Multi-institutional Historical Cohort Study Of Oral Malignant Melanoma in 165 Dogs.

Tetsuya Kobayashi[1,7], Yuko Nakano[1], Ai Watabe[2], Tsuyoshi Kadosawa[2,7], Yusuke Ito[3], Kohji Maruo[3,7], Michio Fujita[4] Tsukimi Washizu[4,7], Rie Imai[5], Takuo Ishida[5,7], Yasuhito Fujino[6], Hajime Tsujimoto[6,7]

1. Japan Small Animal Cancer Center, 2. Rakuno Gakuen University, 3. Gifu University, 4. Nippon Veterinary and Life Science University, 5. Akasaka Animal Hospital, 6. The University of Tokyo, 7. Japan Veterinary Co-Operative Oncology Group (JVCOG)

Introduction

The purpose was to evaluate the outcome and prognostic factors for canine oral malignant melanoma (OMM) treated in Japan with surgery and/or hypofractionated radiotherapy.

Methods

Medical records from 6 institutions between 1/2000 and 12/2010 were reviewed to identify dogs with histologically confirmed OMM. Factors evaluated for prognostic significance included age, breed (Golden Retrievers vs. others), gender, body weight, location of the tumor (the lip or the buccal mucosa vs. the mandibular gingiva, the maxillary gingiva, the tongue or the mucosa of the palate), stage (stage 1 vs. 2, 3 or 4), treatment modalities (surgery, hypofractionated radiation therapy, both) and the usee of a platinum compound.

Survival was calculated by the Kaplan-Meier method and statistical significance was set at $p \leq 0.05$ using log rank analysis for univariate analysis and Cox proportional hazard model for multivariate analysis.

Results

One hundred sixty five dogs were identified. Median age was 12.1 years (3.0-18.0 years). Golden Retrievers were overrepresented (n=22) following by Miniature Dachshund (16), Labrador Retrievers (15) and Beagle (15). Ninety-nine dogs were male (45 castrated) and 66 were female (34 spayed). Median body weight was 12.2 kg (2.1-39.7kg).

Tumors arose from the mandibular gingiva in 67 dogs (40.6%), the maxillary gingiva in 49 (29.7%), the lip or the buccal mucosa in 33 (20%), the mucosa of the palate in 9 (5.5%) and the tongue in 7 (4.2%).

A platinum compound was administered concurrently to 39 dogs, either carboplatin (n= 38) or cisplatin (1). The median number of chemotherapy doses was 4 (1-12). Hypofractionated radiation therapy was delivered using a 300-450-kV orthovoltage x-ray machine (n=78), a 4 MeV linear accelerator (36) or both (1). The total radiation dose was 24 to 40 Gy in 3 to 6 fractions.

In the group treated by surgery alone, 42 (84%) dogs had tumor-free surgical margins, achieved in 12/14 (85.7%) dogs with OMM in mandibular gingiva, 8/12 (66.7%) in the maxillary gingiva, 18/20 (90%) in the lip or the buccal mucosa and 4/4 (100%) in the tongue.

Overall survival was 223 days (11-2,629 days, Fig.1). Median survival was 383 days (11-1,553 days) for dogs that had surgery (n=50), 203 days (19-2,629 days) for dogs that had hypofractionated radiotherapy (n=56) and 218 days (27-1,316 days) for dogs that had both surgery and radiotherapy (n=59). Survival was not significantly different among the treatment groups (p= 0.3778, Fig.2). Significant factors associated with survival by univariate analysis were age (p= 0.0029), breed (p= 0.0155, Fig. 3) and stage (p<0.00001, Fig. 4). Significant factors associated with survival by multivariate analysis were age, breed, body weight, the location of the tumor, stage and the usage of platinum compound. Median survival for dogs with stage 1

