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Improved Research and Experience Sharing of the Ureteroscope Examination Experimental Model in Mini-pigs

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Abstract: ***Objectives**: Currently, there is limited literature available on animal experimental models of pigs, specifically in regards to experimental models of ureteroscopy. **Materials and Methods**: Seven healthy mini-pigs weighing 25kg-30kg, with comparable age, size, and living environment, were selected for the study. Before surgery, intravenous propofol 20 ml was given for general anesthesia. The pig was placed in a supine position, with fixed limbs and separated labia. After disinfection and using a sterile cave towel, the ureteroscope was placed in the urine germinal vestibule, and the external urethral opening was expanded under perfusion fluid. The urethral microscope smoothly entered the urethra, and the ureter opening was identified at 5 o'clock and 7 o'clock. The zebra guide wire was placed into the left ureter, and the ureteroscope was successfully placed into the left ureter. The 5F double J tube was placed in the ureter, and its end remained in the bladder. The ureteroscope was re-entered to check the right ureter opening and another 5F double J tube was placed in the right kidney and down in the bladder. The operation was successfully completed without any abnormalities found. **Results**: The surgical time for establishing an experimental model in 7 mini-pigs varied, with the first pig taking 81 minutes due to lack of experience in water pressure control, search and identification of openings, and re-entering the ureteroscope. The remaining 6 mini-pigs had reduced surgical time, with the last two taking 21 and 19 minutes respectively. The 6 mini-pigs survived normally after surgery. Postoperative X-ray showed bilateral ureteral stents in good position. The animals were observed for breathing, waking up, and normal activities without abnormalities. **Conclusions**: An experimental model of improved mini-pigs for ureteral stent placement has been established using a new method. The assistant clamps the labia to reduce fluid loss, maintains perfusion pressure, and retains a guide wire in the bladder during stent placement on one side. The ureteroscope is guided by two guide wires, significantly reducing operation and anesthesia time, minimizing animal health damage, and lowering mortality rates. This method has reference and promotional significance for future studies.*

Keywords: Mini-pigs, Ureteroscopy, Experimental model.

1. Introduction

Currently, with the increasing research on urological drugs and implant materials, there is a growing demand for animal models [1, 2]. There is limited literature available on animal experimental models of pigs, specifically in regards to experimental models of ureteroscopy. The existing literature lacks detailed content and has limited reference ability, leaving minimal operational experience to learn from [3]. Furthermore, this animal model may result in mortality during experimentation, thus warranting the need for specific improvements to the model.

Miniature pigs have a urological structure similar to that of humans and are therefore often used as animal models for urological experiments. However, there is a lack of detailed descriptions of the specific urological anatomy of miniature pigs and the specific methods of ureteroscopy, and the existing literature is not sufficiently detailed and lacks useful operational experience [4]. In addition, this animal model may die after the ureteroscopic experiment due to improper operation, intraoperative infection, and other reasons, making it difficult to obtain the necessary postoperative data accurately. Therefore, based on the existing data, this study intends to improve the ureteroscopy experimental model of miniature pigs and provide detailed reference materials for the ureteroscopy animal model, which can also provide assistance for the development of materials and drugs related to ureteral animal experiments.

2. Materials and Methods

2.1 General Information

Seven healthy mini-pigs, with similar age, physique, and living environment, weighing between 25kg-30kg, were selected [5]. These pigs were fed a reasonable diet and kept in a clean and hygienic environment.

2.2 Inclusion and Exclusion Criteria

Female experimental mini-pigs were selected, weighing between 25-30kg, with agile movements and flexible responses to external stimuli such as sound and strong light. These pigs had normal eating, drinking, and sleeping habits, normal skin color, and no abnormal phenomena such as anorexia and irritability. The weight, living environment, and feeding conditions of each model were comparable, and their health status was monitored regularly [6].

