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Prepuberal gonadectomy in dog and cat

Literature review

DIPLOMA WORK

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1. Introduction

Prepuberal gonadectomy is defined as ovariohysterectomy (OHE), ovariectomy or castration of kittens and puppies between 6 weeks and 16 weeks of age (Root, 2014). However, in some studies prepuberal gonadectomy refers to animals gonadectomized less than 5 months of age. In another way, prepuberal gonadectomy means the removal of reproductive organs before the onset of puberty. Puberty is the onset of reproductive and sexual maturation and is consisted with the first estrus in females and functional production of spermatozoa in males (Yates et al. 2011).

Prepuberal gonadectomy is mostly performed in the United States were the overpopulation of stray and homeless dogs and cats are a big problem. Each year approximately 5-7 million dogs and cats are surrendered to animal shelters. In United States, the veterinarians in animal shelters have been performing prepuberal gonadectomy on dogs and cats for at least 10 years. The aim is to place animals from shelters into adoptive homes without the opportunity to repopulate. Dog and cat breeders may benefit from prepuberal gonadectomy as well. Breeders can place animals that is qualified as pet animals but are not of the breed standard or that may have heritable defects into homes knowing there will be no repopulation and allowing placement of the animals at a young enough age to facilitate socialization and training (Root 2002).

The aim of this review is to look at the anesthetic and surgical techniques in pediatric animals and to evaluate the benefits and risks regarding prepuberal gonadectomy and if it is reasonable to perform gonadectomy on such young animals.

2. Materials and methods

Before I could start writing this literature review I needed to collect relevant and reliable information concerning the topic. For this I used a virtual private network (VPN). The VPN enabled me to connect to the network of the library of Szent Istvan University from my own computer. By doing this, I was able to collect those articles I needed.

In the process of collecting articles I used different databases: Pubmed, Science Direct, Web of Science, Cab Archive and Cab Abstract. I also collected articles from the American Journal of Veterinary Research. During the research, I used the following keywords: early-age neuter, neuter, spay, ovariohysterectomy, ovariectomy, castration, risk, benefit, gonadectomy, prepuberal and pediatric. I also found articles through the list of references of other articles. Many of those particular articles I needed were quite old and did not exist in the databases but only in paper form. The library helped me to find those I needed.

3. Anesthesia

Anesthesia in pediatric animals is not difficult but differences in physiology, compared to older animals, must be kept in mind when handling the animals, selection of anesthetics, maintaining and monitoring of the animals during the surgical procedure (Root Kustritz, 2002). Physical examination is of high priority before inducing anesthesia and surgery with a particular attention to the respiratory and cardiovascular systems. This is to ensure that the animal is healthy and to exclude congenital abnormalities and infectious disease (Howe, 1999). Concerns relating to anesthesia in pediatric patient includes hypothermia, hypoglycemia and stress. In order to minimize the level of stress, it is recommended to keep pediatric animals together in groups close to the induction (Root Kustritz, 2014).

To prevent hypoglycemia from occurring during anesthesia, feeding close to induction is important. Compared to adult animals, pediatric animals have relatively low muscle mass with even smaller glycogen stores. Pediatric animals have an immature hepatic function, which reduces the capacity to elevate blood sugar by glycogenolysis or gluconeogenesis. So in order to prevent hypoglycemia during anesthesia the fasting time before surgery should be minimized and the animal should receive food instantly after recovery from surgery (Root Kustritz et al., 2014).

Hypothermia is a more common finding in pediatric animals than in adults because of the less amount of subcutaneous fat and the decreased ability to shiver. The supplementation of heat before, during and after is of great importance to ensure a warm environment. Risks in case of hypothermia includes decreased heart rate, deepening of the anesthesia and prolonged anesthetic recovery (Root Kustritz, 2002)

Low doses of anesthetics drugs should be used because of decreased protein binding in circulation, decreased liver metabolism, decreased excretion rate through kidneys and higher respiratory rate. Therefore, most injectable drugs appear more potent and have a longer duration of effect. The recovery time after anesthesia used at gonadectomy is significantly shorter in pediatric animals compared to older animals (Root 2002).

Reported complications during anesthesia of pediatric animals for gonadectomy include drug overdose, cardiac arrest, perioperative regurgitation and aspiration, and change in cardiac rate or rhythm. The occurrence of these complications was not greater in puppies and kittens gonadectomized at less than 12 weeks of age compared to those gonadectomized at 12 to 24 weeks of age or greater than 24 weeks of age (Howe, 1997).

Several anesthetic protocols (**Table 1, 2, 3)** have been reported to be used in early gonadectomy in dogs and cats (Fagella et al. 1993; Fagella et al. 1994). The anesthetic protocols explained by Howe was developed to fulfill several criteria. The protocol was made more or less similar to that used in animals gonadectomized at a traditional age (Howe, 1999).

Table 1

Anesthesia protocol for castration of puppies

Age (weeks)	*Premedication (mg/kg)*	*Induction (mg/kg)*	*Maintenance*
6-14	**Atropine** (0.04)IM, **Oxymorphone** (0.22) IM	Propofol (6.5) IV 15 minutes slowly after premedication	Isoflurane (if necessary)
6-14	**Midazolam** (0.22) IM, **Butorphanol** (0.44) IM	Propofol (6.5) IV slowly 15 minutes after premediacation	Isoflurane (if necessary)
< 20	**Glycopyrrolate** (0.011) IM, **Butorphanol** (0.22) IM	Pentothal (22) IV. Titrated to effect	Isoflurane or Halothane
20-24	**Glycopyrrolate** (0.011) IM, **Butorphanol** (0.22) IM, **Acepromazine** (0.026) IM	Pentothal (22) IV. Titrated to effect	Isoflurane or Halothane

(Root Kustritz, 2002; Howe, 1999; Faggella et al. 1994)

A study from 1994 evaluated the anesthesia during gonadectomy in 6 -14 week old puppies (**Table 1 and 2**). The use of atropine and oxymorphone was rated as the best technique for castration. However, in female puppies the combination of ketamine and midazolam were shown to be the best anesthesia protocol used (Faggella et al. 1994).

