FULL PAPER *Surgery*

# Prognosis of Canine Patients with Nasal Tumors According to Modified Clinical Stages Based on Computed Tomography: A Retrospective Study

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ABSTRACT. To evaluate the efficacy of clinical staging based on computed tomography (CT) imaging over the World Health Organization (WHO) staging system based on radiography for nasal tumors in dogs, a retrospective study was conducted. This study used 112 dogs that had nasal tumors; they had undergone radiography and CT and had been histologically confirmed as having nasal tumors. Among 112 dogs, 85 (75.9%) were diagnosed as adenocarcinoma. Then they were analyzed for survival time according to each staging system. More than 70% of the patients with adenocarcinoma were classified as having WHO stage III. The patients classified under WHO stage II tended to survive longer than those classified under WHO stage III. Dogs classified under WHO stage III were further grouped into CT stages III and IV, and CT stage III patients had a significantly longer survival time than CT stage IV patients. In addition, patients treated with a combination of surgery and radiation had a significantly longer survival time than the patients who did not receive any treatment in CT stage III. On the other hand, different treatment modalities did not show a significant difference in the survival time of CT stage IV dogs. The results suggest that WHO stage III dogs may have various levels of tumor progression, indicating that the CT staging system may be more accurate than the WHO staging system.

KEY WORDS: clinical staging, computed tomography, nasal tumor, survival time.

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Tumors of the nasal cavity and paranasal sinuses are uncommon in the dog, and they account for 1%–2% of all canine neoplasms [2, 3]. Dolichocephalic breeds aged 10 to 15 years are at a greater risk of developing this disease. The most common histological type in canine nasal/paranasal tumors is adenocarcinoma. Most of these tumors are locally invasive but rarely metastasize; however, complete curing is often difficult due to invasion of the tumor into the oral cavity, orbit, and brain [2, 3, 15, 17].

A combination of surgery, radiation, and/or chemotherapy is a standard treatment modality for nasal tumors in dogs [5, 7, 10, 14, 16, 19]. The choice of treatment greatly depends on the location and size of the tumors obtained using radiography.

The staging system proposed by the World Health Organization (WHO) uses the size (T), regional lymph node involvement (N), and distant metastasis (M) for tumor classification; this system has been used as one of the standard classification methods for canine nasal/paranasal tumors [4]. However, it is based on radiography findings, and after the introduction of computed tomography (CT) in small animal practice, CT-based diagnosis has often been used instead [8]. CT can delineate the lesion more accurately, but there have been no reports on the staging system for canine nasal/paranasal tumors based on CT.

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The purpose of this study was to establish a staging system based on CT images for nasal/paranasal tumors in dogs and to retrospectively compare the prognosis obtained using this staging system to that obtained using the WHO staging system.

## MATERIALS AND METHODS

*Patients*: This study used the clinical records of 112 dogs that had undergone both radiography and CT and were histologically confirmed to have nasal tumors. They were admitted to the Veterinary Medical Center at the University of Tokyo between April 1993 and March 2002. The histological diagnosis was made using tissue specimens obtained during surgery or by cytology of the nasal cavity, using a cytobrush® immediately after CT.

*Staging system based on CT findings (CT staging)*: The following 6 parameters were used for CT staging: (1) tumor invasion to the bilateral nasal/paranasal sinus clearly shown on enhanced CT, (2) nasal bone destruction and the tumor mass was glossly found on the nasal plane and/or face (3) involvement of the oral cavity with destruction of the hard palate (4) orbital involvement and the tumor mass compressed eye ball laterally, (5) frontal sinus involvement, and (6) brain involvement with the destruction of the cranium or the cribellum and the tumor mass being invaded into the brain tissue.

CT stage I does not reveal any of the 6 above mentioned findings. CT stage II indicates one of the findings mentioned in (1)–(5), while CT stage III indicates two or more

of these findings. In cases of tumor involving the brain, the patient was classified under CT stage IV.

