THE ROLE OF NEUTERING IN CANCER DEVELOPMENT

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Neutering is recommended under the pretense of providing health benefits to pets while potential negative effects are not well understood and rarely mentioned. Several studies, primarily focused on canines, examined potential undesirable influences of neutering on various health parameters. Most focus on breed specific disease syndromes, or combine data from several different breeds. Information is conflicting and challenging to interpret, especially with regard to the role of neutering and cancer risk in pets. Additionally, proving causality (e.g. “neutering causes cancer”) is difficult as disease development is multifactorial in nature.

The following is a summary of several of the pertinent studies examining the association between neutering and cancer, subdivided by tumor type.

MAMMARY TUMOR

The effect of neutering on the risk of mammary tumors in dogs - a systematic review. Beauvais W. JSAP 2012 Jun;53(6):314-22.

This meta-analysis study represents what is considered the highest order of research in the data publication pyramid. Of 11,149 search results, 13 reports in English-language peer-reviewed journals addressed the association between neutering/age at neutering and mammary tumors. Nine were judged to have a high risk of bias. The remaining four were classified as having a moderate risk of bias. One study found an association between neutering and a reduced risk of mammary tumors. Two studies found no evidence of an association. One reported "some protective effect" of neutering on the risk of mammary tumors, but no numbers were presented. The conclusion was there was limited evidence supporting the evidence that neutering reduces the risk of mammary neoplasia and the evidence that age at neutering has an effect. The risk of bias also indicates a lack of sound basis for firm recommendation for the practice of neutering to provide a benefit of protection against mammary tumor development.

OSTEOSARCOMA (OSA)

Host related risk factors for canine osteosarcoma. Ru G. Vet Journal 1998 Jul;156(1):31-9.

A twofold excess risk for OSA was observed among neutered dogs compared to intact dogs.

Endogenous gonadal hormone exposure and bone sarcoma risk. Cooley DM. Cancer Epidemiol Biomarkers Preve 2002 Nov;11(11):1434-40.

The risk for bone sarcoma in Rottweilers was significantly influenced by age at neuter. Male and female dogs neutered before 1 year of age had an approximate one in four lifetime risk for bone sarcoma and were significantly more likely to develop bone sarcoma than dogs that were sexually intact. There was a significant inverse relationship between duration of lifetime gonadal exposure and incidence rate of bone sarcoma.

HEMANGIOSARCOMA (HSA)

Epidemiologic, clinical, pathologic, and prognostic characteristics of splenic hemangiosarcoma and splenic hematoma in dogs: 217 cases (1985). Prymak, JAVMA 1988 Sep 15;193(6):706-12.

Compared with sexually intact females, neutered females were at significantly increased risk for developing splenic HSA.

Cardiac tumors in dogs: 1982-1995. Ware WA. JVIM 1999 Mar-Apr;13(2):95-103.

The relative risk of any cardiac tumor for neutered females was 4.38 times that for intact females and for neutered males was 1.6 times that for intact males. For cardiac HSA, neutered females had >5 times greater relative risk than intact females. The risk for castrated males was 1.55 times than that for intact males. Intact females were least likely to develop a cardiac tumor, whereas neutered females were most likely to develop a tumor. Neutering appeared to increase the risk of cardiac tumor in both sexes.

Neutering Dogs: Effects on Joint Disorders and Cancers in Golden Retrievers. Torres De La Riva G. PLOS One 2013;8(2):e55937.

The percentage of HSA cases in late-neutered (> 1 year of age) females (7.4%) was greater than intact (1.6%) and early-neutered (< 6 months) females (1.8%). No differences were apparent in males with regard to neutering and the occurrence of HSA.

Long-Term Health Effects of Neutering Dogs: Comparison of Labrador Retrievers with Golden Retrievers. Hart BL. PLOS One 2014;9(7):e102241.

In female Golden retrievers, the rate of HSA increased in dogs neutered > 1 year, but this did not reach significance over intact females. No increase in HSA rate was seen for male or female Labrador retrievers or male Golden retrievers.

Evaluation of the risk and age of onset of cancer and behavioral disorders in gonadectomized Vizslas. Zink MC. JAVMA 2014 Feb;244:309-319.

The odds of neutered female Vizslas developing HSA were 9 times greater than sexually intact females. There was no significant difference in the overall odds of neutered males having HSA, compared sexually intact males. However, specifically looking at males neutered at > 12 months, this group had a significantly higher odds ratio for HSA than did sexually intact males. The anatomic site of HSA development was not specified in this study.

LYMPHOMA (LSA)

Hormonal and sex impact on the epidemiology of canine lymphoma. JA Villamil. J Cancer Epidemiol 2009;2009:591753. doi: 10.1155/2009/591753. Epub 2010 Mar 14.

