Research Paper

Ureteral Obstruction Swine Model through Laparoscopy and Single Port for Training on Laparoscopic Pyeloplasty

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Abstract

This study aims firstly to assess the most adequate surgical approach for the creation of an ureteropelvic juntion obstruction (UPJO) animal model, and secondly to validate this model for laparoscopic pyeloplasty training among urologists.

Thirty six Large White pigs (28.29±5.48 Kg) were used. The left ureteropelvic junction was occluded by means of an endoclip. According to the surgical approach for model creation, pigs were randomized into: laparoscopic conventional surgery (LAP) or single port surgery (LSP). Each group was further divided into transperitoneal (+T) or retroperitoneal (+R) approach. Time needed for access, surgical field preparation, wound closure, and total surgical times were registered. Social behavior, tenderness to the touch and wound inflammation were evaluated in the early postoperative period. After ten days, all animals underwent an Anderson-Hynes pyeloplasty carried out by 9 urologists, who subsequently assessed the model by means of a subjective validation questionnaire.

Total operative time was significantly greater in LSP+R (p=0.001). Tenderness to the touch was significantly increased in both retroperitoneal approaches, (p=0.0001). Surgeons rated the UPJO porcine model for training on laparoscopic pyeloplasty with high or very high scores, all above 4 on a 1-5 point Likert scale.

Our UPJO animal model is useful for laparoscopic pyeloplasty training. The model created by retroperitoneal single port approach presented the best score in the subjective evaluation, whereas, as a whole, transabdominal laparoscopic approach was preferred.

Key words: swine, training, laparoscopic pyeloplasty, single port surgery.

Introduction

Conventional surgery has been laid aside by minimally invasive surgery in many surgical procedures. Different minimally invasive approaches have been described in order to treat ureteropelvic junction obstruction (UPJO) with several advantages that include reduced postoperative pain [1], shorter conva-lescence and minimal disfigurement.

Among minimally invasive approaches, endourology is associated with lower morbidity when compared to laparoscopy. However, reported success rates vary around 15-20% lower than those for open pyeloplasty [2, 3], and it has also been associated with

a higher risk of perioperative hemorrhage [4]. Alternatively, laparoscopic pyeloplasty (LP) success rate matches that of open pyeloplasty [5]. Moreover, and unlike endourological procedures, the latter is not limited by high insertion, crossing vessels, large redundant pelvis and intrinsic obstruction.

Once the benefits of laparoscopic pyeloplasty have been established for UPJO treatment [6], and bearing in mind that it is technically demanding and time consuming, we consider mandatory to develop a validated training program with the aim of mastering the necessary procedural maneuvers. In order to improve endoscopic suturing for laparoscopic pyeloplasty different training protocols have been developed based on physical simulators, virtual simulators, animal models and cadavers, among others [7]. We consider that, in an advanced stage of training, and before applying it to human patients, the LP technique should be performed in highly realistic scenarios, superior to the offered possibilities of physical or virtual simulation, for instance on an animal model of ureteral obstruction.

Different methods have been described for the creation of UPJO animal models [8-10]. In this study we chose an easy to create and reproducible pelvic dilatation method, carried out by the most widely established minimally invasive approach (laparoscopy), and also by a more recent up-to-date "scarless" approach (single port surgery).

The primary endpoint of this study was to compare different surgical approaches in an attempt to minimize complications and access-related injuries when creating an acute ureteral obstruction in a porcine model for training purposes. Concurrently, experienced urologists assessed the experimental model in terms of utility for laparoscopic pyeloplasty training.

Materials and methods

This study protocol was conducted in accordance with the Guide for the Care and Use of Laboratory Animals and approved by the Institutional Ethical Committee for Animal Research. Every effort was made to minimize the number of animals used.

UPJO porcine model creation

Thirty-six Large White male pigs (28.29±5.48 Kg) were used. The ureteral obstruction model was developed by placing a Hem-o-lok ® (Teleflex Medical, North Carolina) in the proximal third of the left ureter. The subjects used in this study were randomly divided into groups, depending on the approach used to create the model: laparoscopic conventional surgery (LAP) or single port (LSP). Both groups were further divided in transperitoneal (+T) or retroperitoneal (+R) approaches.

All surgical procedures were conducted aseptically and under general anesthesia. Perioperative analgesia included an intravenous injection of 1 mg/Kg ketorolac and 1.5 mg/kg tramadol early in the surgery. Additionally, 4 mg/kg of carprofen were administered before the effects of anesthesia had passed and during five days after surgery. Postsurgical infection prophylaxis was carried out by injection of enrofloxacin (7 mg/Kg, IM) during five days postoperatively.

