

Endogenous gonadal hormone exposure and bone sarcoma risk

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Article Abstract

Although experimental and clinical evidence suggest that endogenous sex hormones influence bone sarcoma genesis, the hypothesis has not been adequately tested in an appropriate animal model. We conducted a historical cohort study of Rottweiler dogs because they frequently undergo elective gonadectomy and spontaneously develop appendicular bone sarcomas, which mimic the biological behavior of the osteosarcomas that affect children and adolescents. Data were collected by questionnaire from owners of 683 Rottweiler dogs living in North America. To determine whether there was an association between endogenous sex hormones and risk of bone sarcoma, relative risk (RR) of incidence rates and hazard ratios for bone sarcoma were calculated for dogs subdivided on the basis of lifetime gonadal hormone exposure. Bone sarcoma was diagnosed in 12.6% of dogs in this cohort during 71,004 dog-months follow-up. Risk for bone sarcoma was significantly influenced by age at gonadectomy. Male and female dogs that underwent gonadectomy 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 [RR +/-95% CI = 3.8 (1.5-9.2) for males; RR +/-95% CI = 3.1 (1.1-8.3) for females]. Chi(2) test for trend showed a highly significant inverse dose-response relationship between duration of lifetime gonadal exposure and incidence rate of bone sarcoma (P = 0.008 for males, P = 0.006 for females). This association was independent of adult height or body weight. We conclude that the subset of Rottweiler dogs that undergo early gonadectomy represent a unique, highly accessible target population to further study the gene:environment interactions that determine bone sarcoma risk and to test whether interventions can inhibit the spontaneous development of bone sarcoma