Intact female dogs had a significantly lower risk of developing LSA.

Neutering Dogs: Effects on Joint Disorders and Cancers in Golden Retrievers. Torres De La Riva G. PLOS One 2013;8(2):e55937.

Almost 10 percent of early-neutered (< 6 months) males were diagnosed with LSA, 3 times more than intact males.

Long-Term Health Effects of Neutering Dogs: Comparison of Labrador Retrievers with Golden Retrievers. Hart BL. PLOS One 2014;9(7):e102241.

Male Golden retrievers neutered between 6 -11 months of age had significantly higher rates of LSA than intact males (11.5% compared to 4%.) Female Golden retrievers neutered between 6–11 months had higher rates of LSA compared to intact females (not significant). For Labrador retrievers, neutering at any age had no effect above the level of intact males or females.

Evaluation of the risk and age of onset of cancer and behavioral disorders in gonadectomized Vizslas. Zink MC. JAVMA 2014 Feb;244:309-319.

When controlling for sex, the odds of a neutered Vizsla having LSA were significantly increased than those for sexually intact dogs. Age of neuter did not alter this finding.

Neutering of German shepherd dogs: associated joint disorders, cancers, and urinary incontinence. Hart BL. Vet Med Sci 2016:16;2(3):191-199.

No association between neuter status and LSA in either male or female German shepherd dogs.

MAST CELL TUMOR (MCT)

Cutaneous MCTs: associations with spay/neuter status, breed, body size, and phylogenetic cluster. White CR. JAAHA 2011 May-Jun;47(3):210-6.

Increased risk for MCT development was found in neutered females.

Neutering Dogs: Effects on Joint Disorders and Cancers in Golden Retrievers. Torres De La Riva G. PLOS One 2013;8(2):e55937.

There were no cases of MCT in intact female Golden retrievers versus 5.7% in late-neutered females. No differences were found in the occurrence of MCT in neutered or intact male Golden Retrievers.

Long-Term Health Effects of Neutering Dogs: Comparison of Labrador Retrievers with Golden Retrievers. Hart BL. PLOS One 2014;9(7):e102241.

Neutering had no effect on the development of MCT in male Golden retrievers. No intact female Golden retriever developed MCT and MCT were only seen in female Golden retrievers neutered in the 2–8-year period (incidence in this group was 3.5%.)

No significant differences in the occurrence of MCT were seen in Labrador retrievers of either sex and neuter status.

Evaluation of the risk and age of onset of cancer and behavioral disorders in gonadectomized Vizslas. Zink MC. JAVMA 2014 Feb;244:309-319.

The odds of a neutered Vizsla having a MCT were significantly higher (3.5 times as high) than were the odds for sexually intact dogs.

PROSTATIC TUMORS

Canine prostate carcinoma: epidemiological evidence of an increased risk in castrated dogs. Teske E. Mol Cell Endocrinol 2002 Nov 29;197(1-2):251-5.

Castration increased the risk of prostate carcinoma (PCA). The mean age at diagnosis of PCA in castrated dogs and in intact male dogs was not significantly different. The interval between castration and onset of prostatic problems was highly variable, suggesting that castration does not initiate the development of PCA in the dog, but it could favor tumor progression.

Clinical and pathologic aspects of spontaneous canine prostate carcinoma: a retrospective analysis of 76 cases. Cornell KK. Prostate 2000 Oct 1;45(2):173-83.

The vast majority of canine prostate carcinomas affected elderly sexually intact dogs or dogs that underwent surgical castration after sexual maturity. Duration of testicular hormone exposure was significantly different between dogs with adenocarcinoma and dogs with mixed morphology tumor, but did not appear to influence the frequency or pattern of metastases of these diseases.

TAKE HOME MESSAGE

There are several limitations to the aforementioned studies and it is advisable to interpret conclusions cautiously. The majority are retrospective in nature, and therefore subject to inconsistencies ranging from lack of accurate record keeping, lack of consistency in sample interpretation, and lack of available information. Bias is also a factor for retrospective studies: Most consist of pets presented to teaching hospitals and therefore are not likely representative of larger populations of animals. Many involve breeders, who are likely to be more aware of specific illnesses that occur more frequently in particular breeds. Several are questionnaire based, which selects for only those willing to respond as well as rely on memory rather than precise medical records.

Veterinarians must weigh the available information when making recommendations to owners regarding whether to neuter their pet or not, and at what age to consider performing the surgery. For some cancer types, not only may breeds vary in predisposition but also the possibility of interactions between sex, hormone influences, and timing of hormone alteration should be considered. Rather than making global recommendations regarding neutering, veterinarians should consider individual patient characteristics and owner goals and expectations for their pets.