Minilaparoscopy and Sentinel Lymph Node in Uterine Cancer

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ABSTRACT

Background: The sentinel lymph node (SLN) concept might minimize surgical aggressiveness in gynecological oncology, namely in cervical and endometrial malignancies. Therefore, we assessed the feasibility of SLN identification, dissection, and harvesting by using minilaparoscopic surgical instruments in an animal model. We compared the minilaparoscopic approach, which is known to bring important advantages, with the use of conventional laparoscopic instruments.

Methods: Two groups of 7 female pigs were enrolled in this experiment that was performed by the same surgical team. In group A, all animals were approached by a similar minilaparoscopic surgical instrumentation, namely a 5-mm 30° endoscope (supraumbilical port) and 3 ancillary 3.5-mm trocars. In group B, a 5-mm conventional laparoscopic instrument set was used. The patent blue (4.0 mL) was injected on the paracervical region. The time for SLN coloring, identification, localization, dissection, and excision, as well as complications were recorded. The sealing of the lymphatic vessels was observed in the 2 groups. During this experiment, and for the both groups, the Trendelenburg position was kept the same, as well as the carbon dioxide–pneumoperitoneum pressure. Finally, a laparotomy was then performed to evaluate whether any stained SLN still remained.

Results: All endoscopic procedures were performed without major complications. SLN were identified and excised in all animals in both groups. The SLN localization varied between animals from external iliac to preaortic regions. The surgical times, from skin incision to SLN removal, was 28.4 ± 5.6 minutes for minilaparoscopy and 25.3 ± 6.8 minutes for conventional laparoscopy ($P = .36$). In group B, 1 stained SLN remained and was only detected by laparotomy.

Conclusions: We confirmed the feasibility of the minilaparoscopic surgical approach for identification, dissection, and excision of SLN, as well as for sealing the lymphatic vessels that supply the nodes. This procedure might be considered a potentially better alternative to reduce morbidity during staging procedures for gynecological malignancies.

Key Words: Gynecology, Instrumentation, Malignancy, Minilaparoscopy, Sentinel lymph node, Surgery

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INTRODUCTION

Gynecologists pioneered the laparoscopic approach to abdominal surgical procedures. By the late 2000s, with improvements in training and innovative adaptations of instruments and techniques, minimally invasive approaches for gynecologic malignancies started to be used more often.[1]

Cancer of the cervix is the second most common malignancy in women worldwide.[2] In surgically treated patients with early cervical cancer, lymph node metastasis is the most important risk factor for recurrence and death.[3–5] On the other hand, in developed countries, endometrial cancer is the most common gynecologic malignancy.[2] Evaluation of lymphatic spread in cervical and endometrial cancers staging remains an ongoing area of controversy in the field of gynecologic oncology. Traditionally, to obtain histological diagnosis of nodal spread, the entire lymphatic basin draining a tumor is removed (resulting in prolonged operation duration, increased blood loss, infection, nerve injury, lymphocyst formation, vascular injury, venous thromboembolism, and lower extremity lymphedema).[6,7]

A sentinel lymph node (SLN) is any lymph node that receives direct drainage from the tumor site and is identified by a procedure called lymphatic mapping. SLN biopsy techniques have been developed to decrease complications related to entire lymphadenectomy, to improve detection of micrometastatic disease, and to fine-tune our lymphadenectomy anatomic templates. SLN mapping has been studied in cervical and endometrial cancer with encouraging data.[8–12] The best surgical approach to identify and excise the SLN (laparotomy, laparoscopy, and robotics) is still under evaluation.[13,14]

Currently, efforts of laparoscopic surgeons are aimed at further reducing the morbidity associated with minimally invasive technology, while maintaining the same high standard of surgical results. With a recent focus on minimizing the visibility of scars, minilaparoscopy has reemerged as an attractive option for surgeons because it limits tissue trauma and offers improved cosmetics.