(n= 27), 2 (22), 3 (70) and 4 (24) were 631, 278, 18 and 115 days, respectively. Dogs with stage 2, 3 and 4 OMM had a hazard ratio of 2.1 (95%CI: 1.0-4.5), 3.6 (95%CI: 1.9-6.7) and 6.2 (95%CI: 2.9-13.5) relative to the dogs with stage 1 OMM, respectively. Dogs with OMM at the mandibular gingiva, the maxillary gingiva, the mucosa of the palate and the tongue had a hazard ratio of 2.6 (95%CI: 1.3-5.4), 2.4 (95%CI: 1.2-4.4), 3.8 (95%CI: 1.4-10.5) and 1.4 (95%CI: 0.39-4.8), relative to the dogs with OMM at the lip or the buccal mucosa, respectively.
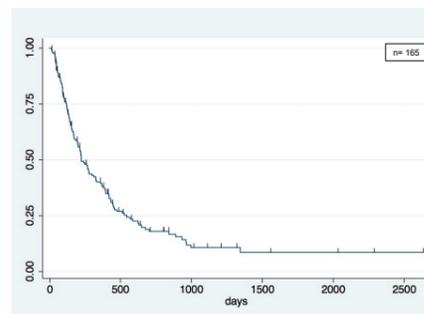

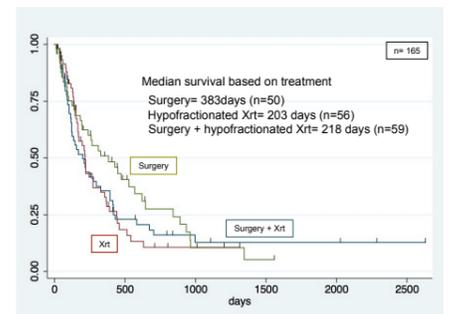Figure 1. Kaplan-Meier curve for overall survival in 165 dogs

Figure 2. Kaplan-Meier survival curves comparing survival based on treatment modalities. Survival was not significantly different among the treatment groups (p= 0.3778).
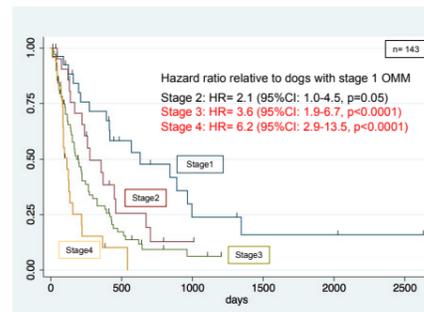

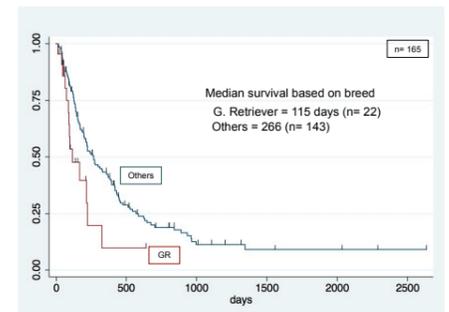Figure 3. Kaplan-Meier curves comparing survival based on stage.

Figure 4. Kaplan-Meier curves comparing survival based on breed. Golden Retrievers with OMM survived significantly less than others (p= 0.0155). Golden Retrievers with OMM had a hazard ratio of 2.7 (95% CI: 1.2-5.8) relative to others.

Conclusion

- Treatment outcomes in our study are comparable to the previous reports in the US.
- There was no difference in outcome depending on the specific treatment administered.
- The prognosis in Golden Retrievers might be worse than in other breeds.
- OMM of the lip or the buccal mucosa might behave better than at other locations.
- Platinum compounds may prolong survival in dogs with OMM.

Current Contact Address:

Tetsuya Kobayashi, DVM, MSpVM, Dip. ACVIM (Oncology)
Japan Small Animal Cancer Center
2-27-4 Nakatomiminami Tokorozawa Saitama, 359-0003, Japan
Tel. 81 (4) 2943-8699, Fax. 81 (4) 2943-8698
E-mail: adriamycin@mac.com, Webstite: www.jsamc.jp