Table 2

Anesthesia protocol for ovariohysterectomy in puppies

Age (weeks)	*Premedication (mg/kg)*	*Induction (mg/kg)*	*Maintenance*
6-14	**Atropine** (0.04) IM **Oxymorphone** (0.11) IM	Propofol (3.4) IV 15 minutes after premedication	Isoflurane
6-14	**Atropine** (0.04) IM **Oxymorphone** (0.11) IM **Tiletamine-zolazepam** (13.2) IM	Isoflurane (by using mask)	Isoflurane
6-14	**Midazolam** (0.22) IM **Butorphanol** (0.44) IM	Isoflurane	Isoflurane
6-14	**Tiletamine-zolazepam** (13.2) IM	Isoflurane	Isoflurane
<20	**Glycopyrrolate** (0.011) IM **Butorphanol** (0.22) IM	Pentothal (22) IV. Titrated to effect	Halothane or Isoflurane
20-24	**Glycopyrrolate** (0.011) IM **Butorphano**l (0.22) IM **Acepromazine** (0.026) IM	Pentothal (22) IV. Titrated to effect	Halothane or Isoflurane

(Howe, 1999; Root, 2002; Faggella et al. 1994)

Faggella and Aronsohn evaluated in their study the pre-anesthetic disposition, depth of sedation, level of resistance following onset of injectable drugs, induction time, induction quality, analgesia and relaxation without inhalation anesthesia (males), extubation time (females), sternal and stand times and last but not least the recovery quality in cats. In male cats, the group anesthetized with tiletamine and zolazepam provided a better analgesia for gonadectomy compared to midazolam and ketamine, which provided the least amount of analgesia. In both males and females the recovery time were significantly longer in those anesthetized with tiletamine and zolazepam. Tiletamine /zolazepam were shown to be the best anesthesia for castration of 6 – 14 weeks old kittens while Midazolam/Ketamine was

recommended to be used for ovariohysterectomy in 6- 14 weeks old kittens (**Table 3)** (Faggella et al. 1993).

Table 3

Anesthetic protocol for OHE and castration in kittens

Age (week)	*Premedication/ Induction (mg/kg)*	*Maintenance*	*Procedure*
6-14	**Tiletamine-zolazepam** (11) IM	Isoflurane	OHE /Castration
6-14	**Atropine** (0.04) IM **Midazolam** (0.11) IM **Ketamine** (11.0) IM **Oxymorphone** (0.07) IM	Isoflurane	OHE/Castration
6-14	**Midazolam** (0.22) IM **Ketamine** (22.0) IM	Isoflurane	OHE/Castration
6-14	**Atropine** (0.04) IM **Midazolam** (0.22) IM **Ketamine** (11.0) IM **Butorphanol** (0.44) IM	Isoflurane	OHE/Castration
<24	**Glycopyrrolate** (0.011) IM **Butorphanol** (0.44) IM **Acepromazine** (0.055) IM **Ketamine** (11) IM	Isoflurane	OHE/castration

(Root Kustritz, 2002; Howe 1999; Faggella and Aronsohn 1993)

A review of early age gonadectomy states that the use medetomidine, ketamine and butorphanol as an anesthetic protocol in cats gives a good analgesia and smooth recovery. This is a more up to date protocol, which might be more common today (Joyce, Yates, 2011).

4. Surgery

Preparation of the pediatric patient for surgery is similar as for traditional gonadectomy but it is important to bear in mind that these patients is in need for extra care (Root, 2002). Since pediatric animals are prone to hypothermia, some points should be kept in mind. Shaving of the surgical site should be as minimal as possible. To keep the animal warm during surgery, warm blankets, warmed bottles or even warm intravenously fluid can be used to preserve the heat. Excessive wetting of pediatric animals during surgery should be avoided and the use of warmed scrub should be considered. As a part of disinfection, alcohol should be avoided to preserve the body heat (Howe 1999, Root 2014). Surgery time is reported to be significantly less for those animals gonadectomized before 12 weeks of age. In addition, the surgical time in females was significantly greater than the surgical time in males, probably because of the more complex nature of surgery (Howe, 1997).

4.1 OHE in kittens and puppies

OHE (Ovariohysterectomy) is the removal of the female reproductive tract, including the ovaries and uterus.

Ovariohysterectomy in kittens and puppies are performed similar to the technique at traditional age of 6 to 7 months of age. In young animals, the incision is started more caudally to the umbilicus than adult animals because the uterus is more easily exposed this way especially in dogs (Howe, 2006). The ventral abdomen, from the xiphoid to the pubis, is clipped and surgically prepared for surgery. An incision is made through the skin and the subcutaneous tissue to expose the linea alba. Consecutively, a stab incision is made into the abdominal cavity (Fossum, 2002). In pediatric animals, the presence of free serous fluid in the peritoneal cavity may be a common finding (Root et al, 2002). To improve visualization, gauze sponges might be used for the removal of free fluid. The Snook ovariohysterectomy hook, which is a remedy to locate the ovaries and uterine horn, is not recommended because of the very friable tissues in young animals. The slightly caudal position of the incision makes the uterus easy to localize by retracting the bladder and looking between the urinary bladder and colon. Careful handling must be kept in mind to avoid excess traction and tearing of tissues due to the very small and friable uterine tissues in puppies and kittens (Howe, 2006)

After the localization of the uterus the suspensory ligament (a fold of peritoneum attached to the ovary) should be visualized and detached without tearing the ovarian vessels. A hole is made in the broad ligament caudally to the ovarian pedicle. One or two clamps are placed across the ovarian pedicle proximal (deep) to the ovary. Another clamp is placed across the proper ligament of the ovary (connection of the ovary to the lateral surface of uterus). The most proximal clamp is positioned to serve as a groove for ligation while the middle clamp holds the pedicle in right position for ligation. The most distal clamp is placed in such a way to prevent backflow of blood after transection.