The clinical stages of the patients were also determined based on the WHO-TNM system of classification (WHO staging). According to this system, stage I indicates that the tumor is unilateral and does not invade the surrounding bone tissues; stage II indicates that the tumor is bilateral or invades the surrounding bone tissues; and stage III indicates that the tumor invades the surrounding tissues/organs.

*Treatment*: The treatment modalities for these patients were selected according to the severity of the diseases and were decided based on the owner's approval. In cases tumor apparently invaded to the brain, oral cavity, or orbit, surgery was not recommended; these patients were mainly treated by radiation alone or radiation with chemotherapy, or they were not treated except supportive therapies with antibiotics or antiinflammatory drugs. For chemotherapy, we intravenously (IV) administered carboplatin (200–300 mg/$m^2$ every 3 weeks for a total of 2–9 times) or cisplatin (50 mg/$m^2$ every 3 weeks for a total of 2–8 times). Radiation therapy was performed using an orthovoltage unit (Hitachi Medico., Co.). Irradiation was performed at 300 kV and 10 mA, with a dose of 4–8 Gy once or twice per week at a total dose of 40–60 Gy.

*Statistical analysis*: The difference in the survival time for the different treatments and the stages between WHO staging and CT staging was evaluated. The Kaplan-Meier method was used to evaluate the survival time, and the Logrank test was used for correlation analysis. $P<0.05$ was considered as significant.

## RESULTS

*Patients*: The patient group comprised 58 males, 13 castrated males, 29 females, and 19 spayed females. The age range was 3 to 17 years, and the mean age was 10.2 years. The most common breed was the Shetland sheepdog (n=29), followed by mixed-breed dogs (n=23), the golden retriever and Siberian husky (n=9 each), and the Shiba dog (n=8). This group included 7 brachycephalic dogs, including 5 Shih Tzu dogs.

The common clinical signs on the first day of admission are listed in Table 1. They were nasal hemorrhage (80.4%), nasal discharge (52.7%), face deformation (37.5%), and sneezing (36.6%). Histological types of tumors are shown in Table 2. Adenocarcinoma was the most frequent (75.9%), followed by chondrosarcoma (10.7%) and osteosarcoma (4.5%). These patient data were similar to those previously reported [2, 3, 5, 11, 13, 20].

*Survival time according to the histological types*: The survival time of the dogs with different histological types is shown in Fig. 1. Dogs with chondrosarcoma had a significantly longer survival time than those with adenocarcinoma (p=0.046) or squamous cell carcinoma (p=0.003).

*Relationship between the clinical stagings and survival time in the dogs with adenocarcinoma*: Survival time of the dogs with adenocarcinoma, which was the most common histological type, determined based on WHO clinical staging and CT staging is shown in Figs. 2 and 3, respectively. According to WHO staging, the dogs in stage II tended to survive longer (median survival time of 17.3 months) than those in stage III (median 11 months; p=0.087). When the dogs with adenocarcinoma were classified according to CT staging, survival time was not significantly different between CT stage I and CT stage II dogs and between CT stage II and CT stage III dogs. However, a significant difference in median survival time was observed between the CT stage III (15.1 months) and CT stage IV (6.6 months) dogs (p=0.016).

Table 1. Clinical signs of the dogs with nasal/paranasal tumors on the first day of admission

| Clinical signs | The number of patients (%) |
|---|---|
| Nasal hemorrhage | 90 (80.4) |
| Nasal discharge | 59 (52.7) |
| Face deformation | 42 (37.5) |
| Sneezing | 41 (36.6) |
| Stuffy nose | 30 (26.8) |
| Snoring | 15 (13.4) |

The most common sign was nasal hemorrhage (80.4%) and approximately half the cases showed nasal discharge. Other clinical signs included sneezing, stuffy nose or snoring, and face deformation.

