

Gonadectomy: What is known, pros and cons, and does age really matter?

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Recent publications have examined the relationship of gonadectomy to the risk of developing cancer, orthopedic conditions, age-related change and associated morbidity/mortality. This talk is aimed at reviewing the current literature and becoming comfortable and conversational about this topic with clients in the exam room.

Outline

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What were you taught? What are we teaching now?

The teaching of small animal theriogenology topics in the veterinary curriculum has evolved significantly over the last 20 years. In fact, I would argue that what is taught on this particular subject has changed more during that time than any other discipline in our profession. Those who graduated prior to 1990 were likely taught a great deal about theriogenology and were accustomed to seeing patients who were intact males and females. Those who graduated between 1990 and 2005 were likely taught very limited small animal theriogenology except to neuter every pet, no matter the gender or age (I fall into this category). For those who have graduated since 2005, there has been a major shift in the mindset of both pet owners and also our profession, and as such, we are all beginning to question and investigate when, and even whether, every pet should be gonadectomized.

Within the current veterinary curriculum at our institution, DVM students are expected to learn reproductive physiology of all species during their first year physiology course (17 lectures total). In the fall semester of the third year, a Reproductive Systems course is taught (4 credit hours) which focuses on clinical theriogenology of all domestic species. Currently, 13 of the 64 lectures (20%) are devoted to small animals, including two lectures/discussions on the effects of neutering. Depending on when and where you attended veterinary school, this probably sounds like a surprising change. I believe that the students who are graduating now will be the ones to encounter this paradigm shift in pet ownership as it relates to the decision of neutering, and thus will likely see more intact dogs and cats throughout their career.

To neuter or not to neuter? Deciphering the Literature

Many terms are used for gonadectomy. For the female, these most often include spay and ovariectomy. For the male, we most often use neuter, castration, or orchiectomy. For the purposes of this discussion, and for searching the literature, **we consider the terms gonadectomy and neuter to mean the same thing: removal of the gonads (and usually the associated structures) from either a male OR female pet.**

An article in JAVMA (May 15, 2017) summarized the welfare implications of gonadectomy on the canine population. With 162 references, it was a comprehensive look at the last 20 yrs of pet ownership, population control implications, and a review of the literature regarding the impact of gonadectomy on quality and quantity of life for pets.

Relative risk is described as the strength of association between the disease (e.g. osteosarcoma) and exposure to the factor (e.g. gonadectomy). For example, if relative risk = 1.0, then exposure to the factor (gonadectomy) does not affect an animal's chance of developing the disease (osteosarcoma). If relative risk >1.0, then exposure to gonadectomy indicates an increased risk for developing osteosarcoma. **Overall prevalence of the disease must be considered for correct interpretation of relative risk.** For example, an increased relative risk for a common disease (e.g. lymphoma) is much more important than an increased relative risk for an uncommon disease (e.g. prostatic neoplasia).

When evaluating the risk vs benefit of gonadectomy for an individual animal, we must consider the following:

- **Prevalence of the disease/condition within *the general canine population***
- **Prevalence of the disease/condition within *that breed***
- **Morbidity and mortality of the disease/condition**

When reviewing the literature, keep the salt handy, and consider the following challenges and limitations when making conclusions:

- Inconsistencies in patient categorization (age at time of Sx), definitions of "early gonadectomy" (<5.5 months vs <12 months)
- With no central database for veterinary medical records, determining incidence of certain diseases is a challenge
- Retrospective studies have the challenges of:
 - Dichotomous binning: e.g. 'intact vs Ovx,' rather than 'years of hormonal exposure'
 - Selection bias in populations
 - Owner participation in surveys; recall bias

Neoplastic Conditions Associated with Gonadectomy

Neoplasia has recently become one of the biggest concerns of pet owners regarding when, and whether, to neuter their pet. While neutering can prevent some types of neoplasia, it has also been shown to increase the incidence of other types of neoplasia. Studies have indicated that cancer is the cause of death in 15-30% of dogs and 26% of cats.

