o espaço subcutâneo. Assim, no SUB 2.0, se um dos cateteres vincar, a passagem da urina pelo dispositivo fica comprometida, ao contrário do que acontece no SUB 3.0, em que o 3º cateter vinca, mas a urina continua a fluir do rim para a bexiga. Para além disso, na versão 2.0 o cateter de cistostomia terminava em forma de *pigtail*, e na versão 3.0 termina num segmento mais reto que pode ser cortado de forma a que o tamanho seja ajustado a cada paciente. Os parâmetros clínicos, laboratoriais e de imagem (ecografia e radiografia) foram monitorizados antes e depois do procedimento. Todos os pacientes tiveram consultas de controlo e lavagem 1 semana, 1 mês e a cada 3 meses após a cirurgia.

As complicações detetadas no período intra-cirúrgico (desde a indução da anestesia até a recuperação da mesma) foram hipotermia e obstipação. A hipotermia foi a única complicação intra-cirúrgica registada que foi transversal a todos os pacientes. A obstipação foi controlada com sucesso com a administração de lactulose. No período pós-cirúrgico (desde a recuperação da anestesia até 7 dias após a cirurgia) foram detetadas as seguintes complicações: obstipação, anemia, disúria, hematúria, anorexia episódios de febre e infeção urinária com bactérias resistentes a múltiplos antibióticos. A febre foi detetada em três pacientes: dois deles atribuído a origem inflamatória induzido pelo trauma da cirurgia e o 3º devido a um processo infeccioso. Neste estudo, dois pacientes morreram durante o período

a curto prazo (7 a 30 dias após a cirurgia), sendo que a causa foram uma infeção urinária com bactérias resistentes a múltiplos antibióticos que foi detetada 5 dias após a cirurgia e no segundo paciente a causa não foi identificada, pelo que mais estudos teriam de ser feitos a fim de se detetar a razão da morte. No período a longo prazo (para além dos 30 dias após a cirurgia) foram apenas observadas complicações num dos gatos, nomeadamente a reincidência de disúria e hematúria. A disúria não associada a infeção do trato urinário foi uma complicação registada no mesmo paciente em dois períodos diferentes, cuja versão do dispositivo colocada foi a 2.0. Neste caso, propôs-se que o cateter de cistostomia, cuja versão 2.0 tinha a terminação em forma de *pigtail*, entrava em contacto direto com o trígono da bexiga, causando irritação e, por isso, sinais clínicos de disúria.

O dispositivo SUB foi colocado com sucesso em todos os gatos, aliviando a obstrução ureteral e reduzindo a azotémia. A concentração sérica de creatinina diminuiu em média de 7.6 mg/dL para 1.9 mg/dL após a sua colocação. O tempo médio de hospitalização foi de 4.8 dias, bastante semelhante a estudos anteriores. Dois gatos morreram dentro de um mês após o procedimento. Os outros três gatos sobreviveram pelo menos 7 a 20 meses, com melhoria da função renal e qualidade de vida.

Os resultados indicam que este procedimento proporciona alívio imediato do bacinete renal, com consequente resolução da lesão renal aguda pós-renal desencadeada pela ureterolitíase obstrutiva, no entanto, neste estudo, está frequentemente associado a complicações.

A colocação do SUB é um procedimento que oferece uma solução a longo prazo para a obstrução ureteral em gatos. No entanto, é necessário um acompanhamento rigoroso e periódico dos pacientes após a cirurgia. Este acompanhamento é crucial para prevenir e tratar possíveis infeções urinárias, que podem comprometer o prognóstico. As infeções urinárias foram uma complicação significativa observada neste estudo, resultando na morte de dois gatos. Portanto, a gestão adequada das infeções urinárias é vital para garantir o sucesso do tratamento com SUB.

Palavras-chave: Obstrução ureteral benigna, Gato, Ureterolitíase, Bypass ureteral subcutâneo, Complicações

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List of abbreviations

ADH – Antidiuretic hormone

AKI – Acute kidney injury

BUN – Blood urea nitrogen

CBC – Complete blood count

CKD – Chronic kidney disease

CRI – Constant rate infusion

CT – Computerized tomography

DSB – Dried solidified blood

ESWL - Extracorporeal shockwave lithotripsy

GFR – Glomerular filtration rate

HVP – Hospital Veterinário do Porto

IRIS – International Renal Interest Society

ISCAID – International Society for Companion Animal Infectious Diseases

NSAID – Non-steroidal anti-inflammatory drugs

PCV – Packed cell volume

PDA – Patent ductus arteriosus

PTH – Parathormone

RBF – Renal blood flow

SDMA – Symmetric dimethylarginine

SUB – Subcutaneous ureteral bypass

TAP – Transversus abdominis plane

TetraEDTA – Tetrasodium ethylenediaminetetraacetic

USG – Urine specific gravity

UTI – Urinary tract infection

UUTU – Upper urinary tract uroliths

UVJ – Ureterovesicular junction

I. INTERNSHIP ACTIVITIES REPORT

During the 6th year of the Master's degree in Veterinary Medicine, in the first semester, I completed my curricular final internship in the Small Animal practice area in Hospital Veterinário do Porto from OneVet Group, from September 19th of 2022 until February 17th of 2023, which counted a total of approximately 900 hours. The internship contemplated a weekly rotation program through the different hospital departments. The schedule consisted of shifts from 8-16h, 9-17h, 13-20h, 20-9h during the week, and on the weekend were 12h shifts, from 9-21h, and 21-9h.

The clinical activities were in the following services: Consultations, Internment, Internal Medicine, Cardiology, Surgery, Dermatology, Oncology, Anesthesiology, and Imagiology.

In consultations, I was able to observe the anamnesis collection and afterward, I was encouraged to perform the general clinical examination, present the findings to the clinician, the list of differential diagnoses, and propose justified complementary exams. I had the opportunity to actively executed these exams, including laboratory testing, radiography, ultrasonography, and urinalysis, among others. With the results, I discussed the treatment plan, the prognosis, and wrote the prescription. Furthermore, it allowed me to learn basic tasks, including performing vaccinations, drugs administration, and blood and urine collection, as well as develop some skills, like communication with the tutors as a tool to obtain a significant anamnesis and as a means to transmit and make the tutor comprehend the clinician.

Regarding the hospitalization, with the help of a nurse and the responsible clinician, I took care of the hospitalized animals. The day started with the clinical examination of all animals and, when needed, catheters were changed, non-invasive blood pressure measurements, and blood samples collection. When necessary, further complementary exams were performed in order to reach a diagnosis or simply for control. I was responsible for the medications, alimentation, and checking the vital parameters in critical patients throughout the shift. In an emergency context, I actively assisted in their assistance: prepared the drugs for administration, performed the intravenous access, watched over the oxygen therapy, and performed intubation, resuscitation techniques, and complementary diagnostic tests. It was also requested to participate in the clinical rounds.

In the surgery department, I got to assist several procedures, including minimal invasion surgeries, ophthalmologic, orthopedic, neurologic, and soft tissue surgeries. I followed the animal from the admission to the discharge of the surgery. I participated in some pre-consultations and discussed the diagnoses and the different surgical approaches with the clinician. I had the opportunity to perform a few ovariohysterectomy and orchiectomy of cats and dogs as a first-hand surgeon. In some cases, I was able to participate in the postoperative period and follow the progression of some cases.

In the anesthesia service, I could learn and discuss the different anesthesia protocols according to the procedure, the patient, the disease, and any comorbidities. I was also able to perform intravenous catheterization, intubations, as well as control of the fluid therapy, vital parameters, and oxygen therapy throughout various procedures.

In the internal medicine service, I had the chance to follow a European board-certified specialist. I contributed to several consultations and discussed the cases and complementary exams, diagnoses, treatment plan, and prognosis. I also got the chance to attend to many gastrointestinal and respiratory endoscopies.

In the cardiology service I assisted various ultrasounds and electrocardiograms. I discussed with the clinicians about the diagnoses and treatments. Additionally, I had the opportunity to witness minimally invasive surgeries such as pacemaker placement, PDA occlusion, and valvule stenosis ballooning.

Regarding the dermatology service, I had the chance to follow a European board-certified specialist. I participated in multiple first, second opinion, and follow-up consultations, mostly concerning atopic dermatitis, external otitis, and acral lick dermatitis. I was allowed to collect cytology samples, with the following Diff-Quick staining and observation in the optical microscope. Additionally, I observed some CT scans of the ear with subsequent ear flushing. I also watched therapy sessions with Phovia Light as a treatment for profound pyoderma.

In the oncology service, I was in multiple first and follow-up consultations. On both, I was invited to discuss the clinical presentation, complementary exams, the possible diagnoses, and the treatment plan. Moreover, I was allowed to follow chemotherapy and electrochemotherapy sessions. Since the most common disease was mammary carcinoma during the days I was in the department, I was encouraged to read and debate about this topic with the clinician.

Concerning diagnostic imaging, when in each service, this department was crucial to help reach a diagnosis. I was invited to do numerous x-rays, in which I learned how to position the animals and choose the right variables. Additionally, I helped in the ultrasounds, in which I was motivated by the clinician to identify the different structures as well as the abnormalities and how the diseases manifest ultrasonographically. I also watched numerous CT scans.

In the urgency service, I was escalated to do night and weekends shifts. I got to watch and help in the emergency care of critical patients, as well as following the hospitalized patients.

For vocational activities, I was highly encouraged to participate in the Journal Club. Me and the other trainees presented a paper and discussed the topic with each other and the responsible clinician. In some of these meetings, a few clinicians presented to us a topic chosen by them, regarding their area of specialization.

II. LITERATURE REVIEW

1. General considerations about the urinary system

1.1. Anatomy of the urinary system of the cat

The kidneys are located in the retroperitoneal space, pressed underneath the dorsal sublumbar muscles. The right kidney is firmly attached and fits in the fossa of the liver, touching the liver's caudate process (König et al. 2004), at the level of the first to fourth lumbar vertebrae. The left kidney is looser and lies more caudally, below the second to fifth lumbar vertebrae. In cats, the kidneys are pendulous and more mobile when compared with the dog (Dyce et al. 2010; Clarkson and Fletcher 2011).

In companion animals, the kidneys are unilobular and bean-shaped, with a smooth surface. Each kidney is composed of a cranial and a caudal pole, a ventral, dorsal, medial, and lateral superficies. The medial border is concave and comprehends the hilus in the middle, in which enters/exits the renal artery and vein, the ureters, nerves, and lymphatic vessels. In 10% of feline kidneys, is reported to exist multiple renal arteries, an important characteristic to consider during a renal surgery procedure, in order to avoid a severe hemorrhage. Surrounding the kidneys, there is commonly a considerable amount of adipose tissue, that can fluctuate accordingly to the animal's body condition (Tillson and Tobias 2012).

Both kidneys are involved by a thin, fibrous capsule, and divided into the outer cortex and the inner medulla. These structures are crossed by the nephrons, which take the urine to the renal pelvis (König et al. 2004; Dyce et al. 2010). The renal pelvis, a dilation of the proximal end of the ureter, gathers urine from the collecting ducts and is continuous with ureters. It has a funnel shape and irregular margins. It is contained within the renal sinus, a fat-containing recess in the hilus (Clarkson and Fletcher 2011).

The ureter is a paired fibromuscular tubular structure that transports urine from the renal pelvis to the bladder, via peristaltic movements. They leave the hilus, and progress retroperitoneally in a caudal direction, along the psoas muscle, and by the pelvic cavity level, after the extern iliac vessels, turn ventrally towards the bladder's trigone (Mathews 2012). Immediately before the vesicular attachment, the ureters turn from a caudal to a cranial direction, forming a j-hook shape. This curvature modifies with bladder repletion: with greater distension, comes a bigger curvature degree (Adams 2017). The insertion is oblique, the ureters run intramurally, within the vesical wall, between the muscular layer and the mucosa, opening in the lumen of the bladder in two slits (Tillson and Tobias 2012). This results in a valve-like effect that combined with the peristaltic movements promote a unidirectional urine flow and prevent vesicoureteral reflux when the pressure in the bladder increases (Segev 2011; Adams 2017).

Histologically, the ureters are divided into three layers: the outer adventitial layer, the middle smooth muscular layers, and the inner mucosae, with the transition epithelium. The tunica muscularis is composed of 3 layers: a central circular and two inner and outer longitudinal layers. However, in the proximal and distal ends, all layers of smooth muscle fibers are longitudinal (Mathews 2012). The ureter's lumen diameter may differ among species and breeds. In healthy cats is reported to be 0,3 to 0,4 mm, a predisposing factor itself for ureteral obstruction, considering even small ureteroliths may occlude the ureter (Hardie and Kyles 2004; Adams 2017). The ureter's length is reported to be 9,19 cm ± 0,34 cm, and the left ureter is usually shorter than the right ureter (Ichii et al. 2022).

The urinary bladder is a musculomembranous distensible organ, located in the pelvic cavity, and its primary role is to store urine. It is composed of an apex, body, and neck (Lipscomb 2012). Its location depends on the repletion state: when empty and contracted, it is globular and lies under the pelvic bones, when it enlarges, alters to a pear shape and the cranial portion reaches the abdomen (Dyce et al. 2010). It is attached to the abdominal wall through the lateral ligaments and the median ligament, a ventral thin structure that connects the bladder to the *linea alba* (Lipscomb 2012).

The bladder is organized into 4 layers: the outer serosa, the detrusor muscle, the submucosa, and the inner mucosal layer, with transitional epithelium. At the dorsal bladder wall, between the ureters and the urethra opening, in the neck, there is the trigone, a noticeable triangular smooth mucosa (Fletcher and Clarkson 2011; Lipscomb 2012). Moreover, there is the internal urethral sphincter, a non-distinguishable anatomic structure, since the oblique interdigitating muscle fibers of the bladder blend through the urethra's smooth muscle (Fletcher and Clarkson 2011; Lipscomb 2012).

The urethra follows different trajectories in females and in males. In females, the urethra leaves the internal urethral orifice at the bladder neck caudally and opens in the external orifice in the vestibule. It exclusively carries urine. In males, the urethra runs through the pelvic canal to an external opening in the penis. It conveys urine, semen and seminal secretions. The male urethra can be divided in the pelvic part and the penile part. The pelvic part is subdivided in two segments: preprostatic segment, extending from the bladder to the seminal hillock, where it is flanked by the deferent ductus openings, and prostatic segment which tranverses through the prostate gland, where is joined by deferent and vesicular ducts. The penile portion of the urethra begins in the ischial arch and terminates in the penis opening (König et al. 2004).

1.2. Physiology of the urinary system

The kidneys are important to maintain homeostasis, as they excrete metabolic waste. They receive 25% of the cardiac output. They respond to water, electrolyte, and acid-base

variations and consequently adapt the reabsorption and secretion rates of these substances. Additionally, they have an endocrine role, responsible for the control of the volume and composition of the extracellular fluids, significantly influencing blood pressure and erythropoiesis (Valender 2013).

This adaptability comes from the great variety of cell types, each of them having specific responses, and are rearranged in a basic functional unit, the nephron. It is composed of the renal corpuscle (glomerulus and Bowman's capsule), only found in the cortex, where the blood is filtered, and the renal tubules, where the ultrafiltrate undergoes modifications due to the selective reabsorption and secretion actions of the different cells. The nephrons merge into a collecting duct system in the kidney cortex, traversing the medulla all the way to the renal pelvis (Valender 2013).

Each glomerulus, a tuft of capillaries, selectively filtrates blood components through a filtration barrier with specific structural and chemical characteristics. It filtrates freely water, electrolytes, and metabolites into the Bowman's space, forming the ultrafiltrate. Other components, in order to be filtrated, depend on various factors such as size, electrical charge, shape, and deformability. Substances with the same or bigger size than a molecular radius of 4 nm or proteins bigger than albumin are retained in the filtration barrier, while molecules with a radius smaller than 2 nm are freely filtered. Concerning the electrical charge, the barrier is charge-selective. The basal membrane has negatively charged residues, repelling negatively charged proteins. Thus, cationic molecules are more easily filtered than neutral and consequently anionic. The shape and deformability highly affect the ability to cross the filtration barrier. The longer and more flexible the molecules, the easier it is to filtrate, whereas the rounder and stiffer ones do not filtrate as freely (Valender 2013).

The glomerular filtration rate (GFR), the ultrafiltrate's volume and concentration depend on the hydrostatic pressure within the glomerulus capillary tuft as well as some intrinsic factors, such as renin-angiotensin-aldosterone system and antidiuretic hormone (ADH) (Valender 2013). Despite disturbances in the mean systemic arterial pressure, the GFR and renal blood flow (RBF) remain constant, an intrinsic renal property (Brown 2011).

Subsequential to ultrafiltrate formation, it goes through the proximal tubule, where at least 60% of the content is reabsorbed: water, sodium, potassium, calcium, phosphate, glucose, bicarbonate, amino acids, and low-molecular-weight proteins (insulin, glucagon, parathyroid hormone). By the end of the proximal tube, more than 99% of glucose, water, and sodium were reabsorbed (Brown 2011; Valender 2013). Furthermore, the proximal tubule cells also secret a wide variety of organic ions, endogenous (creatinine, urea, bile salts, oxalate, urate, prostaglandins, epinephrine) and exogenous (toxins and drugs) (Valender 2013).

Afterward, the filtrate goes through Henle's loop composed of 4 segments: thick descending limb, thin descending limb, thin ascending limb, and thick ascending limb. This

portion allows the kidney to concentrate or dilute the urine, an important characteristic of water balance preservation. The thin descending segment is completely permeable to water and impermeable to salts, whereas the thin ascending limb is impermeable to water and permeable to NaCl. By the end of the thin loop, the filtrate is moderately hypertonic. In the thick ascending limb and distal convoluted tube, there is active reabsorption of salt, contributing to the hyperosmolarity of the interstitium and dilution of the filtrate (Valender 2013).

Reaching the end of the distal tube, the filtrate enters the collecting tubules which merge into collecting ducts. They are permeable to water, and the intensity of water reabsorption is regulated by ADH. The presence of ADH stimulates the water to flow from the tubules to the interstitium and consequently back into circulation. This mechanism is extremely important for the water and blood pressure balance and it is also a determinant factor for urine concentration. Exiting the renal tubules, the urine progresses through the renal pelvis to the ureters, accumulates in the bladder, and when replete, contracts, and the urine is expelled through the urethra (Valender 2013).

1.2.1. Renin-angiotensin-aldosterone system

The juxtaglomerular apparatus, an anatomically distinct region at the vascular pole of the glomerulus, has an important role in the renin-angiotensin-aldosterone system and essential receptors and releases crucial hormones. It is composed of juxtaglomerular cells, granular, modified smooth muscle cells in the proximal wall of the afferent arteriole, the macula densa, specialized cells in the distal convoluted tube between the afferent and efferent arterioles, and the extraglomerular mesangial cells, specialized juxtaglomerular cells (Clarkson and Fletcher 2011; Valender 2013; Junqueira and Carneiro 2017).

This system is an important regulator of the GFR and RBF. It is stimulated primarily by the decrease in renal perfusion pressure (Valender 2013), which is felt by the mechanoreceptors of the juxtaglomerular cells, and the decrease of luminal sodium chloride concentration, detected by osmoreceptors of the macula densa (Brown 2011; Junqueira and Carneiro 2017). This triggers the juxtaglomerular cells to release renin, leading to the conversion of angiotensin I, produced in the liver, to angiotensin II in the lungs (Junqueira and Carneiro 2017). Angiotensin II, a potent vasoconstrictor for systemic arterioles, creates vascular resistance in renal afferent and efferent arterioles, contributing to the increase of systemic blood pressure, activates sodium uptake in the nephron, and stimulates the adrenal gland to release aldosterone and the pituitary to release ADH (Brown 2011). The aldosterone hormone also enhances NaCl retention, and consequently water retention. Thus, all these hormones are considerably important to increase water and salt retention, intravascular volume, and vascular resistance (Valender 2013).

2. Renal function assessment

The measurement of glomerular filtration rate is considered to be the gold standard to evaluate renal function and is strictly related to renal functional mass. It can be evaluated directly or indirectly. Direct tests comprehend the measure of plasma clearance. The principal GFR markers are inulin (the gold standard for GFR measurement) and iohexol (Lefebvre 2011). In clinical practice, it is used iohexol, a substance that is not metabolized and is negligibly bound to proteins, so it is considered to be excreted via glomerular filtration in its totality, within 24 hours. It is injected and plasma samples are collected, with no need for urine collection. However, these techniques are time-consuming, technically challenging, and impractical (DiBartola and Westropp 2020; Loane et al. 2022).

Due to logistical drawbacks, the assessment of renal disease is essentially through the indirect estimation of GFR. Renal disease refers to a functional or morphological abnormality in one or both kidneys, regardless of its severity. This can prompt renal failure which refers to a syndrome that develops when kidneys lose their ability to maintain their regulatory, excretory, and endocrine functions, with consequent undesirable metabolite accumulation and irregularities in fluid, electrolytes, and acid-base homeostasis. It occurs when more than 75% of the nephron population becomes non-functional (DiBartola and Westropp 2020).

The most frequently used renal biomarkers are the binomial blood urea nitrogen (BUN) and serum creatinine, both endogenous nonprotein nitrogenous solutes. Each has a singular value, although they are regularly evaluated together. Azotemia is defined as an increase of nitrogenous compounds concentration in the blood, above their reference intervals. When it is severe, with significant substance retention, combined with the manifestation of adverse clinical signs, including renal and extrarenal signs, is designated uremia. Succinctly, it is a polysystemic clinical syndrome that represents extensive renal functional loss (Palm 2017; DiBartola and Westropp 2020).

Serum creatinine concentration, a surrogate for GFR estimation, is the classic biomarker to assess impaired renal function. It correlates inversely with GFR with an exponential relationship. It is widely used as it is easy to measure, available, economical, and shows minor intra-individual variability. However, it has important limitations that hamper its utility (Kongtasai et al. 2022). Creatinine originates in a nonenzymatic breakdown product of phosphocreatine in muscle. Therefore, creatinine concentration is directly influenced by non-renal factors, such as muscle mass. Depending on the breed, size, and sex, the plasma concentrations may differ. Furthermore, it is important to consider that young animals have lower concentrations, whereas males, as they are more muscular, have higher concentrations. Ideally, each individual patient should have baseline serum creatinine concentration determined for future assessments (DiBartola and Westropp 2020), as serial evaluation in the

same cat increases its sensitivity to GFR change detection (Hall et al. 2014). Nonetheless, as this is not monitored during clinical practice, for reference, in healthy cats, the normal serum creatinine concentration is 0,8 to 1,8 mg/dL (Lefebvre 2011; DiBartola and Westropp 2020). The upper limit of the interval is higher than in dogs (1,3 mg/dL), which can be explained by the feline creatinine daily production being higher, smaller distribution volume, and lower clearance (Le Garreres et al. 2007). In cats, it is also reported to exist a greater inter-individual variability. As a consequence, the reference interval is higher, which can lead to misinterpretation of the values. Therefore, the results must be always interpreted considering the context of each animal (Kongtasai et al. 2022). Creatinine, not metabolized, is freely filtered through the glomerulus at a constant rate and is not reabsorbed. Hence, the determination of serum creatinine provides a reliable estimation of GFR. However, it only provides a rough indication of renal function, as it does not detect early renal damage until a 75% decrease of GFR. This insensitivity results from the natural correlation with GFR (each time GFR decreases by 50%, serum creatinine concentration doubles) and from non-renal factors, such as muscle mass, that can distort the values (Polzin 2017; DiBartola and Westropp 2020). Another major limitation is that it cannot detect renal damage that does not affect the GFR (Kongtasai et al. 2022). Some clinical conditions may decrease serum creatinine concentration, such as muscle-wasted animals (Lefebvre 2011) or diseases, such as portosystemic shunts and hyperthyroidism (Palm 2017).

