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Comparison of Survival After Treatment of Presumed Intracranial Meningioma by Radiotherapy or Surgery in 285 Dogs

Rachel Geiger[1] | Joe Mankin[1] | Holger A. Volk[2] | Steven de Decker[2] | Nate van Asselt[3] | Karanbir Randhawa[3] | Tara Ehling[4] | Charles A. Maitz[4] | Ada Naramor[4] | Joan R. Coates[4] | Catherine Stalin[5] | Lauren Johnstone[5] | Joanna Morris[5] | Ioannis N. Plessas[6] | Alexander Forward[6] | Laurent Garosi[6] | Elena Scarpante[7] | Giunio Cherubini[7] | Tom Harcourt-Brown[8] | Sheila Carrera-Justiz[9] | Jishnu Rao Gutti[9] | Marilia Takada[9] | Joel White[10] | Koichi Nagata[10] | Marc Kent[10] | Renee Barber[10] | Daisuke Ito[11] | Tomohiro Nakayama[11] | Ayaka Oshima[11] | Naoki Sekigucki[11] | Lauren Smith-Oskrochi[1] | Nick Jeffery[1]

[1]Department of Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, Texas, USA | [2]Department of Clinical Science and Services, Royal Veterinary College, Hatfield, UK | [3]Department of Surgical Sciences, University of Wisconsin Veterinary Care, Madison, Wisconsin, USA | [4]Department of Veterinary Medicine and Surgery, College of Veterinary Medicine, University of Missouri, Columbia, Missouri, USA | [5]Small Animal Clinical Division, School of Biodiversity, One Health and Veterinary Medicine, University of Glasgow, Glasgow, UK | [6]Davies Veterinary Specialists, Hitchin, UK | [7]DWR Veterinary Specialists, Cambridgeshire, UK | [8]Langford Vets Small Animal Hospital, Langford, UK | [9]College of Veterinary Medicine, Department of Small Animal Clinical Sciences, University of Florida, Gainesville, Florida, USA | [10]Department of Small Animal Medicine & Surgery, University of Georgia College of Veterinary Medicine, Athens, Georgia, USA | [11]Department of Veterinary Medicine, College of Bioresource Sciences, Nihon University, Fujisawa, Japan

Correspondence: Nick Jeffery (njeffery@cvm.tamu.edu)

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ABSTRACT

Background: The comparative effectiveness of radiotherapy and surgery for treating intracranial meningioma is unknown.
Objectives: To compare survival after treatment of suspected intracranial meningioma by either surgery or radiotherapy.
Animals: Two hundred eighty-five companion dogs with suspected intracranial meningiomas presenting to 11 specialty clinics in three countries.
Methods: Parallel cohort comparison study on retrospective data. Dogs diagnosed with intracranial meningioma by board-certified veterinary neurologists or radiologists and treated by radiotherapy or surgery were identified through medical record searches and presenting and survival data extracted. Lesion site was classified as rostro- or caudotentorial and size was measured on contrast magnetic resonance images. Outcome was all-cause death. Analysis of survival by Cox proportional hazards, including selection for optimal multivariable model using lasso, counterfactual modeling including variables associated with treatment allocation and survival.
Results: One hundred sixty-eight dogs received radiotherapy and 117 received surgery. All analyses indicated reduced survival associated with surgery compared to radiotherapy. There was a median survival after surgery of 297 (IQR: 99–768) days compared with 696 (IQR: 368–999) for dogs treated by radiation, associated with a univariable hazard ratio of 1.802 (95% CI:

Abbreviations: CI, confidence interval; HR, hazard ratio; IQR, interquartile range; lasso, least absolute shrinkage operator; MR, magnetic resonance; MRI, magnetic resonance imaging; SD, standard deviation; T1W, T1-weighted.

1.357–2.394). Counterfactual modeling estimated a mean survival of 480 (95% CI: 395–564) days after surgery and 673 (95% CI: 565–782) days after radiotherapy, representing a decrease in survival of 29%. Location and size of the lesion were not associated with survival duration.

Conclusions and Clinical Importance: Dogs with suspected intracranial meningioma have substantially superior survival after radiotherapy compared to surgery.

1 | Introduction

Brain tumors have been diagnosed at *post mortem* in dogs for many decades [1] but their prevalence and importance became more apparent after cross-sectional imaging became widely available in veterinary medicine [2, 3]. Meningioma is the most commonly diagnosed type in most [3–7], but not all [1], series. The ability to precisely localize brain tumors in animals spurred investigation of a variety of treatment modalities. Although there are no published formal comparison studies, medical management, using anti-seizure medications and glucocorticoids, is associated with poor long-term survival for dogs with suspected meningioma [3, 8–10]. In contrast, direct anti-tumor treatment, mostly radiotherapy [11–15] or surgery [16–19] alone, but also both combined [8, 20, 21] appears to be efficacious. Summary synthesis of these series is difficult, because of differences in reporting and inclusion criteria, but suggests that both treatments generate similar survival outcomes [22].