Neutering has been shown to decrease the incidence of mammary neoplasia in dogs and cats. The risk of developing mammary neoplasia increases with each subsequent estrus cycle, just as many of us were taught in vet school. Mammary cancer is one of the most common types of neoplasia in small animals, with an incidence in the US of roughly 3.4%. This incidence is much higher in Europe, where more pets remain intact. Mammary neoplasia is malignant ~50% of the time in dogs and ~90% of the time in cats. The study conducted by Schneider et al calculated the relative risk of mammary gland

tumors as 0.05% when bitches are neutered prior to their first estrus, 8% when neutered after their first estrus, and 26% when neutered after their second estrus. Thus, the concern for mammary neoplasia is certainly a sound reason to neuter a pet.

Neutering also decreases the risk of ovarian and uterine neoplasia in intact female dogs and cats since these tissues are removed at the time of neuter. Unlike mammary neoplasia, the incidence of these tumors is much lower, as is the associated morbidity and mortality. Testicular tumors in the dog are relatively common, but malignancy and mortality are low. Thus, making the case to neuter a male dog for the sake of preventing testicular tumors, or neutering a female to prevent ovarian or uterine neoplasia, is not as strong of an argument.

For other (non-reproductive) types of cancer, there is great variability and this has been the source of most recent investigations into this topic. **While it may be incorrect to state that neutering causes certain types of cancer, it certainly has been shown that neutering is a risk factor (one of several) for developing certain types of cancer.** See the chart below for a quick summary of the association of neutering with some of the most significant (malignant) types of neoplasia.

Table1: Summary of relative risk for common tumors.*

	Mammary tumor risk/ risk for malignancy	Bone tumor risk	Vascular tumor risk	Lymph tumor risk	Cutaneous tumor risk
All Breeds	9-25% intact; 50-94% malignant	0.3% intact; 98% malignant	0.3% intact; 87% malignant	0.3% intact; 100% malignant	15% intact; ~1% MCT
Effect of spay-status	25-95% reduction in tumor dev.	1.3-5 fold increase	2-9 fold increase	2-4 fold increase	2-4 fold increase (MCT)
Extrapolated risk in spayed animals	0.9-6%	0.4-5%	0.6-2.6%	0.6-1.2%	15-20%; 4% MCT

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There is a decreased incidence of hemangiosarcoma, osteosarcoma, transitional cell carcinoma and prostatic adenocarcinoma in intact male and female and dogs. However, since intact pets (especially females) can be more challenging to own, this risk must be compared to the overall incidence of these diseases in the general canine population compared to certain breeds. Some informative articles have been published in the last 3-5 years gathering retrospective data from several breeds (Vizslas, Rottweilers, Golden Retrievers, Labrador Retrievers, German Shepherds; see reference list). While these articles must be deciphered carefully, they help us gain great insight into breed-specific risks and incidence rates of disease. Regarding the risks of neoplasia related to gonadectomy, we must give strong consideration to the prevalence of the type of neoplasia within the general pet population, and also within a specific breed.

Non-neoplastic Conditions Associated with Gonadectomy

Regarding non-neoplastic concerns, there are a multitude of conditions that have been studied to examine their relationship to neuter status. The table below serves as a quick summary of common conditions and the effect of neutering.