2.3 Surgical Procedure

1) Anesthesia before surgery

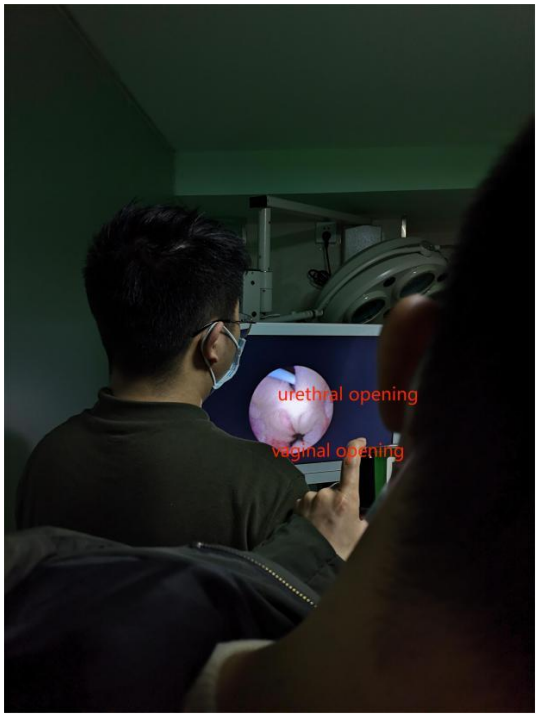
Intravenous general anesthesia was used. Propofol 20ml was injected into the ear vein for intravenous general anesthesia [7]. During anesthesia, 2-3 assistants were needed to properly fix the head, front and hind limbs of the experimental pig, taking care to avoid excessive stimulation of the animal to prevent the experimental animal from struggling excessively

and kicking or interfering with the anesthesia operation.

2) Successful anesthesia assessment

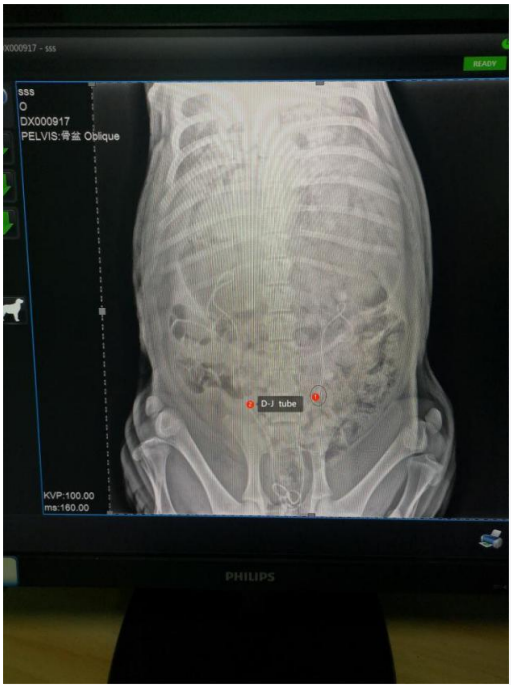
The limbs of the mini-pig should be limp, with no struggling and no corneal reflex. Attention should be paid to observing the animal's skin, lips for cyanosis, and the respiratory movement of its chest and abdomen to avoid excessive anesthesia that may lead to animal death.

Was difficult to expand the urethral opening with the hydraulic infusion pump, and it was found that a large amount of infusion fluid flowed out of the body from the perineum. Therefore, the assistant used his hand to pinch both labia to expand the urethral opening under the infusion fluid, and the ureteroscope was smoothly inserted into the urethra. The female pig's urethra is longer than that of human females, but it is relatively straight and wide. After entering the bladder, the ureteric folds were not visible as in the human bladder. The scope was withdrawn to a position near the neck of the bladder, where there were two ureteric openings at 5 o'clock and 7 o'clock, respectively. The openings were in the form of clefts, which could be expanded with hydraulic pressure. A zebra guide wire was then placed into the left ureter, and the ureteroscope was smoothly inserted into the left ureter along the guide wire. No obvious abnormalities were found during the examination, so a 5F double-J tube was placed in the bladder. The scope was then withdrawn and the zebra guide wire was removed. In a similar manner, after spending some time searching for the urethral opening upon re-entering the scope, the same method was used to expand the urethral opening by pinching both labia, and the right ureteric opening was successfully found, and a 5F double-J tube was inserted into the right ureter during the ureteroscopic examination. In this way, one case of ureteroscopic examination was completed.



(ureteroscopic image)

After following the aforementioned operating procedures of inserting the ureteroscope into the urogenital vestibule and having an assistant pinch the labia majora on both sides to maintain sufficient irrigation pressure, the urethral opening was located and the ureteroscope was smoothly inserted to find the opening of both ureters. After completing the left ureteroscopy and inserting a 5F double-J stent, the ureteroscope was withdrawn but the zebra guide wire was left in the bladder. With the guidance of the previously retained zebra guide wire and a super slippery guide wire, the urethral opening was quickly found again and the right ureteral orifice was smoothly entered. The zebra guide wire was removed and a super slippery guide wire was inserted into the right ureter. The ureteroscope was then reinserted and the right ureteroscopy was completed. Another 5F double-J stent was inserted through the guide wire, reaching up to the right kidney and down to the bladder. The ureteroscope was withdrawn, the guide wire was removed, and the surgery was completed.