Animals were placed in right lateral recumbency. In the laparoscopic groups (LAP+R and LAP+T), the operating field was prepared as follows: the first trocar (10 mm, laparoscope port) was placed in the axillary midline with an open technique; for the transabdominal group, the whole muscular wall was dissected, while for the retroperitoneal group, the peritoneum was maintained intact. Then, the abdominal or retroperitoneal cavity was distended up to a 12 mmHg pressure. Later on, two more trocars were placed under visual control, 5 cm dorsal and 7-8 cm apart on both sides of the first trocar. A 5 mm trocar was placed on the right side and a 10 mm trocar on the left side.

In the single port groups, the abdominal or retroperitoneal cavity was accessed through a 2.5-3 cm incision at the axillary line at the level of the first lumbar vertebrae. The SILS™ Port was correctly inserted once the muscular plane was divided and peritoneum (retroperitoneal group) or the abdominal cavity (transperitoneal group) was reached.

The same surgical method for obstruction of the ureteropelvic junction was employed for all groups. The lower pole of the kidney was dissected, and a 2 cm ureteral segment was isolated and clipped with Hemo-o-lock®. After adequate hemostasis, the retroperitoneal or abdominal cavity space was deflated without drain and the wound was closed in layers.

As study parameters we registered serum creatinine and serum urea and operating times. Serum creatinine and serum urea levels were determined both preoperatively and 10 days after model creation. During model creation, the following procedural times were registered:

Access: from first skin incision to retroperitoneal or abdominal cavity distension.

Field preparation: from the introduction of the first instruments for the dissection of the ureter.

Wound closure: from CO_2 removal to the last skin suture.

Total surgical time: from first skin incision to last skin suture.

In order to assess the degree of abdominal wall injury, an evaluation regarding tenderness to touch

and local wound inflammation was performed during the early postoperative period (1-5 days after the surgery) by the animal housing veterinary in charge. All scores were registered on a 5-point scale, with higher scores related to a higher evidence of pain related behaviors.

Subjective validation of the training model

Ten days after surgery, the animals were randomly operated on by 9 urologists with a previous experience of 10 to 30 laparoscopic procedures, attending an advanced laparoscopic course organized at our center. All surgeons were blinded to this study. Each urologist randomly operated on four animals, each from one study group, and performed the standard Anderson-Hynes dismembered pyeloplasty with two running sutures. Subsequently, all attendants answered a subjective questionnaire for animal model assessment. The questionnaire consisted of four general questions about its similarity with human ureteropelvic junction obstructions, particularly regarding reproducibility, trocar location, approach and maneuvers developed during surgery. Three additional questions were included for each operated model, regarding fibrosis around the ureter, ureteropelvic junction bleeding when dissected, and ureter adhesions, comparing each case to human patients. Questions were scored on a 1-5 scale, with 1 meaning no similarity and 5 reflecting the highest similarity with humans.

Data were processed by the SPSS (Statistical Package for the Social Sciences v.15 Chicago). The results are shown as average ± standard deviation. Data failed Shapiro-Wilk Normality test, and consequently a Kruskal-Wallis test was performed to determine the significant differences between groups. A $p<0.05$ was considered statistically significant.

Results

No complications were found in any of the study groups. There were no intraoperative conversions to transabdominal or open surgery. No differences were identified between both techniques in terms of intraoperative or postoperative complications. No wound infection was present in any of the animals.

Urea and creatinine plasma levels rose above the physiological level 10 days after ureter obstruction (urea (mg/dL): 25.44 ± 8.23 *vs.* 32.62 ± 14.47, p=0.01 and creatinine (mg/dL): 1.91 ± 0.33 *vs.* 3.16 ± 1.01, p=0.001). Animals, however, were in good health condition and neither was found apathetic, inappetent nor showed any signs of pain requiring rescue analgesia.

Regarding abdominal wall injuries, inflammation was found to be slightly higher in the retroperitoneal single port group (LSP+R: 0.73 ± 0.75, LAP+T: 0.68 ± 0.67, LAP+R: 0.67 ± 0.62, LSP+T: 0.64 ± 0.71, p=0.882). On the other hand, tenderness to the touch was significantly greater in both retroperitoneal approaches, with the highest score found in the laparoscopic group (LSP+R: 0.78 ± 0.63 *vs.* LAP+R: 0.88 ± 0.56 *vs.* LSP+T: 0.68 ± 0.68 *vs.* LAP+T: 0.49 ± 0.60, p=0.0001).

