

Does laparoscopic ovariectomy in dogs prevent the development of uterine pathologies at a later age?

Verhindert laparoscopische ovariëctomie bij honden de ontwikkeling van uteruspathologieën op oudere leeftijd?

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ABSTRACT

Ovariectomy and laparoscopic ovariectomy (lap OVE) are the routine spaying procedures in many countries. With these procedures, the uterus remains in situ and later in life, a uterine pathology such as cystic endometrial hyperplasia, pyometra or uterine neoplasia, can potentially develop. The patient files of 308 clinically healthy dogs that underwent elective lap OVE, were retrospectively searched during a study period of twelve years. For 173 dogs (56%), the owners could be contacted for a telephone survey. The median age at the time of lap OVE was 1.2 years (range: 0.4-12.3 years) and median body weight was 17.0 kg (range: 2.0-65.0 kg). At a median follow-up period of 4.5 years (range: 0.2-12.3 years), in none of the dogs, any clinical signs developed related to a uterine pathology. In 14/173 dogs (median age 8.0 years (range: 2.1-11.5 years); median body weight 24.4 kg (range: 2.0-65.0 kg)), early-stage uterine changes (uterine cysts, cystic endometrial hyperplasia, and/or uterine luminal collections) were visible at the time of lap OVE. Two of these fourteen dogs underwent an abdominal ultrasound, at respectively 1.3 and 3.5 years after lap OVE, that identified regression of previous pathologies to a normal uterus. In none of the remaining twelve dogs, any sign of a uterine pathology developed at a median follow-up of 3.9 years (range: 1.1-11.1 years). In this study, it was found that advanced age and even the presence of early-stage hormonally dependent uterine changes should not be considered contraindications to perform lap OVE in clinically healthy dogs.

SAMENVATTING

Ovariëctomie en laparoscopische ovariëctomie (lap OVE) zijn de standaard sterilisatietechnieken in verschillende landen. Bij deze techniek blijft de baarmoeder in situ en kan zich in de toekomst potentieel een pathologie ontwikkelen, zoals cisteuze endometrium hyperplasie, pyometra, of uteriene neoplasie. De patiëntendossiers van 308 klinisch gezonde honden die lap OVE ondergingen, werden retrospectief onderzocht tijdens een studieperiode van twaalf jaar. Van 173 honden (56%) konden de eigenaars bereikt worden voor een telefonische enquête. De mediane leeftijd voor deze honden op het moment van lap OVE was 1,2 jaar (bereik: 0,4-12,3 jaar) en het mediane lichaamsgewicht was 17,0 kg (bereik: 2,0-65,0 kg). De mediane opvolgperiode was 4,5 jaar (bereik: 0,2-12,3 jaar) en bij geen enkele hond ontwikkelden zich klinische tekenen gerelateerd aan een uteriene pathologie. Bij 14/173 honden (mediane leeftijd 8,0 jaar (bereik: 2,1-11,5 jaar); mediane lichaamsgewicht 24,4 kg (bereik: 2,0-65,0 kg)) werden tijdens de lap OVE uteriene pathologieën in een vroeg stadium (uteriene cysten, cisteuze endometrium hyperplasie, en/of uteriene lumenale ophopingen) opgemerkt. Twee van deze veertien honden ondergingen een echografisch onderzoek, respectievelijk 1,3 en 3,5 jaar na lap OVE, waarbij regressie tot een normale baarmoeder werd vastgesteld. Bij geen van de resterende twaalf honden ontwikkelden zich tekenen van een uteruspathologie bij een mediane opvolgperiode van 3,9 jaar (bereik: 1,1-11,1 jaar). In deze studie werd vastgesteld dat gevorderde leeftijd en zelfs de aanwezigheid van hormonaal afhankelijke uteriene pathologieën in een vroeg stadium geen tegenindicatie zijn om lap OVE uit te voeren bij klinisch gezonde honden.