Blood urea nitrogen is the conventional complementary biomarker to evaluate GFR and it is a measure of serum urea nitrogen concentration. BUN and GFR are inversely proportional. Urea is a nitrogenous solute excreted in the urine. They both give equivalent information. The normal BUN concentration in healthy cats is 15 to 35 mg/dL (DiBartola and Westropp 2020). Endogenous and exogenous proteins are subjected to a catabolic process, liberating amino acids, which subsequently are converted to ammonia. This product is subsequently metabolized in the liver to urea. Afterward, this metabolite is freely filtrated through the glomerulus and additionally subjected to passive reabsorption by the renal tubules, which is higher, the slower the tubular flow rate. Thus, the urea excretion rate is not constant, making it a biomarker less reliable to estimate the GFR. Moreover, BUN concentration is greatly influenced by extrarenal factors, such as dehydration and meals with high protein intake, which can increase the values. Therefore, in order to avoid the diet effect on serum BUN concentration, it is recommended to fast for 8 to 12 hours prior to evaluation. Other factors that similarly increase it are gastrointestinal hemorrhage, clinical conditions which enhance catabolism, such as fever, infection, and starvation, and some drugs, including, glucocorticoids. In contrast, extrarenal factors may decrease the BUN concentration such as overhydration, disease states causing polyuria and polydipsia, low protein diets, anabolic

steroids, malabsorption, severe hepatic insufficiency, portosystemic shunting, and drugs, like tetracyclines (Palm 2017; DiBartola and Westropp 2020).

Simultaneous measurement of both serum creatinine and BUN concentrations is more beneficial, compared with creatinine alone. Even though serum creatinine is more reliable for GFR assessment, blood urea nitrogen concentration has a better correlation with the clinical signs and prognosis than creatinine. Additionally, in some cases, for instance, in muscle-wasted patients, creatinine may be underestimated, consequently, BUN is more representative of renal function (Polzin 2017). Nevertheless, the magnitude of their values does not allow the prediction of the cause and extent of renal lesions, as well as the origin of the azotemia (DiBartola and Westropp 2020).

Azotemia, a consequence of renal disfunction, can be subclassified in pre-renal, renal, or post-renal. All these portray different causes for the decrease in GFR with a subsequent increase in renal biomarkers concentration. Creatinine and BUN are the most commonly checked, although there are other substances that contribute to the azotemic status. It is essential to consider that these subcategories may co-exist. Pre-renal azotemia is characterized by the decrease of GFR secondary to hypoperfusion of a morphologic normal kidney. Possible causes might be hypovolemia due to dehydration, poor cardiac output, and pathologic vasodilatory conditions such as shock. The ratio of BUN to creatinine increases, since its reabsorption is intensified in the renal tubules due to a slow flow rate. Usually, this condition is accompanied by an increment in urine concentration. The restoration of euvolemia typically leads to a fast resolution. In intrinsic renal azotemia, the GFR decreases due to intrinsic kidney dysfunction. A cautious evaluation of the serum creatinine concentration is essential, considering the values will be within the reference range until approximately 75% of GFR is impaired and renal dysfunction can occur before it. Post-renal azotemia arises secondary to an obstruction in the urinary system. The ratio of BUN to creatinine is higher, due to lower tubular flow rates. After the obstruction resolution, a rapid correction occurs if any pre-renal or renal azotemia did not develop (Palm 2017).

Since the described blood parameters are limited in detecting early renal dysfunction, symmetric dimethylarginine (SDMA) has been recently proposed as a new promising biomarker to evaluate renal function through indirect GFR estimation. SDMA is a by-product of the methylation of arginine residues in proteins, posteriorly released into circulation. It is eliminated primarily (≥ 90%) by renal clearance without any metabolization and with minor extra-renal influence, making it an accurate endogenous marker. Serum SDMA concentrations are inversely proportional to GFR, with a linear relationship, and directly correlate with serum creatinine (Hall et al. 2014; Loane et al. 2022). It is shown to be increased in cats with chronic kidney disease (CKD), acute kidney injury (AKI) (Loane et al. 2022) and with nephrolithiasis (Hall et al. 2017). It is more sensitive as it detects smaller GFR decreases (average 40% in

cats and dogs, 24% in cats alone) and increases earlier than serum creatinine concentration, by a mean of 14,6 months in CKD cats (range 1,5 - 48 months) (Hall et al. 2014) and a mean of 26,9% (range 0 – 60 months) in cats with nephrolithiasis (Hall et al. 2017). Similar to creatinine, when interpreting the results, it is needed to consider some factors such as age, breed, diet, physical examination findings, and biological variation. Contrarily, it is not affected by muscle mass and sex. However, further studies are needed in order to explore the impact of extra-renal factors on serum SDMA concentrations (Prieto et al. 2020; Sargent et al. 2020).

Cystatin C is another proposed endogenous biomarker for indirect GFR estimation. It is a proteinase inhibitor produced in all nucleated cells, at a constant rate. Although it is freely filtered through the glomerulus, it is reabsorbed in the proximal tubules and totally metabolized, and there is no evidence that cystatin C is not secreted by tubular cells, making it an unreliable GFR biomarker. Various studies failed to demonstrate clinical utility. Even though it is reported to not be influenced by age, sex, breed, body weight, and food intake in cats, it only has a sensitivity of 22%, failing to differentiate healthy and CKD cats. Furthermore, the correlation between serum cystatin C and serum creatinine concentrations is notably weak, and concentration values do not predict the development of azotemia (Syme and Jepson 2017; Kongtasai et al. 2022).

As renal function is impaired, it may prompt further alterations, such as compromised urine concentration ability. Thus, measuring urine specific gravity (USG) is another assessment to evaluate renal function. It is defined as the ratio of urine weight to that of distilled water. It is crucial for differentiation between pre-renal and primary renal azotemia. A urine sample is collected and, with the aid of a refractometer, the refractory index is estimated. The standard value in healthy cats is 1.035 – 1.060. Values between 1.006 and 1.020 are suggestive of CKD, and in advanced stages, isosthenuria is common, with values from 1.008 to 1.012. It is considered hyposthenuria when the refractory index is <1.008. However, some CKD cats are able to retain considerable urine-concentrating ability. USG may be influenced by hydration status, electrolyte status, ADH, diet, individual variation, and external factors like temperature. It is dependent on the number, type, and size of molecules in the urine. Marked glycosuria and proteinuria may cause overestimation of USG, whereas administration of fluids, glucocorticoids, and diuretics may underestimate it. All these factors have to be considered when interpreting the values (Graham 2017; Polzin 2017). In cats, it is reported to have a higher refractive index, so it is needed a particular refractometer for cats, otherwise, values will be falsely increased (Syme and Jepson 2017).

3. Ureteral obstruction in cats

Urolithiasis is defined as the presence of calculi anywhere in the urinary tract and comprehends its causes and effects. It is believed that the uroliths are formed in the kidneys or bladder, and urine flow carries them to the ureters and urethra, respectively (Lekcharoensuk et al. 2005; Grauer 2015; Geddes et al. 2023). It is a multifactorial syndrome in which congenital or acquired pathophysiologic factors increase the risk of excretory metabolite precipitation in the urine (Osborne et al. 2009). Ureterolithiasis is less frequent compared to other locations; however, it can prompt devastating outcomes (Cannon et al. 2007).

Ureteral obstruction is a severe and life-threatening disease, leading to urine flow restriction and post-renal insufficiency, typically resulting in AKI and eventually (Deroy et al. 2017). This is a challenging disease, often requiring sophisticated diagnosis and management, as well as unique surgical skills (Shipov and Segev 2013). Early obstruction relief is crucial to preserve the renal structure and function and to prevent more severe consequences (Hardie and Kyles 2004; Deroy et al. 2017).

3.1. Epidemiology and etiology

Ureteral obstruction is reported with an increasing tendency around the world for the past decades. The most common cause is reported to be ureteroliths, with greater than 98% of the calculi containing calcium oxalate. The cases increment may be explained by the growing awareness of ureterolithiasis as a potential cause of AKI and CKD, as well as the development of new technologies that allowed the surge of new diagnostic imaging modalities (Kyles et al. 2005a; Lekcharoensuk et al. 2005).

Accurate classification is essential in order to determine the proper treatment plan, which depends on the obstruction nature. Concerning the etiology, they can be classified primarily as congenital or acquired. Congenital causes are rare and include ureteral strictures, torsion, kinking, stenosis, circumcaval ureters (Dennis et al. 2010), ureterocele, ectopic ureters (Segev 2011), and ureteral aplasia (Lamb 1998). Acquired ureteral obstructions are the most common and usually result from mechanical obstruction of the ureter (Hardie and Kyles 2004).

They can be further categorized as acute or chronic, static or dynamic, partial or complete, and unilateral or bilateral (Shipov and Segev 2013). The proportion of unilateral versus bilateral ureteral obstructions is 56 to 75% and 25 to 44%, respectively (Berent et al. 2018; Kopecny et al. 2019; Wuillemin et al. 2021; Kennedy and White 2022).

Regarding location, ureteral obstructions can be classified as intraluminal, intramural, or extramural (Shipov and Segev 2013). Intraluminal obstruction is the most common cause of ureteral obstructions in cats. It is typically caused by ureteral calculi, and less commonly due to dried solidified blood calculi, blood clots, and inflammatory debris (Segev 2011).

Intramural causes are associated with ureteral strictures, neoplasia, ureterocele, fibroepithelial polyps, and proliferative ureteritis. Among those, ureteral strictures seem to be the most frequent cause of this type of obstruction, although they are rarely reported (Shipov and Segev 2013). It is defined as circumscribed stenosis, commonly consisting of cicatricial contracture, and is usually found in the right proximal ureter. They often arise as a result of iatrogenic injury, attributed to previous ureteral surgical interventions. Other less frequent causes of ureteral strictures are inflammation due to ureterolithiasis-induced mucosal injury, circumcaval ureters, concurrent ureteroliths, idiopathically and congenitally (Zaid et al. 2011). Extramural compression may occur from retroperitoneal occupying lesions, such as pelvic masses, retroperitoneal fibrosis, circumcaval ureters (Bélanger et al. 2014), accidental surgical ureter ligation during ovariohysterectomy, urinary bladder pathology and prostatic neoplasms (Hardie and Kyles 2004; Shipov and Segev 2013).

Circumcaval ureter, a congenital venous malformation, is a rather common abnormality in cats (35%). It is characterized by a vena cava ventral displacement or duplication relative to the ureter. During embryologic development, the right caudal cardinal vein from the embryo's venous system persists instead of degenerating, entrapping the ureter. Consequently, it may compress or kink the ureter as it passes dorsally to the vena cava, although most of the affected cats do not present any clinical signs (Bélanger et al. 2014). Concerning other obstruction mechanisms, it is also hypothesized the tortuous course around the vena cava, the localized fibrotic reaction within the ureter, the development of a venous ring with gonadal and lumbar veins, and the development of a ureteral stricture during ureteric bud formation in the embryonic stages (Steinhaus et al. 2015). Strictures resulting from circumcaval ureter are commonly observed in the proximal right ureter. (Zaid et al. 2011; Steinhaus et al. 2015).

3.2. Signalment and predisposing factors

Urolithiasis is a multifactorial syndrome, and factors such as gender, age, breed, reproductive status, nutrition, lifestyle, and climate may interfere with the elimination of the metabolites, predisposing certain individuals to their precipitation (Lekcharoensuk et al. 2005; Grauer 2015). It should be taken into consideration that each factor alone plays a limited role in the disease. Thus, the existence of one or more factors is not determinant for the occurrence of urolithiasis (Osborne et al. 2009).

A recent study by Geddes et al. (2023) in a referral hospital in the UK determined a prevalence of upper urinary tract uroliths (UUTU) of at least 4,6%. It eminently recognized two clinical phenotypes for cats with UUTU: an aggressive phenotype with a risk of obstructing in younger cats - obstructive UUTU; and a benign phenotype with a reduced obstruction risk in older cats - non-obstructive UUTU. As a matter of fact, cats who are less than 8 years of age

are 4 times more likely to obstructive UUTU than cats older than 12 years old. The risk factors for UUTU formation are being female, older than 4 years of age, being the most susceptible period 4,0 – 7,9 years, and being one of the following breeds: British shorthair, Ragdoll, Persian, Tonkinese, and Burmese when comparing to non-purebred. Being purebred solely does not increase the risk. Furthermore, the predisposing factors for obstructive UUTU phenotype are being female, younger than 12 years of age, and having bilateral uroliths. Moreover, it was hypothesized that lower body weight might be another risk factor since female body weight was substantially lower (> 1 Kg) when compared with male cats. However further investigation is needed in order to correlate smaller body weight/size, and consequently narrower ureters, with a higher risk of obstructive UUTU in females. It was also demonstrated that cats with obstructive UUTU had higher total and ionized calcium concentrations when compared to cats with non-obstructive UUTU. This suggests that hypercalcemia is a risk factor for UUTU formation and obstructive UUTU phenotype (Geddes et al. 2023).

Water intake is an important factor to take into consideration, as its reduction increases urine concentration and induces oliguria, promoting crystal aggregation. Therefore, the quantity of moisture in the animals' diet may greatly influence the development of uroliths. It was reported that cats fed only with dry food are more likely to have ureterolith-induced ureteral obstruction, and those fed with wet food or with a combination of both are less predisposed (Kennedy and White 2022). Furthermore, some components' concentration may also favor the formation of certain uroliths, such as phosphorus, magnesium, calcium, oxalate, among others (Queau 2019).

Obesity is hypothesized as a risk factor (Palm and Westropp 2011) as bigger amounts of food consumption induce bigger amounts of mineral excretion, which predisposes more for uroliths formation. Lifestyle similarly has a crucial influence, as indoor cats, more sedentary, are associated with reduced voiding and increased urine stasis. The climate seems to also have an important effect on urolithiasis, as higher temperatures cause greater liquid losses, and when not compensated by water ingestion, lead to low urine debit and a decrease in metabolite excretion (Gomes et al. 2018; Kennedy and White 2022).

3.3. Pathophysiology

Urine originates in the glomerulus, and concentrates and accumulates in the kidney tubules. A pacemaker in the renal collecting system originates a peristaltic movement, resulting in a contracting wave transmitted to the ureteral wall. It produces enough pressure to propel a urine bolus along the ureter and into the bladder. The ureteral peristalsis does not depend on innervation, as the contraction is transmitted from one smooth muscle cell directly to the next. Hence after transplantation, the ability to contract and transport urine remains (Lamb 1998).

After ureteral obstruction, there is a complex physiologic response, as the impairment of urine flow results in an intricate syndrome with alterations of glomerular hemodynamics, tubular function, and renal morphology. The adverse events proceeding the obstruction depend on age, degree of obstruction, time length, and whether the obstruction comprehends one or both ureters (Wen et al. 1999; Hardie and Kyles 2004).

The obstruction increases immediately the renal pelvis and intraureteral hydraulic pressure, which when high enough, is transmitted to the nephrons, preglomerular arteries, and interstitial space, leading to a decrease in the GFR and renal blood flow (RBF). The result of the obstructed kidney depends on the nature of the obstruction. The greater the severity of the obstruction, the bigger the alterations of the kidney. In a partial unilateral ureteral obstruction, there will be milder GFR and RBF decrease. In the presence of a complete unilateral ureteral obstruction, these values will be more pronounced. In case of a bilateral ureteral obstruction, the hydraulic ureteral pressure will be significantly higher and consequently, the GFR and RBF will be considerably lower. It can be fatal within 48 - 72 hours (Adams 2017). It was reported, that after obstruction release, renal function impairment was less relevant, but the ability to concentrate urine was more compromised. Furthermore, the longer the duration of the obstruction, the higher the possibility of irreversible damage, due to interstitial fibrosis (Wen et al. 1999). Thereby, early detection and decompression are essential for the preservation of renal function (Lemieux et al. 2021).

In a unilateral ureteral obstruction, when the contralateral kidney function is preserved, it will undergo compensatory hypertrophy, resulting in its enlargement and increasing GFR. Usually, the patient does not become azotemic and clinical signs, when present, are frequently attributed to pain consequential to renal capsule stretching. The mechanical obstruction may promote local inflammation, edema, and muscle spasm, intensifying the clinical signs. Because of the non-specificity of the clinical signs, the unilateral ureteral obstruction may go unnoticed. This compensatory mechanism does not occur in contralateral kidneys with pre-existing CKD, in which clinical signs are more evident. Consequently, the measurement of creatinine clearance is an accurate biomarker of the non-obstructed kidney. Moreover, in the presence of a healthy contralateral kidney, destruction of the ipsilateral kidney is faster, and after obstruction relief, the repairing is slower (Wen et al. 1999; Shipov and Segev 2013).

In obstructive nephropathies, there are a series of mechanisms and mediators involved. There is a leukocyte influx into the injured kidney, consisting mainly of two cell populations: macrophages (predominantly in the first 24 hours) and cytotoxic T lymphocytes. These lead to fibroblast recruitment, contributing to interstitial fibrosis. Other factors, such as angiotensin II, thromboxane $A_{2,}$ and growth factors also contribute to renal sclerosis (Wen et al. 1999).

3.4. Ureteroliths composition

To select the adequate therapeutic and preventive approach, it is important to classify the uroliths through quantitative and qualitative analysis (Lulich et al. 2016; Gomes et al. 2018). Uroliths are highly organized polycrystalline structures, emerging anywhere in the urinary tract. Their formation depends on the alteration of the following conditions: urine pH, the concentration of crystalloids, promoters, and inhibitors of crystallization (Queau 2019). Most uroliths are pure and a small percentage occur with more than one mineral (Kyles et al. 2005a). They can contain the following minerals: calcium oxalate, struvite (magnesium ammonium phosphate), calcium phosphate, apatite, dried solidified blood (DSB), urate, xanthine, brushite, silica, cystine, potassium magnesium, pyrophosphate, and newberyite (Cannon et al. 2007; Houston and Moore 2009). According to the Minnesota Urolith Center, the most common feline uroliths are struvite (49%) and calcium oxalate (41%), followed by purine-based uroliths (urate and xanthine) (5%), silica (1%), cystine (1%), calcium phosphate (1%), and other minerals, with an expression lower than 1%, such as matrix (Osborne et al. 2009).

Over the past decades, there have been significant changes in the location and composition of uroliths in cats (Kyles et al. 2005a; Cannon et al. 2007; Osborne et al. 2009). The number of upper urinary tract uroliths submitted has seen a notable increase in 20 years. Additionally, calcium oxalate and struvite make up approximately 90% of uroliths, with an exponential increase in calcium oxalate uroliths (Lekcharoensuk et al. 2005; Cannon et al. 2007; Osborne et al. 2009).

This tendency is supported by the widespread use of calculolytic diets directed to dissolve struvite uroliths as well as the alteration of maintenance diets to reduce struvite crystalluria (Osborne et al. 2009). Previous research has suggested that magnesium contributes to the formation of struvite calculi in cats, leading the manufacturers to modify their products by reducing magnesium and including ingredients that promote more acidic urine to decrease the potential of struvite formation (Cannon et al. 2007). A study on dietary risk factors in cats with urolithiasis found that these diets increase urine acidity and could actually increase the risk of calcium oxalate formation (Lekcharoensuk et al. 2001). Additionally, it promotes the release of calcium carbonate and calcium phosphate from bone, potentially leading to hypercalciuria. Although calcium oxalate uroliths formation is possible in a wide range of pH levels, extremely acidic urine can affect the concentration of crucial inhibitors of calcium oxalate crystallization, including magnesium, pyrophosphates, and Tamm-Horsfall mucoprotein (Cannon et al. 2007).

Furthermore, hypercalciuria can contribute to the formation of calcium oxalate calculi and may result from multiple pathological conditions, including primary hyperparathyroidism, idiopathic hypercalcemia, impaired renal tubular re-absorption of calcium and increased bone

demineralization. Certain drugs may also promote hypercalciuria, such as corticosteroids, thiazides, as well as dietary factors like increased dietary urinary acidifiers and calcium, and increased intake of vitamins C and D (Milligan and Berent 2019).

However, all this information concerns uroliths, which can be located anywhere in the urinary tract. Little study was done regarding ureteroliths composition, but in a study conducted by Kyles et al. (2005), in which 93 ureteroliths were analyzed, calcium oxalate was present in 98% of them (Kyles et al. 2005a).

3.5. Anamnesis and clinical signs

The clinical manifestation of feline ureteral obstruction can differ significantly among individual patients. It depends on the urolith size, quantity, location, and nature. Urolithiasis may manifest quickly or insidiously, and patients can remain asymptomatic (Gomes et al. 2018). Symptoms might go unnoticed unless there is a unilateral obstruction combined with reduced function of the contralateral kidney or if bilateral obstruction occurs (Adams 2017). Ureteral calculi may occasionally be discovered incidentally during abdominal imaging studies conducted for reasons unrelated to urinary issues (Shipov and Segev 2013).

Clinical signs are typically nonspecific and can be caused by uremia or pain resulting from direct ureteral stimulation at the obstruction site, as well as stretching of the collecting system and renal capsule (Segev 2011). They usually include hyporrexia, weight loss, lethargy and vomiting. In a severely azotemic patient, symptoms such as polyuria, polydipsia, anorexia, and oral ulcerations may be also present. Due to ureteral colic, abdominal pain and dysuria/stranguria may be apparent (Kyles et al. 2005a; Berent 2011). Hematuria can also be a presenting symptom of urolithiasis due to mechanical injury from uroliths and associated inflammation (Palm and Westropp 2011). It is possible to observe oliguria and anuria; however, their absence cannot rule out complete unilateral ureteral obstruction as urine production from the contralateral kidney may continue even if it doesn't significantly contribute to the overall GFR (Segev 2011).