The combination of the SLN technique and minilaparoscopy could be an alternative to achieve the goal of a less aggressive surgical procedure. The former is the least invasive method to assess lymph nodes by histologic examination and the latter seems to be one of the least invasive surgical approaches. To add the advantage of minilaparoscopic approach to the benefit of the SLN concept on an oncologic staging system, we evaluated the feasibility of SLN excision by minilaparoscopy in a porcine model, and we compared it with the conventional laparoscopic approach.

MATERIALS AND METHODS

The aim of the study was to test, using an in vivo porcine model, the feasibility of minilaparoscopic approach for SLN identification, dissection, and excision using the new 3.5-mm rotating bipolar coagulator. We did the same experiments in a second control group with 5-mm conventional laparoscopic instruments. Animal experiments were performed following EU Directive 2010/63/EU and the Portuguese law for animal welfare (*Diário da República*, Portaria 1005/92).

Animal Model

To accomplish the aim, 18 female pigs (*Sus scrofus domesticus*) weighing between 35 and 45 kg were submitted for the surgical procedure. The first 4 animals, used to establish anatomical landmarks and technical steps, were not included in the following protocol. Two animal groups were formed with 7 animals each. Group A was submitted for minilaparoscopy and group B for conventional laparoscopy. Animals were randomly assigned to groups and the animals' mean weight was 38 ± 2.1 kg in group A and 38 ± 3.2 kg in group B. All the pigs were 12 weeks of age.

Pig Preparation

All procedures were performed with the animals under general anesthesia with endotracheal intubation and mechanical ventilation. The pigs had no access to food (8 hour) nor water (4 hour) before the surgical procedure. Animals were premedicated with a combination of azaperone (4 mg/kg, intramuscularly [IM]), midazolam (1 mg/kg, IM), and atropine (0.05 mg/kg, IM). Anesthesia was induced with propofol (6 mg/kg, intravenously) and maintained with continuous propofol infusion (20 mg/kg/h, intravenously) and buprenorphine (0.05 mg/kg, IM).

Surgical Procedures

The animals were placed in exactly the same Trendelenburg position (25°) and immobilized. In group A, the pneumoperitoneum (14 mm Hg) was created using a Veress needle at a supraumbilical position, where an optical trocar (30160GC; Karl Storz 6-mm trocar set; Karl Storz, Tuttlingen, Germany) was introduced and a 5-mm 30° endoscope (26046BA; HOPKINS II forward oblique telescope; Karl Storz) was used to have a general view of the abdominal cavity. After observing the pelvis, under direct visualization, 3 3-mm ancillary trocars (30114GZL; Karl Storz minilaparoscopy trocar set) were inserted, 1 suprapubically and 2 laterally to the epigastric arteries, in the left and right lower abdominal quadrants, respectively. The bladder was fixed to the anterior abdominal wall with a *TLIFT* (VECTEC, Vichy, France) to get a better exposure of the surgical field. Internal iliac vessels were visualized followed by the identification of external iliac vessels, aorta, and vena cava. Patent-V blue (4 mL) was injected in the paracervical region (Spinocan 26G 120 mm; Braun, Melsungen, Germany). A few minutes after blue injection on the paracervical region, the lymphatic mapping was observed, showing the colored lymphatic channels toward the lymph nodes that retained the blue dye. In this experience, 36-cm-long minilaparoscopic instruments (Karl Storz Endoskope minilaparoscopy instruments set) were used, choosing among graspers, cold scissors, suction/irrigation, and the recent 3.5-mm bipolar coagulator (Karl Storz Robi).

After opening the retroperitoneum, all blue-stained lymph nodes were classified as sentinel and were finely dissected and excised separately with minilaparoscopic instruments. Any small bleeding was immediately controlled with the bipolar instrument that was used also for sealing the lymphatic vessels.

The procedure time, defined as the interval between the start of skin incisions to SLN removal, was recorded as well as difficulties and complications at each step of the procedure. The intraoperative complications were defined as bowel, bladder, ureteral, or vascular injuries, and an estimated blood loss $>$ 200 mL. Estimated blood loss was estimated from the contents of suction devices.