Total operative time was significantly longer in the LSP+R group (48.78 ± 11.23 min, p=0.001), followed by LSP+T (32.37 ± 16.00 min) and laparoscopic groups: LAP+T (25.33 ± 4.50 min) and LAP+R (24.75 ± 8.84 min).

The most time-consuming procedural step was wound closure, except in the LSP+R group, in which the access and field preparation took longer than wound closure (Table 1). The time spent in creating access was similar for laparoscopic and LSP+T groups, and increased significantly for LSP+R group (p=0.014).

The time needed for incision closure was significantly decreased in the LAP+R group, compared to the LSP groups, but not when compared with the LAP+T group. The latter showed the shortest time for field preparation (p=0.001).

As for the ureteral obstruction training model, attendants assessed it with high scores (above 4 over 5) in all general aspects (reproducibility: 4.00 ± 0.80, port placement: 4.00 ± 0.87, approach: 4.14±0.85 and surgical maneuvers: 4.43 ± 0.70). Regarding particular aspects, the highest valued approaches in terms of fibrosis, adhesions, and bleeding were LAP+T and LSP+R (Table 2).

Table 1. Mean operative times.

	Access* (p=0.014)	Field preparation* (p=0.001)	Wound closure* (p=0.008)	Total time* (p=0.001)
LAP+T	8.98±2.75	3.78±1.03	9.82±2.02	25.33±4.50
LAP+R	8.41±5.34	4.77±1.50	8.23±2.48	24.75±8.84
LSP+T	8.65±4.72	6.55±2.76	11.74±3.09	32.67±6.16
LSP+R	13.77±2.39	17.76±10.26	11.61±1.82	48.78±11.23

(*) statistically significant differences found after group comparison.

Table 2. Surgeons' subjective scores on the animal model.

	Fibrosis * (p=0.004)	Adhesions* (p=0.005)	Bleeding
LAP+T	3.47±1,28	3.41±1.18	2.94±1.30
LAP+R	2.90±0.88	2.30±0.94	2.50±0.71
LSP+T	3.00±0.94	3.06±1.09	2.65±1.22
LSP+R	3.50±1.21	3.25±1.30	3.62±0.96

(*) statistically significant differences found after group comparison.

Discussion

Despite its greater technical difficulty and steep learning curve, laparoscopic pyeloplasty is often performed, and may eventually replace, open pyeloplasty and endourological techniques as the surgery of choice [6].

The main problem of LP is that it requires high skills in intracorporeal suturing. Although some methods have been described to avoid the need for or reduce the complexity of this procedural step (mechanical suture [11], laser welding or surgical adhesives [12]), the only effective method to reduce the LP learning curve is to use a robot [13]. However, its application is limited due to its high cost [14, 15].

In order to master intracorporeal suture and get the required skills and knowledge, the completion of a steep learning curve is necessary [5]. Currently, there is no universal model accepted for training in laparoscopic surgery. Available training programs usually resort to physical and virtual simulators, as well as experimental animal models. Simulators enable basic laparoscopic skills development, such as hand-eye coordination, suturing and knot-tying abilities; however, they are considered unrealistic, for they cannot simulate bleeding or show tissue fibrosis, adhesions, etc. This is why we agree with Stolzenburg et al [16], who consider that the use of experimental animals, respecting the three R's (Reduce, Refine and Replace), is essential for training and adequate skills acquisition on advanced laparoscopic techniques prior to its application on human patients

The benefits of using animals for advanced urological laparoscopy training have already been stated [17], especially for radical prostatectomy [18, 19], and pyeloplasty [1].

The main objective in this study was to assess different minimally invasive surgical approaches for the development of ureteropelvic junction obstruction animal models, and its subsequent application for Anderson-Hynes LP training.

Previously reported UPJO models were used exclusively for research in therapeutic and diagnostic methods. As far as we know, UPJO swine model has

not been used for training. Zhang *et al* [7] reported the use of a healthy porcine animal model for laparoscopic pyeloplasty training by using a small intestine segment to simulate the enlarged renal pelvis. In our opinion, this model is perfect for enhancing intracorporeal suturing skills, whereas it is not as suitable as ours for dissection maneuvers, as it lacks fibrosis, adhesions, etc.

According to the consulted literature, the ureteral obstruction can be performed, among other methods, by ligature [10, 20], suture-ligature [12], or electrical injury [9]. These methods require an average 6 weeks for the development of the pathology, increasing overall costs of the model creation. Total obstruction of the ureter carried out with the application of an endoclip fully develops in 10 days, reducing the time lapse between model creation and surgical procedure, and consequently indirectly decreasing overall costs.