Physical examination findings are nonspecific, but they might give crucial information that aids in the diagnosis. Patients usually are prostrated, with pale mucous membranes, different degrees of dehydration, hypersalivation/nausea, and uremic oral ulceration. On abdominal palpation, they may exhibit abdominal pain and asymmetrical kidneys, in which the diseased kidney is usually enlarged and firm (Kyles et al. 2005a; Shipov and Segev 2013). However, a recent study documented renomegaly as an infrequent condition (Bua et al. 2015).

The disparity in clinical presentations of feline ureteral obstruction presents a significant challenge to clinicians, making it difficult to establish precise therapeutic guidelines for this

heterogeneous patient population. Therefore, each animal should be evaluated and treated on a case-by-case basis (Shipov and Segev 2013).

3.6. Diagnosis

Diagnosing ureteral obstruction in cats can be difficult, it typically involves assessment of the medical history, clinical signs, and laboratory results (Segev 2011), and for a more definitive diagnosis, it requires imaging techniques (Bartges and Callens 2015).

The goal is to detect the disease at the earliest stage, determine its severity, and classify the nature of the obstruction. As part of the diagnostic assessment, the kidneys' ability to return to normal function after obstruction relief should be evaluated (Shipov and Segev 2013).

3.6.1. Laboratory abnormalities

Although laboratory tests do not provide a definitive diagnosis, they are essential as they can indicate the presence of underlying conditions that may increase a patient's susceptibility to urolith formation, such as hypercalcemia. Additionally, some alterations may suggest urinary tract impairment, leading to further diagnostic exams that approximate to the ureteral obstruction diagnosis. Lastly, their detection is crucial, as therapeutic modalities may depend on the abnormalities and for monitoring purposes (Bartges and Callens 2015).

Kyles et al. (2005) evaluated the clinical, clinicopathologic, radiographic, and ultrasonographic abnormalities in feline ureterolithiasis. It was reported that the most frequent alteration in blood analysis was azotemia (83%), with different degrees of azotemia that may be explained by whether calculi are bilateral or unilateral, the level of renal function impairment, the level of ureteral obstruction, and the degree of prerenal azotemia. Interestingly, 76% of cats with unilateral ureterolithiasis had azotemia, which suggests impairment of the contralateral kidney. The second most prevalent was hyperphosphatemia (54%), followed by anemia (48%), hyperkalemia (35%), hypocalcemia (22%), and hypercalcemia (19%). In the same study, when comparing unilateral and bilateral ureterolithiasis, it was observed that serum creatinine, BUN, and phosphate concentrations were substantially higher in patients with bilateral ureteral obstruction (Kyles et al. 2005a).

While urinalysis may not always yield specific information in cases of ureteral obstruction, it can disclose certain indicators such as hematuria, pyuria, cylindruria, crystalluria, and bacteriuria (Shipov and Segev 2013). The presence of crystalluria is not a reliable indicator of uroliths in cats, as the presence of crystals does not predict the presence of uroliths, and vice-versa. Also, crystals may not accurately predict the urolith type. Urine specific gravity can provide valuable information about the chemical composition of the urine,

which is an important factor in urolith formation, as higher urine specific gravity may suggest an increase in the concentration of urolithic precursors. Similarly, pH levels may help predict the urolith type, since calcium oxalate, purines, and cystine are less soluble in acidic urine, while struvite calculi are less soluble in alkaline urine (Bartges and Callens 2015).

Urine culture and antibiotic sensitivity testing may also be pertinent, as some bacteria may promote urolith formation. Also, it is important to monitor the patient for any secondary urinary infection that might be caused due to mucosal damage induced by calculi, incomplete urine voiding, or entrapment of the bacteria within the urolith (Bartges and Callens 2015). In cats, the most frequently isolated bacteria in cases of infection are *Escherichia coli* and *Enterococcus faecalis*. These bacteria are commonly found as commensals in the feline gastrointestinal tract and have the potential to cause ascending colonization. Less frequently, bacteria isolated may include *Staphylococcus epidermidis*, *Pseudomonas aeruginosa, Streptococcus spp., Klebsiella pneumoniae,* and *Enterobacter aerogenes* (Kyles et al. 2005a; Berent et al. 2014; Berent et al. 2018; Kopecny et al. 2019; Pennington et al. 2021).

3.6.2. Imaging modalities

3.6.2.1. Radiography

Radiography of the abdomen is one of the initial imaging methods employed to identify ureteroliths (Bartges and Callens 2015). The main purpose is to document the urolith size, number, and location since they are usually underestimated when resorting solely to ultrasonography (Berent 2011). In cats, abdominal radiographs alone have a sensitivity of 83%, and when combined with ultrasonography, it increases to 90%. As the majority of ureteroliths are composed of calcium oxalate and calcium phosphate, both radiopaque on survey radiographs, ureterolithiasis diagnosis is possible (Kyles et al. 2005a). In radiographs, it is possible to detect small, round, and radiopaque opacities, a dilated and tortuous ureter, and/or a kidney with bigger dimensions (figure 1) (Seiler 2018).

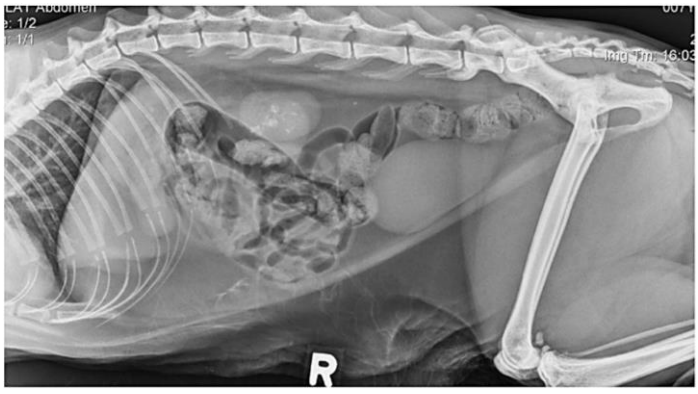

Figure 1. Lateral radiography of a cat showing multiple radiopaque opacities in the kidneys and retroperitoneal space, where the ureters are located (adapted from Palm and Westropp, 2011).

In the lateral projection is usually easier to identify the uroliths, although ventrodorsal or dorsoventral projections may aid to determine the affected ureters (Palm and Westropp 2011). In a study conducted by Nesser et al. (2018), it was evaluated the radiograph distribution of ureteroliths. It was determined that a greater portion of ureteroliths were located in the proximal ureter and mid-ureter compared to the ureterovesicular junction (UVJ). Furthermore, a correlation has been demonstrated between the size of ureteroliths and their location, with larger ones being more frequently located in the proximal segment of the ureter (Nesser et al. 2018). This might be explained by the decreasing lumen area from the proximal ureter to the mid-ureter (Ichii et al. 2022). In the same study, the authors reported a higher incidence of calculi at the UVJ in male cats. Interestingly, it has been documented that ureteroliths might change positions through antegrade or retrograde movement (Nesser et al. 2018).

Using exclusively conventional radiography techniques might bring some disadvantages, including missing small calculi, colonic contents and soft tissues overlapping preventing their visualization, and missing radiolucent uroliths (Kyles et al. 2005a). Especially in feline patients, ureteroliths are often smaller than 2 mm, which falls below the detection threshold of radiographic imaging (Clarke 2018a). Furthermore, due to the two-dimensional nature of radiographs, accurate assessment of ureteroliths location can be challenging. This limitation can result in misinterpretation when attempting to evaluate the side of the obstruction or to distinguish between bilateral or unilateral ureterolithiasis (Kyles et al. 2005a; Palm and Westropp 2011). Additionally, the retroperitoneal contrast on abdominal radiographs may be reduced due to conditions, such as nephritis, ureteritis, and retroperitoneal effusion accumulation, tampering with the diagnosis. Similarly, this loss of definition can also occur in the peritoneal cavity secondary to uroabdomen, peritonitis, and peritoneal fluid accumulation (Clarke 2018a).

3.6.2.2. Ultrasonography

Abdominal ultrasonography is a noninvasive and easily accessible diagnostic imaging technique for assessing the upper urinary tract in felines (Wormser et al. 2019). It is the initial imaging method employed to identify ureteroliths (Lulich et al. 2016). It is a valuable tool to determine the extent of hydronephrosis and hydroureter, as well as the precise location of the obstruction (Kyles et al. 2005a; Berent 2011). The presence of hydronephrosis and hydroureter proximal to an obstructive lesion is sufficient to diagnose ureteral obstruction (Lulich et al. 2016). It is also the method of choice to evaluate renal geometry, architecture, and vascularity (Seiler 2018). It has a sensitivity of 77% - 98% for the detection of ureteroliths and 44% for the

detection of strictures when used as the unique imaging modality (Kyles et al. 2005a; Wormser et al. 2019).

A typical image of ureterolithiasis is a hyperechoic structure causing distal acoustic shadowing, consistent with ureteroliths, and is accompanied by a proximally tortuous and dilated ureter, as well as hydronephrosis (figure 2) (Shipov and Segev 2013). However, in the presence of renal pelvic and ureteral dilation, with no signs of urolith shadowing, strictures should be considered. In some cases, there is evidence of peri-ureteral hyperechoic tissue at the stricture site (Zaid et al. 2011). The optimal approach for evaluating the renal pelvis is through dorsal and transverse planes. If the ureters are dilated, they can be traced caudally from the renal pelvis. The upper urinary tract, prior to the obstruction site is filled with anechoic fluid (Seiler 2018). Determining the width of the renal pelvis is crucial to establish the appropriate treatment (Berent 2011).

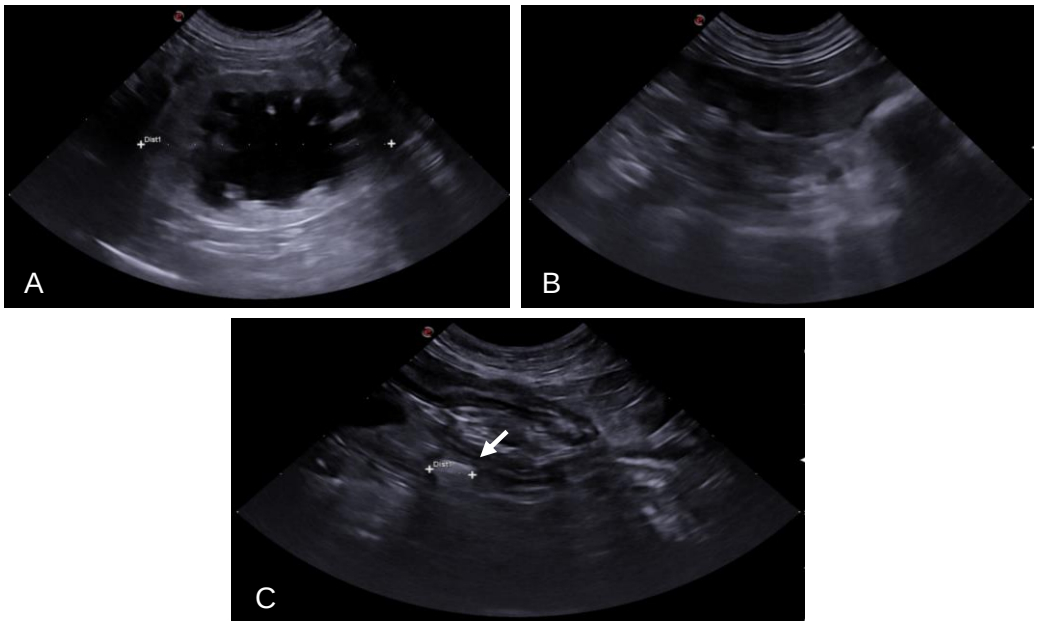

Figure 2. Ultrasonographic images of a cat with a renal pelvis and ureter dilation (original, provided by HVP).

Subtitle: A: dilated renal pelvis; B: dilated ureter; C: ureterolith (arrow).

Although ultrasonographic detection of pyelectasia can occur in healthy cats with a normal renal structure and function, the severity of renal pelvis dilation increases with renal dysfunction and parenchymal irregularities. Based on a retrospective study, it was determined that renal pelvis dimensions greater than 13 mm demonstrated 100% sensitivity in diagnosing obstructive nephropathy. However, it should be noted that several of these patients had smaller renal pelvis dimensions. Therefore, due to a broad range of overlap with smaller renal

pelvis sizes, those measuring less than 13 mm are not indicative for a particular urinary disease, and does not exclude ureteral obstruction (D'Anjou et al. 2011).

In feline patients, during ultrasonographic surveys, several factors can hamper the identification of the underlying cause of ureteral obstruction, including small body size, patient mobility, and small ureteral diameter making it more susceptible to being obscured by adjacent structures. Additionally, the echogenicity and acoustic shadowing may not always correspond to the underlying cause of the obstruction. For example, blood clots' echogenicity can vary, leading to them being missed or misdiagnosed as ureteroliths. Localizing the site of the obstruction can present difficulties, especially in early obstructions, as the ureter dilation may not extend to the obstructing site, because it begins proximally. Furthermore, larger ureters tend to facilitate the detection of uroliths. (Wormser et al. 2019; Testault et al. 2021). Lastly, the tortuous nature of the hydroureter can also constitute a challenge while attempting to follow the ureter and diagnose the underlying cause (Wormser et al. 2019).

3.6.2.3. Computed Tomography

When the ureteral obstruction is not apparent in radiographic and ultrasonographic surveys, and if highly suspected, computed tomography (CT) should be considered. The advantage of this imaging modality is the visibility of the whole urinary tract without the superposition of any adjacent structure (Seiler 2018), the distinction between partial and complete obstructions (Berent 2011) and superior estimation of the ureteroliths size (Wormser et al. 2019). Contrast-enhanced CT allows the delineation of the renal vasculature, highlighting its structure and abnormalities. Using a lower dose of contrast medium can produce satisfactory imaging results, which may be beneficial for patients with impaired renal function (Seiler 2018). However, there is risk associated which must be considered. Cats with ureteral obstruction often have GFR decreased, consequently reduced renal elimination of the contrast, culminating in inadequate filling of the obstructed kidney. Furthermore, considering cats might be azotemic during the diagnosis, there is a nephrotoxicity risk during the nephrogram phase (Berent 2011).

Nonetheless, Testault et al. (2021) conducted a study that compared the effectiveness of nonenhanced CT and ultrasonography in detecting ureteroliths in cats. This was the first study to assess the utility of nonenhanced CT, proving its feasibility (figure 3). Similarly to previous studies, nonenhanced CT detected more calculi than ultrasonography. Moreover, it was more efficient to give the correct lateralization and localization of the calculi, valuable information to decide the medical or surgical approach (Testault et al. 2021).

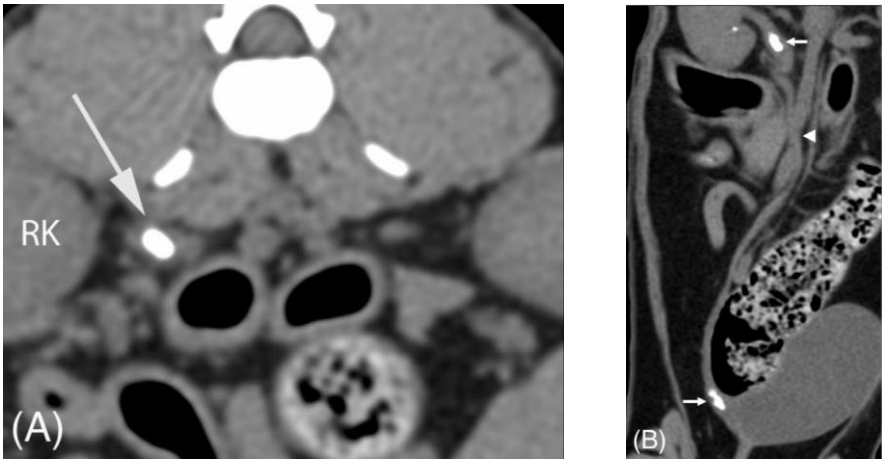

Figure 3. Nonenhanced CT scan of 2 different cats (adapted from Testault et al., 2020).

Subtitle: A: calculi lodged in the right proximal ureter (RK – right kidney). B; two calculi within the right ureter, one proximal and one distal (arrows). Ureter has a circumcaval trajectory (arrowhead).

3.6.2.4. Percutaneous Antegrade Pyelography

When radiography and ultrasonography are inconclusive to determine the diagnosis and there is a strong clinical suspicion of ureteral obstruction, percutaneous antegrade pyelography may be deemed an adequate alternative (Palm and Westropp 2011; Lemieux et al. 2021). It is regarded as the most accurate test to diagnose ureteral obstruction, with a sensitivity of 100% (Adin et al. 2003) and does not demand renal function (Testault et al. 2021), nor causes nephrotoxicity (Etedali et al. 2019). The procedure, performed under general anesthesia and using ultrasound guidance, consists of the contrast medium injection directly in the renal pelvis and the immediate obtainment of an abdominal radiograph. The volume of contrast injected must be the same as urine withdrawn from the renal pelvis previously. It can be executed in azotemic patients without reduction in image contrast (Seiler 2018). Nevertheless, it is important to take into consideration the disadvantages, such as renal puncture and urine leakage into the abdomen (Berent et al. 2014).

This diagnostic method offers improved visualization of the renal pelvis and ureters, enables localization of the ureteroliths and strictures, and aids in the determination of whether a complete or partial obstruction is present (Berent 2011). The passage of the contrast medium into the bladder confirms ureteral patency. Thereby, in a complete ureteral obstruction, it is possible to observe pyelographic evidence of renal pelvic and a ureteral segment dilation, with or without tortuosity, and the contrast comes to an abrupt termination in the ureter, without extending distally throughout the rest of the ureter and into the bladder (figure 4). Regarding partial ureteral obstructions, it might be observed pyelographic evidence of renal pelvic and ureteral segment dilation, with or without tortuosity, and a marked reduction in ureter diameter is evident, along with a delayed transit of the contrast into the bladder (Etedali et al. 2019).

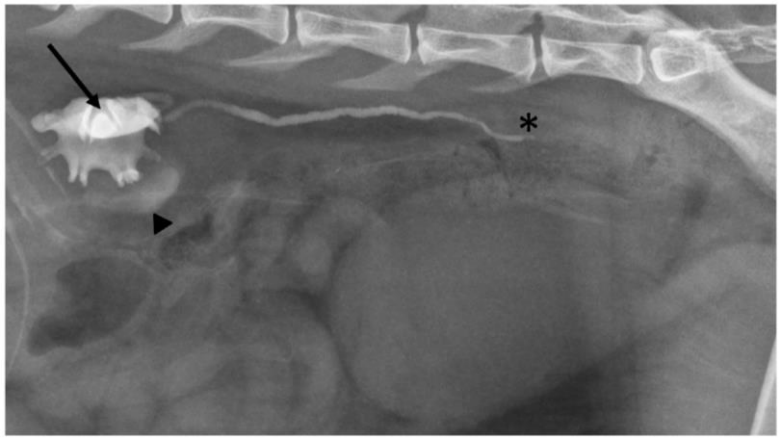

Figure 4. Pyelographic image of a cat with a right ureteral obstruction, lateral view (adapted from Etedali et al., 2019).

Subtitle: evident contrast in the dilated renal pelvis (arrow) and in the segmentally dilated and tortuous ureter (asterisk). A small amount of peri-renal leakage is observed (arrowhead).

3.7. Treatment

At diagnosis, numerous cats with ureteral obstructions are severely ill, particularly when the contralateral kidney is dysfunctional. They may exhibit various degrees of AKI and electrolyte imbalances, as well as other comorbidities (Clarke 2018a). It is reported that cats with ureteral obstruction are often diagnosed with concurrent CKD (Lemieux et al. 2021). The management can involve either medical or surgical intervention (Kyles et al. 2005b).

The main objective is to perform immediate renal decompression and stabilization, as it is crucial for the preservation of renal function, as well as allowing patency to be established (Berent 2014). The clinical, laboratory, and imaging parameters are essential to determine the urgency of the intervention (Kyles et al. 2005b). Nevertheless, ureteral obstructions should always be managed as an emergency, regardless if the obstruction is partial or complete (Lulich et al. 2016).

The selection of the treatment for ureteral obstructions is based on factors such as the nature and location of the obstruction, the severity of clinicopathological abnormalities, the hypothesis of renal infection, and the risks associated with each available procedure (Segev 2011). However, clinicians are challenged to consider non-conventional treatments and explore less invasive alternatives, so the interference with GFR is minimal (Lulich et al. 2016).

3.7.1. Conservative treatment

Typically, medical management, initiated upon ureteral obstruction diagnosis, is implemented firstly in all types of ureteral obstructions in order to relieve the pressure, stabilize the patient, and allow appropriate planning for further treatment (Hardie and Kyles 2004;

Berent 2011; Merindol et al. 2023). When the condition of obstructive ureterolithiasis is stable, medical management may be considered the only treatment. Sometimes, this approach is the only one available, due to owners' financial limitations (Merindol et al. 2023).

Conservative treatment is clinician-dependent (Berent 2014) and must be adapted to the patient's needs (Merindol et al. 2023). Medical management, which partially comprehends expulsive therapy (Palm and Westropp 2011), should involve administering fluid therapy with balanced isotonic crystalloids. The rate of intravenous fluids should be determined based on physical exam findings, and it should take into consideration the maintenance fluid needs, dehydration deficits, and ongoing fluid losses. Due to overzealous, it is usual for cats to get overhydrated, and combined with decreased renal excretion, it is required careful monitoring of body weight, edemas, central venous pressures, electrolyte concentrations and respiratory sounds (Berent 2011; Clarke 2018a). Additionally, it can be combined with the administration of loop diuretics, such as furosemide, or osmotic diuretics, such as mannitol (Hardie and Kyles 2004; Lulich et al. 2016). The latest should be administered initially as a bolus and then in a constant rate infusion (CRI). Anuric and cardiac-compromised patients are not eligible (Berent 2014). Furthermore, corticosteroids, such as prednisolone and dexamethasone, can be considered at anti-inflammatory doses to decrease ureteral inflammation, promoting uroliths' passage (Merindol et al. 2023). Alpha-1 adrenergic antagonists, such as prazosin, can also be used with the purpose of decreasing the pressure and easing spasms by acting on the ureter's smooth muscle, although there is no scientific evidence (Berent 2014; Lulich et al. 2016; Merindol et al. 2023). Other muscle relaxers have been suggested, such as amitriptyline and glucagon, but are reported to be less effective (Berent 2014). A more recent study reported that the use of tamsulosin has been effective in the treatment of calculi-induced ureteral obstructions, particularly in cases of small distal ureteroliths (Chae et al. 2022). If deemed necessary, antibiotics should also be provided, particularly in patients with pyelonephrosis-induced ureteral obstruction (Merindol et al. 2023).