After SLN extraction, bilateral dissection was performed to achieve visualization of the aorta and the vena cava and, subsequent completion of pelvic and para-aortic lymphadenectomy was carried out. Finally, a laparotomy was then performed to evaluate whether there was any remaining SLN. After the procedure, the pigs were euthanized by anesthesia overdose.

In group B, exactly the same procedure, by the same surgical team, was performed but with 5-mm conventional laparoscopic instruments. To avoid possible bias comparing the groups, all the experiments were performed by the same surgical team.

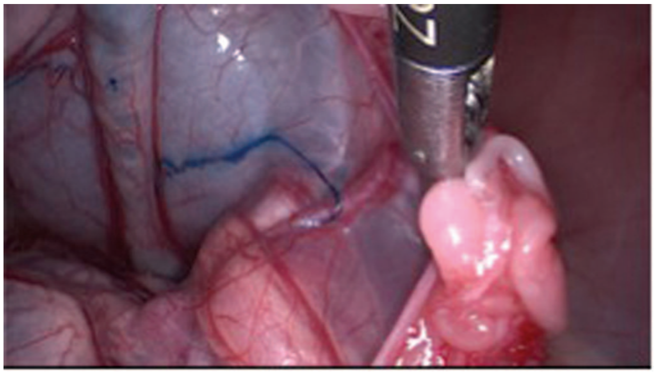

Figure 1. Lymphatic afferent vessels colored by blue dye after cervical injection.

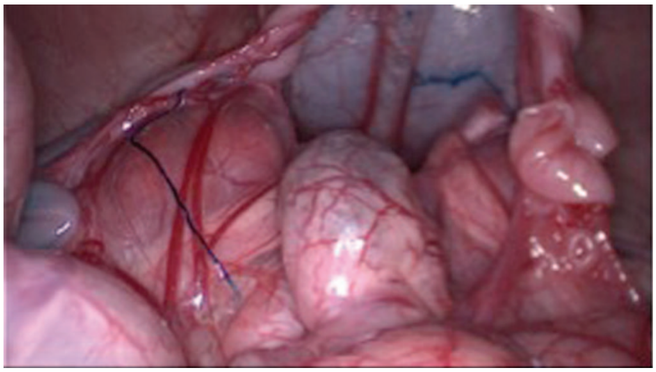

Figure 2. Lymphatic afferent vessels colored by blue dye to the sentinel lymph node.

Data Recording

All surgical endoscopic procedures were recorded on an advanced image and data archiving (AIDA) device from Karl Storz. Vital and physiological parameters (heart rate, arterial pressure, and respiratory distress) were monitored by the research team.

Histologic Analysis

The lymph nodes were analyzed without freezing. Lymph nodes were fixed in neutral buffered formaldehyde for 24 to 72 hours, then cut into 0.1-cm-thick slices, and embedded in a paraffin block per node. Multiple sections were prepared from each block. A set of 3 4-μm-thick sections was cut every 250 μm. Sections were stained with hematoxylin and eosin.

Statistical Analysis

All quantitative data are presented as mean $\pm$ SD. Statistical analysis was performed using the statistical software SigmaStat (version 3.5; Systat Software Inc, San Jose, California).

Independent samples Student *t* test analysis was used to compare surgical times, and statistical significance was set at $P < .05$. We also present Cohen *d* measure of effect size, whereby 0.2 equates to a small effect, 0.5 equates to a medium effect, and effects > 0.8 equate to large effects.[15]