Table 2. Histological types of canine nasal tumors

| Histological diagnosis | Number of patients (%) |
|---|---|
| Adenocarcinoma | 85 (75.9) |
| Chondrosarcoma | 12 (10.7) |
| Osteosarcoma | 5 (4.5) |
| Squamous cell carcinoma | 3 (2.7) |
| Transitional cell carcinoma | 3 (2.7) |
| Nasal mucous gland tumor | 1 (0.9) |
| Others | 3 (2.7) |
| Total | 112 (100) |

Adenocarcinoma was the most frequent (75.9%), followed by chondrosarcoma (10.7%) and osteosarcoma (4.5%).

*Survival time of dogs treated with different modalities in the dogs with adenocarcinoma*: The survival time obtained on using different treatment modalities was evaluated in WHO stages II and III. The number of dogs classified under WHO stages I was not sufficient for analysis. In WHO stage II dogs, no significant differences were demonstrated by treatment modalities. In WHO stage III dogs, those treated with a combination of surgery and radiation tended to survive longer (median; 7 months) than those that did not receive any treatment (median 1.8 months; p=0.055) (Fig. 4). No other significant difference was observed between the treatments.

The survival time of dogs classified under each CT stage

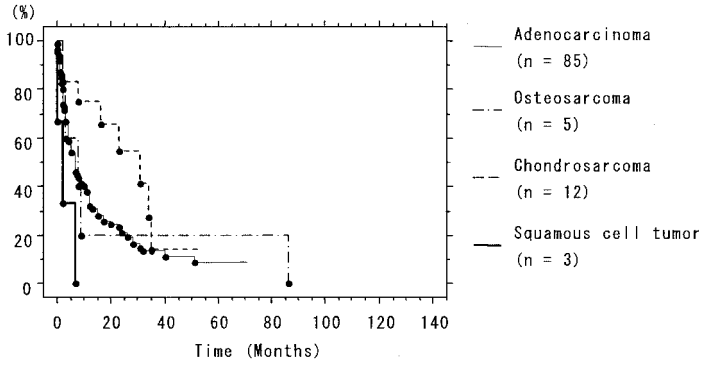


Fig. 1. Survival time of the dogs according to the histological types. The dogs with chondrosarcoma had a significantly longer survival time than those with adenocarcinoma (p=0.046) or squamous cell carcinoma (p=0.003).

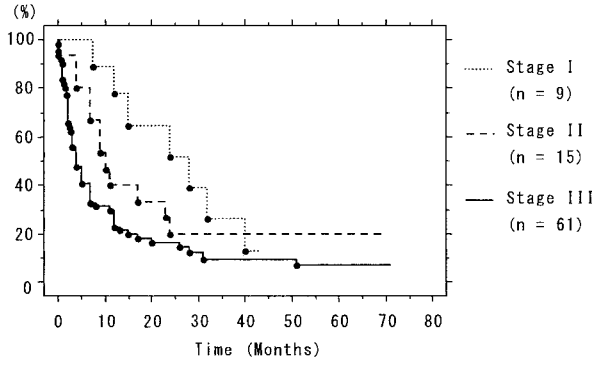


Fig. 2. Survival time of the dogs with adenocarcinoma according to WHO staging. Survival time was not significantly different between the WHO stage I and WHO stage II dogs, while it tended to be different between the WHO stage II and WHO stage III dogs (p=0.087).

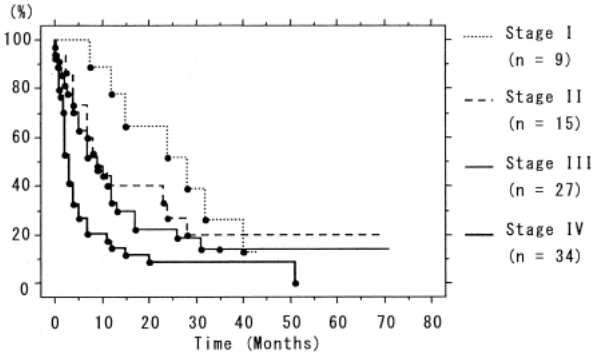


Fig. 3. Survival time of the dogs with adenocarcinoma according to the CT stages. Survival time was not significantly different between the CT stage I and CT stage II dogs and between CT stage II and CT stage III dogs. However, it was significantly different between the CT stage III and CT stage IV dogs (p=0.016).