Due to potential pain associated with this condition, it is essential to implement effective pain management for optimal feline welfare. Preventive and multimodal analgesia should be applied, considering the type, severity, and duration of the process, as well as comorbidities. Pain management focuses on analgesia, as well as comfort while reducing adverse effects. Therefore, the administration of an opioid, such as methadone or buprenorphine is ideal. Whenever possible, NSAIDs, including robenacoxib and meloxicam, should be combined, as they promote effective analgesia. Additionally, adjuvant analgesics, such as ketamine, gabapentinoids, and tramadol are also successful in minimizing pain (Steagall et al. 2022).

Medical dissolution may be a viable option for non-obstructive uroliths that are asymptomatic, do not contribute to recurrent infection, or cause compression of renal parenchyma due to their large size. This is generally reserved for uroliths composed of struvite,

cystine, or purine. However, this should not be attempted in cats with upper urinary tract uroliths, since approximately 98% of these contain calcium oxalate, which makes them not amenable to medical dissolution (Lulich et al. 2016).

During the procedure, patients should be closely monitored for disease evolution. Serial measurements of serum creatinine and BUN concentrations are sensitive indicators to assess progression. However, in the presence of prior kidney disease, severe azotemia might persist, and these parameters are not reliable. Serial imaging surveys are crucial to monitor the efficacy of medical management. In ureterolithiasis cases is essential to observe if calculi move in an antegrade or retrograde direction (Kyles et al. 2005b; Palm and Westropp 2011).

When unresponsive to therapeutics, severely azotemic and hyperkalemic patients, and immediate resolution is not possible, placement of a nephrostomy tube, hemodialysis, or peritoneal dialysis should be considered (Berent 2011; Shipov and Segev 2013). The objective is to reduce azotemia, provide enough time to assess whether the ureteroliths will pass spontaneously, and enhance the cat's clinical status prior to surgery (Kyles et al. 2005b).

In a recent study by Merindol et al. (2023), it was concluded that medical management has a low success rate of 30%, with a reoccurrence of 22%. Successful outcomes were observed primarily in young cats and distal ureteroliths were more likely to pass into the bladder compared to proximal ureteroliths. In the same study, smaller uroliths, particularly those measuring less than 1,44 mm in length, had a 50% chance of successfully passing. Thus, when suggesting medical management to the pet's owner, they should be informed of the high prevalence of failure, few cats are eligible, and choosing this approach, carries a significant risk of irreversible renal damage, as the results may take some time to manifest, and most patients do not respond (Merindol et al. 2023).

Considering the high likelihood of recurrence of ureterolithiasis in cats, it is important to carefully consider the benefits of avoiding surgery. However, these benefits must be balanced against the risks associated with medical treatment. Above all, the preservation of renal function should be prioritized as a critical factor in the decision-making process. Also, it is clear that medical management should be attempted for a short time duration, particularly considering that the obstruction often is present prior to clinical manifestation and admission for medical care (Shipov and Segev 2013). Nevertheless, as the increased risk of complications is linked to inexperienced operators, surgical procedures should only be deemed in the presence of experienced surgeons (Lulich et al. 2016).

3.7.1.1. Nephrostomy tube

In situations where immediate permanent fixation is not feasible due to factors such as procedural complexity, lengthy duration, or patient instability for anesthesia, the placement of

a nephrostomy tube offers a viable alternative. It is indicated in cases of severe hydronephrosis, life-threatening azotemia, and in patients with current renal insufficiency (Berent 2014). This approach allows prompt and temporary relief of the ureteral obstruction, which helps to stabilize the patient. It offers the additional benefit of evaluating the remaining function of the affected kidney before proceeding with further and more permanent surgical interventions (Kyles et al. 2005b; Berent 2011).

The placement, a rather short procedure, involves inserting a tube directly into the renal pelvis to drain urine. It can be placed percutaneously with ultrasound or fluoroscopic guidance, or placed surgically. In cats, it should be applied surgically, because their kidneys are more mobile. Thus, nephropexy must be performed to prevent any leakage (Berent 2011). For its placement, it is required renal pelvis dilation, so in acute ureteral obstructions, this procedure might not be feasible (Hardie and Kyles 2004).

This procedure is associated with some major complications, such as urine leakage, which can lead to uroabdomen, and tube dislodgement, which can be prevented by nephropexy, numerous sutures around the catheter to the skin, and an abdominal wrap. Furthermore, pneumothorax, hemorrhage, and infection are other less frequent complications (Berent et al. 2014).

A study conducted by Berent et al. (2012) investigated the clinical efficacy of placing a locking-loop pigtail nephrostomy tube for the purpose of temporary ureteral diversion in cases of ureteral obstruction. It was used for different purposes, such as the prevention of urine leakage following ureterotomy, placement of a ureteral stent or identification of a renal pelvis rupture, and the maintenance of renal pelvis decompression. Additionally, it served as a means to drain and flush obstructive pyelonephritis, as well as being a component of the intracorporeal nephrolithotripsy protocol. Based on the authors' experience, relying solely on a nephrostomy tube is not recommended, and when possible, definitive treatment is preferable. In the same study, notable improvement in renal function was observed, as evidenced by a nearly threefold decrease in serum creatinine concentration within a span of three days. While major complications related to the use of the locking-loop pigtail nephrostomy tube were relatively infrequent, their occurrence had significant negative consequences. In prior studies, complications were reported in 46% of patients that underwent this procedure; however, those articles described the placement of Folley catheters, red rubber catheters, and large fenestrated latex catheters for drainage. In this study, with 22 locking-loop pigtail nephrostomy tubes placed, only 3 patients had complications. The preliminary results suggest that a locking-loop pigtail nephrostomy tube is a safe and effective option for temporary renal pelvis decompression (Berent et al. 2012).

3.7.2. Extracorporeal shockwave lithotripsy

Extracorporeal Shockwave Lithotripsy (ESWL) is an advanced non-invasive technique and involves the use of high-energy shockwaves that are generated outside the body and targeted toward the urinary stones. The calculi are shocked thousands of times with different energetic levels, causing them to fragment into smaller pieces, so they can flow into the bladder for natural voiding (Milligan and Berent 2019). The success of this technique depends on certain factors, such as size, composition, and location (Cléroux 2018).

This procedure offers several advantages, including reduced patient discomfort, faster recovery times, and avoidance of surgical incisions. However, ESWL can cause damage to the surrounding tissue, such as renal fibrosis and hemorrhages. When breaking the stones, debris may accumulate and reobstruct, thus ureteral stent placement is always advised, as it passively dilates the ureter, facilitating the fragments' passage. ESWL is contraindicated in patients with uncontrolled urinary infections, coagulopathies, anatomic obstruction distal to the ureterolith, and in pregnant cats (Cléroux 2018; Milligan and Berent 2019).

Despite it being effective in dogs, ESWL is rarely considered in cats for the treatment of ureterolithiasis, due to the high risk of reobstruction given their small ureters and the incapacity to break down calcium oxalate uroliths. Moreover, feline kidneys are particularly susceptible to shockwave-induced injuries, reinforcing that cats are not suitable candidates for ESWL (Shipov and Segev 2013; Milligan and Berent 2019).

3.7.3. Surgical treatment

For the past decades, the management of ureterolith-induced ureteral obstruction in cats has been within the purview of surgeons. Development of new technologies allowed new surgical techniques, and evolving of ureterolithiasis management (Lulich et al. 2016). The technique is chosen accordingly to the number of uroliths, location, nature of the obstruction, renal pelvis diameter (Berent 2014), renal function at diagnosis (Lanz and Waldron 2000), as well as the surgeon's preference (Kyles et al. 2005b; Wormser et al. 2019) and probability of regaining renal function (Segev 2011).

3.7.3.1. Eligibility criteria for surgery

Conservative management must be discontinued when patients are unresponsive to the therapeutic after 24 to 48 hours. The imaging criteria is progressive renal pelvis dilation, in serial ultrasound surveys, as well as static obstructions. Moreover, surgical intervention is directly advised if there is decline of the patient's clinical status, including fever, growing inappetence and lethargy, as well as ureter rupture and leakage. It is also recommended in

the presence of progressive renal function deterioration, such as increasing azotemia and hyperkalemia, and persistent oliguria/anuria. Although, if the patient has life-threatening hyperkalemia, fluid overload, or low urine output (< 1 mL/Kg/h), despite euhydration or overhydration, the minimum 24 hours medical treatment should not be attempted (Kyles et al. 2005b; Shipov and Segev 2013; Lulich et al. 2016; Berent et al. 2018). In the detection of a urinary infection, surgery must be delayed for at least 48 hours. In this period of time antibiotic therapy is administered in order to address the infection (Berent et al. 2018).

3.7.3.2. Anesthetic protocol

In feline patients with ureterolithiasis, GFR and RBF decrease and many have concurrent CKD. Many anesthesia drugs undergo renal metabolism and/or excretion to some extent. As a result, in the presence of renal disease, the pharmacodynamics and pharmacokinetics of these medications may be altered. Moreover, patients with renal diseases often have comorbidities associated, such as azotemia, electrolyte imbalance, dehydration, and anemia. It is also known that anesthetic and sedative drugs have effects on RBF and GFR. Thus, it is crucial to consider these alterations when outlining the anesthetic plan, adjusting the dosage, and choosing the correct drugs (Clarke-Price and Grauer 2015).

Azotemia is frequently associated with plasma acidification, decreasing plasma protein binding to drugs. Therefore, high concentrations of active drugs are free, increasing the risk of overdose (Clarke-Price and Grauer 2015). Further, drugs might decrease cardiac output and blood pressure, a danger to compromised renal function. Favoring anesthetic agents that preserve, improve cardiovascular function, and minimize renal vasoconstriction is crucial for patients with renal disease (Weil 2010; Rezende and Mama 2015).

Premedication with sedatives and analgesics reduce stress and provide analgesia, decreasing the amount of induction and maintenance agents for general anesthesia. Opioids such as methadone or butorphanol are effective options for sedation and analgesia. It can also be used low doses of acepromazine for sedation. Alpha2-agonists, such as dexmedetomidine, should be avoided as they promote vasoconstriction and decrease cardiac output. The anesthesia induction can be safely achieved using propofol, alfaxalone, a combination of an opioid (fentanyl or hydromorphone) and a benzodiazepine (midazolam), or a combination of ketamine and midazolam. For maintenance of general anesthesia, isoflurane or sevoflurane can be administered. It's important to note that these agents can decrease GFR, but this can be counteracted by administering a CRI of an opioid, such as fentanyl, to minimize these side effects. The use of drug combinations allows for the reduction of individual drug doses, thereby minimizing the negative effects associated with higher doses (Weil 2010; Clarke-Price and

Grauer 2015; Mateo et al. 2015; Rezende and Mama 2015). Oxygen and intravenous fluid therapy should be secured throughout the whole anesthetic procedure (Weil 2010).

Systemic analgesia may not always provide complete pain relief, which is why local anesthesia is often used as an adjunct to block pain. High doses of opioids can have negative effects on feline patients, so using local anesthesia allows for lower doses of opioids or even their complete substitution. Techniques commonly used in cats with ureterolithiasis include epidural anesthesia, incisional line blocks, intraperitoneal blocks, or a combination of these methods. These can provide targeted pain relief and enhance overall pain management during and after surgical procedures (Luca et al. 2017).

Close monitoring of the patient is crucial, with particular attention to blood pressure to ensure adequate kidney perfusion (Weil 2010). Hypotension is frequently observed during prolonged anesthesia, with an incidence of 82%. This can be attributed to factors such as drug-induced vagal tone or hypothermia. For prevention, it is important to employ measures such as fluid therapy and early intraoperative management (Mateo et al. 2015; Luca et al. 2017).

Hypothermia is the most common intraoperative complication, with a prevalence of 87% to 93%. It is hypothesized that cats' bigger body surface area and body weight ratio make them prone to heat loss. It is correlated with a prolonged duration of general anesthesia, so minimizing the duration of anesthesia is recommended whenever possible. Hypothermia should be prevented, as it can promote serious consequences, including arrhythmias, coagulopathies, and reduced oxygen to the tissues (Mateo et al. 2015; Luca et al. 2017).

In a study by Mateo et al. (2015), several risk factors during anesthesia for the treatment of ureteral obstruction were identified. They found that hyperkalemia, advanced age, higher ASA status, and emergency interventions were associated with higher perioperative anesthetic mortality rates. This information is important as it helps guide anesthesia drug selection and the implementation of close monitoring protocols to ensure patient safety (Mateo et al. 2015).

3.7.3.3. Traditional interventions

A wide range of surgical procedures is currently available for the management of ureteral obstruction in feline patients, namely, ureteronephrectomy, pyelolithotomy, ureterotomy, ureteroneocystostomy, ureteral anastomosis and renal transplantation (Hardie and Kyles 2004; Kyles et al. 2005b; Berent 2014).

Ureteronephrectomy consists of the removal of the kidney along with the ureter. It is only advised in severe hydronephrosis, unresectable ureteral stricture, and renal abscesses (Kyles et al. 2005b; MacPhail and Fossum 2019). Even though it is associated with a few procedure-associated complications, it is not recommended in azotemic patients. It is reported that over 30% of older cats develop chronic kidney disease, so it is crucial to preserve all renal

function. Furthermore, this procedure does not treat the underlying cause, and since many cats eventually develop ureteroliths in the contralateral ureter, kidney removal is strongly discouraged (Berent 2011).

Pyelolithotomy is the removal of the urolith from the renal pelvis and proximal ureter, through incisional procedures. It is typically performed when the calculi are too large or in a location that renders alternative minimally invasive approaches inadequate. However, a notable drawback of this technique is its challenging execution in the absence of ureteral dilation (MacPhail and Fossum 2019).

Ureterotomy is a surgical procedure involving an incision made in the ureter to remove ureteroliths, to repair strictures or other obstructive lesions within the ureter. It allows direct access to the ureter's affected area, facilitating the removal of the obstruction (Hardie and Kyles 2004; MacPhail and Fossum 2019). It is the most performed traditional surgical technique (Kyles et al. 2005b; Berent 2011). Major complications associated are urine leakage leading to uroabdomen, persistent ureteral obstruction secondary to preexisting stricture and inflammation, reoccurrence of ureteral obstruction, and postoperative ureteral stenosis (Kyles et al. 2005b; Roberts et al. 2011; Culp et al. 2016). It is reported that the survival to discharge is approximately 79%, and only 31% resolved azotemia after surgery (Roberts et al. 2011; Culp et al. 2016). Therefore, the mortality rate is up to 21%. It is crucial to carefully consider the potential benefits of the procedure in light of the high mortality rate (Roberts et al. 2011).

Ureteroneocystostomy involves the resection of the distal damaged ureteral segment, which is then repositioned and anastomosed to the bladder (Hardie and Kyles 2004; MacPhail and Fossum 2019). It is the second most used traditional surgery. This is applicable to the distal two-thirds of the ureter; however, when a bigger portion is resected, tension-reducing techniques should be considered in order to avoid tension in the ureter. It can be done by allying to the procedure renal descensus and psoas cystopexy. This surgical technique is associated with complications, more frequently than ureterotomy, such as urine leakage and postoperative persistent ureteral obstruction (Kyles et al. 2005b).

Ureteral anastomosis or ureteroureterostomy is a surgical procedure employed to reconstruct the ureter by connecting two ureter segments, to restore its continuity. It may be necessary to associate renal descensus and psoas cystopexy to reduce ureteral tension. However, it is technically difficult to perform and it carries a high risk of postoperative obstruction, especially in cats due to their smaller size. Therefore, it is generally recommended to explore alternative surgical methods as a first-line approach whenever feasible (Lanz and Waldron 2000; Hardie and Kyles 2004; Kyles et al. 2005b; MacPhail and Fossum 2019).

In a study by Kyles et al. (2005b), in which cats with ureterolith-associated ureteral obstruction were all treated with traditional surgery techniques, it was reported that the perioperative mortality was 18% and major complications were observed in 31%. Nonetheless,

it is important to note that these surgeries were conducted in two universities known for their extensive expertise in ureteral surgery. Therefore, less experienced clinicians in microsurgical techniques may encounter higher rates of morbidity and mortality (Kyles et al. 2005b).

3.7.3.4. Alternative interventions

Due to the potential adverse outcomes and mortality risks associated with traditional surgeries, there has been ongoing research into alternative approaches. The goal is to identify less invasive techniques that can provide immediate renal decompression, stabilize the kidney, allow the rapid establishment of ureteral patency, and prevent postoperative complications, such as leakage and stenosis (Berent 2011; Berent 2014).

In the most recent consensus regarding the treatment and prevention of uroliths in dogs and cats, by Lulich et al. (2016), the management of obstructive ureteroliths in cats should involve, as first-line treatment, the placement of a subcutaneous ureteral bypass (SUB) or ureteral stent. Achieving optimal results requires the use of fluoroscopic imaging, appropriate training, and an experienced operator (Lulich et al. 2016).

3.7.3.4.1. Ureteral stent

The placement of an indwelling ureteral stent is a minimally invasive intervention and can be used as an alternative to traditional surgery for the treatment of ureteral obstructions. The primary goal is to divert urine from the renal pelvis into the bladder, bypassing the obstruction (figure 5). This promotes passive ureteral dilation, assists in the management of post-interventional edema, and facilitates the spontaneous passage of stones. Stenting provides prompt relief of ureteral obstruction and renal stabilization, effectively eliminating the risk of postoperative urine leakage, and acting as a preventive measure against the migration of nephroliths. In cats, the most used are the multi-fenestrated polyurethane catheter with a double-pigtail configuration, in which one coil is placed in the renal pelvis and the other coil in the bladder, preventing migration (Berent et al. 2014; Berent 2014; Clarke 2018b).

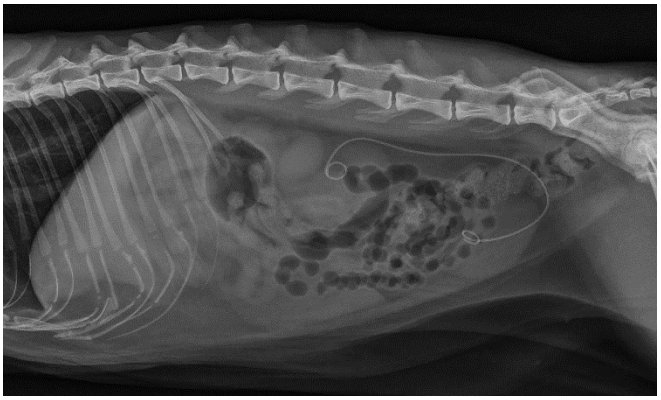

Figure 5. Lateral radiography of the ureteral stent after placement (adapted from Clarke, 2018b).

Ureteral stents can be inserted using different approaches, including cystoscopy by a percutaneous approach only in female cats, or open surgery. The ureteral stent insertion can be antegrade via pyelocentesis, retrograde via cystotomy, or through a ureterotomy incision. In most cats, males and females, it is performed surgically, using an antegrade technique with intraoperative fluoroscopy. The procedure consists of a nephrostomy needle access into the renal pelvis, and subsequently, a guide wire advances through the ureter, into the bladder, and out, through a previously done small caudodorsal cystostomy incision, creating a through-and-through access. The ureter dilator is then passed in an antegrade manner. Next, the ureteral stent is advanced similarly in an antegrade way through the guide wire, following the dilator and expelling it out through the cystostomy incision. In some cases, to allow the passage of the ureteral stent beyond the obstruction, it might be needed dissection of the periureteral tissue, so the ureter can be straightened, or resort to traditional ureteral surgery techniques, such as ureterotomy, ureteroneocystostomy, and ureteral anastomosis; however, it increases the risk of leakage (Berent et al. 2014; Culp et al. 2016; Wormser et al. 2016).

Ureteral stent placement has lower complication rates compared to traditional surgical techniques, predominantly consisting of minor complications. However, major procedure-related complications were observed in approximately 7 to 9% of cases. These complications included uroabdomen resulting from ureteral tear, leakage at the site of ureterotomy or bladder stay suture, and penetration of the renal parenchyma. Minor complications, occurring in around 21% of cases, consisted of ureteral mucosal intussusceptions and guide wire wall penetrations, which did not have any significant clinical impact on the patients. Other intraoperative complications included multiple pyelocentesis attempts, failure to direct stent placement, and stent migration. Immediate postoperative complications, within the first 7 days, were observed in 4 to 9% of cases and included stent migration, pollakiuria and stranguria, congestive heart failure, pancreatitis, and hepatic lipidosis. Short-term complications, within 30 days after ureteral stent placement, were noted in approximately 10 to 15% of cases and included stranguria and pollakiuria, and stent migrations. In the long-term period, occurring

beyond 30 days, the reported complication rate was approximately 10 to 33%. These complications comprehended reobstruction, recurrence of ureteral strictures, pyelonephritis, proliferative ureteral mucosal hyperplasia/uteritis, stent migration, vesicuoureteral reflux, encrustation, and sterile cystitis (Horowitz et al. 2013; Berent et al. 2014; Kulendra et al. 2014; Manassero et al. 2014; Wormser et al. 2016).

The most described complication at any time after ureteral stent placement was dysuria (pollakiuria and stranguria), in 38% of cats undergoing ureteral stent placement. However, signs were generally temporary, resolving spontaneously or with medical management, typically involving steroid administration or α-adrenergic blockage. The exact causes of this condition remain uncertain; however, one potential explanation is the irritation of the bladder caused by the distal coil of the ureteral stent. This could be attributed to the incorrect selection of stent length or the mechanical rigidity and positioning of the coil. The dorsolateral position of the coil leads to direct mechanical contact with the trigone and the proximal urethra, leading to lower urinary tract signs (Berent et al. 2014; Kulendra et al. 2014; Wormser et al. 2016; Deroy et al. 2017).

Another frequently reported complication was urine leakage, resulting in uroabdomen. This complication was documented in approximately 15% of cases and was primarily attributed to the ureterotomy procedure required to allow the passage of the guide wire through the site of obstruction. Feline patients developing abdominal effusion were less likely to survive to discharge (Culp et al. 2016).

Post-obstructive diuresis was also identified as a serious complication posterior to ureteral stenting. It was reported in all cats submitted to ureteral stenting (Culp et al. 2016; Balsa et al. 2019). It is defined as polyuria after a urinary obstruction relief, with a urine output >2 mL/Kg/h. This is a major concern, as it can lead to dehydration and electrolyte disturbances when not appropriately managed. Longer and more severe post-obstructive diuresis is associated to greater changes in serum creatinine, BUN, and potassium concentrations. Contrarily, less severe post-obstructive diuresis is associated with greater changes in serum pH, bicarbonate concentrations, and base excess. Its duration is intimately associated with ICU and hospitalization days, as more severe post-obstructive diuresis remits to longer internments (Balsa et al. 2019).