The proximal clamp is removed and a ligation is made in the groove. For ligation, absorbable suture materials should be used (Fossum, 2002). Suture materials containing polydioxanone may cause calcinosis circumscripta and avoidance of this material is recommended. Calcinosis circumsscripta is a disorder causing progressive, well-demarcated calcium deposits

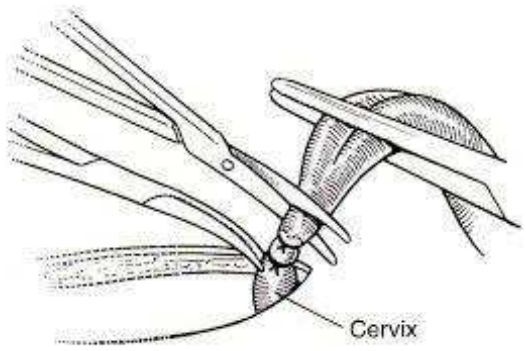

Figure 1: Ligation near cervix before transection (Fossum, 2002).

suture material should be chosen. Continuous stiches are preferred. The last step is to close the skin with an unabsorbed suture material (Fossum, 2002).

4.2 OVE in kittens and puppies

Ovariectomy (OVE) is the removal of the ovaries excluding the uterus. Bilateral ovariectomy has been preferred over ovariohysterectomy due to smaller incisions, reduced abdominal trauma, reduced surgery and anesthesia time (Howe, 2006). The technique is performed by making a ventral midline incision, starting from the umbilicus and directed further caudally. Location of the ovary is done by either visualization or palpation. The ovary in cats are usually more eminent than the ovary in dogs. After location of the ovary, a window is made in the broad ligament. The window should be made in a relative avascular area to prevent bleedings. Compared to dogs the cats may have more utero-ovarian venous anastomosis. A hemostat carrying suture material is passed through the window in the broad ligament and a ligation is made over the ovarian pedicle (**Figure 1**). A secondary ligation might be made for additional security. Thereafter, another ligation is passed through the window and the ligation is made over the uterine horn. If necessary, a secondary ligation may be performed. Two forceps are placed across the ovarian pedicle between the ligatures and the ovary. The same is done between the ovary and the uterine horn (**Figure 2**). Transection is done between the two forceps and visualize for any bleedings. Checking the transected ovary is extremely important in order to ensure the complete removal of the ovary. Any remnants can lead to ovarian remnant syndrome. Closure of the abdominal cavity is done the same way for ovariohysterectomy (Ehrhardt, 2012).

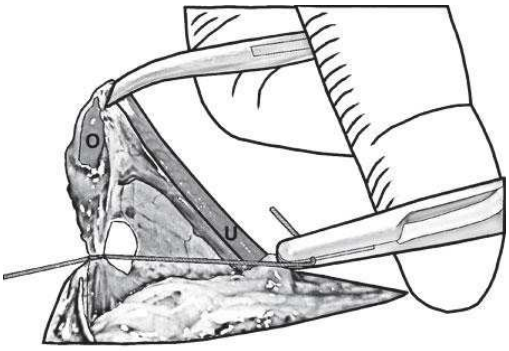

Figure 2: Ligation of ovarian pedicle. (Ehrhardt 2012)

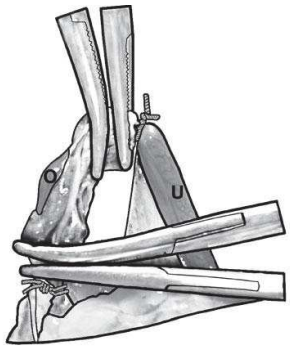

Figure 3: Forceps are placed in position and transection between each of them should be performed (Ehrhardt 2012)

4.3 Castration in kittens

Castration in kittens is performed similar to adult individuals (Root, 2014). Two separate incisions are made on the midline of the scrotum. The testis of the pediatric cat is incredibly small and highly moveable and can occasionally be difficult to stabilize in the scrotal region. Hence, fixation of the testis in the scrotum is necessary before performing the incision (Howe, 2006). The incision should be made directly over the testis at the ventral aspect of the scrotal sac. Using a careful traction, the testis is exposed. It is important to realize that the pediatric spermatic cord is short and the tissues are extremely friable so exteriorized of the testis to the same distance as the adult cat cannot be performed without potential tearing of the spermatic cord (Root 2014, Howe 2006).

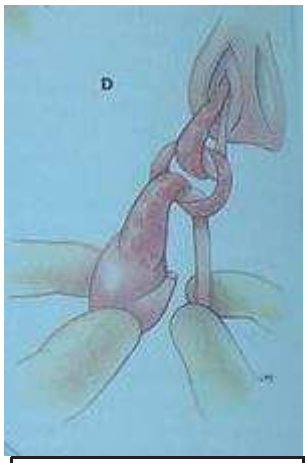

Figure 4: Open castration technique: ligation of spermatic vessels and ductus deferens (Fossum, 2002)

Figure 5 : Closed castration: ligation of spermatic cord (Fossum, 2002)

Two techniques, closed castration and open castration, can be used in cat. Closed castration technique is performed by tying the spermatic cord onto itself while the open castration technique is done by tying the spermatic vessels to the ductus deferens on each side (**Figure 4 and 5**). Even though both techniques can be used the closed technique is preferred (Root et al, 2014). Since the spermatic cord is quite short it can make it difficult to perform the tying so ligature or hemostatic clips is recommended for hemostasis (Howe et al, 2006). The incision after the castration is left open to heal by second intention (Looney et al. 2008).