RESULTS

Following the blue dye injection on the paracervical region, the blue lymphatic channels were identified **(Figures 1 and 2)** as well as the ending blue lymph node, which was considered the SLN. The average time for coloring of the SLNs was 7.9 ± 1.1 minutes in group A and 7.3 ± 1.1 minutes in group B [$t(12) = 0.98$; $P = .35$, $d = 0.524$ – medium effect size]. The retroperitoneum was accessed in the standard fashion with care to avoid bleeding from vessels and capillaries, which might stain the retroperitoneum, resulting in greater difficulty in following the blue lymphatic channels. Identification, dissection, and excision of SLNs were performed with success in all pigs. The overall results of our study are summarized in **Table 1.** The average times to perform the experiments were 28.4 ± 5.6 minutes in group A and 25.3 ± 6.8 minutes in group B [$t(12) = 0.94$; $P = .36$, $d = 0.507$ – medium effect size]. From every animal, at least one colored lymph node was excised; in some cases, 2 lymph nodes were. Concerning the SLN locations, most of the SLNs were found in the right iliac and left iliac vessels regions, 3 on the promontory region, 1 on the right obturator, and 1 on the preaortic region. Lymphatic vessels were sealed with the rotating bipolar instruments. According to our feedback, the minilaparoscopic bipolar dissector offered better small vessel hemostasis and a more efficient sealing of the afferent lymphatics **(Figure 3).** The colored lymph nodes were sent to histology

Table 1.
Individual Data After Patent Blue Injection and SLN Detection

Group	SLN			Complications	Operative Time, min
	Coloring Time, min	***n***	Location		
A: minilaparoscopy					
1	8	1	Right iliac vessels		35
2	8	1	Right obturator		36
3	6	2	1 promontory; 1 right iliac vessels	Bleeding 30 mL	31
4	9	1	Left iliac vessels		27
5	9	2	Left iliac vessels		22
6	8	1	Preaortic		25
7	7	1	Right iliac vessels		23
Mean ± SD	7.86 ± 1.07				28.43 ± 5.65
B: conventional laparoscopy					
1	7	1	Left iliac vessels		38
2	6	1	Left iliac vessels		16
3	8	1	Promontory		23
4	8	1	Right iliac vessels		26
5	6	1	Left iliac vessels		22
6	7	2	Right iliac vessels and left iliac vessels		24
7	9	1	Promontory		28
Mean ± SD	7.29 ± 1.11				25.29 ± 6.75
P	.35				.36
Cohen *d*	0.524				0.507

Abbreviation: SLN, sentinel lymph node.

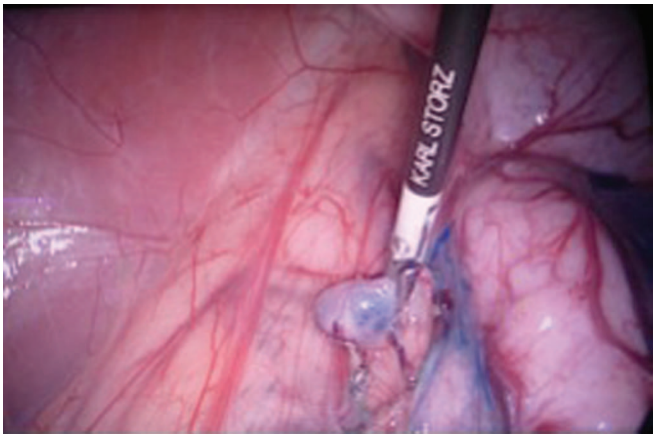

Figure 3. Minilaparoscopic sentinel lymph node identification and dissection with 3.5-mm Robi Kelly forceps.

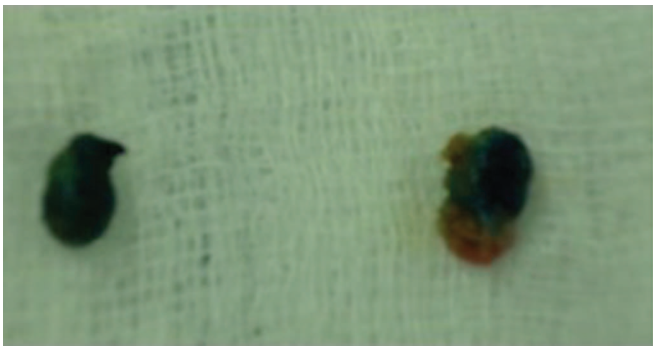

Figure 4. Lymph node colored in blue.