INTRODUCTION

Elective spaying of female dogs is routinely performed by surgical ovariectomy (OVE) (Van Goethem et al., 2006). Ovariectomy has some advantages when compared to ovariohysterectomy (OVH), including a shorter incision size, less tissue trauma, decreased incidence of hemorrhage, and a shorter surgical duration (Van Goethem et al., 2006). Ovariectomy can easily be performed by laparoscopic technique (lap OVE), offering even more advantages to the dog as well as to the surgeon, including decreased postoperative pain, decreased hospitalization time, decreased recovery time, decreased amount of intraabdominal adhesions, and increased postoperative mobility (Shariati et al., 2014; Binder et al., 2018).

Despite evidence in the literature that ovariectomy is preferable over ovariohysterectomy (DeTora and McCarthy, 2011), ovariohysterectomy still remains the spaying technique of choice for many veterinary surgeons. Their motivation is the concern that future uterine pathologies might develop after OVE. This is based on the high incidence of genital tract pathologies at adult age in female intact dogs (Concannon et al., 1991; Schaefers-Okkens and Kooistra, 1997; Egenvall, 2001).

Uterine pathologies most commonly encountered in intact dogs are cystic endometrial hyperplasia (CEH), pseudo-placentational endometrial hyperplasia, pyometra, endometrial polyps, adenomyosis, serosal inclusion cysts, disorders of sexual development, and uterine neoplasia (Schlafer, 2012). Most of these occur in older dogs (8-10 years) and are promoted by cyclic hormonal stimulation (Schaefers-Okkens and Kooistra, 1997). Uterine serosal inclusion cysts are solitary or multiple thin-walled structures found on the serosal surface of the uterus in multiparous bitches (Sievert et al., 2020). Cystic endometrial hyperplasia is characterized by an irregular thickening of the uterine wall making the uterus more susceptible for the development of pyometra (Schlafer, 2008). Pyometra occurs in up to 24% of intact female dogs with early-stage clinical signs of lethargy, anorexia, and vaginal discharge (Egenvall, 2001; Hagman, 2004). Benign uterine tumors, mostly consisting of leiomyoma, are uncommon with a prevalence of 0.03%, while malignant tumors, such as leiomyosarcoma and endometrial adenocarcinoma, are rare with a prevalence of 0.003% (Brodey, 1967; Hedlund, 2007). Uterine tumors generally have a slow clinical progression resulting in only vague abdominal signs until pyometra occurs, the tumor creates an abdominal mass effect, or the tumor metastasizes (Tsioli et al., 2011).

In this retrospective study, owners of clinically healthy dogs that underwent elective lap OVE were contacted with regard to the potential development of any uterine pathology at any time after the procedure. The hypothesis was that no uterine pathology would occur after lap OVE. For dogs that already had early-stage hormonally-induced uterine changes at the time

of lap OVE, it was hypothesized that this would regress and the uterus would return to normal.

MATERIALS AND METHODS

Study population

The medical records of dogs that underwent elective lap OVE between January 2009 and February 2021 in the Small Animal Teaching Hospital, Faculty of Veterinary Medicine, Ghent University were searched. Dogs with a disorder of sexual development (DSD) and/or pre-existing urinary incontinence (UI) were excluded.

Breed, age, bodyweight, and body condition score (BCS) information was gathered from the patient file. Descriptive statistics were used to describe the data. Based on their age at surgery, dogs were categorized into three groups, pubertal (<1.5 years), adult (1.5-6 years), and older (>6 years).

Intraoperative findings

The surgical reports were checked for the intraoperative presence of uterine changes. In these reports, uterine cysts were defined as solitary or multiple cystic structures originating from the outer wall of the cranial uterine horn. Cysts smaller than 1 cm in diameter were considered early-stage. Uterine CEH was defined as the presence of an irregular or thickened uterine wall. Evaluation of the size of the uterine wall was done taking into account the estral stage of the dog. Uterine luminal collections, a precursor for pyometra, were defined as the presence of undulating luminal content visible during manipulation of the uterine horns. Minor (<1 cm) dilation of the complete uterine horn was considered early-stage.