In a study from 2014, different surgical techniques in prepuberal gonadectomy (8-12 weeks of age) and those of traditional age (6-8 months of age) were compared. All together 183 male kittens were used for this study and the number of animals were assign to two groups: knot group (n=92) and ligature group (n=91). Technique used in the knot group was to tie the spermatic cord on itself. On the other hand, the technique used in the ligature group was to place a ligature around the spermatic cord. Both techniques were performed without opening the vaginal tunica. The results showed the surgical time to be significantly shorter in the knot group than the ligature group. Comparing the prepuberal gonadectomy to traditional age gonadectomy the surgical time was shorter for prepuberal gonadectomy. Furthermore, the

fastest and cheapest technique for male prepuberal gonadectomy was the knot technique, since no suturing were required (Porters et al. 2014b).

4.4 Castration in puppies

Pediatric castration of puppies is performed with a few modifications to the technique in adult dogs (Howe, 2006). Testis are usually descended into the scrotum around 12 – 14 weeks. This makes it more difficult, especially compared to cats were the testis are already in the scrotum at birth (Root, 2014). If the pediatric patient has one or both testicles retained, postponing of the castration until the testicle is descended into scrotum is recommended because the anesthetic and surgical risk associated with the retained testicle (cryptorchidism) is greater (Porters et.al, 2014). Before performing the castration, the entire scrotal region is clipped and prepped for surgery. In adult male dogs, irritation on the scrotum may occur. However in young animals the clipping and surgical preparation does not result in irritation of the scrotum because the scrotal sac is not yet well developed as in adult male dogs (Howe, 2006).

The castration technique in puppies can be performed similar to the scrotal incision in kittens or by prescrotal incision.

4.4.1 Open prescrotal castration

Initially, the verification of the testis is important. A slight pressure is added to the scrotum to advance one of the testis in the prescrotal area (cranially to the scrotum). An incision is made through the skin and subcutaneous tissue just above the displaced testicle. The incision is continued through the spermatic fascia to exteriorize the testicle. Thereinafter, the parietal vaginal tunic is opened. A hemostat is placed across the tunic where it is attached to the epididymis. The ligament between the tail of epididymis and the tunica is separated digitally by traction. Caudal traction is applied to exteriorize the testicle. The ductus deferens and the vascular cord is ligated individually. A common ligature is made around them both at the end. The suture material must be of absorbable suture material. A hemostat is placed proximally to the ligation. The cord is transected between the ligation and the hemostat. The second testicle is advanced from the same incision and the same procedure is implemented as the first one. At last, three layers close the incision. First, the fascia is closed by using either interrupted or continuous pattern. Continuous pattern is used for closure of the subcutaneous tissue. The skin is closed with loosely tied interrupted pattern.

4.4.2 Closed prescrotal castration

Closed castration is performed similar to the open castration except the opening of the parietal vaginal tunics. The spermatic cord is exteriorized maximally by separating fat and fascia from the parietal tunics. Traction is applied to the testicle to ensure torsion of the fibrinous attachment between the spermatic cord tunics and the inner wall scrotum. The spermatic cord and tunics are ligated together. Transection of the entire spermatic cord is done after a successful ligation. The closure of the incision is done similarly to the open prescrotal castration technique.

5. Benefits and risks

5.1 Mammary neoplasia

The greatest benefit of prepubertal gonadectomy is the decreased risk of development of mammary neoplasia (Root, 2014). Mammary tumors are the most common tumors in female dogs while the incidence of mammary tumors in female cats are roughly half that seen in dogs and there is no obvious protective effect of having a litter for dogs and cats (McKenzie, 2010). The incidence of mammary tumor especially in intact females increases with age.

In cats the incidence of mammary tumors is 2.5 % and malignant adenocarcinomas is the most common. Over 90 % of the mammary tumors found in female cats are malignant while in dog 50 % of mammary tumors are malignant (Root et. al, 2007). The incidence of mammary tumors is breed specific in Japanese domestic breeds and Siamese and these are more prone to development of mammary tumors. Occurrence of mammary tumors in dogs is 3.4 % with 50 % being fibroadenomas and 50 % malignant adenocarcinomas (Root, 2002).

Gonadectomy decreases the incidence of mammary tumors tremendously, especially gonadectomy before the first estrus. Number of estrus cycles before ovariohysterectomy can increase the risk of development of mammary tumor in dogs and cats. The risk of the occurrence of mammary neoplasia in dogs have been reported to be 0.5 % for females spayed before the first estrus, 8% of females spayed before the second estrus and 26 % for females spayed after the second estrus. Compared to gonadectomized animals, intact dogs and cats have seven times higher risk of developing mammary tumors with age (Root, 2007).

A study from 2005 reported a 91 % reduction in the risk of developing mammary tumor in cats if they were ovariohysterectomized before the age of 6 months and 86% reduction in risk if spayed before the age of one year compared to intact females. Furthermore, the study showed a protective effect if the cats were spayed between 13 and 24 month of age. Compared to intact females, the risk of feline mammary carcinomas increased if ovariohysterectomy were performed after the age of two years (Overley, 2005).

5.2 Pyometra

Pyometra is an infection of the uterus under the influence of the hormone progesterone. Bacterias can reach the uterus with an ascending infection from the distal portion of the genitourinary tract. The failure to clear bacterias from the uterus after estrus may lead to pyometra (Nelson, Couto, 2014). Pyometra occurs most commonly in aged female dogs and have a lesser occurrence in cats. Ovariohysterectomy is the best solution to prevent or treat pyometra. The mortality rates regarding pyometra are reported to be around 4.2% to 17 % in dogs and 8% in cats (Root et. Al., 2014). Ovariohysterectomy decreases the risk of pyometra considerably in dogs and cats. However, uterine stump pyometra may occur if some ovarian tissue is still present (ovarian remnant syndrome) because of the production of progesterone (McKenzie, 2010).