Chronic lower urinary tract infection was diagnosed 11% of patients who underwent ureteral stenting. Interestingly, the occurrence of these complications was more frequent in patients undergoing ureteral stenting as compared to those who underwent traditional ureteral surgery. This disparity could potentially be attributed to the longer duration of stenting, which promotes bacteria colonization of the ureteral stent, and consequently biofilm formation, making the infection clearance more difficult. Thus, feline patients at high risk for infection, such as immunosuppressed, are not good candidates for ureteral stent implantation. Similarly

to Human Medicine, the ureteral stent should be replaced or removed days to weeks after to minimize these complications (Wormser et al. 2016).

Encrustation was identified as an additional complication necessitating ureteral stent exchange, in 20 to 26% of cats undergoing ureteral stenting (Berent et al. 2014; Deroy et al. 2017). It is characterized by the mineralization and accumulation of stone debris on the surface of the stent, leading to obstruction. In a study conducted by Manassero et al. (2014), it was observed that all cases of encrustation occurred in patients who had undergone ureteral anastomosis. It is plausible to suggest that the implementation of a SUB device in these cases could have prevented the occurrence of this complication (Manassero et al. 2014).

In a study conducted by Berent et al. (2014), the technical and clinical outcomes of ureteral stenting were investigated in cats with benign ureteral obstruction. The authors found that patients with ureteral strictures posed greater challenges for successful stent placement. This difficulty could be attributed to factors such as the proximal location of the obstruction, the length of the non-obstructed ureter, and the narrowed ureter lumen. Consequently, navigating the dilator and stent through the stricture and the normal ureteral lumen proved to be more challenging. Furthermore, cats with ureteral obstruction have a higher risk of reobstruction. This may be due to the presence of fibrous tissue in the stricture, which prevents normal passive dilation of the ureter. As a result, reobstruction is likely to happen at the site of the stricture (Berent et al. 2014).

Stent exchange was required in 23 to 32% of cases due to reobstruction, stent migration, stent irritation, severe or persistent dysuria, ureteral reflux, ureteral stent fracture, and mineralization (causing obstruction) (Nicoli et al. 2012; Berent et al. 2014; Kulendra et al. 2014; Wormser et al. 2016; Deroy et al. 2017).

The median survival time for feline patients treated with ureteral stenting was 419 to 480 days (range 2 to 2800 days) (Nicoli et al. 2012; Berent et al. 2014; Kulendra et al. 2014; Manassero et al. 2014; Wormser et al. 2016). The degree of renal function is an important factor since CKD cats with IRIS stage 1 or 2 lived longer than IRIS stage 3 or 4 (Horowitz et al. 2013). The mortality rate was reported to be approximately 8% to 19%, and in most cases was related to the lack of improvement in renal function (Nicoli et al. 2012; Berent et al. 2014; Kulendra et al. 2014; Wormser et al. 2016; Deroy et al. 2017).

Based on the findings in the aforementioned recent studies, ureteral stenting emerges as a valuable and safe approach for managing feline ureterolithiasis. In comparison to traditional ureteral surgery techniques, ureteral stenting demonstrates lower mortality rates and facilitates prompt decompression of the renal pelvis, leading to faster resolution of azotemia (Berent et al. 2014; Culp et al. 2016). However, with the introduction of the SUB device, complications have decreased in both the short- and long-term compared to ureteral

stents. As a result, if the SUB device is an available option, it is preferable to choose it over ureteral stents in cats (Milligan and Berent 2019).

3.7.4. Subcutaneous ureteral bypass

The SUB device is a minimally invasive treatment option for the treatment of the various causes of benign and malignant ureteral obstruction. In cats, it has been found to have fewer complications both in the short-term and long-term when compared to other surgical alternatives (Berent and Weisse 2020). Additionally, SUB device placement allows shorter surgery times and shorter hospitalization times when compared to other surgical procedures (Deroy et al. 2017; Livet et al. 2017). The procedure is technically challenging, and previous training is advised as it has been shown to reduce complication rates. Previous studies have reported a learning curve associated with the procedure, suggesting that greater expertise leads to higher success rates (Berent and Weisse 2020).

3.7.4.1. SUB™ 3.0 characteristics

An indwelling subcutaneous ureteral bypass (SUB) is a locking-loop nephrostomy catheter and a multi-fenestrated cystostomy catheter, both attached to a connector that attaches to a subcutaneous shunt port (SwirlPort™) through a third catheter (actuating catheter) (Figure 6). It creates an artificial ureter, allowing the urine to flow from the kidney directly into the bladder, bypassing the ureter (Berent and Weisse 2020).

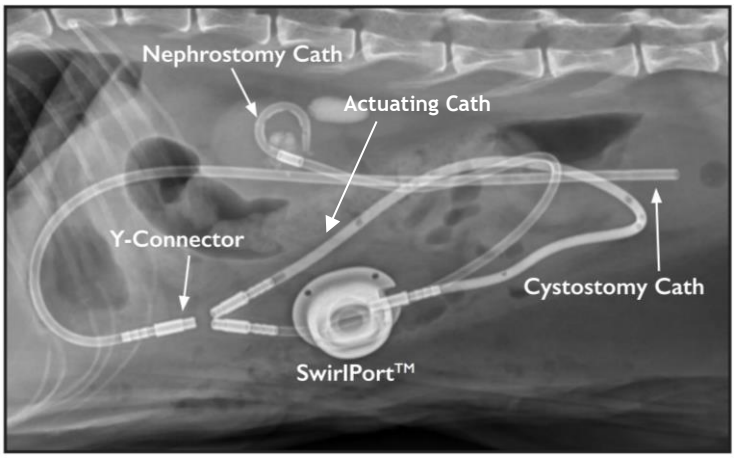

Figure 6. Lateral radiography of the SUB™ device 3.0 after placement, with the principal elements identified (adapted from Berent and Weisse, 2020).

The port is placed in the subcutaneous space, in a ventral position. It allows access to periodic system flushing and drainage, and urine sampling. Thus, this design helps maintain long-term patency and allows the injection of a solution to prevent occlusion and biofilm

formation. The end of the nephrostomy catheter features a pigtail conformation and it is multi-fenestrated. Before the beginning of the coil, there is a black radiopaque marker which enables the operator to visualize the last fenestration under fluoroscopy and ensure accurate positioning of the catheter. To prevent leakage or dislodgment, and provide security, after the marker, there is a Dacron cuff and a silicone sleeve that is surgically glued to the renal capsule. Inside the catheter, there is a locking string that prevents the pigtail to uncoil and dislodge. In smaller renal pelvises, the nephrostomy tube can be turned into a ureterostomy tube by cutting and removing the locking string and consequently removing the lock. The cystostomy catheter has a straight multi-fenestrated end. With similar objectives, it has a Dacron cuff and a silicone sleeve that are surgically glued and sutured to the bladder capsule (Berent and Weisse 2020).

Depending on whether the ureteral obstruction is unilateral or bilateral, there are different options. In a unilateral ureteral obstruction is typically used a 3-arm “Y-connector”, whereas, in a bilateral ureteral obstruction, it can be used a 4-arm “X-connector” or two 3-way “Y-connectors” and two ports (Figure 7) (Berent and Weisse 2020).

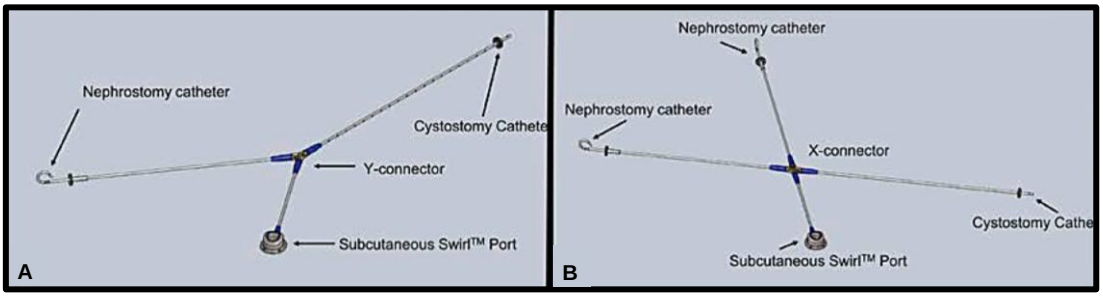

Figure 7. Schematic of a unilateral and a bilateral SUB™ 3.0 (adapted from Berent and Weisse, 2020).

Subtitle: A: unilateral SUB with a “Y-connector”; B: bilateral SUB with a “X-connector”.

The SUB was redesigned with the purpose of decreasing the most frequent complications, shortening procedure times, minimizing subcutaneous dissection, and making device exchange easier for the operator if needed. In SUB™ 3.0, the greatest innovation was the introduction of a connector in which the nephrostomy and cystostomy catheters attach, along with the addition of a third catheter that directly connects the connector to the port. This design modification allows the first catheters to remain indwelling in the abdominal cavity, while the latter catheter traverses the abdominal wall to connect to the port. Therefore, if a kink were to occur in the actuating catheter, the urine flow would not be disrupted. In the previous version, SUB™ 2.0, in which the nephrostomy and cystostomy catheters were attached directly to the port (Figure 8), one of the main complications was kinking of the tubing at the entry of the body (Berent and Weisse 2020).

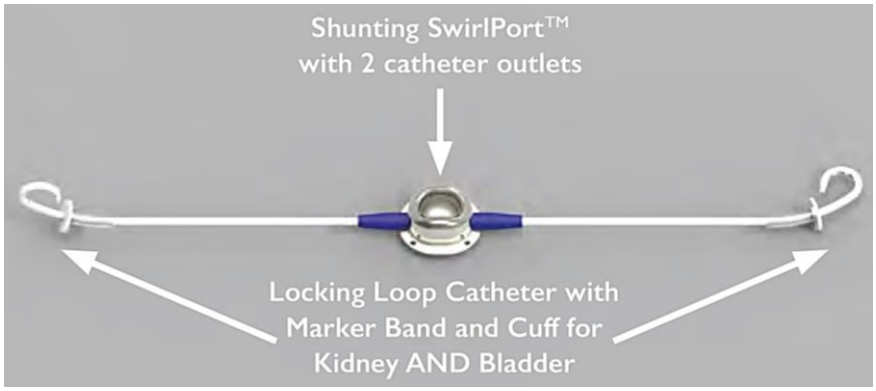

Figure 8. The SUB™ 2.0 assembled outside the patient (adapted from Berent and Weisse, 2018).

3.7.4.2. Preoperative management

Elective procedures should be postponed until patients can be properly stabilized. In this preoperative time, a physical examination should be done. When auscultated a heart murmur, cats should undergo echocardiography (Wuillemin et al. 2021). Blood analysis should also be done in order to identify the abnormalities, correct them and control the progress. Other routine exams should be done, including radiography and ultrasonography, essential tools to detect the nature and location of the obstruction. However, when they are inconclusive, an antegrade pyelogram should be performed at the same anesthesia time as the surgery. Cystocentesis should also be done, but if it is not possible to do it before surgery, urine should be collected intra-operatively through the catheter placed in the renal pelvis (Rezende and Mama 2015; Luca et al. 2017; Kulendra et al. 2020; Pennington et al. 2021).

Prior to SUB placement, patients should be submitted to medical treatment for 24 to 72 hours for stabilization, treatment of any UTI, and possible spontaneous ureterolith passage. It is crucial to reduce azotemia, treat hypovolemia and dehydration, correct electrolyte imbalances, and improve urinary output (Mateo et al. 2015; Wuillemin et al. 2021). Preoperative medical management consists of intravenous fluid therapy, analgesia, mannitol, and α-1 adrenergic antagonists (prazosin) that should be discontinued at least 8 hours before surgery (Mateo et al. 2015; Livet et al. 2017; Berent et al. 2018; Vrijsen et al. 2021; Wuillemin et al. 2021). The treatment of any UTI is recommended for at least 48h before surgery, based on a urine culture and sensitivity test. Further medication might be administered, including proton pump inhibitors, antiemetics, histamine H2 receptors, and phosphate binders accordingly to the patient's needs (Berent et al. 2018; Pennington et al. 2021).

When medical management fails to produce a response, patients who are stable enough should undergo prompt SUB placement. However, for patients who cannot tolerate a

lengthy anesthesia period, the placement of a nephrostomy tube or intermittent hemodialysis should be considered as an alternative (Berent et al. 2018).

3.7.4.3. Surgery procedure

The surgical access is via ventral midline laparotomy to expose the affected kidney and the bladder apex. The peri-renal is then dissected off the caudal pole of the kidney, exposing 1 to 2 cm of the renal capsule (Berent and Weisse 2020).

The nephrostomy catheter is placed using the modified-Seldinger technique, with fluoroscopy guidance. The renal pelvis is punctured by an 18G over-the-needle catheter, from the caudal pole of the kidney. A pyelocentesis is performed for bacterial culture, followed by an antegrade pyelogram with 50% contrast:saline solution to visualize the ureteral obstruction and guide the placement of the guidewire. A 0.035” J-tip guidewire is advanced through the catheter carefully coiled inside the renal pelvis to avoid perforation. While securing the J-tip wire, the catheter is removed, and then the 6.5Fr nephrostomy catheter with the hollow cannula inside are advanced over the guidewire. As kidneys are usually fibrotic, it might be difficult to advance the catheter. After entering the renal pelvis, the cannula is partially retracted while the catheter is advanced into the renal pelvis. When the black radiopaque marker is ensured to be within the renal pelvis, the locking string is then pulled and fixated, forming a pigtail at the end of the catheter. The coil should not be pushed too tight as it could kink at a fenestration. The Dacron cuff and silicon sleeve are advanced down the nephrostomy catheter to the renal capsule, where is surgically glued. Posteriorly, a contrast study should be done under fluoroscopy to ensure the correct placement, filling, and drainage, without leaking through the kidney or ureter (Berent and Weisse 2020) .

According to the surgical guide by Berent and Weisse (2020), it is advised to use a different approach when renal pelvises are smaller than 8 mm. Authors find it easier and safer to place the nephrostomy tube down the ureter, instead of coiling it in the renal pelvis. However, care must be taken to avoid perforation of the renal pelvis and ureter. For this technique, the locking string is cut and removed from the nephrostomy catheter, leaving a gently curved ureterostomy catheter. The kidney is punctured in a more caudolateral aspect, with an 18G over-the-needle catheter, through which passes a 0.035” angle-tipped hydrophilic guidewire to cannulate the ureter. However, when the renal pelvis is smaller than 5 mm, it is needed an extraordinary step. First, a 22G IV catheter can be used to puncture the renal pelvis, followed by the ureter’s cannulating with a 0.018” angle-tipped hydrophilic guidewire. Then, the 22G catheter is removed and exchanged by an 18G IV catheter, and subsequently the 0.018” guidewire is exchanged by a 0.035” angle-tipped hydrophilic guidewire. The 18G is removed over the guidewire, and the nephrostomy catheter, together with the hollow cannula, is

advanced down the guidewire and into the ureter. Although, once the hollow cannula pierces through the renal parenchyma, the catheter surpasses it into the renal pelvis and is advanced until the black radiopaque marker is within the renal pelvis and the catheter is down the ureter. Finally, the Dracon cuff and the silicone sleeve are slidden down and glued to the renal capsule (Berent and Weisse 2020).

For cystostomy catheter placement, in the urinary bladder apex, a purse-string suture is placed. A small stab incision is made in the center, with the aid of cautery to prevent post-operatory hematuria and blood clot formation. When bilateral SUBs are implanted, both catheters should be placed close to the bladder apex, just off the midline. The cystostomy catheter, together with the hollow cannula, is advanced into the bladder until the Dracon cuff comes against the bladder's serosal surface. When the bladder is small, the catheter's tip should be trimmed, to ensure it does not come in contact with the trigone and cause irritation. The purse-string suture is then secured around the catheter and the Dacron cuff is surgically glued and sutured to the bladder. Next, a leakage test must be done by infusing saline through the hollow cannula (Berent and Weisse 2020).

For connecting the catheters, it starts with applying blue boots at the end of all catheters, with the tapered end first. When necessary, nephrostomy and cystostomy catheters should be cut shorter and adapted to the patient's size. The 2-arms of the "Y-connector" usually face caudally, with the nephrostomy catheter attached laterally and the actuating catheter medially. The cystostomy catheter connects to the arm facing cranially. In the nephrostomy catheter, the blue boot must slide over the locking string, pinning it. When connecting the catheter, the connector's barbs wedge and lock the string, ensuring the pigtail does not uncoil. With a scalpel, the excess is cut against the metal barb, so it does not hang, as it causes incomplete seal and leakage. Lateral to the ventral abdominal incision, on the ipsilateral side, the subcutaneous tissue is dissected off the muscle, halfway between the xiphoid and the pubis. With a hemostat, a 2-3 fingers wide hole is pierced, approximately 4 cm from the port location (to prevent kinking) through which transverses the actuating tubing. It is then cut to fit the patient, placed a blue boot (tapered end first), and connected to the port. When the device is closed, it is leak tested. A Huber needle attached to a T-port, 3-ways-stop-cock, and two syringes is inserted in the port and the system is drained. The "Y-connector" is the first leak tested by digital compressing the nephrostomy and cystostomy catheters when infusing the fluid. Next, the port is tested by pressing the proximal actuating tubing. If no leak is observed, the system is secure. System patency is confirmed with an additional contrast test, in which contrast is infused through the port to the whole device. The port is sutured subcutaneously to the ventral body wall. The omentum is used to cover the entry site and the abdomen is closed. Once the surgical procedure is done, fluoroscopy is performed to ensure the kinks and leakage absence, the radiopaque markers' correct location, and the proper location of the Dacron cuffs.

3.7.4.4. Postoperative management

All patients should be closely monitored during the postoperative period. The fluid therapy rates should be adapted for each individual cat, based on the assessment of hydration status, body weight, urine output, PCV, serum total solids, and blood gas partial pressure. To quantify urine excretion, urinary catheterization should be implemented postoperatively, under the same anesthesia time (Balsa et al. 2019). However, due to the inherent risks associated with this procedure, the catheters were promptly removed when alternative methods of monitoring hydration became feasible. Serum biochemical analyses should also be performed to evaluate BUN, creatinine, phosphorus, potassium, sodium, and total and ionized calcium concentrations. All these variables should be checked every 12 to 24 hours until hospital discharge (Berent et al. 2018; Kulendra et al. 2020; Vrijsen et al. 2021; Wuillemin et al. 2021).

Analgesia should be assured and tailored to each patient, according to the clinician's preferences. Antibiotic therapy can be initiated preoperatively as a prophylactic measure. However, when it is not, it should be initiated after surgery and for the following 2 weeks, in order to reduce biofilm formation. If the results of the bacterial culture come positive, empiric antibiotic therapy should be discontinued and an antibiotic based on the results is administered for 4 to 6 weeks (Livet et al. 2017; Berent et al. 2018; Vrijsen et al. 2021; Wuillemin et al. 2021). It is reported that patients not receiving antibiotics postoperatively have an increased risk of developing a positive urine culture after discharge (Kopecny et al. 2019). An esophagostomy tube may be placed in cats with severe azotemia and anorexia. It is also important to guarantee hydration of the patients with prior diagnosed cardiac diseases since it does not increase cardiac output like intravenous fluid therapy, preventing congestive heart failure. Ultrasonographic surveys may be performed daily to evaluate pelvic and ureteral dilation and identify postoperative complications. Prompt identification and management of any postoperative abnormalities are important for the patient's recovery. Previously to hospital discharge, it is advised a SUB device flushing with the aid of ultrasonography, to ensure the absence of occlusions (Berent et al. 2018; Wuillemin et al. 2021).

3.7.4.5. Follow-up

Ensuring regular follow-up examinations of the animal is crucial for adequate monitoring of the SUB device, renal function, and overall clinical status of the patient. The most recent guidelines recommend re-evaluations 1 week, 1 month, and then every 3 months posterior to SUB placement (Berent and Weisse 2020). During these periods, a serum biochemical profile, CBC, urinalyses, body weight, and systolic blood pressure should be measured. Furthermore, it should be performed a urinary tract ultrasonography with the renal pelvis measurement and subsequent SUB device flushing (Livet et al. 2017; Berent et al. 2018;

Kulendra et al. 2020; Butty and Labato 2021; Pennington et al. 2021; Wuillemin et al. 2021; McEntee et al. 2022). In individuals with an elevated risk of infection and encrustation, a more frequent flushing protocol should be implemented (Berent and Weisse 2020).

In the presence or suspicion of calcium oxalate stones, the administration of potassium citrate is recommended, with concurrent monitoring of urine pH and serum potassium concentrations. Furthermore, in persistently azotemic patients, renal diet is advised, while those with serum creatinine levels within the reference range should be fed a prescribed neutralizing stone diet. When serum phosphorus is > 5 mg/dL (reference range 2,1 to 5,7 mg/dL), owners are advised to administer aluminum hydroxide. Persistently ionized hypercalcemic patients should be submitted to hyperparathyroidism testing, entailing measuring of serum PTH, parathyroid hormone-related protein, ionized calcium, and vitamin D. If idiopathic hypercalcemia is diagnosed, dietary fiber supplementation should be prescribed. If no improvement is observed after four weeks, administration of alendronate is recommended.

3.7.4.6. SUB flushing

SUB flushing is a sterile procedure with minimal restraint of the patient and is often ultrasound-guided. It is advised 1 week, 1 month, and thereafter every 3 months post-surgery. The process is initiated with hair clipping over the port and aseptically preparing the skin. With the patient in dorsal recumbency, the Huber needle, with a 3-way stop-cock and two syringes attached, is perpendicularly inserted in the port's silicone diaphragm until it reaches the metal. One of the syringes is utilized to collect a urine sample for urine culture and urinalyses. While monitoring the renal pelvis, the device is vigorously flushed to provoke turbulence, and air bubbles along with distension should be detected. After withdrawing the fluid previously injected, to avoid renal pelvis overdistension, the process is repeated for the urinary bladder, and similarly, air bubbles should be identified. Subsequently, the renal pelvis is completely drained, the T-FloLoc syringe, containing a solution of tetra-EDTA (tetrasodium ethylenediaminetetraacetic), is connected to the system. The inclusion of this substance is essential in mitigating the risk of device occlusion, mineralization, and biofilm formation. The solution is then slowly and intermittently injected, allowing it to drain down the SUB between each pulse. Throughout this procedure, close monitoring of the renal pelvis is essential, ensuring that any distension resolves within a few seconds. If the distension persists, the flushing should be immediately discontinued.