Altogether, time spent to create the obstruction is also increased when intracorporeal suture is used. With this method, Desai *et al* [20] reported a total operative time of approximately 60 minutes, which is higher when compared to the 25 minutes needed in our laparoscopic transabdominal group. Furthermore, Chiu *et al* [12] reported an average of 16 minutes for the placement only of the suture-ligature. Although in our study the time spent for clip placement was not recorded, it was under five minutes in all cases.

Until recently, laparoscopy and endoscopy were the only standard MIS approaches. Over the last years, new approaches have emerged, such as single port surgery and NOTES (Natural Orifice Transluminal Endoscopic Surgery). These approaches have been developed in an attempt to reduce incision related complications, including hernia [21], hemorrhage [22], pain, and scaring. Although the only published reports rely on short term results, it seems that they provide comparable therapeutic outcomes [23], lower morbidity, better aesthetic results, and reduced postoperative pain when compared with conventional laparoscopic surgery [24].

In order to assess which MIS approach is best, parameters registered in our study were all related to patient benefits: postoperative pain, intraoperative and postoperative complications, and total operation time. No complications were found in any of the groups.

Retroperitoneal route has been proved to offer anesthetic advantages requiring a less marked Trendelenburg position in LRP [25], faster access to the ureteropelvic junction [26] and easier identification of the aberrant vessels [27].

On the other hand, problems derived from the

retroperitoneal access are the same as the advantages of the transperitoneal approach: better operating field with improved organ vision and wider working space, which usually leads to improved operating times. Considering the latter, among retroperitoneal groups, LSP+R group had increased total surgical time as it took longer to establish access and carry out field preparation, compared with the rest of the groups. We believe this difference in access times derives from the extra care taken not to open peritoneum. Furthermore, single incision group required more time in surgical field preparation, especially when positioned in retroperitoneum, due to movement limitation, loss of instrument triangulation and the parallel arrangement of instruments [24].

In 2004 Cathelineau *et al* [25], reported no differences in postoperative pain between the transperitoneal and the retroperitoneal LRP. In our study, tenderness to touch was less evident in transabdominal approaches in both laparoscopic and single port approaches. According to Desai *et al* [29], this fact could be caused by the flank neuralgia syndrome due to injury or entrapment of the subcostal nerve. On the other hand, when assessing retroperitoneal access, the single port group showed fewer signs of tenderness to touch than the laparoscopy group. The opposite situation occurred when the transperitoneal access was assessed.

For training model validation, urologists assessed the presence of adhesions as significantly lower in LAP+R group, compared to the other groups. Similarly, in LAP+R, fibrosis obtained a significantly lower score compared to the LSP groups. More specifically, fibrosis and bleeding of the LSP+R group was higher, showing that this approach generates a more intense reaction than through laparoscopy. However, there were more ureteral adhesions in the transabdominal group.

Overall, bleeding was the lowest valued parameter for all groups, which was expected as it is easier to achieve correct hemostasis in a porcine model than in a human patient, due to different cell biology, blood supply, and tissue textures [30].

One of the limitations of our model, compared to the aforementioned UPJO models created by partial ureteral obstruction, is the lack of fulfillment of clinical considerations, as the pathophysiology differs greatly from such encountered in UPJO under natural conditions in human patients. We gave priority to an easy to create and fast to develop UPJO model, and tried to achieve a model that fulfilled surgical anatomic criteria of the condition, aiming at its validation as training tool for the practice of laparoscopic Anderson-Hynes pyeloplasty.

In conclusion, we consider the use of experimental animal models essential for advanced laparoscopic surgery training. However, we emphasize the need to use these animals under strict control, and only after basic laparoscopic skills have been mastered with physical or virtual simulators, or cadavers. Above all, there should be a careful balance between acquisition of knowledge and new skills, and the potentially unnecessary harm to animals.

Creating an UPJO animal model by application of an endoclip to the ureter is easy, fast and reproducible, independently of the surgeon's inherent laparoscopic skills. The LSP+R constituted the highest scored approach in terms of anatomical similarity with human patients. However, from our point of view, the former is not suitable for model creation, as it causes more pain and inflammation postoperatively, and requires longer operating times than the other minimally invasive alternatives. All variables considered, the transabdominal laparoscopic approach is the best option for UPJO model development. It requires short operating times, causes less postoperative pain and achieves a good subjective assessment by urologists.

Acknowledgements

Competing Interests

None of the authors have any competing interests that might conflict with this study.

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