(Figures 4, 5, and 6). No major complications were observed in our series. Neither urinary nor digestive tract injuries were reported. There was 1 case of intraoperative bleeding (30 mL), which was controlled by minilaparoscopic instruments. Minilaparoscopic port sites required no suture closure. After the experiments, all animals were submitted to laparotomy. In the group B, there was 1 SLN that was only detected after laparotomy.

DISCUSSION

SLN techniques are now part of the standard treatment for breast cancer,[16] melanoma,[17] and selected cases of vulvar cancer.[18] The application of the SLN concept for malignancies of intra-abdominal organs is still under evaluation and testing. SLN biopsy has been one of the most important innovations in surgical oncology in recent years; it is being reported as a less invasive procedure that brings more information to clinicians.[9,10]

In SLN biopsy–negative patients, regional lymphadenectomy may no longer be a requirement, promising

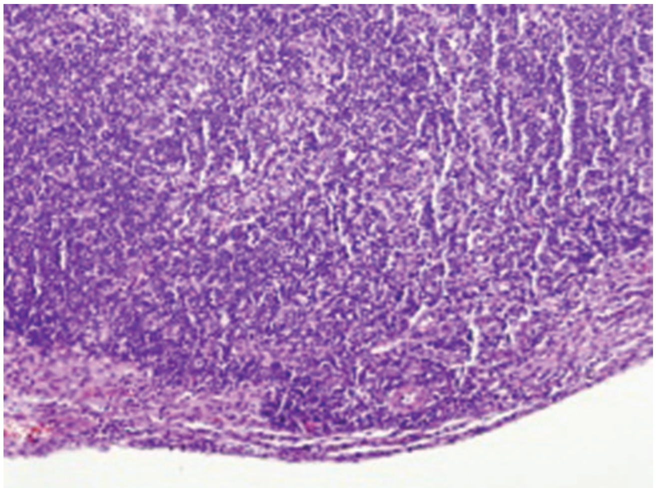

Figure 5. Excised sentinel lymph node. (Hematoxylin and eosin 4×).

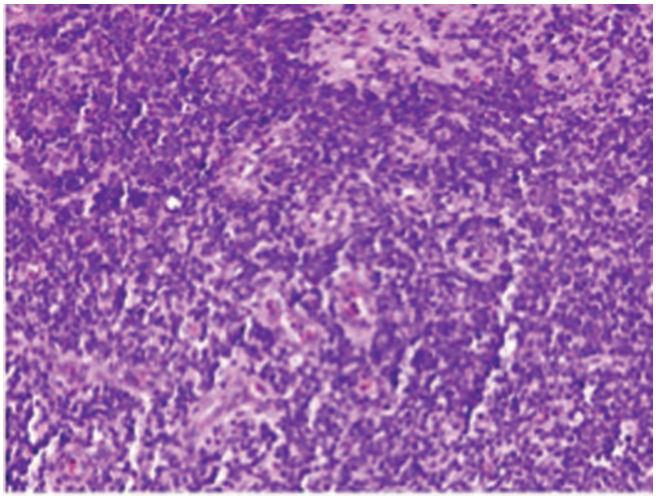

Figure 6. Excised sentinel lymph node. (Hematoxylin and eosin 20×).

fewer potential complications such as lymphedema, lymphocysts, nerve injury, vascular injury, and venous thromboembolism. In uterine cancers, SLN biopsy holds the hope of more accurate identification of uterine drainage and staging of the primary tumor, as well as, potential applications in fertility-sparing surgical procedures.[19]

The SLN detection rate is significantly higher through laparoscopy than through laparotomy after vital dye pericervical injection.[13] In cervical cancer, lymphatic mapping can be conducted by laparotomic or laparoscopic approaches. It would appear perfectly logical to perform lymphatic mapping laparoscopically. The ad-