5.3 Benign prostatic hypertrophy

The increase in both cell number (hyperplasia) and size (hypertrophy) of the prostate gland in male dogs increases with age. This disease is manifested clinically in 75 %- 80 % by 6 years of age. Castration is reported to decrease the size of the prostate gland and the smaller the gland is the less likely it is to become infected (Root, 2014).

5.4 Behavior

Gonadectomy and the following decrease in gonadal steroid hormones have been linked to the decrease in sexual behaviors. The decrease of sexual behaviors in cats after gonadectomy is beneficially. The undesired behaviors reduced to the greatest after castration in male cats are sexual behaviours, roaming and urine spraying. In male dogs the benefits of castration is decreased mounting, urine marking and roaming. These effects of castration is not associated with the age at gonadectomy in male dogs or cats (Root 2012).

A study observing the long-term risks and benefits of prepuberal gonadectomy in cats resulted in decreased occurrence of hyperactivity and increased occurrence of shyness among strangers. This concerned those animals gonadectomized before 5.5 months of age. Aggression towards veterinarians, sexual behaviors and urine spraying were shown to have a reduced occurrence in early-age gonadectomy (Spain et al. 2004a). Another study showed that prepubertal gonadectomy did not result in increased behavioral problems compared to

those observed after traditional-age gonadectomy (Howe et al. 2000). Lower incidence of abscesses in males was associated with early-age gonadectomy. After a follow –up of 5 to 6 years, there was no longer any differences between the ages at gonadectomy in terms of risk of abscesses (Spain et al. 2004)

Intact cats were found to be more aggressive towards each other and less affectionate towards humans than those gonadectomized at 7 weeks and 7 months of age (Stubbs et al. 1996).

A prospective cohort study evaluating the risk and benefits with early age gonadectomy in dogs resulted in an increased rate of aggression and excessive barking. However, these associations were probably an artifact of the screening procedures of the shelter for aggression and probably not a result of early age gonadectomy (Spain et al. 2004b). Another cohort study showed that there was no increased occurrence of behavioral problems in early-age gonadectomy compared to gonadectomy performed at a traditional age (Howe et al. 2001).

To provide short-term and long-term information regarding the behavioral characteristics was the aim of one study in shelter cats undergoing prepubertal and traditional age gonadectomy. The undesired behavior was not affected by the age at gonadectomy (Porters et al. 2014b).

5.5 Society

Population control is the primary benefit of gonadectomy. The reduction of the total number of kittens and puppies is extremely important in order to decrease the number of animals abandoned annually and to reduce euthanasia. In United States, each year 5-7 million dogs and cats are surrendered to different animal shelters. Out of these approximately 3 to 4 million are euthanized. Early age gonadectomy is most commonly performed in humane organizations rather than veterinary practices in order to keep the population of animals to as minimum as possible. Gonadectomy performed before adoption ensures that no repopulation will occur while housed at the shelter and prevent repopulation when adopted. Additionally, the adoptability increases tremendously if animals are gonadectomized.

5.6 Urinary incontinence

Urinary incontinence is a common disorder in gonadectomized animals (McKenzie, 2010). It is believed to be connected to hormonal deficiency where the lack of estrogen can lead to oestrogen-responsive urinary incontinence. Other factors that may be associated with urinary incontinence includes the length and width of the urethra, position of the bladder, age and breed (Nagakura, Clark, 1992).

In a study where the long-term risk and benefits of early-age gonadectomy in dogs were evaluated there was a significant interaction between the age of gonadectomy and sex and the different risks between the males and females. In those animals gonadectomized before the age of 5.5 months the incidence of cystitis was considerably higher among female dogs but none of the described dogs had more than two episodes of cystitis. The occurrence of urinary incontinence among female dogs was associated with decreasing age at gonadectomy. Those females that were gonadectomized before the age of 3 months seemed to be at highest risk compared to those gonadectomized at above 3 months of age. Over a period of 6 years, the incidence of urinary incontinence was 12.9 % in those female dogs gonadectomized before the age of 3 months and 5.0 % for female dogs gonadectomized older than 3 months of age (Spain, Scarlett, Houpt, 2004).

A more recent study evaluating the occurrence of urinary incontinence in ovariohysterectomized female dogs were divided into three different age groups: <6 months, 6-18 months and last > 18 months of age. The result of the three age groups were 5.5 %, 4.8 % and 5.9 %, respectively, which showed no considerably differences in the age group at the time of ovariohysterectomy and urinary incontinence. There was, however, significant differences in the body weight and urinary incontinence. In smaller dogs, the rate of incontinence was 1.37 % and in medium to large dogs the rate was 9.12 %. In another way, larger dogs (>15 kg) were seven times more likely to develop urinary incontinence than smaller breeds (<15 kg). The follow-up time of this study was ranged from approximately 4 to 7 years so a portion of the dogs evaluated may develop urinary incontinence in the following years. The association between the body weight and incontinence was reported to be independent from age groups, litter numbers and reason for ovariohysterectomy (Forsee et. al., 2013).

5.7 Urethral diameter

Several studies have evaluated the incidence of decreased urethral diameter. The alteration in sexual status connected to gonadectomy did not predispose male cats to a decreased urethral diameter (Root et al. 1996; Howe et al. 2000).