II, III and IV treated with different modalities is shown in Figs. 5, 6 and 7, respectively. The number of CT stage I dogs was not sufficient for statistical analysis. In CT stage III dogs, those treated with a combination of surgery and radiation survived significantly longer (median 17 months) than those that did not receive any treatment (median 5 months; p=0.003) (Fig. 6). However, there was no significant difference in the survival time obtained using the different treatment modalities in CT stage II and IV dogs (Figs. 5 and 7).

## DISCUSSION

The patient signalment of the dogs used in this study was almost similar to that in previous reports. The most common breed in this study was the Shetland sheepdog; dolichocephalic dogs accounted for 93.8% [2, 5, 6, 11, 13–15]. In this study, both the mean and median age of tumor occurrence were 10 years, which was similar to those previously reported [2, 3, 9, 11, 14–16]. Histologically, 82% of the tumors were carcinomas; this percentage was higher than that obtained in the previous reports [2, 3, 16].

Mean and median survival time in all the patients were 15.2 months and 7 months, respectively, and these time periods were similar to those obtained in the previous reports [9, 12, 15, 17]. The dogs with chondrosarcoma had a better prognosis with a mean survival time of 21.5 months than those with squamous cell carcinoma with a mean survival time of 2.3 months; these data are similar to those obtained in the previous reports [1, 7, 18, 20].

Clinical staging of WHO by using TNM classification has been in practice since many years, and this system is based on radiographic findings. In this system, it may be hypothesized that nasal tumors develop from one side of the nasal/paranasal cavity and grow toward the contralateral nasal cavity first; subsequently, they invade to the nasal bones and finally, they infiltrate into the surrounding tissues. However, in some cases, nasal tumors may extend to the orbitary fossa first and not to the contralateral nasal cav-

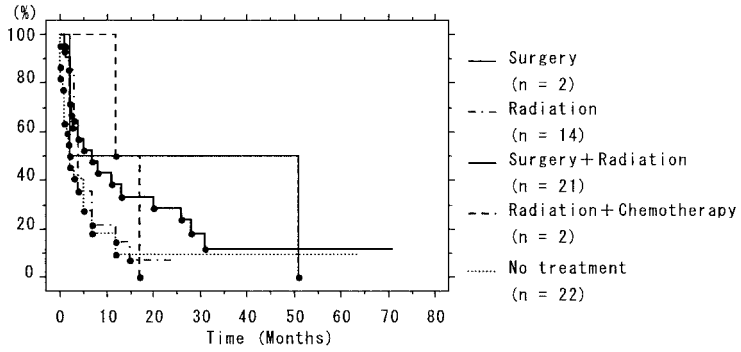


Fig. 4. Survival time of WHO stage III dogs with adenocarcinoma that were treated with different modalities. Dogs treated with a combination of surgery and radiation tended to survive longer than those without treatment (p=0.0055).

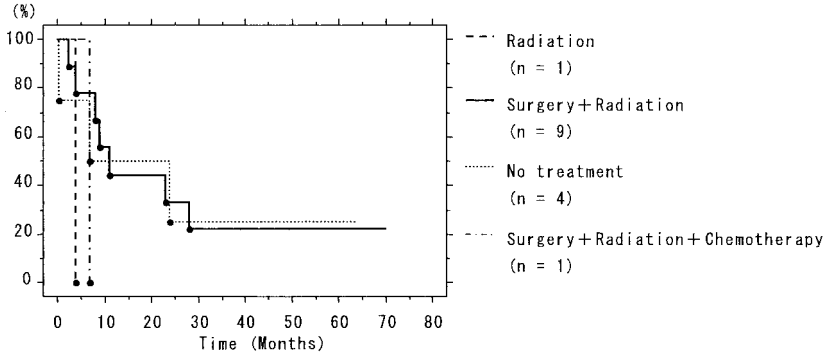


Fig. 5. Survival time of CT stage II dogs with adenocarcinoma treated using different modalities. There was no significant difference in the survival time between the treatment modalities.

