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THE NEUTERING CONTROVERSY

Understanding Data on Hormones, Behavior and Neoplasia

***Vanna M. Dickerson**, DVM, MS*
***Janet A. Grimes**, DVM, MS, DACVS-SA*
***Mandy L. Wallace**, DVM, MS, DACVS-SA*
University of Georgia College of Veterinary Medicine

The decision to spay and neuter companion animals has been a subject of much debate for decades. From a population control standpoint, the answer seems simple. The American Society for the Prevention of Cruelty to Animals estimates that roughly 7.6 million animals enter shelters in the United States each year, a large proportion of which are euthanized.[1] Given this staggering number, decreasing the number of births through spaying and neutering seems like a straightforward decision; however, it is not that simple.

New research has brought to light potential downsides to spaying and neutering that should be considered. How does one answer the questions raised by a responsible pet owner regarding their individual animal? This article discusses literature exploring potential links between gonadectomy and various neoplastic and nonneoplastic disorders in dogs.

NEOPLASIA

Many studies have explored the potential relationship between gonadectomy and various forms of neoplasia. Most available literature is retrospective in nature; therefore, proof of direct causation is lacking. Bias secondary to unknown environmental factors, veterinary care, and diet, among other factors, is difficult to address retrospectively. Gonadectomy has been associated with an increase in lifespan, which may be a source of bias as many forms of neoplasia are more common in dogs of advanced age.[2]

Reasons for choosing to spay or neuter an animal are also multifactorial. For instance, owners of purebred dogs may be more likely to choose gonadectomy in a pet with a known familial history of disease. Incidence for a particular neoplasia following gonadectomy may also be breed specific.

JUDGMENT CALL
The decision to spay or neuter a pet should be an individual one with a thorough discussion between the owner and the veterinarian about what risks are present and how they may affect the particular patient. Male Labrador retrievers castrated before 6 months of age had a significantly higher incidence of cranial cruciate ligament (CCL) rupture and elbow dysplasia than intact males.

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Nonetheless, repeatable trends provide guidance for future studies investigating the pathophysiology and influence of sex hormones on cancer. Prospective studies including a greater number of patients and attention to decreasing potential confounding factors should be performed.

Urogenital and Mammary Neoplasia

Decreasing the risk of mammary cancer, along with eliminating the risk of ovarian, uterine, or testicular cancer, are among the most common reasons cited to encourage spaying and neutering of companion animals.

Castration is associated with improvement in some undesirable behaviors, such as roaming, mounting, and urine marking in male dogs.

Mammary cancer in dogs carries a 50% chance of malignancy, with surgery being the treatment of choice.[3] Removal of the ovaries before the first heat cycle reduced the risk of mammary cancer to 0.5% in one study, compared to a 26% risk when a dog is spayed after 2 or more estrous cycles.[4] This protective effect is decreased after the first estrous cycle and lost once a mammary tumor has developed.[3,5] A recent systematic review of literature evaluating the impact of ovariectomy on the risk of canine mammary neoplasia determined that evidence supporting the protective link is weak, largely because of the potential for bias in the majority of the studies investigated.[6]

Although castration greatly reduces the risk of canine prostatic diseases such as benign prostatic hyperplasia (BPH), castration is not protective against prostatic neoplasia. Several studies have shown an increased incidence of prostatic cancer in castrated dogs compared to intact male dogs, with a risk increase 2 to 4 times that of intact males.[7] One study found an increased risk for all types of prostatic neoplasia in castrated dogs, including transitional cell carcinoma (TCC), adenocarcinoma, and carcinoma.[8] Limitations to these studies include that no case controls were included and the impact of age at castration was not evaluated.