Owner questionnaire

At the time of the study, owners were contacted for a telephone survey (two attempts at direct contact) and were asked to answer a standardized questionnaire, focusing on the potential development of uterine pathologies. Dogs were considered to have a uterine pathology when this was diagnosed by a veterinarian based on clinical signs, bloodwork, medical imaging, or autopsy. Also when the owner noticed any of the typical clinical signs associated with uterine pathologies, including lethargy, polyuria/polydipsia, and/or vulvar discharge, the dogs were categorized as having a uterine pathology.

RESULTS

Study population

During the past twelve years (from January 2009

Table 1. Dogs divided by age category.

	Pubertal (<1.5 years)	Adult (1.5 - 6.0 years)	Older (>6 years)
Number of dogs	95	55	23
Age (in years)*	0.8 (0.4 - 1.46)	3.2 (1.5 - 5.9)	8.8 (6.03 - 12.3)
Body weight (in kg)*	16.5 (2.0 - 45.5)	16.2 (2.0 - 65.0)	24.0 (5.0 - 54.0)

*Age and body weight depicted as median followed by range.

till February 2021), elective lap OVE was performed in 308 dogs. Twenty-two dogs were excluded because of the presence of possible confounding pathologies, including 16 dogs with UI and six dogs with a DSD. For 113 dogs, no follow-up information was available (59 owners did not respond after two attempts at direct contact, 19 telephone numbers were no longer in use, 17 patient files did not contain a phone number, 6 numbers appeared to be wrong, 5 telephone numbers were international paying, 5 owners did not want to collaborate, 1 owner did not remember any relevant information, and 1 owner had passed away). A total of 173/308 (56%) dogs entered the study.

The median age at the time of lap OVE was 1.2 years (range: 0.4-12.3 years) and the median body weight was 17.0 kg (range: 2.0-65.0 kg). Based on the age at lap OVE, there were 95 pubertal dogs, 55 adult dogs, and 23 older dogs (Table 1).

Intraoperative uterine changes

In 14/173 (8%) dogs, one or more uterine changes were found. The median age of these dogs was 8.0 years (range: 2.1-11.5 years) and the median body weight was 24.4 kg (range: 2.0-65.0 kg). In total, 19 uterine diseases were observed in these 14 dogs during lap OVE. These pathologies consisted of CEH in 10/14 (71%) dogs, a uterine cyst in 6/14 (43%) dogs, and uterine luminal collections in 3/14 (21%) dogs (Figure 1).

In pubertal dogs, no uterine pathologies were observed. In adult dogs, 3/55 (5%) uterine pathologies were found. These included a uterine cyst in 2/55 (4%) dogs, and early-stage CEH in 1/55 (2%) dogs. No uterine luminal collection was observed. In older dogs, 16/23 (70%) uterine disorders were found, spread over 11 dogs. These pathologies included early-stage CEH in 9/23 (39%) dogs, uterine cysts in 4/23 (17%) dogs, and uterine luminal collections in 3/23 (13%) dogs.

Uterine pathologies at follow-up

The median follow-up period (time between lap OVE and telephone survey) was 4.5 years (range: 0.2-12.3 years). In none of the 173 dogs in this study, a uterine pathology developed during this follow-up period.

For the 14 dogs that had uterine changes at the time of lap OVE, a median follow-up time of 3.9 years (range: 1.1-11.1 years) was reached. Ten of them were presented to the Small Animal Teaching Hospital with different complaints, including dermatologic complaints (n=4), mammary tumors (n=3), neurological problems (n=1), vulvar discharge (n=1), and hepatomegaly (n=1). In two of these dogs, an abdominal ultrasound was performed as part of the work-up. The first dog was diagnosed with vaginitis after antibiotic treatment, 1.3 years after lap OVE. The second dog underwent an ultrasound control for hepatomegaly,