(X-ray)

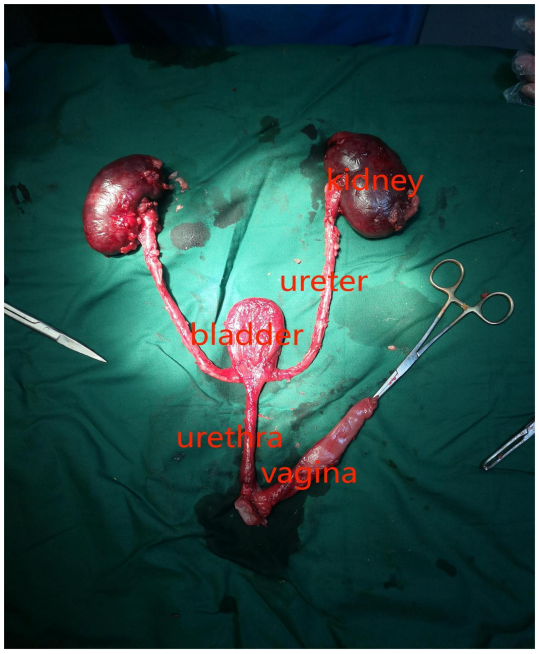
3. Results

Due to the anatomical characteristics of the male pig, ureteroscopy is more difficult, and female pigs were chosen for the animal model in this study. There are differences between the female pig's urinary reproductive system structure and that of humans: 1) The urethral opening is located in the vestibule of the vagina. The ureteroscope needs to enter the vestibule of the vagina first and fill it with water pressure. Multiple folds are visible inside, among which the urethra is located in the middle and top, and the vaginal opening is below the urethra. The remaining folds are blind ends and need to be carefully identified during the operation. 2) The characteristics of the ureteral opening are that the pig's ureteral opening is located near the inner opening of the urethra, and the ureteroscope needs to return to the inner opening of the urethra after entering the bladder. In addition, the end of the ureteral opening lacks a circular muscle and appears as a valve-like structure, which acts as an anti-reflux valve. Therefore, it is difficult to find the ureteral opening during the experiment. Our experience is to retreat the ureteroscope to near the inner opening of the urethra, and increase the flushing pressure to lift the valve-like structure and directly expose the ureteral opening. Our experience shows that the ureteral diameter of pigs weighing between 30-35 kg is sufficient for the successful passage of a 9.8 F ureteroscope, which can meet the needs of the experiment.

The surgery time for establishing the experimental model in the 7 miniature pigs varied greatly, with the first one taking the longest time, up to 81 minutes. The main reason was the lack of experience in operating this animal model, such as controlling water pressure, adjusting water flow rate, finding and identifying the urethral orifice and ureteral orifices, and the lack of experience in finding the urethral orifice and ureteral orifices when reinserting the ureteroscope after placing the stent in one ureter. The first miniature pig had an additional anesthetic during the operation and died after a long period of anesthesia. The surgical time for the remaining 6 miniature pigs gradually decreased, with the last two taking 21 minutes and 19 minutes respectively. After the experiment was completed, the animals were returned to their pigsty and their breathing was observed, and their lips and skin were checked for signs of cyanosis or poor peripheral perfusion. About 4-10 minutes later, all animals woke up smoothly, gradually regained normal activity in 5-8 minutes, and survived normally. Postoperative abdominal X-ray examination of the miniature pigs showed that the positions of the bilateral ureteral stents were good. Continued observation of their activity, eating, drinking, urination and defecation was necessary. Comparison of the modified experimental method showed that the experimental time was significantly shortened, the anesthesia time of the experimental animals was also reduced, and the time for the miniature pigs with shorter postoperative anesthesia to recover eating and activity was also correspondingly shorter.

On X-ray, the stent was observed in all cases and its complete removal was confirmed on necropsy after a few days. Homogeneous degradation due to erosion was observed along the entire stent surface, while maintaining a patent lumen. Throughout the process, the ureteral stents remained stable and exhibited lower maximum tensile strain and higher stiffness. The IVP assessment revealed that, at all time-points after stent insertion, the level of hydronephrosis did not exceed grade 2. Overall, the animals that received stents showed a lower average grade of hydronephrosis. Based on histopathological grading of nephropathy and ureteral pathology, stented kidneys and ureters demonstrated better pathological conditions, indicating improved biocompatibility. There were no significant differences observed in the stented kidney. As expected, histological analysis showed greater changes in the stented ureters compared to the non-stented ureters in each pig. Overall, no significant inflammatory or necrotic cells were found.