TCC of the urinary bladder is a relatively uncommon but devastating neoplasia in dogs. TCC is generally more common in female dogs than male dogs; however, gonadectomy has been associated with an increased incidence in both sexes.[9] One study found castrated males to have a 3.6 times higher risk than intact males for development of urinary bladder TCC.[8]

Hemangiosarcoma

Splenic hemangiosarcoma (HSA) is a common disease in dogs. Early retrospective studies demonstrated a predisposition for development of splenic HSA in spayed female dogs compared to intact female dogs.[10] A recent retrospective study evaluating golden retrievers presenting to a single referral institution found a higher incidence of HSA in females spayed after 12 months of age (rate of diagnosis, 7.4%) compared to intact females (1.6%) and females spayed before 12 months of age (1.8%).[11] This suggests that either early spaying is protective against HSA in golden retrievers, or, more likely, that duration of sex hormone exposure is not a causative factor in development of the disease.

Neuter status did not affect the rate of diagnosis of HSA in male golden retrievers in this study. The study evaluated more than 700 golden retrievers; however, the number of dogs with HSA was small: 10 females and 10 males. In this study, patients diagnosed with HSA at ages older than 9 years were excluded, which may have introduced bias as splenic HSA has previously been documented to be more common in dogs between 8 to 13 years of age.[10]

A recent retrospective study, in which the data were obtained by questionnaires available to owners of vizslas through the Vizsla Club of America website, found spayed female vizslas had a higher incidence of HSA than intact female vizslas; however, diagnoses were not confirmed by review of medical records. The study found spayed female vizslas to have 9 times the risk of intact females for developing splenic HSA.[12] Neuter status did not affect odds of HSA diagnosis in male vizslas. The number of affected dogs was moderate in this study, with a total of 43 female and 30 male vizslas diagnosed with HSA.

Despite the pitfalls of retrospective studies, collectively these data suggest a possible link between gonadectomy and the incidence of HSA in female dogs. This was corroborated in a review of the Swiss Canine Cancer Registry; over 1900 cases of

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HSA were identified, and spayed females were at a 1.6 to 2.2 times higher risk of developing HSA when compared to intact females.[13] The underlying pathophysiology of this apparent increased risk is unknown, and warrants further investigation. Studies with higher numbers of dogs affected with HSA are necessary to determine if a true link exists between gonadectomy and development of HSA.

Osteosarcoma

Osteosarcoma (OSA) is another type of neoplasia for which a possible increased risk after gonadectomy has been suggested. OSA primarily affects large-breed dogs, and it is associated with poor long-term survival rates despite aggressive treatment. Experimental studies have shown variable relationships between sex hormones and OSA, with some suggesting suppression and others promotion of the disease.[14] The pathophysiology of the potential link between sex hormone exposure and OSA risk in dogs has not been investigated.

An increased risk of hip dysplasia and cranial cruciate ligament (CCL) rupture has been demonstrated in castrated male dogs.[34] The same study reported spayed females have an increased risk of CCL rupture, but no increased risk of hip dysplasia compared to intact females.

A large case-control study evaluating dogs from several institutions found the risk of developing OSA in gonadectomized dogs to be 2 times that of intact dogs, regardless of sex.[15]

A study evaluating approximately 700 rottweilers with 86 confirmed cases of appendicular OSA found that gonadectomy before 12 months of age significantly increased the risk of developing OSA.[14] This study was conducted via owner questionnaire; however, veterinarians were contacted to confirm diagnoses. Interestingly, gonadectomized dogs in this study had a longer life expectancy than intact dogs. This may contribute to the apparent increased risk of OSA in gonadectomized dogs, as OSA is frequently diagnosed in geriatric patients.

Mast Cell Tumors

Mast cell tumors (MCT) represent approximately 25% of all cutaneous neoplasms in dogs, with prognosis varying based on grade.[16] A study including approximately 150 dogs with cutaneous MCT found that gonadectomized vizslas were 3.5 times more likely to be diagnosed with MCT than intact vizslas across both sexes in one study.[12] Additionally, gonadectomized vizslas were diagnosed with MCT at a significantly younger age than intact vizslas.