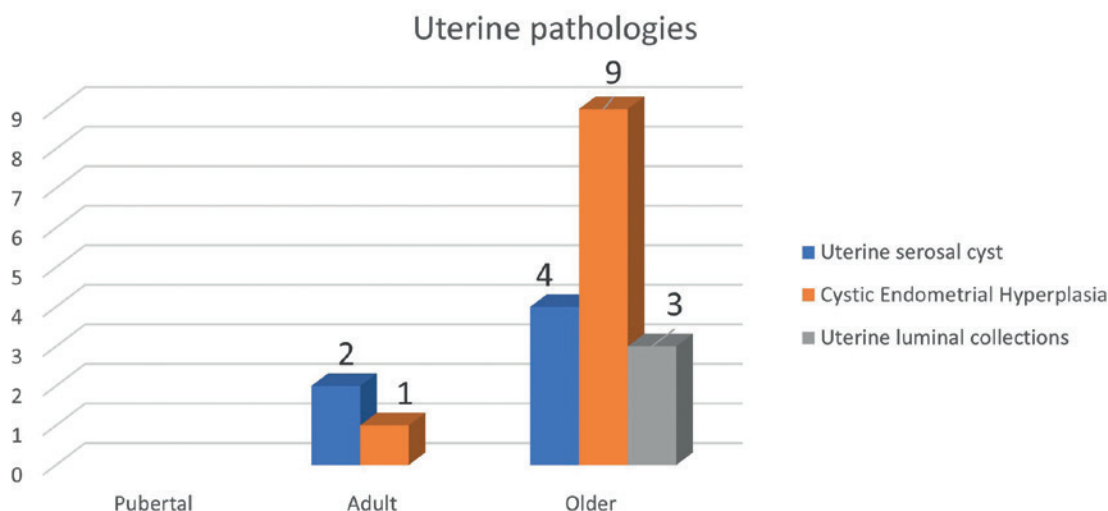


Figure 1. Distribution of the observed uterine pathologies per age group.

3.5 years after lap OVE. Both dogs had early-stage CEH at the time of lap OVE, whereas an atrophic thin-walled uterus without any cysts in the wall nor uterine luminal collections, was detected at follow-up. In the other eight dogs, there were no indications for the presence of any uterine pathology based on physical examination. At the time of the survey, 12/14 (86%) dogs in this follow-up study were alive and 2/14 (14%) dogs had died. The cause of death was not related to the genital system.

DISCUSSION

In none of the dogs in this study, appreciable uterine pathologies developed after elective lap OVE. Furthermore, in two dogs with early-stage CEH at the time of lap OVE, there was ultrasound confirmation that the uterine changes reversed after lap OVE. Both findings support the use of lap OVE as the routine neutering procedure, also in clinically healthy adult and older dogs.

The 173 dogs in this study were followed for a median time of 4.5 years, during which no uterine pathologies developed. This result supports earlier research on 141 dogs after open OVE (Janssens and Janssens, 1991, Schaefer-Okkens and Kooistra, 1997), and a more recent study on 125 dogs after lap OVE (Coriveau et al., 2017), where none of the dogs developed pyometra. Since both CEH and pyometra require chronic hormonal stimulation of the uterine wall to develop, and since OVE removes hormonal stimulation, the risk of uterine pathology is reliably eliminated (Hagman, 2004), provided the dog is not exposed to exogenous hormones. Even more interesting was that the 14 dogs identified with early-stage uterine disease (uterine cysts, CEH, and uterine luminal collections) did not progress to clinical disease after lap OVE. Instead, in the two dogs in which ultrasound examination of the abdomen was performed, the uterine horns had regressed to a normal, atrophic size. The same probably also occurred to the other dogs, since physical examination, consisting of abdominal palpation and vulvar inspection, did not reveal any abnormalities. This strongly suggests that early-stage, non-neoplastic uterine pathologies are reversible after lap OVE. An earlier experimental study has indeed shown that CEH can be induced by the presence of a uterine irritant combined with the administration of progestagens, and that withdrawal of progestagens, even in the continued presence of a uterine irritant, may lead to uterine recovery (Chen and Lee, 2006). To the authors' knowledge, this is the first clinical report of CEH regression after OVE.