5.8 Feline lower urinary tract disease (FLUTD)

Feline lower urinary tract disease is a syndrome with symptoms like hematuria, pollakiuria, dysuria and urination in inappropriate locations. The reported occurrence of FLUTD is 0.6 % (Senior. D 2006). In a large study, the incidence of FLUTD appeared to have an increased risk in gonadectomized cats. Obese cats appeared to have an increased risk of developing FLUTD

5.10 Growth plate closure

Gonadal hormones facilitate the closure of growth plates in long bones (Root, 2012). High doses of estrogen inhibit the growth of long bones and stimulate physeal closure. Both estrogens and androgens promote the calcium deposition at the physes and eventually migrating osteoblast will secrete components of bone matrix. The time of first estrus in females or the presence of sperm in the ejaculate in males promote the closure of physes and cessation of the growth of longitudinal bones. Physeal closure begins as early as 4 months in intact cats and is completed by approximately 20 months of age. The proximal radial physes closes the earliest (4-7 months) while the distal radial physes closes the latest (14-20 months). Some physes will close prepubertally while other will close later (Root et al., 1997)

Figure 4: Radiograph of cats neutered at 7 weeks, 7 months and sexually intact, respectively. Animals neutered at 7 weeks and 7 months were presented with a delay physeal closure. In sexually intact cats a complete physeal closure of distal radius was observed.

Different studies show that there is a relationship between prepubertal gonadectomy and delayed growth plate closure (Salmari et al. 1991; McNicholas et al. 2002; Root et al. 1997; Stubbs et al. 1996).

The aim of one study was to determine the time of proximal and distal radial physeal closure and the length of radius in adult male and female cats that were gonadectomized at two different ages or left intact. The cats were divided into groups according to sex and age. The first group consisted of those animals gonadectomised prepubertally (7 weeks), second group of those gonadectomized postpubertally (7 months) and the third and last group were those left intact. The proximal radial physeal closure did not differ in time in male cats of all three groups. However, in female cats there was a delayed proximal physeal closure in those gonadectomized at 7 weeks old compared to those gonadectomized at 7 months of age or left intact. The closure of the distal radial physes of both male and female cats were delayed in those animals gonadectomized at 7 weeks or 7 months of age compared to intact animals (**Figure 4**). Age at time of gonadectomy had no effect. Since the closure of distal radial physes occurs postpuberally the closure may be

dependent on the presence of gonadal steroids. The radial length differed in groups for both female and male cats at 24 months of age. Males gonadectomized at 7 weeks or 7 months ended up to have a final radial length of 13 % greater than the intact males, while female cats gonadectomized at the same time as males ended up to have a final radial length of 9 % greater than intact females (Root et al., 1997).

Another study concerning dogs got similar results as the above-mentioned study in cats. In all neutered dogs, compared to sexually intact animals, the maturation of radial and ulnar physes was delayed and there was a delay in physeal closure in animals gonadectomized at 7 weeks old compared to those gonadectomized at 7 months of age. Compared to intact animals the length of radius was greater in all neutered males. Females spayed at 7 weeks of age had a greater radial length than those animals spayed at 7 months of age or those left intact. The growth rate of gonadectomized animals were unaffected prior to 7 months of age, however, gonadectomized animals continued to grow for a longer period compared to intact animals where the growth rates declined after 7 months of age (Salmeri et al., 1991).

Spontaneous femoral capital physeal fracture in adult cats were evaluated in 2002. All the cats used in this study were neutered. As the same as previous studies it is strongly suggested that neutered male cats are more predisposed to these kind of fractures than those left intact and a major risk factor is prepubertal gonadectomy. However, the 26 cats used in this study had a higher mean body weight, which could have been a contributed factor for the physeal fractures. Prepubertal gonadectomy can be a cause of higher body weight (McNicholas et al. 2002).

5.11 Rupture of cranial cruciate ligament

The incidence of cranial cruciate ligament rupture were shown to be higher in early gonadectomized animals from a study using Golden retrievers. The occurrence of cranial cruciate ligament rupture reached 7.7 % in females and 5.1 % in males. The mean age of the first early gonadectomized dog with cranial cruciate ligament was 3.6 years. In intact males and females, there was no incidence of cranial cruciate ligament rupture (De La Riva et al., 2013). The results from another study indicated that early age gonadectomy was a significant predisposing factor of excessive tibial plateu angle in dogs with cranial cruciate ligament rupture. Dogs with tibial plateu angle in both rear limbs were 13.6 % times as likely to have been gonadectomized before 6 months of age (Duerr et al., 2007). Other factors that might

contribute to cranial cruciate ligament rupture are obesity since gonadectomized animals are more prone to gain weight. Delayed growth plate closure in early gonadectomized animals might increase the angulation of stifle, which can predispose the animals to rupture of the cruciate ligament (Root, 2012)

5.12 Obesity

Obesity is considered to be the most common nutritional disorder in dogs and cats (Root et al. 2002). Early gonadectomy was associated with a decreased incidence of obesity in dogs in one study (Spain et al., 2004). In another study, comparing sexually intact dogs with gonadectomized dogs, the incidence of obesity was higher in those gonadectomized and the increased risk was significant during the first 2 years only. However, the risk of obesity was not influenced by the age at gonadectomy. In the sexually intact animals, male dogs had a 40 % less chance to become obese compared to intact females. In gonadectomized animals, however, there was no differences between males and females (Lefebvre et al. 2013). Gonadectomy of cats had the similar outcome as for dogs with significantly increase in body fat and body weight compared to intact animals (Ngyen et al. 2004). The age at gonadectomy was not an influencing factor.

One study evaluating the heat production in cats concluded that the resting metabolic rate in cats decreased after gonadectomy. Males and females gonadectomized at 7 weeks or 7 months of age had a lower heat coefficient than sexually intact males and females. Higher heat coefficient reflect higher metabolic rates, therefore, intact animals had a higher metabolic rate than gonadectomized animals. Those cats gonadectomized at 7 weeks of age did not differ from those gonadectomized at 7 months of age (Root et al. 1996a).