Table 2: Effect of neuter and breed predispositions.*

	Population most affected	Estimated incidence	Breed predisposition	Effect of neuter	Effect of early neuter
Perioperative complications	F/S	6-27%	Large dogs		unknown
Ovarian remnant syndrome	F/S	1-2%	Large Dogs		unknown
Pyometra	F/I	25% by age 10		90+% reduction	no effect
Urinary incontinence	F/S	2-20%	Boxer, Doberman, Rottweiler, Old English Sheepdog, Giant Schnauzer	5+ fold increase	unknown
Urolithiasis: struvite	F/C	0.3-1%	Spaniel, Pekingese, German Shepherd Dog, Dachshund	7 fold increase	unknown
Urolithiasis: Oxalate	M/C	0.3-1%	Small, Toy Breeds	7 fold increase	unknown
Cystitis (recurrent)	F/S	14% (0.3%)	German Shepherd Dog, Dachshund, Doberman, Pincher, Spaniel, Golden Retriever	3-5 fold increase	unknown
Benign prostatic hyperplasia	M/I	50-80%	Unknown	90+% reduction	risk decreased
Joint Disorders	F/S, M/C	3-25%	Golden retriever, Boxer, German Shepherd Dog, St. Bernard, Labrador retriever	1.5-5 fold increase	risk increased
Cognitive dysfunction	M/C			Increased progression	unknown
Inappropriate urination	M/I	3-8%	Beagle, Bichon Frise, Cocker Spaniel	reduction	no effect
Roaming	M/I			reduction	no effect
Aggression	M/I, M/C, F/C	5-20%	English Springer Spaniel, German Shepherd Dog, Mixed	Inter-dog aggression reduced; Aggression toward family member increased	No effect; risk increased
Anxiety-related behavior	F/C, M/C	7-10%	Vizsla, German Shepherd, Beagle, Golden Retriever, Labrador Retriever, Mixed	2-4 fold increase	risk increased
Obesity	F/C, M/C	3-5%		3-20 fold increase	unknown

*Used with permission from author: C. Scott Bailey. Non-cancerous conditions associated with spay/neuter status in the canine. 2016. Clinical Theriogenology, Vol 8;3: 203-206.

Regarding reproductive concerns, the two most important are pyometra and benign prostatic hyperplasia (BPH), both of which increase with age in intact animals. The risk of pyometra is significant, increases with age, and the morbidity and mortality can be quite high (especially if

untreated). Thus, pyometra alone is a strong argument towards neutering in females. Even in exceptional purebred dogs that have been used for breeding purposes, we recommend ovariohysterectomy as soon as sufficient litters are obtained (to prevent pyometra, to help prevent mammary neoplasia, to eliminate the risk of unwanted pregnancies, and to make her a more convenient pet). With regard to BPH, it is a common disease of intact males, the incidence increases with age, but the morbidity and mortality are typically low (when identified early and managed correctly).

Obesity has long been critically evaluated for its relationship to neutering. Several studies have demonstrated neutering as a risk factor for obesity (although not the only risk factor for obesity). The literature is actually sparse when it comes to examining the effect of neutering on metabolic rate. Some speculate that it is not a direct effect on metabolic rate, but rather a resultant lack of drive or desire to explore created by the loss of hormones. Although experts cannot all agree on the mechanism by which it happens, all agree that there is a correlation between neuter status and body condition score (BCS). Most DVMs caution clients about this and even recommend a decrease in caloric intake following neuter. In most pets, this can be effectively managed by diligent clients. Thus, obesity alone is not an effective argument toward allowing a pet to remain intact.

Neuter status has also been demonstrated as a risk factor for various joint disorders, most notably cranial cruciate rupture and hip dysplasia, in multiple studies. Similar to obesity, orthopedic conditions likely have several risk factors. When reading the literature, it is speculated that this increase in orthopedic disorders could be due to a loss of ligament integrity from the lack of positive hormonal influence in both males and females, or perhaps a loss of muscle tone from the lack of testosterone in male dogs. Although obvious to us, it is worth discussing with clients that we should not become so fixed on the decision to neuter that we lose sight of other important risk factors for joint disorders such as lack of activity and obesity. For example, there seems to be an increased incidence of capital physal fractures in castrated male cats, but this may be partially due to increased weight gain in gonadectomized males. Breed predisposition should also be emphasized with regard to joint disorders and the decision of when to neuter, especially in dogs. In breeds predisposed to orthopedic problems, it is certainly worth considering leaving them intact for as long as is reasonable given their situation.

