

The Role of Neutering in Cancer Development



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KEYWORDS

• Neuter • Cancer • Sex hormone • Spay • Castration

KEY POINTS

- Sex hormone receptors have been found in some canine and feline tumors and implied in others through sex predilection or response to neutering.
- A few studies indicate that some tumor types may be increased in surgically altered dogs; other tumor types may be decreased in neutered animals.
- Neutering has other effects on certain behaviors, noncancerous diseases, and lifespan that may outweigh cancer risks.
- Recommendations may be different for owned animals and those in a shelter or rescue setting.
- Veterinarians and pet owners should discuss the risks and benefits of neutering for each individual.

INTRODUCTION

Sex hormones normally influence many tissues in the body, and hormone receptors are present in some canine and feline neoplasms: mammary tumors,^{1–6} meningiomas,^{7,8} perianal gland tumors,⁹ and likely others. The administration of exogenous hormones has been associated with the development of some tumors, such as progesterins in the development of canine and feline mammary tumors.^{10,11} Signalment of dogs that present with certain tumor types have been associated with variable sex predilection, implying hormonal influence. Other tumors may regress or have decreased recurrence after surgical alteration.^{12–14} Recently, increased scrutiny of the role of neutering in dogs on disease incidence has resulted in some interesting findings, and questions, on the potential role of sex hormones in cancer development in this species (**Table 1**).

Steroid hormones interact with cells in several ways: (1) diffusion through the cellular membrane and binding to cytoplasmic (androgen) or nuclear (estrogen) receptor proteins. The activated receptor then interacts with coregulator proteins and binds to

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Vet Clin Small Anim 44 (2014) 965–975
<http://dx.doi.org/10.1016/j.cvs.2014.06.003>

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Table 1	
Tumor types that may be influenced by gonadectomy	
Concerning Breeds	
Tumors with increased risk post-castration	
Cardiac tumors	All
Osteosarcoma	All, purebred dogs, Rottweilers (<1 y of age at castration)
Prostatic tumors (carcinoma, adenocarcinoma, transitional cell carcinoma)	All
Transitional cell carcinoma of the urinary bladder	All
Lymphoma	All, Golden retrievers (<1 y of age at castration)
Tumors with decreased risk post-castration	
Testicular	All
Tumors with increased risk post-spay	
Cardiac tumors	All
Cardiac hemangiosarcoma	All
Osteosarcoma	Purebred dogs, Rottweilers (<1 y of age at spay)
Splenic hemangiosarcoma	All, Vizslas, Golden retrievers (>1 y of age at spay)
Mast cell tumor	All, Vizslas, Golden retrievers
Lymphoma	All
Tumors with decreased risk post-spay	
Ovarian tumors	All
Uterine tumors	All
Mammary tumors (canine, with spay before 3rd estrus)	All
Mammary tumors (feline, with spay before 3rd estrus)	All

hormone-responsive elements in the promoter regions of the DNA, which causes transcription of hormone-regulated proteins.¹⁵ (2) Hormones may bind to receptors that interact with other transcription factors that bind to the DNA, causing indirect activation of proteins.¹⁶ (3) Receptors may not require binding of the hormone to induce DNA transcription, rather may be activated through other growth factor pathways.¹⁶ In humans, estrogen and testosterone affect breast and prostatic cancer growth and viability in a large percentage of patients, leading to treatments that modulate hormone levels or block their receptors.¹⁶

MAMMARY TUMORS

Historically, the influence of spaying on mammary tumor development has been the most well-studied veterinary sex hormone–tumor link. In sexually intact female dogs, mammary neoplasia is the most common form of cancer, based on many current large European cancer registries' databases.^{17–20} Because early neutering is rare in these countries, these data help us to understand the risk in intact female dogs. Incidence of mammary tumors increases over time, which also correlates with increased exposure to female sex hormones.^{17,21,22} Exogenous hormone exposure also increases the risk of tumor development.¹⁰ Significant tumor risk occurs around 7 to

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