In a prospective control study of kittens the falciform fat thickness was evaluated by radiographic assessment. It revealed significant differences between gonadectomized and intact cats. The fat measures was greater in cats gonadectomized at 7 weeks and 7 months of age compared to intact cats. However, there was no differences between those gonadectomised at 7 weeks of age and those at 7 months of age (Stubbs et al. 1996).

5.13 Infectious disease

A higher incidence of infectious diseases has not been reported to occur in cats gonadectomized at an early age (Howe et al. 2000). In dogs, however, the incidence of parvoviral enteritis was higher in those dogs gonadectomized at less than 24 weeks of age compared to those gonadectomized at greater than 24 weeks of age (Howe et al. 2001).

In one trial, the aim was to determine the effect of anesthesia and surgery on serological responses to vaccination in kittens. The serological responses of kittens gonadectomized at the time of first vaccination at 8 weeks of age did not differ from those kittens gonadectomized one week before or one week after first vaccination or from those kittens that were not gonadectomized. Finally, gonadectomy at or near the time of first vaccination will not impair antibody responses in kittens (Reese et al. 2008).

5.14 Surgical complications

Short-term complications of prepubertal gonadectomy in dogs and cats was investigated in one study. Animals were divided into three different groups with animals being gonadectomized at <12 weeks old, 12-23 weeks old and >24 week old. In those animals gonadectomized at 12 weeks and above 24 weeks of age the overall complication rate was 6.5 % and 10.8 %, respectively, which showed that older animals had a significant greater overall complication rate than younger animals. However, there was no differences between animals at 12 weeks and 12-23 weeks of age. Additionally, those animals gonadectomized later than 24 weeks had significantly more minor complications than those at 12 weeks of age (7.8 % and 3.6 % respectively). Among those gonadectomized at 12 weeks of age, females had significantly more overall and minor complications than males, probably because of the more complex surgery in females. The most common complication was problems with the surgical incision. Cats had a lower frequency of complication probably because of the easier surgery in cats compared with dogs (Howe, 1997).

5.16 Neoplasia

In aged dogs, testicular neoplasia is common with a reported incidence of 0.9 %. Sertoli cell tumors, Leydig cell tumors and seminomas are reported to be the most common. Gonadectomy is preventative and no influence of the age at gonadectomy has been reported (Root 2012).

Transitional cell carcinoma is the most common tumor of the urinary bladder in dogs. The incidence is 1% of all malignant tumors in dogs and it rarely occur in cats. The tumor is more common in females than males. Gonadectomized animals have 2 to 4 times higher risk for development of transitional cell carcinoma compared to intact animals. No differences at the age of gonadectomy is reported and an exact cause and effect had not been defined (Root 2007; McKenzie 2010).

Osteosarcoma is a bone tumor with a very low prevalence. The overall occurrence is 0.2 % and is usually seen in large breed dogs (Root 2012). A study showed a twofold increase in the occurrence of osteosarcoma in gonadectomized animals (Ru et al. 1998). Bone sarcoma was diagnosed in 12.5% in Rottweiler dogs in one study. An increased risk of developing osteosarcoma was seen in males and females gonadectomized before 1 year of age compared to dogs that were intact (Cooley et al. 2002).

Overall incidence of haemangiosarcoma in dogs and cats are 0.2% and 0.03% respectively. The occurrence of haemangiosarcoma is reported to increase in gonadectomized animals. Gonadectomized female dogs had a four time greater risk of developing haemangiosarcoma than intact females while gonadectomized males had only a slight increased risk of developing haemangiosarcoma compared to intact males. No information was provided on the age at gonadectomy (Reichler, 2009).

5.17 Secondary sex characteristics

The external genitalia in cats and dogs gonadectomized at an early age is less developed compared with animals gonadectomized at a more traditional age or left intact (Stubbs et al. 1996; Root et al. 1996b; Salmeri et al. 1991). Male cats gonadectomized at 7 weeks of age were not capable of complete penile extrusion and only 1/3 to 2/3 of the penis length could be visualized (Root et al. 1996b). However, in a second study all male cats, castrated or left intact, were capable of penile extrusion at one year of age. Additionally, in cats

gonadectomized at 7 weeks of age the penile spines were absent, atrophied in those gonadectomized at 7 months of age and in those left intact the penile spines were fully developed (Stubbs et al. 1996).

The os penis in dogs gonadectomized prepubertally was shown to be smaller and the radiodensity was decreased compared to dogs gonadectomized at 7 months of age or left intact (Salmeri et al. 1991). In both female dogs and cats the vulva appeared smaller in those gonadectomized at 7 weeks and 7 months of age compared to intact females (Salmeri et al. 1991; Stubbs et al. 1996).

Table 4
Effect of gonadectomy in dogs and cats

Condition	*Occurrence*	*Effect of gonadectomy*	*Species affected*	*Comment*
Mammary neoplasia	Very common	Decreased	Dog and cat	Greatly reduced if spayed before the first estrus
Pyometra	Very common	Decreased	Dog and cat	Prepubertal gonadectomy is not shown to have a more diminishing effect.
Benign prostate hypertrophy	Very common	Decreased	Dog	No effect of the age at gonadectomy
Behavior problems	Common	Variable	Dog and cat	Conflicting studies: less aggression, sexual behaviors and urine spraying
Urinary incontinence	Common	Increased	Dogs	In one study, the decreasing age at gonadectomy increases the incidence of urinary incontinence
Hip dysplasia		Increased	Dog	The incidence of hip dysplasia was higher in prepuberal gonadectomized dog

Table 5
Effect of gonadectomy in dogs and cats (continue)