Six pigs underwent long-term placement of ureteral stents without adverse events. All 6 pigs had an unremarkable postoperative course and the ureteral stents were found to be appropriately positioned on fluoroscopic imaging and were removed without complications. Retrograde pyelography revealed no urinary extravasation in any of the ureters, and there were no gross ureteral defects noted. There was no evidence of significant urine ascites in the abdomen at the time of ureteral collection, and the average creatinine values did not increase. Microscopic examination of the ureters showed no evidence of transmural injury, but revealed urothelial damage, moderate to marked inflammation, muscular disruption, and granulation tissue. At low magnification, full-thickness injury to the tissue layers was observed, with degeneration, necrosis, and loss of urothelium, accompanied by adjacent granulation tissue, hemorrhage, and inflammatory infiltrate. At higher magnification, there was no evidence of degeneration, necrosis, or loss of urothelium. Within the lamina propria, there was the presence of granulation tissue, hemorrhage, fibrin, and edema with mixed inflammation, predominantly neutrophils.



(urinary system of mini-pigs')

4. Discussion

The anatomical structure of the urogenital tract in small pigs (females) is similar to that of humans, making it a useful model for ureteroscopy examination. However, there are unique differences in their anatomy that can make the operation more time-consuming and potentially harm the health of the experimental animals or interfere with the interpretation of experimental results, particularly for those lacking experience in establishing a ureteroscopy model [8]. To address this, an improved method for establishing a ureteroscopy experimental model in small pigs is proposed. This involves the assistant clamping the labia to reduce fluid loss and maintain perfusion pressure, which facilitates the quick identification of the urethral orifice. Additionally, a guide wire is left in the bladder when removing the ureteral stent on the opposite side, allowing for the rapid identification of the urethral orifice and efficient completion of the ureteroscopy examination on the other side under the guidance of dual guide wires. This significantly shortens the surgical operation time, reduces anesthesia time, and minimizes the dosage of anesthetic drugs required to enter the experimental animal's body, resulting in the conservation of anesthesia drugs, reduced harm to the experimental animal's health, and lower mortality rates. This method has potential for further application and promotion.

Ureteroscopy is a minimally invasive surgical procedure used to diagnose and treat conditions of the urinary tract, particularly the kidneys and ureters [9]. It involves the insertion of a flexible or rigid scope through the urethra and into the bladder, and then through the ureter and into the kidney. Ureteroscopy is commonly used to remove ureteral calculi or to perform biopsies of the urinary tract. Mini-pig models have become increasingly popular in biomedical research due to their anatomical and physiological similarities to humans [10]. Mini-pigs have a similar urinary tract to humans, including a similar ureter diameter, which makes them a useful model for ureteroscopy research. Improvement of the experimental model of ureteroscopy in mini-pigs would likely involve modifications to the surgical procedure or the mini-pig model itself in order to better replicate the human ureteroscopy experience. This could include improvements to the visualization of the urinary tract during the procedure, modifications to the equipment used during the procedure, or changes to the anesthesia and pain management protocols for the mini-pigs [11].

Mini-pigs have been used as an animal model for studying ureteroscopy due to their anatomical and physiological similarities to humans [12]. Their urinary tract is similar to that of humans in terms of the size of the ureters and the structure of the kidney. The use of mini-pigs in ureteroscopy research can help researchers develop and refine new surgical techniques, test new equipment, and evaluate the safety and efficacy of new drugs and procedures [13].

Some potential areas for improvement in the experimental model of ureteroscopy in mini-pigs could include: 1) Anesthesia and pain management: Ureteroscopy can be a painful procedure for animals, and pain management and anesthesia protocols can be improved to minimize pain and discomfort. 2) Visualization of the urinary tract: Improved visualization of the urinary tract during the procedure can improve the accuracy and safety of the procedure. This could involve the use of advanced imaging techniques such as fluoroscopy or ultrasound. 3) Equipment: Improvements in the equipment used during the procedure could help to make the procedure more efficient, accurate, and safe. For example, the use of improved endoscopes or lasers could improve the precision of the procedure and reduce the risk of complications. 4) Experimental design: Improvements to the experimental design could help to better replicate the human ureteroscopy experience in mini-pigs. This could include the use of a more standardized protocol for the procedure or the inclusion of more animals in the study to increase the statistical power of the results.

5. Conclusion

Overall, the use of mini-pigs as an animal model for studying ureteroscopy has the potential to provide valuable insights into the safety and efficacy of new surgical techniques and equipment. By improving the experimental model, researchers can continue to advance our understanding of this important medical procedure and improve outcomes for patients.

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