Less frequently, fluoroscopic guidance is used, particularly when ultrasonography is inconclusive or unavailable. Nevertheless, ultrasound should be used to obtain accurate renal pelvis measurements, so optimal functioning of the device is ensured. To confirm patency,

100% iohexol is injected and contrast agent filling the catheters, the renal pelvis and bladder should be observed. Following the withdrawal of the previously injected contrast, the T-FloLoc, mixed with 1 mL of contrast, is slowly infused in pulses (Berent and Weisse 2020).

The tetra-EDTA solution serves multiple functions, including its role as an antimicrobial and demineralization agent. As a result, there are established protocols available for flushing SUB devices affected by mineralization and infection (Berent and Weisse 2020).

3.7.4.7. Complications

In comparison to other treatments, the occurrence of short- and long-term complications associated with the SUB placement is minimal. Recent advancements in the device's design and implementation have contributed to a continuous reduction in these complication rates. The majority are attributed to technical deficits and outcomes are influenced by the operator’s experience and perioperative management. Hence, it is advisable for the procedure to be performed by professionals with extensive expertise and prior training since there is a learning curve associated with optimal results (Berent and Weisse 2020).

Complications associated to SUB device placement are essentially intraoperative and postoperative (within the first 7 days). The reported intraoperative complication rate is approximately 0% to 7%, and includes catheter leakage, blood clot obstruction, catheter kinking, backward coiling of the nephrostomy catheter, iatrogenic renal hemorrhage, subcapsular bleeding, hemorrhage during esophagostomy placement, hypothermia, and hypotension (Berent et al. 2018; Kulendra et al. 2020; Wuillemin et al. 2021). Two studies have reported higher rates of intraoperative complications (15% to 17%), with complications being the misplacement of the nephrostomy catheter and the locking loop not being tight enough. This could potentially be attributed to the absence of fluoroscopic guidance during the procedure (Livet et al. 2017; Butty and Labato 2021). Postoperative complications have been reported to occur at a rate ranging from 31% to 43%. They include blood clot obstruction, device leakage potentially leading to uroabdomen, UTI, fluid overload, anemia, corneal ulceration, dysuria, seizures, azotemia worsening, device kinking, seroma, severe bruises of the ventral abdominal wall, intermittent hyperthermia. Short-term complications, within 30 days after ureteral stent placement, were noted in 20 to 30% of cases and comprehended blood clot obstruction, stone obstruction, UTI, sterile cystitis, seroma, and urethral obstruction. In the long-term period, occurring beyond 30 days, the reported complication rate was 30 to 52%. The complications were occlusion due to mineralization, device kinking, blood clot obstruction, UTI, and urethral obstruction (Livet et al. 2017; Luca et al. 2017; Berent et al. 2018; Kulendra et al. 2020; Butty and Labato 2021; Vrijsen et al. 2021; Wuillemin et al. 2021).

Device urine leakage is more frequently observed during the intra- and postoperative periods, occurring at a rate of 0 to 3% of patients. This particular complication is often linked to technical errors, such as not cutting the locking string close enough to the catheter. Consequently, urine leakage is observed at the junction of the shunting port and the nephrostomy catheter, where the locking string is secured (figure 9). Leakage may also be due to inadvertent puncture with the guidewire and catheters or Dacron cuff detachment (Berent et al. 2018; Berent and Weisse 2020; Dirrig et al. 2020; Kulendra et al. 2020).

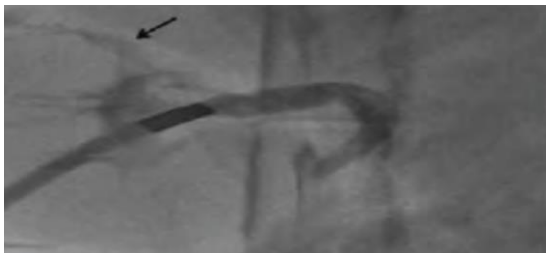

Figure 9. Contrast leakage (black arrow) in the kidney's cranial pole, due to unintentional puncture with a guidewire (adapted from Berent and Weisse, 2018).

Subtitle: contrast leakage (arrow).

Chronic hematuria was reported in 12% of the cases after SUB device placement, similar to ureteral stenting (18%). Many cats had a history of DSB calculi, suggesting idiopathic renal hematuria. This postoperative complication is reported to significantly reduce overall survival time (Berent et al. 2018).

Device kinking is observed intraoperatively, occurring at a rate of 2% and more commonly in a long-term period, in 5 to 15% of cats with SUB devices placed. This is frequently attributed to technical errors, such as the nephrostomy catheter being coiled too tightly or the device being misplaced. The latest typically happens when the device entrance through the abdominal wall is not sufficiently distant from the end of the blue boot (figure 10). This issue is often observed when patients are moved into different positions, such as crouching and laying extended (Berent et al. 2018; Berent and Weisse 2020; Wuillemin et al. 2021). With the new SUB^{TM} 3.0 design, the addition of the actuating catheter, connecting both nephrostomy and cystostomy to the port, reduced the kinking complication to 0% (Berent and Weisse 2020).

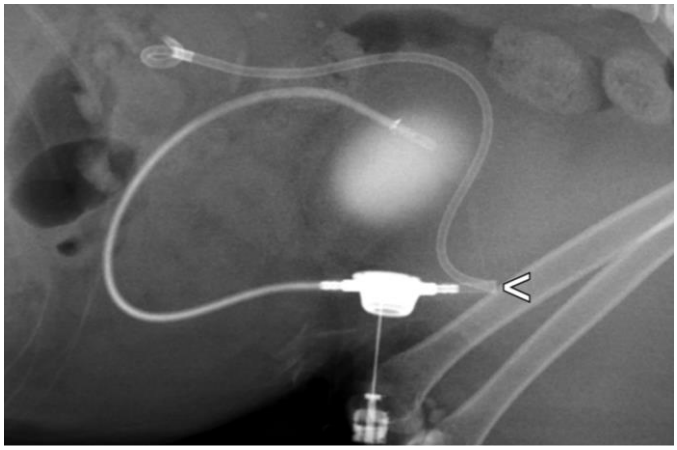

Figure 10. Positive contrast fluoroscopic examination of a cat's unilateral right-sided SUB system, revealing a kink in the nephrostomy catheter at the point where it traverses the abdominal wall (adapted from Dirrig et al. 2019).

Subtitle: kinked nephrostomy catheter (arrowhead).

Sings of dysuria, unassociated with UTI, were reported in 5 to 9% of cases (Berent and Weisse 2020). Prior to the placement of the SUB device, it has been reported that 23% of cats experienced non-infectious dysuria, which can be indicative of ureteral colic or lower urinary tract disease (Berent et al. 2018). The latter condition, with an incidence of 13 to 39%, might be explained by the cystostomy catheter coming in contact with the trigone, causing irritation (Livet et al. 2017; Wuillemin et al. 2021). Recent guidelines recommend trimming the end of the cystostomy catheter to ensure a proper fit for the patient (Berent and Weisse 2020). Symptomatology can be managed with short-term analgesia and NSAIDs/corticosteroids; however sterile cystitis may occur multiple times in the patient's life (Horowitz et al. 2013; Livet et al. 2017). When compared to the ureteral stent rates (38%), the SUB device rates are lower, likely attributed to the cystostomy catheter location. While the SUB's cystostomy catheter is positioned in the urinary bladder apex, the ureteral stent extends into the lumen, with the coil positioned near the trigone and urethra opening, causing irritation (Berent and Weisse 2020).

Urinary tract infection is a complication transversal to all periods, posterior to SUB placement, occurring in 17 to 31%. Patients with SUB devices are more susceptible to UTIs. This increased risk can be attributed to the surface of the implant providing a suitable substrate for biofilm development. Biofilm formation allows bacteria to evade the host immune system and antimicrobial therapy, leading to inadequate bacterial elimination and the persistence of the infection (Livet et al. 2017). Multiple studies have identified predisposing factors for positive urine culture following SUB placement. It has been reported that cats with a positive urine culture prior to surgery are more likely to develop a UTI postoperatively (Livet et al. 2017; Berent et al. 2018; Kopecny et al. 2019; Pennington et al. 2021; Wuillemin et al. 2021). Also, at the end of anesthesia, it was observed that cats with higher rectal temperatures were

significantly less prone to having a positive urine culture at 1 and 3 months post-surgery (Pennington et al. 2021). Moreover, cats not receiving antibiotics postoperatively had a higher risk to develop positive urine cultures after hospital discharge (Kopecny et al. 2019). Urethral catheters are similarly associated with UTIs, due to ascending infection and colonization of the system. The longer the catheterization, the higher the risk of developing a UTI (Berent et al. 2018; Weese et al. 2019). *Enterococcus spp.* is the most common bacteria isolated in UTIs in cats. Although it is regularly associated with subclinical bacteriuria, it is important to consider its presence in feline patients with urinary implants. *Enterococcus spp.* has intrinsic and acquired resistance to antimicrobial agents and can form biofilms, making it more challenging to treat the infection effectively (Berent et al. 2018; Kopecny et al. 2019). The treatment of subclinical UTIs is still a debate (Kopecny et al. 2019), but according to the recent ISCAID guidelines antibiotics are rarely prescribed and discouraged in the absence of clinical signs. Regarding the treatment of clinical UTI, specifically cystitis, the same guidelines indicate amoxicillin and trimethoprim-sulfonamides, for 3 to 5 days, as first-line treatment. However, if sensitivity tests come as resistant or the patient does not tolerate these antibiotics, nitrofurantoin, fluoroquinolones, and 3rd generation cephalosporins should be used. For pyelonephritis, it is crucial to promptly initiate empirical treatment with fluoroquinolone or cefpodoxime, ceftazidime, or cefotaxime. Once urine culture and sensitivity testing results are available, empiric treatment should be reassessed and antibiotic therapy should be based on the results, for 10 to 14 days (Weese et al. 2019). Interestingly, since the introduction of the routine tetraEDTA flushing solution 1 week, 1 month, and then every 3 months postoperatively, chronic UTIs have decreased from 8% to 0% (Berent and Weisse 2020).

Device obstruction was observed in 24% of cases, and the primary causes include the presence of stones (12%), blood clots (8%), and mineralization (17 to 24%) (Berent et al. 2018; Wuillemin et al. 2021). Blood clot obstruction is more frequently observed during the intraoperative and immediate postoperative periods. Factors influencing blood clot occlusion were catheter orientation to the port and preoperative serum creatinine concentration. In approximately half of the cases, flushing the device with tissue plasminogen activator can successfully manage the obstruction. However, if the occlusion persists despite the flushing, the catheter may need to be exchanged. Mineralization, with consequent device occlusion, was the most commonly observed long-term complication (25%). This complication is predominantly seen in cystostomy catheters and factors associated with mineralization include small shunting port and postoperative ionized hypercalcemia. It is reported to reduce overall survival time. Surgery intervention was required along with catheter exchange in 53% of cases. However, since the implementation of the tetraEDTA flushing solution in 1 week, 1 month, and every 3 months thereafter, mineralization rates decreased to 7% (Berent et al. 2018; Berent and Weisse 2020).

3.7.4.8. Outcome and prognosis

The SUB device, in multiple studies, has been successfully implanted in all patients submitted to this procedure, with immediate renal pelvis decompression. The median survival time was 827 to 881 days. No patient's death is attributed to surgery or persistent ureteral obstruction (Horowitz et al. 2013; Berent et al. 2018; Butty and Labato 2021; Wuillemin et al. 2021). Additionally, most feline patients die from non-urinary causes, and those dying from urinary causes, have shorter survival times (Berent et al. 2018; Wuillemin et al. 2021). The overall mortality after SUB placement is 51%, and the hospital discharge mortality rate is 6%, 10% after 1 month, 17% after 3 months, and 26% after 1 year (Berent et al. 2018). Overall survival time is significantly influenced by preoperative factors, such as a previous history of CKD, strictures and weight loss, and preoperative fluid overload development. Regarding postoperative factors, CKD IRIS stage (stages I and II have increased survival times), serum creatinine concentration (1 mg/dL increase, increases the death risk by 26%), and postoperative fluid overload development also affect overall survival time (Berent et al. 2018; Wuillemin et al. 2021).

Median hospitalization time is 4 days (ranging from 1 to 11 days), and the survival rate at hospital discharge is approximately 88 to 94% (Horowitz et al. 2013; Berent et al. 2018; Wuillemin et al. 2021). Factors associated with survival to discharge are oliguria/anuria, development of fluid overload, congestive heart failure, pancreatitis, and lack of renal function. (Horowitz et al. 2013; Berent et al. 2018). Hospitalization time is influenced by serum creatinine and BUN concentrations preoperatively, preoperative positive urine culture, ureteral obstruction duration, bilateral SUB device placement, blood transfusion, development of fluid overload, serum potassium concentration, postoperative hyponatremia, and postoperative diuresis (Horowitz et al. 2013; Berent et al. 2018; Balsa et al. 2019; Wuillemin et al. 2021).

Despite being technically challenging and requiring experienced veterinarians, SUB device placement is a feasible treatment option. It allows prompt renal pelvis decompression and consequent reduction of azotemia levels in most cats. Despite complications, when the owners were surveyed, they reported that their cats had a good quality of life following SUB device placement. Complications are somewhat frequent, but with proper management, feline patients with ureteral obstructions can have a good to excellent prognosis. However, cats with CKD may experience disease progression, resulting in shorter survival times and a less favorable prognosis (Berent et al. 2018; Wuillemin et al. 2021).

III. PLACEMENT OF A SUBCUTANEOUS URETERAL BYPASS FOR THE TREATMENT OF URETERAL OBSTRUCTION IN CATS: A RETROSPECTIVE STUDY

1. Introduction and objectives

Bening ureteral obstruction is a multifactorial and life-threatening disease, with increasing tendencies in cats (Kyles et al. 2005a; Geddes et al. 2023). Ureteral obstruction may manifest quickly or insidiously, and once diagnosed, urgent intervention is required to decompress the renal pelvis and prevent renal function decrease (Lulich et al. 2016; Gomes et al. 2018). Calcium oxalate is the most common type of ureteroliths, which do not dissolve with medical treatment (Kyles et al. 2005a; Lekcharoensuk et al. 2005).

Various approaches have been documented for managing ureteral obstruction. Medical management alone has demonstrated low success rates, highlighting the need for surgical intervention in most cases (Merindol et al. 2023). Traditional surgical techniques are invasive and associated with high morbidity, hence there is growing interest in exploring new interventional options. Ureteral stenting is reported to be an effective approach for treating ureteral obstruction. However, it is associated with a higher risk of long-term complications and its placement is technically challenging. In certain cases, ureteral stenting is contraindicated, such as in the presence of ureteral strictures or immunocompromised patients. Additionally, due to the smaller dimensions of a cat's ureters, for some patients ureteral stenting is not feasible (Berent et al. 2014; Deroy et al. 2017).

SUB device placement has been described as a viable alternative treatment for any type of benign ureteral obstructions. It consists of a nephrostomy catheter and a cystostomy catheter connected to a subcutaneous shunting port. This provides immediate renal pelvis decompression and allows for the urine to flow from the kidney directly to the urinary bladder, bypassing the ureter (Berent and Weisse 2020). Compared to ureteral stents and traditional surgical procedures, SUB device placement is deemed a superior treatment for ureteral obstruction, as surgical times are shorter, complication rates lower, and has more promising outcomes (Wormser et al. 2016; Deroy et al. 2017). Additionally, it is an indwelling system that allows maintenance through periodic flushes, providing long-term solution for ureteral obstructions (Berent and Weisse 2020).

The objective of this study was to evaluate the outcome and determine the complications of SUB device placement in cats, for the treatment of ureteral obstructions, in *Hospital Veterinário do Porto* (HVP).

2. Material and methods

Medical records of all feline patients diagnosed with benign ureteral obstruction and underwent SUB device placement in *Hospital Veterinário do Porto* (HVP), between November 2021 and June 2023, were retrospectively reviewed. Data was collected from the computerized medical database *WinTouch 2023*, using the coding "*bypass ureteral subcutâneo unilateral*" and "*bypass ureteral subcutâneo bilateral*". The diagnosis of ureteral obstruction consisted in an abdominal ultrasonography, with the detection of pyelectasis, associated with hydroureter, and an antegrade pyelography, performed immediately prior to SUB device implantation. The inclusion criteria for this study were based on the presence of the following information in the medical records: preoperative history, concurrent diseases, preoperative diagnostic results from imaging and blood analysis, drugs administered, anesthetic and surgical details, and SUB device placement associated complications.

All cases were referred to HVP, and pre-surgical information gathered from patient's reports and analysis were included in this study. Additionally, one patient's owner opted to have their follow-up consultations with their primary veterinarian, and the information from those reports was also included.

The data recorded concerning the population's characterization and preoperative information were: age, sex, breed, body weight, reproductive state, clinical signs, previous history of CKD or concomitant diseases, laboratory results (serum concentrations of creatinine, BUN, potassium, phosphorus, PCV (packed cell volume), urine pH, hematuria, pyuria, proteins, and USG at admission, ureteral obstruction cause, ureteroliths localization, renal pelvis transverse measurement and presence of hydronephrosis and hydroureter. The information collected from the perioperative period comprehended, whenever possible, intraoperative and postoperative complications, the presence of anemia, serum concentrations of creatinine, electrolyte assessment, postoperative body weight and hydrations status, and hospitalization time. For the short- and long-term periods, whenever possible, it was recorded data regarding SUB device complications, serum concentrations of creatinine, blood pressure measurements, and urine culture results.

Complications associated with the SUB device placement were divided into intraoperative (from anesthesia induction until full recovery), postoperative (from recovery to 7 days post-surgery), short-term (7 to 30 days after surgery), and long-term (>30 days after surgery) complication details. Complications that persisted beyond a single time period were described on the period in which they initially manifested. Complications were further classified as major and minor. Major complications refer to treatment-related adverse events that require additional therapy, increased care, or prolonged hospitalizations, whereas minor complications, in contrast, required minimal to no treatment.

In the preoperative period, all patients were medically managed for at least 24 hours, to ensure stabilization and possible spontaneous calculi passage. Patients with any urinary tract infection (UTI) received antibiotic therapy for a minimum of 48 hours, previous to SUB device placement, to allow bacteriuria reduction. The medical management typically consisted of IV fluid therapy with Ringer lactate and analgesia. Diuretics, antiemetics, proton pump inhibitors, and angiotensin II receptor blockers (telmisartan) were administered as necessary, according with the clinicians' preferences. Metamizole was used as an antipyretic agent for the treatment of fever. In addition to medical management, the placement of a nephrostomy tube could be considered if deemed necessary by the clinicians. All the patients admitted in the hospital without an ultrasound report underwent an abdominal ultrasonography, focusing in the urinary tract. The renal pelvis diameter in a transverse plane, calculi location, presence of contralateral calculi and nephroliths, and number of calculi found were recorded. Abdominal radiography was equally performed, and whenever a heart murmur was detected, patients were submitted to an echocardiography. Cystocentesis was performed preoperatively in most patients, and the obtained urine samples were subsequently sent to two different laboratories for urine culture and antibiotic sensitivity testing.

In HVP, the criteria for the placement of a SUB device include: the presence of hydroureter and hydronephrosis, imaging evidence of an obstructive lesion, renal pelvis dilation > 5 mm, and lack of response to medical management after 24 hours.

In all patients, before SUB device placement, antegrade pyelography was performed intraoperatively, using an 18 or 22G over-the-needle catheter. For contrast, it was used a 50:50 mixture of sterile saline (0,9% NaCl) and iohexol. In cats who did not have a cystocentesis performed previous to surgery, a pyelocentesis was performed and urine sample was equally submitted to urine culture and antibiotic sensitivity testing.

For pre-anesthesia, the drugs routinely used were a combination of methadone (0,25 mg/Kg slow IV), dexmedetomidine (0,002 mg/Kg IV), and midazolam (0,1 mg/Kg IV). General anesthesia was induced with propofol (2 mg/Kg slow IV) and maintained with volatile sevoflurane. Additionally, locoregional anesthesia (TAP block) was performed with ropivacaine (7,5 mg/mL). For those patients who did not receive preoperative antibiotic treatment, antibioprophylaxis was initiated intraoperatively. The preferred antibiotic for this purpose was cefazolin, administered at a dosage of 22 mg/kg. The initial dose was given at the start of the surgery, followed by subsequent doses every 1 hour and 30 minutes to maintain therapeutic levels. In some patients a fentanyl CRI and a lidocaine, ketamine and dexmedetomidine CRI were administered intraoperatively and continued immediately postoperatively for a short period of time.

Two different commercial SUB device versions were applied in this study: SUB™ 2.0 and SUB™ 3.0. The differences to the latest version lay in an additional catheter connecting

the nephrostomy and cystostomy catheters in the abdominal cavity, passing through the abdominal wall and attaching to the subcutaneous port. Furthermore, the design of the cystostomy catheter end has been modified, transitioning from a multifenestrated locking-loop to a straight configuration. The SUB device placement procedure was performed, with the aid of fluoroscopy, as described in the surgical guide provided by Norfolk Vet Products (Berent and Weisse 2018; Berent and Weisse 2020). By the end of the surgery, a fluoroscopic study is performed in order to ensure that the device is properly placed in the kidney and bladder, as well as to confirm the absence of urine leakage, kinking, or catheter misplacement.

Postoperatively, immediately after the surgery, close monitoring was implemented until the patient fully recovered from anesthesia. This involved continuous observation and assessment of vital signs, such as heart rate, respiratory rate, blood pressure, temperature, and mucosal colors. Until hospital discharge, all feline patients received pain management to ensure their comfort, typically through the administration methadone or buprenorphine. Additionally, antibiotic therapy with cefazolin was continued for a duration of up to 7 days to prevent any potential postoperative infections. While hospitalized, cats had a routine physical examination performed at least twice a day to check for any signs of complications such as fever (> 39,5 ºC), fluid overload, and dysuria. Serum creatinine concentrations were monitored every 48 to 72 hours. Prior to hospital discharge, control blood analysis and abdominal ultrasound were performed in all patients.

The hospitalization time was determined as the period between the day of the SUB placement until the day of hospital discharge. The criteria for hospital discharge were based on the patient's overall clinical condition, good pain management, and a significant decrease in serum creatinine concentration. For the patients discharged with anorexia, stimulation of food and water consumption were advised. After stabilization, and if not implemented before by the owners, renal or urinary diet implementation was suggested to the owners.

Concerning follow-up evaluations, it was advised 1 week, 1 month, and thereafter every 3 months posterior to SUB placement. On each re-evaluation, it was performed a SUB device flush, blood pressure measurement, serum creatinine concentration, and urine culture. If a UTI was detected, more frequent SUB device flushes were recommended. If deemed necessary by the clinicians, additional blood analyses could be conducted, including complete blood count (CBC), assessment of electrolyte concentrations and a biochemical profile. Any complications that arose were noted and addressed during each appointment or through phone follow-ups. The follow-up data extended until the writing of the study was included.