Gonadectomy was not found to affect the rate of MCT diagnosis in Labrador retrievers.[17]

A case-control study evaluating more than 300 dogs with MCT in multiple breeds found a 4 times higher risk of development of grade 2 or 3 MCT in spayed females over intact females and a 1.4 times higher risk in castrated males over intact males.[18] In contrast, gonadectomy did not significantly affect the diagnosis of MCT in a retrospective study evaluating golden retrievers.[11]

A large study evaluating more than 400 dogs with MCT disease in England found fewer MCT diagnoses in neutered dogs than in intact dogs.[19]

Collectively, these studies suggest neuter status may only be associated with diagnosis of MCT in certain breeds.

Lymphosarcoma

Lymphosarcoma (LSA) is the most common type of hematopoietic neoplasia in dogs. High-grade LSA may be fatal within weeks if not treated aggressively with chemotherapeutic agents, and even with appropriate treatment it is associated with a median survival time of approximately 1 year.[20] Male golden retrievers castrated before 12 months of age were 3 times more likely to be diagnosed with LSA compared to intact male golden retrievers; LSA was not diagnosed in males castrated after 12 months of age.[11]

When evaluating LSA in vizslas, gonadectomized vizslas were 4.3 times more likely to be diagnosed with LSA than intact vizslas across both sexes.[12]

Gonadectomy was not found to affect the rate of LSA diagnosis in Labrador retrievers.[17]

Larger-scale studies evaluating the impact of gonadectomy on other canine breeds have not been performed.

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NONNEOPLASTIC DISORDERS

Behavior

The impact of gonadectomy on behavioral disorders is important to consider, as frustrations with behavior often lead to relinquishment of companion animals to shelters. Given the vast impact of training and experiences when evaluating behavior in dogs, the potential for significant bias in behavioral studies is high.

While there is minimal to no strong evidence clearly linking gonadectomy to various diseases, owners of at-risk breeds should consider all factors.

Castration is associated with improvement in some undesirable behaviors, such as roaming, mounting, and urine marking in male dogs.[21] Inter-male aggression may also improve or resolve after castration, although other forms of aggression seem to be less affected.[22]

Fear behavior during veterinary visits has not been associated with reproductive status.[23]

A study in female German shepherd dogs demonstrated a possible increase in reactivity to unfamiliar people and dogs following ovariohysterectomy.[24] This study did not evaluate the dogs before surgery, was not blinded, and only evaluated 14 dogs.[24]

Behavioral disorders, such as storm phobia, may be more common in vizslas gonadectomized before 6 months of age than in intact vizslas.[12]

A case-control study evaluating a variety of dog breeds found a possible association between gonadectomy and separation anxiety, although the number of intact animals in both the case and control groups in this study was low.[25]

Gonadectomy has also been discussed as a contributing factor to cognitive decline in geriatric dogs. One study suggested intact male dogs may have slower progression of cognitive impairment than castrated male dogs.[26] This study had relatively low numbers and was only able to comment on male dogs because of the lack of recruitment of intact females.

Urogenital Disorders

Urinary incontinence is a disorder with an incidence of up to 1% in intact female dogs, compared to >20% in spayed females.[27] There is conflicting evidence regarding the importance of early versus late spaying and its impact on development of urinary incontinence in female dogs, with some studies reporting an increased incidence and frequency of episodes of incontinence in early-spayed dogs, while other studies report no difference between early and late spaying.[27] Larger-breed dogs are at higher risk than smaller-breed dogs.[28,29]

This condition can be quite frustrating for owners and veterinarians alike to manage; therefore, it should be taken into consideration when deciding to spay female dogs. Given the suspected association with gonadectomy, owners of dogs with signs of urinary incontinence as puppies may consider waiting at least until after the first heat cycle to perform spay surgery.