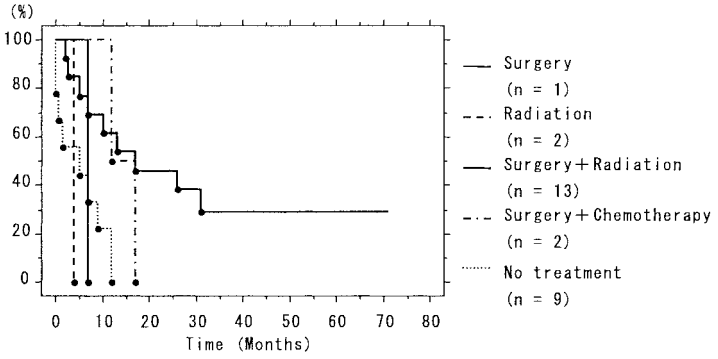


Fig. 6. Survival time of CT stage III dogs with adenocarcinoma treated with different modalities. Dogs treated with a combination of surgery and radiation survived significantly longer than those treated without any treatments (p=0.003).

ity. This progression may depend on the site of the primary lesion. CT staging-the new staging system discussed in this paper-is based on CT imaging, which delineates the size and location of the tumor more clearly and with greater accuracy.

Among 112 patients, 18 were classified under WHO stage I; 23, under WHO stage II; and 71, under WHO stage III, respectively. When using the CT staging system, the number of patients in CT stages I, II, III, and IV was 18, 22, 32, and 40, respectively, indicating that CT staging may enable further differentiation of the level of progression of WHO stage III patients.

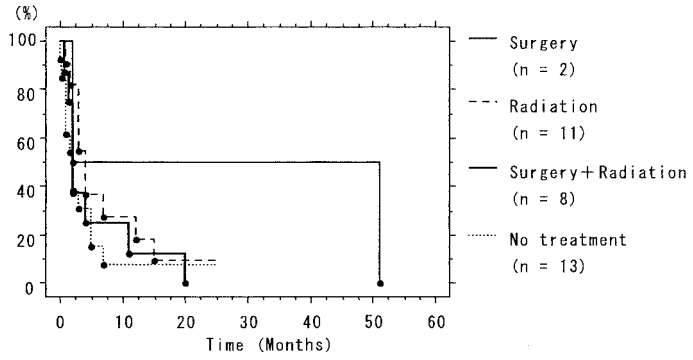


Fig. 7. Survival time of CT stage IV dogs with adenocarcinoma treated with different modalities. There was no significant difference in the survival time between the treatment modalities.

When the survival time in the dogs with adenocarcinoma, which was the most common histological type, between the WHO stages was compared, the WHO stage II patients tended to survive longer than the WHO stage III patients. When the survival time in the dogs with adenocarcinoma between the CT stages was compared, the CT stage III patients had a significantly longer survival time than the CT stage IV patients. This result also showed that WHO stage III included patients with various levels of tumor progression, and that CT stages III and IV were practically effective to differentiate the progression level of patients with nasal/paranasal tumors.

Since this was a retrospective study and the treatment modality for each patient was not randomized, the survival time according to the treatment modalities was compared in dogs with adenocarcinoma for certain stages having a sufficient number of patients for analysis. In the WHO stage II patients, no significant difference was observed between the survival time of the different treatment modalities. In WHO stage III dogs, those receiving a combination of surgery and radiation therapy tended to survive longer than those that did not receive any treatment. No significant difference was observed between the survival time of the different treatment modalities in CT stage II. In CT stage III, dogs receiving a combination of surgery and radiation therapy showed a significantly longer survival time than those that did not receive any treatment. The survival time of CT stage IV dogs did not significantly differ depending on the treatment modalities possibly due to the terminal stage of tumor.

In conclusion, the CT staging system in this study may differentiate the WHO stage III patients with greater precision, and it was effective in estimating the prognosis of, at least, dogs with adenocarcinoma, particularly those classified under CT stages III and IV.

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