The flushing process consisted of the patient is positioned in dorsal recumbency, and a Huber needle, equipped with a 3-way stopcock and two syringes, is inserted perpendicularly into the port's silicone diaphragm. Typically, the procedure is performed without the requirement of sedation. However, in case of anxious patients, a sedative was administered.

Firstly, a urine sample is collected to urine culture and antibiotic sensitivity testing. Subsequently, while monitoring the renal pelvis and then the urinary bladder, the device is vigorously flushed to assess SUB device patency. Finally, after emptying the renal pelvis, the T-FloLoc syringe with the tetraEDTA solution is slowly and intermittently flushed into the system.

For feline patients dying during the study period, time post-surgery and cause of death were recorded. The cause of death was further classified as urinary or non-urinary related causes.

3. Results

3.1. Case selection, historical and clinical data

Five feline patients with 5 completely obstructed ureters were evaluated and included in this study. All (100%) had successful SUB placement.

Feline patient 1 was 8 years old, female, spayed, domestic short-hair, with a body weight of 2,94 Kg. It was presented as a surgical referral to ureteral stenting, after presenting with weight loss, vomiting, and abdominal pain on palpation. It has a previous history of CKD, with creatinine levels within the reference range in the consultation previous to ureteral obstruction diagnosis. As the ureteral stent was not able to pass through the ureter, a SUB device was placed. Patient 2 was 7 years old, male, neutered, domestic short-hair, with a body weight of 3,09 Kg. It was presented as a surgical referral to SUB device placement, after presenting hyporrexia and weight loss. Patient 3 was a 7-year-old female, spayed, domestic short-hair, with a body weight of 4,45 Kg. The iatotropic signs were abdominal alopecia, vomiting, anorexia, lethargy, weight loss, and fever was detected during physical examination. It was presented at HVP as a surgical referral to SUB device placement. Feline patient 4 was 12 years old, female, spayed, domestic short-hair, with a body weight of 2,96 Kg. It was admitted to HVP as a surgical referral to SUB device placement and the iatotropic signs were vomiting, weight loss, and polyuria, and on physical examination dehydration was detected. Patient 5 was 11 years old, female, spayed, domestic short-hair, with a body weight of 4,36 Kg. It was referred to HVP for ureteral stent removal, after presenting to the primary veterinary clinic with nausea, anorexia, on physical examination dehydration and abdominal distension, and on ultrasonography survey observing intra-abdominal free fluid. This cat had a previous history ureterolith-induced ureteral obstruction, which was treated 2 years prior with ureteral stenting. Patients 1, 4, and 5 had a previous history of CKD (table 1).

Table 1. Demographic data of the 5 patients included in this study.

	Sex	Age	Reproductive status	Breed	Body weight (Kg)	Clinical signs	Previous clinical history
Patient 1	Female	8	Spayed	DSH	2,94	Weight loss, vomiting, abdominal pain	CKD
Patient 2	Male	7	Neutered	DSH	3,09	Hyporrexia, weight loss	None
Patient 3	Female	7	Spayed	DSH	4,45	Abdominal alopecia, vomiting, anorexia, lethargy, wight loss, fever	None
Patient 4	Female	12	Spayed	DSH	2,96	Vomiting, anorexia, weight loss, polyuria, dehydration,	CKD
Patient 5	Female	11	Spayed	DSH	4,36	Nausea, anorexia, dehydration, abdominal distension, intra-abdominal free fluid	CKD, ureterolith-induced ureteral obstruction

DSH – domestic short-hair; CKD – chronic kidney disease.

3.2. Clinicopathologic and laboratory data preoperatively

In a pre-surgical assessment, the mean PCV 30,3% (range: 20,9% to 34,8%; reference range: 26% to 47%), with only patient 5 having a non-regenerative anemia prior to SUB placement. The mean serum creatinine and BUN concentration was 7,6 mg/dL (range: 1,9 to 11,9 mg/dL; reference range: 0,8 to 1,8 mg/dL) and > 205,1 mg/dL (range: 122,7 to 324,0 mg/dL; reference range: 17,6 to 32,8 mg/dL), respectively. Thus, all patients were azotemic before medical treatment. The mean serum creatinine concentration just before surgery, and after fluid therapy was 4,1 mg/dL (range: 1,68 to 7,32 mg/dL), and only patients 1, 4, and 5 were azotemic. The mean serum potassium concentration was 4,7 mg/dL (range: 3,6 to 5,6 mg/dL, reference range: 3,4 to 4,6 mg/dL), with patients 4 and 5 being hyperkalemic (5,6 mEq/L and 5,4 mEq/L, respectively) and patient 1 being in the superior limit of the reference range. Concerning the serum phosphorus concentration, the mean was 10,1 mg/dL (range: 4,8 to 15 mg/dL; reference range: 3,0 to 6,9 mg/dL), with patients 1, 4, and 5 being hyperphosphatemic. The average was calculated with only four patients, as patient 3 did not have it measured.

Almost all feline patients, had a urinalysis and urine bacterial culture performed before SUB device placement. Patients 1 and 5 had a pyelocentesis performed intraoperatively, prior to placement of the SUB device, and patients 2, 3, and 4 had cystocentesis performed in the primary veterinary clinic or upon admission to HVP. Regarding urinalysis type II, there were no data reported for patient 5. Patients 2, 3, and 4 had the presence of hematuria, patients 2 and 3 had leucocytes in the urine, and it was detected proteins in cats 2 and 4. The urine pH of patient 2 was acidic (pH = 5; reference range: 5,5 to 7,5). In patient 3, urine sediment contained

calcium oxalate crystals. Urine culture was negative in all patients. Mean USG was 1.017 (range: 1.012 to 1.027; reference range: > 1.035), being cats 1, 2, 3, and 4 below the inferior limit.

The aforementioned data is summarized in table 2.

Table 2. Summary of preoperative blood and urine analysis results of all the patients.

	PCV (%)	SCr before MT (mg/dL)	BUN before MT (mg/dL)	SCr preoperatively (mg/dL)	Potassium (mEq/L)	Phosphorus (mg/dL)	Urine sediment	USG
Patient 1	32,1	8,03	122,7	7,32	4,5	7,5	-	1.012
Patient 2	29,3	1,9	153,7	1,68	4,6	4,8	Blood; leukocytes; proteins	1.020
Patient 3	34,6	9,18	285,0	1,3	3,6	-	Blood; leukocytes; proteins; CaOx crystals	1.027
Patient 4	34,8	7,0	324,0	6,05	5,6	12,9	Blood; proteins	1.014
Patient 5	20,9	11,85	> 140	5,31	5,4	15,0	-	-

PCV – packed cell volume; SCr – serum creatinine; BUN - blood urea nitrogen; MT – medical treatment; CaOx – calcium oxalate.

3.3. Diagnostic imaging

Preoperative echocardiography was performed on cats 2 and 4 after hearing a heart murmur during auscultation and after suspecting fluid overload, respectively. No underlying heart diseases or fluid overload were found.

Abdominal radiography was performed on patient 2 at the primary veterinary clinic, and it was observed radiopaque opacities in the kidney and retroperitoneal space, where the ureters would be.

Abdominal ultrasonography was performed on the five patients as the definitive method for diagnosis and reports were available for review. The totality of the abdominal cavity was assessed revealing abnormalities only in the urinary tract. In patient 1, it was observed hydronephrosis in the right kidney and ipsilateral hydroureter. The renal pelvis dilation was 6,3 mm and it was detected a ureterolith lodged in the first third of the ureter. The left kidney presented lesions compatible with CKD, including kidney atrophy, irregular conformation, and absence of corticomedullary differentiation. In feline patient 2 it was observed a bilateral ureterolithiasis. It was observed hydronephrosis and hydroureter on the left side. The exact measurements of pelvis dilation were not recorded, but it was registered a dilation on the right side with < 5 mm, and on the left side with > 8 mm. Nephroliths were detected on both renal pelvises, and a single calculus was observed in the proximal third of the left ureter. Additionally, sediment was observed in the bladder. Regarding case 3, it was reported hydronephrosis of

the right kidney and hydroureter on the right side. The ipsilateral renal pelvis had a dilation of 15,0 mm and there was a single calculus lodged in the proximal third of the ureter. On the left kidney, it was detected nephroliths. In patient 4, on the right side, it was observed hydronephrosis, hydroureter, and nephroliths. The renal pelvis dilation was 18,5 mm and a single calculus was located in the middle of the ureter. On the left side, it was detected a ureterolith on the ureteropelvic junction with a mild renal pelvic dilation (2,8 mm), but no ureteral abnormalities were noted. In patient 5 it was reported intra-abdominal free liquid and a sample was collected, revealing not to be compatible with urine. On the left kidney it was detected hydronephrosis, and the renal pelvis had a dilation of 10 mm. The ureteral stent was properly positioned within the renal pelvis and a single calculus was observed in the proximal portion of the ipsilateral ureter, within the ureteral stent. After nephrostomy tube placement the renal pelvis dilation reduced to 5 mm.

Table 3. Summary of the important data gathered on the abdominal ultrasound.

	Ureteral obstruction side	Pelvis dilation (mm)	Ureterolith location	Presence of nephroliths
Patient 1	Right	6,3	Proximal	No
Patient 2	Left	> 8	All extent	Left and right
Patient 3	Right	15,0	Proximal	Left
Patient 4	Right	18,5	Middle	Right
Patient 5	Left	10,0	Proximal	No

Intraoperative fluoroscopy was performed in all the patients, confirming the abnormalities identified during the ultrasonography surveys. In patient 5, it was additionally used to verify the patency of the ureteral stent, by injecting iohexol into the renal pelvis. The contrast flow was observed to abruptly cease before reaching the location of the calculus, and no contrast was observed in the remaining portion of the ureter or the bladder, confirming a ureteral stent obstruction.

3.4. Medical management

Prior to SUB device placement, all cats received IV fluid therapy with Ringer lactate. The rate of fluid administration was adjusted based on the degree of dehydration on each cat. The duration of IV fluid therapy prior to the procedure averaged 3,4 days (range: 1 to 6 days). In patient 5, which was admitted with dehydration, 3 days after hospitalization (and before surgery) euhydration was reached. Additional preoperative management included administration of buprenorphine for analgesia (n=3, patients 3, 4, and 5), an antiemetic, maropitant (n=3, patients 3, 4, and 5), and a proton pump inhibitor (n=2, patients 3 and 5).

Patient 3 received antibiotic therapy with ampicillin before surgery, for a duration of 5 days, due to fever upon hospitalization. Moreover, due to obstipation, lactulose was administered. In patient 4 was detected hypertension and telmisartan was administered.

As patient 5 was anorectic, a nasogastric tube was placed upon hospitalization. Also, a nephrostomy tube was implanted, until stabilization of the patient, and 4 days after, upon removal, a subcapsular hemorrhage developed. In the same animal, ampicillin was administered for 5 days before surgery.

The duration of admission-to-surgery varied among the patients, with patient 1 being admitted for 4 days, patients 2 and 4 for 1 day, patient 3 for 5 days, and patient 5 for 6 days.

None of the patients in the present study responded to medical management as an expulsive therapy. Such was confirmed by an abdominal ultrasonography, immediately before surgery, which revealed no significant improvement in the condition. Consequently, all patients underwent SUB device placement.

3.5. SUB device placement

A SUB device was successfully placed in all patients. Feline patients 1 and 2 had a SUB^{TM} 2.0 placed (figure 11A), and patients 3, 4, and 5 had SUB^{TM} 3.0 placed (figure 11B). Thus, a coiled cystostomy catheter was used in patients 1 and 2, and a straight cystostomy catheter was used in patients 3, 4, and 5. Furthermore, there is an additional catheter (actuating catheter) that links the nephrostomy and cystostomy catheters, through the abdominal wall, to the subcutaneous port.

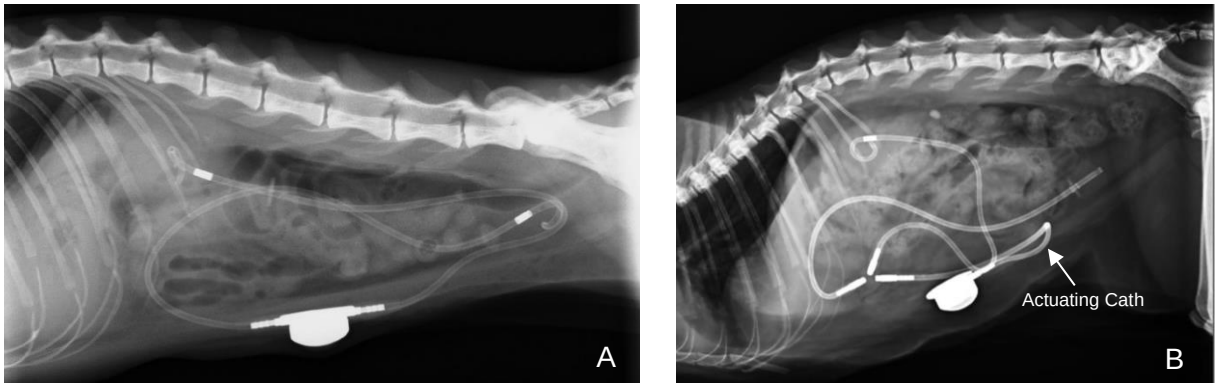

Figure 11. Abdominal radiography of two different cats after SUB placement with two versions (original, provided by HVP).

Subtitle: A: feline patient 2 with the SUB 2.0 device; B: feline patient 3 with the SUB 3.0 device.

All five cats had a unilateral SUB device placed, due to a ureterolith-induced ureteral obstruction. Patients 1, 3 and 4 placed a SUB device on the right side and patients 2 and 5

had a SUB placed on the left side. In patient 5, in the same anesthetic time and before SUB device placement, the previous placed ipsilateral ureteral stent was removed.

The device's patency was verified intraoperatively with the aid of fluoroscopic imaging. Contrast was injected through the port into the system, and to verify the absence of leakage, kinking or obstruction. None of these was detected in any of the patients.

3.6. Post-procedural data

The average serum creatinine concentration was 4,1 mg/dL (range: 1,32 to 6,6 mg/dL; reference range: 0,8 to 1,8 mg/dL). The postoperative PCV was recorded in all patients, except for number 4, and the mean was 24,7% (range: 14,7 to 32,6%; reference range: 26,0 to 47,0%). These values were collected in an average of 24 hours post-surgery (range: 12 to 48 hours).

In patient 1, in the first 48 hours, PCV decreased to 22,2%, creatinine decreased to 6,7 mg/dL, and it was detected a mild hypernatremia (159 mEq/L; reference range: 147 to 156 mEq/L). Additionally, dehydration was documented along with weight loss (235 g). Three days after SUB device placement, serum creatinine concentration decreased to 3,11 mg/dL and PCV increased to 25,2%. Moreover, it was detected leukocytosis 25,21 x 10^9/L (reference range: 5,5 to 19,5 x 10^9/L), as well as neutrophilia 24,35 x 10^9/L (reference range: 3,12 to 12,58 x 10^9/L) and lymphopenia 0,37 x 10^9/L (reference range: 0,73 to 7,86 x 10^9/L). Enrofloxacin was associated to cefazolin and the parameters' values decreased. Hypernatremia remained with the same values and it was reported a hyperkalemia of 5,6 mEq/L (reference range: 3,4 to 4,6 mEq/L). It was also reported that, even though urine was not being measured, the patient's urination frequency increased and the dehydration degree increased 24 hours post-procedure. The IV fluids rate was increased. In the next hours, the dehydration degree decreased and euhydration was reached and electrolyte balance was reestablished 3 days postoperatively.

Patient 2, preoperatively with creatinine values within the reference range after medical management, had an increase to 2,25 mg/dL in the 24 hours after SUB device placement. Additionally, it was detected leukocytosis (21,56 x 10^9/L; reference range: 5,5 to 19,5 x 10^9/L), neutrophilia (19,41 x 10^9/L; reference range: 3,12 to 12,58 x 10^9/L), and mild hypernatremia (158 mEq/L; reference range: 147 to 156 mEq/L), hyperkalemia (4,7 mEq/L; reference range: 3,4 to 4,6 mEq/L) and hyperchloremia (124 mEq/L; reference range: 107 to 120 mEq/L). On the subsequent hours, serum creatinine concentration returned to normal values. Three days postoperatively, anemia was detected, with a PCV of 23,3% (reference range: 26,0 to 47,0%).

In patient 3, serum creatinine concentration and PCV remained within the reference range, and no abnormalities were recorded.

Concerning patient 4, serum creatinine concentration decreased within the first 12 hours post-operatively to 5,8 mg/dL and the patient remained hyperkalemic (5,9 mEq/L; reference range: 3,4 to 4,6 mEq/L). No data was recorded regarding postoperative CBC analysis. Furthermore, an initial state of dehydration was reported, along with weight loss (295 g) 48 hours following the relief of ureteral obstruction, which was subsequently compensated for.

Regarding patient 5, serum creatinine concentration decreased within the first 24 hours post-operatively to 4,5 mg/dL and serum potassium concentration decreased, remaining mildly hyperkalemic, closely above the superior limit of the reference range (4,7 mEq/L; reference range: 3,4 to 4,6 mEq/L). Immediately following surgery, a CBC was performed, and anemia worsening was detected (14,7 %; reference range: 26,0 to 47,0%). Subsequently a blood transfusion was administered and PCV increased to 17,0%. Furthermore, dehydration was reported, along with weight loss (380 g) 48 hours following the relief of ureteral obstruction.

The first blood analysis and clinical signs aforementioned are summarized in table 4, with only the important parameters being registered.

Table 4. Summary of the important data gathered on the first postoperative blood analysis and clinical signs observed.

	PCV (%)	Serum leukocytes (x 10^9/L)	Serum neutrophiles (x 10^9/L)	SCr (mg/dL)	Sodium (mEq/L)	Potassium (mEq/L)	Hydration status (%)	Weight loss 48 hours postop (g)
Patient 1	22,2 (↓)	25,21 (↑)	91,1 (↑)	6,6 (↑)	159 (↑)	4,0	6 - 7	235
Patient 2	29,4	21,56 (↑)	19,41 (↑)	2,25 (↑)	158 (↑)	4,7 (↑)	< 5	No
Patient 3	32,6	13,78	11,25	1,32	156	4,2	< 5	15
Patient 4	-	-	-	5,8 (↑)	155	5,9 (↑)	6	295
Patient 5	14,7 (↓)	-	-	4,5 (↑)	-	4,7 (↑)	6 - 7	380

PCV – packed cell volume; SCr – serum creatinine; ↓ - below reference range; ↑ - above reference range.

Prior to hospital discharge, all patients underwent an abdominal ultrasonography and serum creatinine concentration was assessed, for monitoring purposes. The ultrasonography revealed pyelectasis reduction and the absence of free fluids in the abdominal cavity. Additionally, a brief inspection of the SUB device was conducted to ensure the proper positioning. Regarding the serum creatinine concentrations, a decrease was observed in all patients to an average of 1,9 mg/dL (reference range: 0,8 to 1,8 mg/dL). Patient 1 had a concentration of 2,75 mg/dL, patient 2 had 1,7 mg/dL, patient 3 had 1,32 mg/dL, and patient 4 had 1,91 mg/dL. Since patient 5 passed away before hospital discharge, their data was not included in the calculation of the mean.

The average hospitalization time was 4,8 days (range: 3 to 8 days). Patient 1 had the longest hospital stay, lasting 8 days. Patients 2 and 4 were both hospitalized for 4 days, while patient 3 had the shortest hospitalization period, lasting 3 days. Patient 5 was not included in the mean calculation, because it did not survive to hospital discharge.

3.7. Intraoperative complications

Hypothermia was reported in all patients. Specifically, patient 1 exhibited hypothermia with the lowest temperature reaching 33,5ºC, patient 3 had a temperature of 32,4ºC, and patient 4 registered a temperature of 33,8ºC. Patients 2 and 5 did not have recorded values, but it was documented that they also experienced hypothermia during this period.

3.8. Postoperative complications

In patient 1, it was reported anemia. Following the placement of the SUB device, the cat exhibited persistent anorexia, leading to the insertion of a nasogastric tube 72 hours later. The tube remained until hospital discharge, because the anorexia persisted. Due to a lack of defecation, an abdominal radiography was conducted, revealing feces accumulation and distension of the distal portion of the colon. Lactulose was administered until resolution.

In patient 2 was registered a mild seroma and discomfort around the port. Buprenorphine and meloxicam were administered to alleviate the symptoms. Additionally, the patient experienced episodes of pyrexia, which were effectively managed with the administration of metamizole. Anemia was also reported. Six days postoperatively, the patient started to have symptoms of dysuria (pollakiuria and stranguria). After 3 days of administering robenacoxib and buprenorphine, the symptoms were successfully managed.

As patient 3 persisted with obstipation, the administration of lactulose was maintained until the patient's hospital discharge. Five days after SUB device placement (3 days after hospital discharge), it was hospitalized again because of a suspected urinary infection, due to episodes of dysuria (pollakiuria and stranguria) and hematuria were detected by the owners, along with lethargy, tenesmus, and anorexia. On physical examination, fever was detected. On blood analysis, results demonstrated leukocytosis (20,72 x 10^9/L; reference range: 5,50 to 19,5010^9/L), neutrophilia (17,92 10^9/L; reference range: 3,12 to 12,58 10^9/L), mild hypernatremia (157mEq/L; reference range: 147 to 156 mEq/L) and hyperchloremia (122 mEq/L; reference range: 107 to 120 mEq/L). An abdominal ultrasonography was performed and marked thickening of the vesical wall and renal pelvis mild dilation was observed. Cystocentesis and urine culture with sensitivity testing was performed. For treatment, enrofloxacin was empirically administered and it started the T-FloLoc infection protocol suggested by the Norfolk Vet Products (Berent and Weisse 2020). Three days after the second

hospitalization, hematuria started and amoxicillin with clavulanic acid was combined to enrofloxacin. Five days post-hospitalization, the bacterial culture and sensitivity testing results came positive for extended spectrum β-lactamase (ESBL) *Enterobacter spp.,* resistant to multiple drugs and only sensitive to amikacin and minocycline. Thus, previous antibiotics were stopped and minocycline was initiated. On the same day, T-FloLoc infection protocol was stopped as no results were observed. Gradually, euthermia was reached, and it started eating, but dysuria and hematuria were persistent. Nevertheless, after 10 days of the second hospitalization, it was discharged. Twenty days after SUB device placement (11th day of minocycline), owners came to another appointment to re-evaluate. There were no abnormalities in the blood analysis. Abdominal ultrasound was performed and it was observed a less thickened vesical wall, an absence of peri-renal reactivity, and hydronephrosis. Cystocentesis was performed and urine was sent for a bacterial culture and sensitivity testing. Urinalysis revealed hematuria and pyuria. Urine cytology revealed abundant inflammatory cells and intra- and extracellular bacteria. Three days later, there was another appointment due to vomits and dysuria. An abdominal ultrasound was performed, revealing the absence of evident vesical wall thickening. Maropitant and omeprazole were administered. Results from urine culture came positive for ESBL *Klebsiella spp.*, and minocycline kept being administered. On the next day, dysuria and hematuria signs were milder. Two days later (25 days after SUB device placement), it was hospitalized due to fever, anorexia, and lethargy. Twenty-six days after the SUB device placement, the owners decided for euthanasia. The cause of euthanasia was classified as urinary.

