CORRESPONDENCE

Re: A Quality-Adjusted Time Without Symptoms or Toxicity (Q-TWiST) Analysis of Adjuvant Radiation Therapy and Chemotherapy for Resectable Rectal Cancer

To our knowledge, Gelber et al. (1) have provided the first quantitative scrutiny of quality-of-life management of patients treated for locally advanced rectal cancer. The authors conclude, "Use of combined chemotherapy and radiation therapy as an adjuvant to surgery for patients with poor-prognosis resectable rectal cancer is justified." To which may be added—in comparison with postoperative adjuvant radiation therapy alone. There also appears to be an assumption, which generally conforms with the literature, that adjuvant postoperative radiation therapy alone does not improve survival.

However, the usual treatment decision confronting the patient is combined treatment versus no treatment. In the absence of a comparison, have the authors examined their data by deleting the impact of those toxic events or delayed reactions attributable to radiation therapy in the control group? Such complications, including death, were cited in the published manuscript from which the current study is derived (2).

Reasonably predictive estimates of quality of life after various treatment options are valuable in helping the patient with rectal cancer to make difficult choices. By embracing the side effects of treatment alternatives, Gelber et al. are to be congratulated for their accomplishment in this difficult field. However, quality of life has many elements. Some dimensions, such as performance status and economic considerations, can be quantified.

Other elements, such as pain, psychological factors, and genitourinary function, are more difficult to integrate. We have a long way to go before reliable clinical utility can be achieved.

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References


Note

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Response

We thank Dr. DeCosse and Ms. Cenerazzo for their compliments regarding our work. The requested examination of our data can be performed simply by taking the average months in TOX (i.e., time with toxicity) associated with the radiation therapy-alone arm and putting them into the TWiST clinical health state for the analysis. The results in this case continue to demonstrate a substantial advantage for the combined-modality approach. This analysis, however, is based on the assumption that radiation therapy alone does not improve disease-free survival or overall survival. We agree that more evaluations that incorporate aspects of quality of life into treatment decision-making are needed.

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Comparing the Age at Prostate Cancer Diagnosis in Humans and Dogs

Prostate cancer is the most frequently diagnosed noncutaneous cancer in U.S. men and kills more than 40,000 men annually in this country (1). It is interesting that the dog is the only nonhuman species in which spontaneous prostate cancer occurs frequently (2). Clinically apparent prostate cancer in pet dogs exhibits aggressive biologic behavior, with metastasis to regional lymph nodes or lungs present frequently at the time of diagnosis (3,4). Canine prostate cancer also shares with its human counterpart a high propensity for skeletal metastasis. Recently, we documented that high-grade prostatic intraepithelial neoplasia (PIN), the likely precursor of many human prostate cancers (5), occurs spontaneously in the canine prostate in association with invasive carcinoma (6). Canine PIN shares many of the morphologic and immunophenotypic features of human PIN, including basal layer disruption, an increased proliferative index, and increased microvessel density compared with that of benign epithelium (6).

Our work (6,7) suggests that pet dogs offer a naturally occurring animal model to study factors that regulate the initiation and progression of prostate cancer. Recently, we developed an algorithm to convert the chronologic age of dogs to physiologic age in human years. This algorithm is based on mortality data from more than 23,000 pet dogs in the computerized Veterinary Medical Data Base and takes into consideration breed- and body size-specific differences in life expectancy (8). The purpose of this study was to compare the age at prostate cancer diagnosis in dogs with previously published age-specific incidence data from humans.

The age at diagnosis of spontaneous prostate cancer in 686 pet dogs was obtained from the Veterinary Medical Data Base. For each dog, chronologic age at diagnosis was converted to physiologic age expressed in human years by use of the following algorithm (8):
Physiologic age (human years) = 
\[ \{[-0.107 \times X - 2^2] + \{[0.2911 \times X + 4.9979] \times C\} + \{-0.0013 \times X + 0.0221\} + \{-3.6437 \times X\} + 37.4, \]
where \( X \) is the breed- or body size-specific median age at death (years) and \( C \) is the chronologic age of dogs in years. Physiologic age at diagnosis for the 686 dogs with prostate cancer was compared with the age of 110 men diagnosed with prostate cancer prior to the use of serum prostate-specific antigen screening (9). These human data were selected for comparison because the canine prostate cancers were diagnosed following the onset of clinical signs, rather than by screening with a biochemical marker.

The physiologic age at prostate cancer diagnosis, expressed in human years, was similar between the two species (Fig. 1). In both species, prostate cancer was uncommon in young males. Only 4% of cases occurred in dogs younger than the equivalent of 45 human years; only 1% of cases in humans were diagnosed before the age of 50 years. Mean and median physiologic ages at the diagnosis of prostate cancer in dogs, expressed in human age equivalents, were 67 years and 73 years, respectively. Mean age at diagnosis for the men with prostate cancer was 70 years. Forty-four percent of prostate cancers were diagnosed in dogs at greater than 70 years of physiologic age. Similarly, 56% of the human cancers were diagnosed in men 70 years of age or older.

Because dogs of small body size (versus large body size) or mixed breed (versus pure breed) have increased longevity (8), we have used an algorithm that standardizes the chronologic age of dogs of different breeds and body sizes to physiologic age expressed in human years. This analysis has important implications for comparative oncology research, because this approach can be used to determine the influence of physiologic age on the development of prostate cancer and other naturally occurring cancers in pet dogs.

We conclude that the development of spontaneous prostate cancer in dogs and humans is similarly influenced by age. Appropriate in vivo animal models are needed to study factors that regulate the development and progression of prostate cancer. Our data further strengthen the hypothesis that pet dogs may serve as a relevant model to increase our understanding of prostate carcinogenesis.

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References


Notes

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