UNIVERSITY OF CALGARY
FACULTY OF VETERINARY MEDICINE

This review accompanies the relevant episode of the Cutting Edge veterinary podcast. In each episode of this podcast, 3rd year students in the University of Calgary's veterinary medicine program fill you in on the most up-to-date literature and evidence-based practices on topics that matter to you, the practising veterinarian.

Factors to Consider when Determining the Age of Desexing in Dogs

STUDENTS: Rachael Morrison, Bailey Harper and Heather Burnett
FACULTY MENTORS: Drs. Marina McConkey and Ning Cheng

Introduction

For many years, it has become common to routinely spay and neuter (desex) dogs around six months of age regardless of size and breed (1). Recent literature has raised questions regarding the evidence behind this decision pertaining to risks of neoplasms and development of joint disorders. Desexing was typically performed at or before six months of age for several reasons. Some of those reasons include controlling overpopulation and smaller vessels to ligate during surgery (2). There are a multitude of factors involved in determining at which age an owner should choose to desex their dog. These factors include but are not limited to musculoskeletal disorders, reproductive neoplasia and disorders, as well as non-reproductive neoplasia. The main issue that we will discuss is that of musculoskeletal disorders.

Almost all the research in the last decade has been done by one institution, and one group of authors in particular. The research that is currently available is based on specific breeds that are already predisposed to certain diseases. The data available is then skewed because those breeds are more likely to develop those cancers/disorders. Breed examples are Golden Retrievers and hemangiosarcomas, and German Shepherds and hip dysplasia.

Musculoskeletal Disorders

A topic of discussion is how early desexing can influence the occurrence of certain joint disorders especially in large breed dogs. The risk of desexing dogs before they reach skeletal maturity is that it can lead to increased occurrences of cranial cruciate ligament (CCL) injury, hip dysplasia (HD) and elbow dysplasia (ED) especially in large breed dogs (3, 4, 5, 6, 7, 8, 9, 10). The basis of this is the concept that desexing dogs before their growth plates have closed changes the longitudinal bone growth. These changes then increase the risk of joint incongruencies leading to the previously mentioned disorders (11).

A link between gonadal hormones and longitudinal bone growth exists in other species such as rats, rabbits, and humans. Rats, with removal of estrogen through ovariectomies, experience an increase in longitudinal bone growth (11). There is a dose-dependent decrease in

longitudinal bone growth with estrogen supplementation in rats (11). The administration of estrogen to desexed juvenile rabbits leads to earlier fusion of the growth plates (3). This link between gonadal hormones and longitudinal bone growth continues to be studied in human medicine (4).

Recent studies have tried to characterize the relationship between early desexing and occurrence of joint disorders in dogs. A study by Simpson et al found that Golden Retrievers who were ≤6 months old at the time of desexing had a significantly increased risk for CCL injury and osteoarthritis (OA) (4).

Another study was done by Torres de la Riva et al at the UC Davis teaching hospital (5). They looked at the records of Golden Retrievers between the ages of 1-8 years (759 animals total) and divided the population into 3 groups: desexed at ≤6 months, desexed >6 months, and intact. They did not find any cases of CCL injury in either intact males or females. This study did find that there was a significant increase in the occurrence of CCL injury in early desexed dogs. They found incidences of 5% in males and 8% in females for CCL injury. They also found that early desexed male dogs had more than twice the risk of developing HD.

In a review published in 2019 by Urfer et al the risk of CCL injury increased in desexed dogs compared to intact dogs from the general population. There was more variability in the risk of HD, ED and OA depending on breed, sex, and age of desexing (6).

Hart and colleagues have conducted several studies using the database of the UC Davis teaching hospital on dogs aged 1-8 years (7, 8, 9, 10). In 2014 they published a study comparing the incidence of joint disorders and cancers in desexed and intact Golden and Labrador Retrievers over a 13 year period (9). Similar to the Torres de la Riva study (5), they divided the animals into 3 groups: desexed at ≤6 months, desexed >6 months, and intact (8). They found that for both breeds, the group desexed at ≤6 months had a significant increase in the incidence of at least one joint disorder (HD, ED and CCL injury) compared to their intact counterparts. Golden Retrievers had a larger increase in risk going from 5% to 27% in males and from 5% to 20% in females. The increase seen in Labrador Retrievers was from 5% to 10% in males and to 12% in females. There was a difference found between breeds on which joint disorders had the largest increase. For male Golden Retrievers, HD and CCL injury were most increased compared to male Labrador Retrievers where it was CCL and ED that increased the most.

Another study by Hart published in 2016 using the same database examined the medical records of German Shepherds over a period of 14.5 years with 1170 dogs total (8). They found that the rate of joint disorders was significantly higher in those desexed before one year of age (21%) when compared to those left intact (7%). They observed the same trend in females desexed before one year old (increase from 5% to 16%). The most frequent joint disorder associated with early neutering was CCL injury.