The relationship to urolithiasis and cystitis illustrated in the table above cannot be ignored. Although originally speculated as a decrease in urethral diameter following neuter, this has since been disproved as the cause. Many now speculate that perhaps it is the frequent flushing of the urethra (marking territory) that helps keep urolithiasis at bay in intact animals. Regardless of the cause, urolithiasis is certainly a very treatable condition with low morbidity and mortality in dogs and thus, is not an argument against neutering.

All of the non-neoplastic conditions that have been associated with neutering should be considered on an individual animal basis. Is it a predisposed breed? What is the dog's job (family pet, working dog, etc)? Is it even realistic to allow the dog to remain intact given its job? **Although we cannot ignore that there is a relationship between some of these conditions and neutering, sometimes neutering is just what needs to be done, regardless of the consequences down the road.**

What is your opinion? Does your opinion matter?

Every DVM should have an opinion on this topic. And we don't all have to share the same opinion. Most importantly, our professional opinion should be well-founded on facts and we should be able to make sound, defensible recommendations to each client. Science is important. Facts are important. Research is important. But at the end of the day, no one sees the ENTIRE picture more clearly than the family's veterinarian. Thus, **your professional opinion is the most important** and your

opinion should be clearly communicated to the owner without reservation. *As veterinarians, the most impactful statement that we make to owners regarding their pet's health is, "If he were my dog, I would _____."*

What does all of this mean for a DVM in private practice?

In unowned/shelter animals, decisions for neutering should be made from a population medicine or kennel perspective. This is typically performed at an early age in both males and females, and most of those animals are adopted and go on to live a long, healthy life. In these situations, there is a delicate balance between making the best decision for the pet versus making the best decision for prudent use of financial resources for the entire population of animals housed in that facility.

However, for owned animals, these decisions should be made on an individual case-by-case basis. Consider this joint position statement from the Society for Theriogenology and the American College of Theriogenologists regarding the mandatory spay-neuter requirements put forth by some municipalities:

The American College of Theriogenologists (ACT) is the certifying college for veterinarians board certified in reproduction (specialists), and the Society for Theriogenology (SFT) is an organization of veterinarians with a special interest in reproduction in veterinary medicine. The ACT and SFT believe that companion animals not intended for breeding should be spayed or neutered; however, both organizations believe that the decision to spay or neuter a pet must be made on a case by case basis, taking into consideration the pet's age, breed, sex, intended use, household environment and temperament. The use of generalized rules concerning gonadectomy (removal of the ovaries or testes) is not in the best interest of the health or well-being of the pets or their owners.

Based on the research available, it is clear there are a number of health benefits of the sex steroid hormones and that this benefit varies with age, sex, and breed. Therefore, although spay-neuter is the responsible choice for most pets, it is in the best interest of each individual patient for its veterinarian to assess the risks and benefits of gonadectomy and to advise his/her clients on what is appropriate for each individual pet at each stage of its life.

*expanded statement with references: http://c.ymcdn.com/sites/www.therio.org/resource/resmgr/docs/spay-neuter_basis.pdf

In almost all of the conditions discussed, both neoplastic and non-neoplastic, gonadectomy prior to puberty or sexual maturity may make the risks of some diseases higher. This is especially true in breeds which are predisposed to certain conditions. In those situations, it may be worthwhile to leave the animal intact until 12-18 months of age (musculoskeletal maturity) *IF that is a realistic option.*

No matter how far we come in our knowledge of this topic, our most important job is to see the whole picture. The animal's behavior, disposition, and ability to do its job (usually as the family pet) should still remain the key factor influencing the decision for gonadectomy.

References and resources:

- www.therio.org (SFT membership info, including full library access; conference info; DVM search tool; SFT proceedings)
- www.avis.org (free resource for DVMs; mtg proceedings available from several organizations)
- Pubmed (www.pubmed.gov),
 - Can read abstracts, but may not be able to access full text of all articles without a subscription (or library access through SFT, etc).

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