Delayed growth plate closure		Increased	Dog and cat	Higher incidence in those gonadectomized prepubertally.
Cranial cruciate ligament		Increased	Dog	Higher incidence in prepubertal gonadectomy
Obesity	Common	Increased	Dog and cat	No effect of the age at gonadectomy
Parvoviral infection		Increased	Dog	Higher incidence in those gonadectomized less than 24 weeks of age
Surgical complications		Decreased	Dog and cat	Less in those gonadectomized prepubertally
Transitional cell carcinoma	Uncommon	Increased		Not influenced by the age at gonadectomy
Osteosarcoma	Uncommon	Increased		Not influenced by the age at gonadectomy
Haemangiosarcoma	Uncommon	Increased		Not influenced by the age at gonadectomy
Testicular neoplasia	Uncommon	Decreased		Not influenced by the age at gonadectomy
Size of vulva		Decreased	Dog and cat	Not influenced by the age at gonadectomy

6. Conclusion

Pediatric anesthesia and surgery are considered safe procedures as long as the different pediatric physiology is taken into account. Compared to adults, the organs in young animals are still immature and not fully developed. Since the kidney and liver function more slowly than older animals the anesthetic agents will have a prolonged effect in the body before they are metabolized and excreted. The advantage of pediatric anesthesia is the usage of low doses and the recovery is quite short. The benefits with the surgery in pediatric animals is the shorter time, less invasiveness and minimal bleeding. The surgery is performed more or less similar to adult animals but due to the more friable tissues extra care should be practiced.

The primary reason for prepubertal gonadectomy is the population control. In the United States, there are millions of homeless animals and the number of animals euthanized each year is excruciating. Prepuberal gonadectomy make sure that animals cannot repopulate after adoption and this contribute to the prevention of more homeless animals. Other benefits of gonadectomy is reduction in mammary tumors, pyometra and benign prostatic hypertrophy. Mammary tumors have shown a tremendous reduction in animals gonadectomized before the first heat while pyometra and BPH is not connected to the age at gonadectomy. Prepuberal gonadectomy has shown an alteration is sexual behavior and reduction in roaming, urine marking and aggression towards veterinarians. In one study, the cats had a lower incidence of abscesses, which can be in correlation with less roaming and aggression (Spain et al. 2002).

Obesity may be a problem in gonadectomized animal. Different studies have compared animals at 7 weeks of age, 7 months of age and those left intact. The falciform thickness, which were evaluated by radiography, appeared to be thicker in gonadectomized animals. Gonadectomy results in lower metabolic rate, which may be one of the reasons of gaining weight. There was no differences, however, between prepuberal and traditional age gonadectomy.

Different orthopedic problems have been connected to prepuberal gonadectomy. There is some conflicting studies regarding hip dysplasia. One study found differences between those gonadectomized before and after 5 months of age while another study found no increased incidence of hip dysplasia in animals gonadectomized prepuberally. However, the incidence of hip dysplasia in the first mentioned study was 6.7 %, which is relatively low occurrence. The closure of the growth plates appear to be delayed in gonadectomized animals and there seems to be a slightly higher incidence in those gonadectomized prepuberally. Prepuberal

gonadectomy is showed to have a predisposing effect on the rupture of cranial cruciate ligament.

Different tumors appear to have an increased incidence in gonadectomized dogs and cats. Transitional cell carcinoma, osteosarcoma and hemangiosarcoma is reported to have an increased incidence while testicular tumors have a reduced occurrence. Even though the incidence of these tumors are increased with gonadectomy the occurrence is less than 1 % which is a very low occurrence rate. The rate of these tumors are not higher in animals gonadectomized at an early age.

Gonadectomy showed to alter the size of sexual organs in both males and females. The vulva appeared smaller in those gonadectomized and male cats had problems with extruding the penis in one study. This is not considered serious and will not be a disadvantage for the animal. The incidence of urinary incontinence after gonadectomy is a bit conflicting since one study got a higher incidence of urinary incontinence in animals gonadectomized at an early age while a more recent study found no correlation between urinary incontinence and gonadectomy.

Many of the studies published look at the comparison between gonadectomized and intact animals without the regard for age at the time of gonadectomy. It can appear that there are more risks than benefits with gonadectomy but many of the diseases have a very low incidence and are easily treatable. Many of the studies are relatively old and more recent studies have not been performed. No significant short- and long-term effect have been reported when comparing prepuberal gonadectomized dogs and cats to those animals gonadectomized at a more traditional age. Performing early-age gonadectomy is considered safe and does not differ much from gonadectomy at a more traditional age.

7. Summary

The aim of the study was to do a review of studies regarding prepuberal gonadectomy and to look at the anesthesia, surgical techniques and possible benefits and risk. Prepuberal gonadectomy is the removal of reproductive organs in males and females less than 5 months of age.

Prepuberal gonadectomy is considered safe regarding the anesthesia and surgery. Low doses of anesthesia is needed and the animal will recover rapidly. Surgery is less invasive and minimal bleedings are observed. Surgical techniques are done similarly as traditional age gonadectomy with only a few exemptions. The clipping and disinfection of the surgical area should be as minimal as possible to preserve the body heat.

The benefits and risks of prepuberal gonadectomy does not differ significantly from traditional age gonadectomy. Prepuberal gonadectomy is showed to have an increased incidence of delayed growth plate closure and rupture of cranial cruciate ligament. Furthermore, gonadectomized animals are prone to gain more weight than intact animals. Different types of neoplasia in different organs tend to have an increased occurrence in gonadectomized animals but the incidence is quite low.

The primary benefits of prepubertal gonadectomy is the population control and the decreased incidence of mammary tumors. Gonadectomy before the first heat seems to be preventative for the development mammary tumors. Other diseases connected to the reproductive organs, such as pyometra, benign prostatic hypertrophy and testicular neoplasia, will have a great reduction. The behavior is shown to have, especially in cats, a reduction in the sexual behavior and less roaming and urine marking.

Prepuberal gonadectomy does not differ much from gonadectomy at traditional age and can be performed safely without any common and serious risks.

8. Acknowledgement

9. References

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