Pyometra is a condition of female dogs that is prevented by gonadectomy. Pyometra carries an incidence of approximately 25% by 10 years of age in intact female dogs. Though pyometra can be cured by ovariohysterectomy, the morbidity rate of dogs treated for pyometra is quite high, with an overall mortality rate of 10% reported in one study.[30]

BPH is a condition of male dogs that is prevented by castration.[31] BPH is diagnosed in nearly 100% of intact male dogs by the age of 9 years old. Although clinical signs are not always present, BPH predisposes dogs to prostatitis and may lead to dyschezia and subsequent perineal hernia due to tenesmus. Perineal hernias can lead to life-threatening entrapment of the urinary bladder, intestines, and other structures.[32]

Immune-Mediated Diseases

One study found an increased incidence of multiple immune-mediated disorders in gonadectomized dogs of both sexes, including atopic dermatitis, immune-mediated hemolytic anemia, hypothyroidism, immune-mediated thrombocytopenia, hypoadrenocorticism, and inflammatory bowel disease.[33] One possible explanation outlined in this study was a lack of sex hormone-induced involution of the thymus, as thymic hyperplasia has been associated with autoimmune disorders.

Orthopedic Disorders

An increased risk of hip dysplasia and cranial cruciate ligament (CCL) rupture has been demonstrated in castrated male dogs.[34] The same study reported spayed females have an increased risk of CCL rupture, but no increased risk of hip dysplasia compared to intact females.

Castrated male golden retrievers had nearly double the risk of hip dysplasia in one study, in addition to an increased risk of CCL rupture.[11]

Male Labrador retrievers castrated before 6 months of age had a significantly higher incidence of CCL rupture and elbow dysplasia than intact males.[17] This same study found an increased risk of hip dysplasia in spayed female Labrador retrievers compared to intact females, but no difference in incidence of elbow dysplasia or CCL rupture.

Gonadectomy before closure of physes is associated with lengthening of bones, which may contribute to an increased incidence of orthopedic disease. Since gonadectomy has also been associated with obesity, this could be a confounding factor contributing to the apparent association between sex hormones and orthopedic disease.[35] Additionally, case numbers in these studies were low.

CONCLUSION

Unfortunately, there is no clear answer when deciding whether one should spay or neuter an individual dog. While there is minimal to no strong evidence clearly linking gonadectomy to various diseases, owners of at-risk breeds should consider all factors. Given the potential for an increased lifespan, many owners may wish to accept the potential for cancers often associated with geriatric age to avoid nuisance behaviors associated with an intact animal and diseases such as pyometra or BPH.

Evidence for a link between gonadectomy and increased risk of the neoplastic, behavioral, immunologic, or orthopedic diseases mentioned in this article is weak and needs to be further explored with appropriately designed research studies. These risks may also be breed specific. The decision to spay or neuter a pet should be an individual one with a thorough discussion between the owner and the veterinarian about what risks are present and how they may affect the particular patient. TVP

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Vanna Dickerson

Vanna Dickerson, DVM, MS, is a small animal surgical resident at the University of Georgia. Dr. Dickerson attended veterinary school at University of Georgia, followed by an internship at Friendship Hospital for Animals in Washington, DC. After her internship she completed a research fellowship at University of Georgia, with a focus on models of kidney disease in cats.

Janet Grimes

Janet Grimes, DVM, MS, DACVS-SA, is an assistant professor of soft tissue surgery at University of Georgia. Dr. Grimes attended veterinary school at University of Georgia, followed by an internship at Texas A&M University. She then completed a small animal surgical residency at Auburn University. Dr. Grimes was previously a faculty member at Louisiana State University. Her research interests include canine hemangiosarcoma and sentinel lymph node imaging.

Mandy Wallace

Mandy Wallace, DVM, MS, DACVS-SA, is an assistant professor of soft tissue surgery at University of Georgia. Dr. Wallace attended veterinary school at Mississippi State University, followed by an internship at Colorado State University. After her internship, Dr. Wallace completed a PennHIP research fellowship at University of Pennsylvania, followed by a combined small animal surgical residency and master's program at University of Florida. Her research interests include hepatic vascular anomalies, minimally invasive surgery, and the impact of gonadectomy on canine diseases.

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