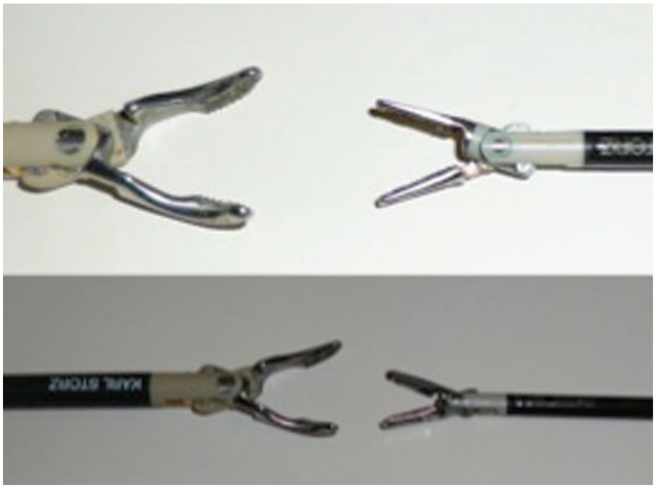

Figure 7. The 5-mm rotating bipolar versus minilaparoscopic Robi Kelly.

vantages are several and obvious: first, the laparoscopic surgical approach allows a more delicate and bloodless dissection of the retroperitoneum; second, laparoscopy permits magnification of the image, which facilitates visualization of blue lymphatic vessels; and third, if positive nodes are identified, the surgeon has the opportunity to end the procedure, thus avoiding radical hysterectomy, and offer to patients chemoradiation with minimal delay and reduced morbidity compared with laparotomy.

Minilaparoscopy re-emerged has an even better approach involving the use of miniaturized scopes and instruments to further reduce perioperative morbidity and enhance cosmetic healing.

Most surgeons have been hesitant to adopt minilaparoscopy into their practice expressing concerns regarding the instruments (not functional or not strong enough). Furthermore, some have complained that 3-mm instruments do not offer the same array of end-effector options or functionality of the 5-mm instruments. Recently, minilaparoscopic surgical techniques have benefited from additional product development with a focus on improving instrument strength and optics. The transition from 10- to 5-mm ports was a change from big to small, whereas the transition from 5 to 3 mm is visible to invisible.[20]

During these experiments, the research team found those thinner instruments to be very functional with no increase in complexity. The new minilaparoscopic rotating bipolar instrument **(Figure 7)** greatly facilitates a bloodless, precise tissue dissection, shortens the operation time, prevents unnecessary application of intraperitoneal foreign bodies, reduces the costs, and brings more convenience to the surgeon.

Another advantage of minilaparoscopy is the possibility of performing it under local anesthesia, generally with sedation, thus avoiding general anesthesia complications.[21] It may be easier to schedule and reduce the costs of SLN excision. It decreases the extent of intraoperative injury, avoids incisional herniation, and reduces postoperative pain.

In addition, the use of small-diameter laparoscopes and instruments is feasible with low carbon dioxide pressures,[22] thereby reducing possible complications related to pneumoperitoneum.

This is the first study that compares minilaparoscopic versus conventional laparoscopic approaches for this type of procedure. Further studies with larger samples, lower carbon dioxide pressures, and local anesthesia should be done. Also, human studies should be performed.

The minilaparoscopic approach to SLN is a promising concept in the minimally invasive surgical domain.

CONCLUSIONS

Minilaparoscopic approach to SLN identification, dissection, and excision is a feasible and reproducible procedure. Our comparative study revealed no statistically significant time difference between the minilaparoscopic and conventional laparoscopic procedures. With the smaller tools, a gentle and fine dissection of the anatomical planes, lymphatic nodes, and vessels was observed. Additionally, better sealing of lymphatic afferent vessels that supply the nodes was obtained.

This procedure can be considered a potentially better alternative to reduce morbidity during staging procedures for gynecologic malignancies.

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