Hart et al did another study using the same teaching hospital database (UC Davis) comparing different breeds (9, 10). They looked at 35 different breeds of dogs and compared the risk of disorders in relation to age of desexing. One major finding was a general increased risk of joint disorders with early desexing in relation to increased body size. Many of the small breeds noted did not show a significant increased risk for CCL injury, HD, or ED. They found that some giant breeds such as Great Danes or Irish Wolfhounds did not follow this trend and did not display an increased risk of joint disorders at any age of desexing. The authors once again found sex to be a variable that changed the significance of the risk of early desexing on joint disorders.

For example, in Rottweilers the risk of joint disease was higher in females. In males: intact: 8%, <6 months: 10%, females; intact: 16%, <6 months: 43%. This larger scale analysis supports many conclusions made by the previous papers discussed. Hart et al's (9) study highlights the complexities of the relationship between early desexing and joint disorders in two ways. First it is breed dependent which is shown by comparing Golden and Labrador Retrievers. They are similar in size and weight yet have significant differences in the way they responded to early desexing and joint disorders. This implies that expected adult weight is not enough to predict the outcome of early desexing on its own. Secondly it is sex-related. This is shown by the difference in the size of response between sexes of the same breed. This implies that breed-specific recommendations alone may not be adequate.

There is a well-established link between obesity in pets and joint disease (12). There has also been data to show that desexing animals can predispose them to obesity due to decreased metabolic rate (6). Many of the studies discussed confirmed that there is a relationship between obesity and desexing (4, 5). Yet those same studies did not show a relationship between body condition score and the risk of joint disorders. This implies that excess weight may worsen the joint disorders once present, but it may not be responsible for causing the disorders themselves.

Reproduction

Mammary Cancer

There is a belief in the veterinary community that desexing before the first estrus cycle in female dogs is protective against the development of mammary cancer. Many papers throughout the literature have supported this claim (13, 14, 15). The landmark paper on the topic was published in 1969 (15) and the data from this paper is often misinterpreted. The study states that the relative risk of mammary carcinoma is 0.5%, 8% and 26% for dogs spayed before their first cycle, after one cycle and after two cycles respectively. Overall, desexed dogs had a 12% increase in mammary cancer risk when compared to intact animals. These numbers do not represent the actual incidence, but some interpret them this way. The incidence of mammary tumors found in a Swedish insurance company database was 13% (16). Another finding from the landmark paper (15) is that animals desexed before 2.5 years of age (with a maximum 4 estrus cycles) showed a sparing effect for mammary cancer. However, there were only 87 dogs for case control matches in this study.

In a study of submitted histopathology samples, there was no difference in the odds ratio for diagnosis of neoplasia in mammary gland samples between intact or desexed females (17). Also, the outcome of the histopathological diagnosis was significantly associated with the breed of dog. Boxers, German Shepherds, and Jack Russell Terriers had increased odds ratio when compared to Labrador Retrievers.

Sorenmo and colleagues (14) completed a study on 137 dogs and determined that the most impactful effect of desexing related to mammary cancer was improving survival time of dogs with mammary neoplasia receiving a concurrent tumor resection. They reiterate the previous claim that the sparing effect of desexing on mammary carcinoma was minimal after 2.5 years. However, the data was collected via retrospective questionnaire completed by owners which introduces significant recall bias.

A systematic review published in 2012 used the Cochrane guidelines to evaluate the current evidence on the topic by evaluating many frequently cited papers (18). They found low to high levels of bias in all of them. Regarding the Schneider et al (15) paper in particular, they found that: it was not made clear if there was control for breed in the analysis, there were no confidence intervals or P values given only claims of significance, it was not stated if the cases were randomly selected and there was a small population of dogs used to reach these conclusions. Generalized areas of bias for the other papers included the age of the papers (many >40 years), which means new epidemiological methods were not used to evaluate the data. Also, major potential confounding factors were not considered, such as age, breed, and previous treatment with a synthetic estrogen product.

Overall, due to the considerable bias in the literature, the claim that desexing before the first heat cycle significantly decreases the risk of mammary carcinomas in dogs is not well supported (18). Further unbiased literature needs to be published before using the risk of mammary carcinomas in dogs to decide on age of desexing. However, it is important to note that there may still be a risk present, but the magnitude is unknown. The current literature suggests that it is important, like with all disorders, to consider the breed of the dog and its relative risk for mammary tumors. It is also key to note that the incidence is much lower than the relative risk reported in the Schneider et al (15) paper.

Urethral Sphincter Mechanism Incompetence (USMI):

A common current belief around USMI in dogs is that it can be reduced by spaying after the completion of at least one heat cycle. Although some studies have found a correlation with age of desexing and USMI occurrence (19, 20), others have shown no correlation or other factors to be of importance (21, 22). Vulvar conformation as well as adult body weight have been shown to interact with the age of desexing for occurrence of USMI (19, 21). A statistically significant relationship between age of desexing and USMI was found in dogs >25kg but not in smaller dogs (21). Also, dogs >15kg were at a near 7 times risk for developing USMI overall compared to smaller dogs (19). Both studies on weight had potential confounding factors. There were no intact animals included for a control even though USMI also occurs intact animals (22). Also, timing of diagnosis affects how cases are reported and included in research. For USMI, this depends on when owners bring their dog in and the dependability of their recollection. A systematic review of USMI literature using the Cochrane guidelines evaluated the evidence as weak and that the current literature is insufficient for recommendations on timing of desexing (20).