In patient 4, the complications were hyperthermia, hyporrexia and weight loss. Hyperthermia was effectively controlled with metamizole and it started eating after hospital discharge. Furthermore, it was reported hypertension during this period, which was a decompensation due to the procedure, as it was already diagnosed previously. It was managed with telmisartan.

Regarding patient 5, three days after the placement of the SUB device, a hematoma was identified at the suture site, and it was accompanied by the discharge of an exudate consistent with pus. An ultrasonography assessment was performed, revealing the presence of intra-abdominal fluid along with a peritoneal reactivity, indicative of peritonitis. Urography was conducted, confirming the SUB device patency and correct positioning. In addition to the ongoing administration of ampicillin, enrofloxacin was added as an adjuvant treatment. Successive ultrasound examinations showed a decrease in peritoneal reactivity, decrease in intra-abdominal fluid, and better clinical status, following the initiation of this combined antibiotic therapy. The anemia continued to worsen, requiring two additional blood transfusions on the 5th and 6th days post-surgery. Although PCV value increased 4,8%, it never reached the reference interval. From the 9th to the 10th day of hospitalization, PCV decreased 2% and

abdominal dilation was reported. Ten days after surgery, the patient was transferred to the primary veterinary clinic and died on the same day.

3.9. Long-term complications

Patient 2, five months postoperatively, had clinical signs of dysuria and hematuria. Urine culture results came negative, so administration of buprenorphine, robenacoxib, prazosin was initiated. One month later, the symptoms continued and there were sporadic episodes of vomiting. Robenacoxib was discontinued and exchanged by prednisolone and it was successfully managed.

No more complications were reported at the time of this report. Follow up for patients 1 and 2 was 20 months and patient 4 was 7 months.

3.10. Follow-up information and outcome

In patients 2 and 4 serum creatinine concentrations decreased until reaching the reference range. Patients 1 until the writing of this study, could not decrease the values below the superior limit of the reference range. In all patients, until hospital discharge, renal pelvis dilation was reported to decrease substantially.

The median survival time in this study was 296 days (range: 16 to 623 days). No cat died intraoperatively or due to persistent ureteral obstruction after surgery. Two out of the 5 patients died after SUB device placement, within one month. Patient 3 died of a multiresistant urinary infection and patient 5 died unexpectedly probably due to a non-urinary cause. Survival rate from 1 month to 6 months was 60%.

4. Discussion

For all five feline patients described in this study, the placement of a SUB device was successful and provided immediate relief of the ureteral obstruction, resulting in the decrease of the serum creatinine concentration. The placement of a SUB device does not prevent the primary cause of ureterolithiasis, it only allows resolution of the obstruction. This allowed the treatment of the associated ureterolithiasis, regardless of the severity of the clinical signs and laboratory abnormalities. There were no instances of intraoperative or immediate postoperative mortality in any of the cats.

In a recent study by Geddes et al. (2023), two different clinical phenotypes of upper urinary tract uroliths (UUTU) were identified: obstructive UUTU, which is more aggressive and common in younger cats; and non-obstructive UUTU, which is milder and more prevalent in older cats. Various risk factors were identified for non-obstructive UUTU, including being

female, older than 4 years old, and being certain breeds such as British Shorthair, Ragdoll, Persian, Tonkinese, and Burmese. The most susceptible age range for UUTU formation is between 4,0 and 7,9 years. For the obstructive UUTU phenotype, being female, younger than 12 years old, and having bilateral uroliths were identified as predisposing factors. Interestingly, those under 8 years old are 4 times more likely to develop obstructive UUTU. Considering the present study's population, 4 out of 5 patients, were female and within the age range commonly associated with high risk of developing obstructive UUTU, aligning with the predisposing factors. However, none of them were purebred. No specific information about the diets or indoor/outdoor status of the cats was recorded in this study, and it is important to note that these factors can indeed have an impact on the development of ureteral obstruction. Therefore, considering this information would provide a more comprehensive understanding of the disease and its management.

The clinical presentation of feline ureterolithiasis can vary significantly between individuals, and the associated clinical signs are often nonspecific (Kyles et al. 2005a; Segev 2011; Gomes et al. 2018). The most common clinical signs, practically observed in all patients, were vomiting/nausea, weight loss and hyporrexia/anorexia, which may be attributed to the presence of azotemia, as indicated by the elevated serum creatinine and BUN concentrations. Clinical sings such as abdominal pain on palpation and abdominal alopecia, in patients 1 and 3, respectively, might be attributed to stretching of the renal collecting system and capsule, direct stimulation of the obstruction site and ureteral colic (Berent 2011; Segev 2011). In patient 3, fever was reported at physical examination, and is explained by an ongoing infection. On urinalysis type II, calcium oxalate crystals were detected. It is reported that most ureteroliths (98%) contain calcium oxalate, and, even though crystals may not accurately predict the urolith type, it can provide a valuable suggestion about the ureterolith composition (Bartges and Callens 2015). Patient 5 presented with intra-abdominal free fluid upon admission, as observed in the abdominal ultrasonography. However, the fluid's constitution was not further characterized in the available data, making it challenging to determine its exact origin.

Preoperative serum creatinine and BUN concentrations were increased in all patients at some point in time, during the period between diagnosis and treatment. It is reported that CKD has a prevalence of 1,2% in cats, which increases to 3,6% in cats that are aged nine years or older (Conroy et al. 2019). Additionally, it was concluded in previous studies that nephroliths can lead to CKD (Hall et al. 2017). In patients 2 and 4, these values were increased as expected, as they had a bilateral ureterolithiasis. Even though only one of the ureters was completely obstructed, the contralateral was partially obstructed, justifying the abnormal values. Patients 1, 3, and 5 had a unilateral ureteral obstruction and were concurrently azotemic. It would be expected for the serum creatinine and BUN concentrations to remain within the reference range, as a healthy contralateral kidney would compensate by increasing

its GFR (Wen et al. 1999; Kyles et al. 2005a). However, in patient 1, there was pre-diagnosed CKD, explaining the abnormal serum creatinine increase. Patients 3 and 5 had nephrolithiasis on the contralateral kidney, which also compromises the renal function.

In patients 1, 2, 3, and 4, USG was below the reference limit (USG > 1.035). This can be explained by patient 1 having previous history of CKD, patient 2 having nephroliths and patients 3 and 4 having both.

In past studies, for the diagnosis of ureteral obstruction, a combination of ultrasonography and radiography is advised, as sensitivity increases to 90% (Kyles et al. 2005a). However, in a most recent study, the sensitivity of ultrasonography alone for the diagnosis of ureterolithiasis is reported to reach 98% and 44% for the diagnosis of ureteral strictures when performed by specialized operators (Wormser et al. 2019). In the latest consensus on recommendations concerning the management and prophylaxis of urolithiasis, the utilization of ultrasonography is advocated as a diagnostic tool, with radiography being potentially useful in cases where diagnostic uncertainties exist. Additionally, it states that the presence of hydronephrosis and hydroureter proximal to an obstructive lesion is considered enough for diagnosis (Lulich et al. 2016). In this study, ultrasonography alone was the imaging method of choice to reach a definitive diagnosis. It was performed by veterinarians with extensive expertise, increasing the sensitivity. In all patients, hydronephrosis and hydroureter were observed, along with one or more ureteroliths. However, it is important to note that the diagnostic failure rate for detecting ureteral strictures is substantial, implying that there is a significant possibility of it going undetected. Moreover, in cases of initial ureteral obstructions, the degree of dilation observed in the renal pelvis and ureter may not be significant, leading to potential misinterpretation or misleading findings.

The hypothesis proposing the origin of ureteroliths as nephroliths that have undergone migration from the renal pelvis into the ureter, resulting in subsequent obstruction, is widely acknowledged within the scientific community (Lekcharoensuk et al. 2005; Grauer 2015; Geddes et al. 2023). Thus, those cats with nephroliths are considered to be more susceptible of developing a ureterolith-induced ureteral obstruction (Geddes et al. 2023). This was reported in patient 5, where a reobstruction was observed after undergoing ureteral stent placement two years prior. Furthermore, in patients 2, 3, and 4, on abdominal ultrasound surveys, nephroliths detected, indicating their increased susceptibility to develop a reobstruction or contralateral ureteral obstructions. Specially in patients 2 and 3, as they are in the predisposed age range to develop an obstructive UUTU. Therefore, close monitoring of the location of these nephroliths during follow-up appointments is imperative.

The identification of the location and size of the ureteroliths can provide helpful information in assessing the potential success of medical management. It is reported that success rate is low (30%) for the passage of ureteroliths into the bladder. This success rate

was observed mainly in young cats with distal ureteroliths measuring less than 1,44mm in size (Merindol et al. 2023). In the present study, none of the patients were young and none of them had ureteroliths in the distal portion of the ureter. However, in the absence of information about the size of the calculus, it is very difficult to elude if conservative treatment would be successful. Information of the size of the calculus would be very important to help in the decision for a previous attempt for conservative treatment

The only intraoperative complication reported was hypothermia, which all patients experienced. This was reported as the most common complication in a few studies, with a prevalence of 87 to 97%. Such might be explained by cats' bigger body surface area and body weight ratio make them more vulnerable to heat loss, and the long surgical time with exposition of the viscera associated with lavage solutions (Mateo et al. 2015; Luca et al. 2017).

In Human Medicine it is reported that fever happening within the first 4 days postoperatively are likely non-infectious. These fevers are primarily triggered by the release of cytokines, which act on the anterior hypothalamus and stimulate the production of prostaglandins, thereby mediating a febrile response. Research indicates that the extent of tissue trauma is directly proportional to the release of IL-6, which, in turn, correlates directly with the magnitude of fever experienced during the postoperative period (Narayan and Medinilla 2013). In another recent study it was reported that the second most frequent cause of pyrexia in cats is inflammatory (non-infectious) conditions. Also, leukocytosis and neutrophilia can be associated to different causes, including stress, infection and inflammation. When multiple episodes are documented, the stress factor can be excluded. (Spencer et al. 2017). During the postoperative period, occurrences of pyrexia were frequent, as it was documented in patients 2 and 4, within the first 12 hours and 2 days, respectively. In both cases, pyrexia episodes had a duration of 2 days. Additionally, as none of these patients had positive urine bacterial cultures, infection was discarded and it was attributed to an inflammatory reaction due to the SUB device placement surgery. In patient 2 fever was accompanied with leukocytosis and neutrophilia, but it was also attributed to inflammation.

In a recent study by Balsa et al. (2019), the occurrence of post-obstructive diuresis was investigated following ureteral stenting and SUB device placement in cats. It was observed that after relief of urinary obstruction, there was an increase in urine output, which could potentially lead to dehydration and electrolyte imbalances. The study found that 100% of the feline patients undergoing ureteral obstruction decompression experienced post-obstructive diuresis. Furthermore, it concluded that higher concentrations of serum creatinine, BUN and potassium concentrations lead to more severe post-obstructive diuresis (Balsa et al. 2019). In case of patient 1, an increase in urination frequency was reported, accompanied by subsequent dehydration, electrolyte imbalance and rapid weight loss. While urine output was not directly measured in this study, the reported findings are consistent with post-obstructive

diuresis, which may explain the observed laboratory abnormalities. Dehydration was also observed in patients 4 and 5 following SUB device placement, as well as rapid weight loss, which might similarly be explained by post-obstructive diuresis. Interestingly, the three patients mentioned had the highest preoperative serum creatinine concentrations (8,03 mg/dL, 7,0 mg/dL, and 11, 69 mg/dL) when compared to other patients, which may further justify the clinical signs of dehydration as post-obstructive diuresis. In the same study, it was reported that more severe post-obstructive diuresis is associated with longer hospitalization times (Balsa et al. 2019). This finding was observed in the case of patient 1 (8 days of hospitalization) and patent 5 (it died before hospital discharge, but hospitalization time would have been more than 10 days). However, it is important to note that the prolonged hospitalization time in the case of patient 1 cannot be solely attributed to post-obstructive diuresis. Instead, it was a combination of factors including anorexia and obstipation that contributed to the overall poor clinical condition of the patient, leading to the need for an extended hospital stay. Similarly, in patient 5, hospitalization time was concurrently associated to the non-regenerative anemia which required 2 blood transfusions. In the case of patient 4, this phenomenon was not observed, as the hospitalization time was only 3 days. This could possibly be attributed to the absence of electrolyte imbalances, a good overall clinical state, and the ability to easily correct the dehydration.

In the preoperative period, patient 3 presented with multiple episodes of fever and ampicillin was initiated upon admission. A urine culture was performed and no bacteria were isolated, so a urinary infection was discarded. In the postoperative period, the patient exhibited clinical signs of dysuria and hematuria. Subsequent urine culture and antibiotic sensitivity tests were performed twice with an interval of 15 days, yielding positive results for *Enterobacter spp.* and *Klebsiella spp*., both of which displayed resistance to multiple antibiotics. As a result, a post-surgery urinary tract infection was diagnosed. Three hypotheses were proposed to explain the occurrence of this infection. The first hypothesis suggests that the patient had a preexisting mixed UTI prior to surgery. The clinical signs upon admission, especially fever, could be explained by an ongoing UTI. During the preoperative phase, empirical antibiotic therapy was administered in response to episodes of fever, and this treatment continued for 3 days before cystocentesis. As a result, the strains of bacteria susceptible to ampicillin were eradicated, leading to a decrease in bacterial concentrations in the urine. Thus, bacteria were unable to be isolated in the urine culture, possibly resulting in a false negative, as reported in a previous study (Pennington et al. 2021). Consequently, following the placement of the SUB device, the bacteria, which were resistant to ampicillin, multiplied and started forming biofilms that facilitated their evasion of the antibiotic treatment (Berent et al. 2018; Pennington et al. 2021). Hence, when the proper antibiotic started being administered, the infection could not be controlled. On the other hand, mixed UTI are relatively uncommon (Garcês et al. 2022).

Also, the two isolated bacteria are opportunistic pathogens found in clinical surfaces and equipment, rarely causing concurrent infection (Moxley 2013), leading to the next hypothesis. The second hypothesis proposes the contamination of the second urine sample during its collection, storage or transportation. The third theory suggests the possibility of a laboratory error during the process of the second urine culture.

In the present study, the average hospitalization time was 4,8 days, with a range of 3 to 8 days. This can be compared to previous studies where the average hospitalization time was reported as 4,6 days (range: 1 to 11 days) (Berent et al. 2018). It is worth noting that the results obtained in this study are similar. For the calculation of this average, patient 5 did not count, as it died before hospital discharge. However, as expected, patients needing blood transfusions require longer hospitalizations times (Berent et al. 2018) and patient 5 would have been hospitalized the longest, for more than 10 days.

Patient 1 on follow-up appointments and successive serum creatinine concentration re-evaluations, revealed a progressive decrease of the creatinine levels. However, once the serum creatinine concentration reached a certain threshold, it remained consistently elevated above the upper limit of the reference range. It is known that longer durations of ureteral obstructions increase the risk of irreversible renal damage (Wen et al. 1999). In case of this patient, the surgery was delayed for 4 days; however, ureteral obstruction is often present before clinical manifestation and admission (Shipov and Segev 2013). The delay in performing surgery, along with the presence of preexisting CKD, likely contributed to additional permanent renal injury and subsequently higher serum creatinine concentrations.

In patients 1 and 3 obstipation was reported and confirmed on abdominal radiography. Constipation, a rather common condition in cats, is defined as the retention of feces within the colon or rectum, typically accompanied by infrequent bowel movements (< 3-4 defecations per week) and/or dyschesia. Obstipation is a severe form of constipation, and typically requires medical intervention for resolution (Unterer 2017). Constipation is a multifactorial condition, and there are several factors that can predispose, including increasing age, obesity, diet, previous history of constipation and CKD (Benjamin and Drobatz 2020). Hospitalized cats are particularly susceptible due to factors such as reduced physical activity, reluctance to defecate while in hospital environment, increased risk of dehydration and hypokalemia during illness, and the administration of opioids (Hall 2017). Concerning patient 1, obstipation was detected following surgery, and after being hospitalized for 8 days. The development of this condition can potentially be attributed to a combination of factors, including postoperative dehydration, lack of activity, and the opioids administered during anesthesia. Additionally, the patient had a prior history of CKD, in which the ability to concentrate the urine was impaired, as indicated by a USG of 1.012 upon hospital admission. This chronic water loss resulted in compensatory water absorption from the colon, leading to dehydration of the feces and ultimately contributing

to obstipation (Quimby 2016). In patient 3, obstipation was diagnosed before surgery, on the 4th day of hospitalization, and there was no registration of feces since the 1st day of hospitalization. Such can be explained by the anorexia and fever experienced before and upon hospital admission, as well as the stress associated with hospitalization, lack of activity and reluctance on defecating while kenneled. Nevertheless, in both cases, successful management was achieved through the administration of lactulose.

According to the Norfolk surgical guide for the placement of the SUB™ 3.0, it was not reported any case with worsening of the azotemia postoperatively (Berent and Weisse 2020). However, in this study, patient 2, in the 24 hours postoperatively, had serum creatinine concentration transitorily increased above the threshold. Such can be explained by the trauma associated to the nephrostomy catheter insertion, leading to brief renal malfunction.

Furthermore, in patients 1 and 2, mild anemia was observed within 48 hours and 72 hours after surgery. Considering preoperative PCV was within the reference range, and no dehydration was reported prior to the surgical procedure, it can be inferred that the reported anemia is attributable to intraoperative blood loss.

Regarding patient 5 a more severe and non-regenerative anemia was detected. In the preoperative period, after the nephrostomy tube removal, there was a subcapsular hemorrhage, contributing to PCV decrease. Post-surgery, there was a significant decline of 6,2% in PCV, suggesting substantial blood loss during the surgical procedure. Interestingly, even after the initial blood transfusion, the PCV continued to decrease. This phenomenon can be probably attributed to the pre-existing diagnosis of CKD, which was exacerbated by the ureteral obstruction, subsequently worsening renal insufficiency. While the precise cause of death remains unknown, it is suspected that the aggravation of CKD played a considerable role. However, it is noteworthy that until the day of the transfer, during which the patient passed away, there was a progressive improvement in the clinical condition, making the death unexpected. A plausible hypothesis, given the sudden nature of events and considering the pre-existing low PCV and the acute nature and sudden abdominal distension, is the possibility of an internal hemorrhage. Another potential explanation could be an exacerbation of the previous infectious peritonitis. Further investigation and evaluation would have been needed to fully understand the circumstances surrounding the patient's demise.

Patient 2 experienced dysuria as a major complication in the postoperative and long-term periods, presenting with clinical signs such as pollakiuria and stranguria, along with the presence of hematuria. After obtaining negative results in all urine bacterial cultures performed, and the absence of fever and another signs of infection, these clinical signs were deemed non-infectious. In the Norfolk surgical guide for the placement of the SUB™ 3.0, it is reported that the percentage of dysuria decreased from 9% to 5% after changing from the version 2.0 to the most recent one (Berent and Weisse 2020). The comparison between the SUB device 2.0 and

3.0 revealed a change in the shape of the cystostomy catheter, transitioning from a coiled form to a straight configuration. In this case, as it was placed the SUB device 2.0, it was hypothesized that the cause of dysuria was the coiled end of the cystostomy catheter coming in contact with the trigone, due to its conformation and size. This contact likely led to an inflammatory response in the opening and proximal segment of the urethra, responsible for the observed clinical signs, as similarly reported in previous studies (Livet et al. 2017; Wuillemin et al. 2021). Furthermore, the new surgical guide suggested that the cystostomy catheter end should be trimmed to adapt to the patient's bladder size (Berent and Weisse 2020). Interestingly, in this study, feline patients who received the SUB device 3.0 did not experience non-infectious dysuria. Therefore, it was proposed that the previous conformation of the cystostomy catheter could be responsible for the observed clinical signs when compared to the newer version of the SUB device. However, it's important to consider that the suggestion made about the relationship between the modified catheter conformation and the absence of non-infectious dysuria in cats is based on only four cases, which is a small population size.

In the present study, the mortality was 40%, and the two patients that died were in the short-term period. In previous studies, the mortality rate in this period was 10 to 12% (Berent et al. 2018; Wuillemin et al. 2021), which is substantially lower. The cause of death was attributed to urinary complications in one case and non-urinary complications in another. Specifically, in one patient the cause of death was due to a urinary infection with bacteria resistant to multiple antibiotics, and in the other patient was likely related to a late postoperative hemorrhage. The overall survival time was also much lower, in this study was 296 days and in previous studies was 827 to 881 days (Horowitz et al. 2013; Berent et al. 2018; Butty and Labato 2021; Wuillemin et al. 2021). These disparities can be explained by the small population size and the short duration of the study.

5. Limitations

The retrospective nature of this study imposed several limitations. Incomplete records and inconsistencies in the evaluation procedure among patients hindered the ability to conduct a coherent analysis. Furthermore, apart from the surgical intervention, the patients in this study were treated by various clinicians, and the treatment approaches were not standardized. Bigger population size and longer follow-up periods could have helped better characterize the complications, survival time, and mortality in the different periods.

To enhance the clinical assessment, a comprehensive and thorough collection of the patients' clinical history would have been beneficial. This would include meticulous documentation of their lifestyle (indoors/outdoors), dietary habits, water consumption, and frequency of urination. Such information on these variables could have facilitated the

identification of associated risk factors and subsequently enabled the recommendation of lifestyle modifications to mitigate the risk of reobstruction (Gomes et al. 2018; Queau 2019). The assessment of serum ionized calcium would also have been important to document as it is reported to be a risk factor for obstructive ureterolithiasis (Geddes et al. 2023).

The lack of documentation regarding the postoperative exact measurements of the renal pelvis dilations is indeed a significant limitation in the study. Gathering such information would have been crucial to determining whether all patients experienced a complete or partial decrease of the pyelectasis and to assessing the time it took for this change to occur. The inclusion of this data could have provided valuable insights into the impact of the intervention and its effectiveness in managing ureteral obstruction.

6. Conclusion

In all five patients, the consequences of ureteral obstruction were successfully resolved. The dilation of renal pelvises decreased, and there was a significant reduction in serum creatinine levels, revealing resolution of the post-renal AKI induced by obstructive ureterolithiasis.

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