For pubertal dogs, the routine spaying technique is lap OVE (Van Goethem et al., 2006), but for adult and older dogs, OVH is commonly advised (Urfer and Kaerberlein, 2019). This recommendation is based on the relatively frequent occurrence of uterine pa-

thologies in older intact dogs (DeTora and McCarthy, 2011). In a study on 228 adult dogs, performed to evaluate the optimal age for a preventive ultrasonographic screening of the uterine health, a prevalence of 18% CEH, 11% uterine luminal collections, and 1% uterine masses was found (Melandri et al., 2019). This concurs with the present study, where 5% uterine pathologies were found in adult dogs ($n=55$); this number increased to 70% in older dogs ($n=23$). The current recommended surgical technique for uterine pathologies, such as uterine cysts or CEH, is OVH (Sasidharan et al., 2021). However, the emergence of laparoscopic technique has been a strong driving force towards OVE (Charlesworth et al., 2019). The standard technique for elective spaying of young dogs has switched in the last decade from OVH to OVE (DeTora and McCarthy, 2011). The authors expect that evidence-based guidelines will be drawn up in the future that determine when OVH is medically necessary. The current advice at the authors institution is to perform lap OVE as a standard spaying technique independent of age, and only switch to laparoscopic-assisted OVH in case of late-stage uterine pathologies, recognizable as segmental uterine luminal collections, or in case of uterine tumors.

No uterine tumors were detected in this study. This is not surprising since the prevalence is only 0.03% and they are almost exclusively diagnosed in older intact dogs (Brodey, 1967; Hedlund, 2007). The rare occurrence of uterine tumors does not justify the use of an OVH technique with an increased morbidity compared to the OVE technique (Van Goethem et al., 2006).

After OVE, hormonal stimulation of endometrial and other uterine tissues will cease, reversing these tissues to their normal, unstimulated size (Schaefer-Okkens and Kooistra, 1997). This is, however, not a true atrophy, but rather a dormant state since a high percentage of these uterine cells was found to still express estrogen and progesterone receptors six months after OVE (Schäfer-Somi et al., 2017). Exogenous estrogen exposure can therefore still result in uterine pathologies in ovariectomized dogs (Noakes et al., 2001). Nevertheless, the same is true after OVH, where the endometrial tissue remaining at the cervical stump will result in stump pyometra in case of exogenous hormone exposure (Ivaldi et al., 2022).

This study has several limitations. Only 173 of the 308 dogs that underwent lap OVE, were included in the study (56%). Twenty-two dogs were actively excluded because of the presence of confounding pathologies, and for 113/308 dogs, owner questionnaires were lacking. This percentage of respondents is not uncommon for retrospective long-term telephone surveys and percentages above 50% are deemed representative (Goodwin et al., 2020). Three age groups were defined to allow comparison of occurrence of uterine pathologies. For the pubertal group, an upper age limit of 18 months was chosen. Since large breed dogs can take up to two years to reach puberty, this

led to the wrongful inclusion of one large breed dog (19-months-old) to the adult group instead of the pubertal group. However, no uterine abnormalities were found in this dog. More importantly, only two of the 14 dogs with uterine pathologies at the time of the lap OVE were evaluated by abdominal ultrasound later. While the authors assume that no uterine pathologies were present in the other twelve dogs, since physical examination at the Small Animal Teaching Hospital in ten dogs and annual health checks by their veterinarian in the remaining two dogs did not reveal any abnormalities, it is possible that a non-clinical uterine pathology was present. In a gonadectomized animal, there still remains a minimal risk for the development of a non-hormonally induced uterine tumor (0.003%). These tumors will gradually increase in size creating abdominal discomfort, often causing pyometra because of uterine luminal collections, and might result in distant metastasis (Tsioli et al., 2011). The authors are confident that these signs would have been picked up and thus are confident to conclude that no uterine pathologies were present at the time of follow-up.

CONCLUSION

Despite the presence of many adult and older dogs in this study, in none of the clinically healthy dogs, uterine pathologies developed after lap OVE. This supports the use of lap OVE as the standard spaying technique in clinically healthy adult and older dogs. Early-stage hormonally induced uterine changes did not progress and were documented in two dogs to resolve after lap OVE.

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