Prostatic Neoplasia:

Desexing increases the incidence of prostatic neoplasia by 2.84 times (23). However, this brings the risk to only 0.6% (13). As prostatic neoplasia is rare it should not be considered a major factor when determining age of desexing.

Pyometra:

Data from a Swedish insurance company revealed that the incidence of pyometra at 10 years of age was 13% (16). As it can be eliminated by desexing at time of diagnosis, it is not a disorder that should be considered of major importance when determining age of desexing.

Testicular neoplasia:

The most common type of testicular tumor is Leydig tumors which rarely metastasize. Sertoli cell tumors, although highly metastatic, have been found to have a lower prevalence (24). As non-metastatic disease is eliminated by neutering, and occurrence of highly metastatic tumors is low, testicular tumors should not be a major factor for determining age of desexing.

Other Neoplasms

There are four neoplasms associated with desexing: hemangiosarcoma (HS), osteosarcoma (OSA), lymphoma/lymphosarcoma (LS) and mast cell tumors (MCT) (5, 7, 8, 9, 10, 27, 28). The risks of these neoplasms are not only associated with desexing but also with the breed of dog. For Golden Retrievers it has been said that desexing quadruples the risk of cardiac HS, doubles the risk of splenic HS, and creates a 2-4 times increase in OSA (5, 7, 26, 27). In Rottweilers, desexing triples to quadruples the occurrence of OSA in females (26, 27). For LS there was a generalized increased risk in desexed females compared to males although the numbers were slightly different for each study (5, 7, 8, 9, 10).

In a study done by Hart et al in 2016 desexing did not increase the risk of the neoplasms studied in German Shepherds (8). A study done by Torres de la Riva et al in 2013 showed early desexed Golden Retrievers had an increased occurrence of LS compared to intact dogs (5), late desexing increased the occurrence of HS, with a mean age of 7.6 years, and no significance was found in MCT. Their study ended at dogs aged 8 years old and animals could have developed conditions after the study ended.

In the study done by Hart et al in 2020, the breeds that had a significant risk for developing one of the four neoplasms are Golden Retrievers, Boxers, Bernese Mountain dogs, Standard Poodles, Border Collies and Cocker Spaniels (9). Generalized findings from this study were that larger breed and female dogs had higher rates of neoplasms when desexed, and that genetics and breed predispositions play a large role.

Desexing Vizslas over 12 months of age significantly increased the risk of MCT and LS (25). Desexed females had an increased risk of HS and MCT (5, 7, 8, 9). For OSA and LS, there was an increased risk associated with desexing (28) but they had a stronger correlation with breeds and genetics than timing of desexing.

Bias in the literature

There were many different biases in the populations of dogs chosen. Many of the studies are retrospective and done through referral specialty hospitals, so the data may not be applicable to all populations. The population sizes are varied, especially in giant breeds and the more uncommon breeds. Some populations had 1000 dogs and others had 60. Another potential issue is that desexed dogs may be receiving more consistent vet care and be diagnosed with more disorders than the general population, especially those presenting to a tertiary level referral center. It is also argued that desexed animals in North America are usually owned and receive more regular vet care (6).

Conclusion

The current evidence suggests desexing after bone growth closure is protective against the development of joint disorders in predisposed dog breeds. Large breed dogs tend to be more affected by the removal of gonadal hormones (German Shepherds, Labradors, Golden Retrievers). However, breed and sex are both factors that must be considered in addition to predicted adult size. Different breeds of similar size and dogs of opposite sexes are affected differently by the removal of gonadal hormones. Studies of Golden Retrievers and Labradors did not find a correlation with increased BCS and joint disease with respect to reproductive status. Therefore, increased risk of joint disease is an important factor to consider when determining the best age to desex. The consequences of the risk in comparison to other factors, must be analyzed at depth to determine the ideal age for each patient. Recent research has shown that it is important for dogs to be skeletally mature before desexing (4, 5, 7). It is important to note that large breed dogs are not skeletally mature by 6 months. More research is needed to determine definitive ages when certain breeds should be desexed (6).

More research is needed into mammary neoplasia and desexing, as well as USMI. The landmark study (15) is often misquoted as reporting the occurrence of mammary cancer instead of the relative risk. Bias was found in many of the research papers on this topic, along with USMI. Dogs >25kg most likely should not be desexed until after at least one heat cycle (18).

Desexing increases the risk of certain non-reproductive neoplasias, however, these neoplasias may also be strongly associated with genetics and breed. There needs to be more research done to make any type of association with timing of desexing and the risks of neoplasia.

Based on the discussed findings we recommend waiting for skeletal maturity before desexing large breed dogs. Although other factors are likely important, there is not sufficient evidence at this point to support earlier desexing from a health perspective.

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