A randomized clinical trial comparing radiotherapy with surgery is the optimal method to obtain reliable and accurate information regarding treatment recommendations. However, currently it would be difficult to construct such a trial because it would need considerable funding (to ensure that owners would be willing for their dogs to undergo randomly selected treatment that might also have differential costs and care implications). The alternative is to rely on observational data accrued through routine care and treatment in specialist clinics. Unfortunately, there are many pitfalls in analysis of observational data [23], and in human medicine it is well recognized that, for many reasons, the results of observational data analysis and formal trials can differ [24], implying that judicious interpretation is necessary.

Simple univariable analysis (such as Cox regression) and relying solely on p values to interpret effects often leads to inappropriately rigid and inaccurate conclusions from observational data. Instead, alternative, more complicated, models that develop "counterfactuals" from available data permit more subtle and reliable comparison between treatment groups. Such analysis estimates treatment effects by incorporating into the model differences in treatment allocation and survival effects of other clinical variables (such as age, lesion location *etc.*). This type of approach, which includes propensity scoring for example, has become increasingly used in human medicine [25] and the statistical methods are now widely available in software packages.

In this study we aimed to collect data from a large number of dogs diagnosed with meningioma and treated by either radiotherapy or surgical excision and compare the overall survival between treatment groups. We collected information on factors that influence treatment allocation and outcome for inclusion in the counterfactual modeling process to obtain the best estimate of difference in survival between the two treatment modalities.

2 | Methods and Materials

This was a multicenter retrospective investigation that included dogs treated for suspected meningioma between 2007 and 2023. Records were reviewed from 11 institutions. Ethical approval for this study was provided by the Ethics Review Panel of the Royal College of Veterinary Surgeons (UK; application #: 2022-097).

This treatment comparison study has several pragmatic characteristics that aid in increasing generalizability of the results [26]. First, the diagnosis of meningioma was based on recognition of features considered typical of meningioma on magnetic resonance (MR) images, rather than histopathology, because most dogs that undergo radiation therapy for brain masses do not have biopsy diagnosis (and for comparative purposes there is a need to have similar entry criteria for both categories of treatment). Second, treatment for each dog was primarily categorized as "radiotherapy" or "surgery," while recognizing that there were differences in the precise delivery of each intervention. Similarly, categorization of therapy was by intention-to-treat and so animals that did not complete a designated therapy (most often radiotherapy) were still included in outcome analysis. Third, the outcome measure was all-cause death (see below). Importantly, such pragmatic studies provide an overall, broad-brush view of the relative benefits of competing therapies, but do not imply that specific sub-groups might not exhibit different outcomes. Those questions must be addressed in more focused future studies.

Dogs were included if they had a board-certified radiologist or neurologist magnetic resonance imaging (MRI) diagnosis of a single intra-cranial, extra-parenchymal mass with the primary differential diagnosis of meningioma and received definitive-intent therapy to their tumor in the form of surgery or radiotherapy. The broad criteria necessary for a strong presumptive diagnosis of meningioma are long recognized [27] and more formally summarized recently [28].

Dogs were excluded if they were younger than 2 years old [29], had an estimated life expectancy of < 6 months due to concurrent malignancy or comorbidity, or if they had diabetes mellitus. Dogs were excluded if the goal of therapy was palliative as described in medical records. Dogs receiving both radiotherapy and surgery for treatment of meningioma were excluded because they are subject to survivor bias (only dogs that survive 1 type of therapy are available to receive the second therapy) [30, 31], and so would not be a fair comparator group. Dogs were also excluded if they had peri-ocular or spinal meningiomas, multiple concurrent intra-cranial masses, or history of another intra-cranial tumor treated with radiation therapy or surgery.

Surgical cases with image-based meningioma diagnosis but differing histopathology were included to permit fair comparison with radiotherapy cases. Given the retrospective and multi-institutional nature of this study, radiation therapy equipment, protocols, dose delivery, technique (when applicable), treatment planning systems, immobilization equipment, and quality assurance varied between sites (as is well recognized [32]) but was in each instance defined by the on-site radiation oncologist. For the purposes of this study, radiotherapy protocol for each dog was designated by 1 radiation oncologist (LS-O) into 1 of the following categories: conventionally-fractionated radiotherapy (16–20 fractions of 2.5–3 Gray/fraction [Gy/fx]), hypofractionated radiotherapy (6–12 fractions, 4–6 Gy/fx), hypofractionated stereotactic radiotherapy (3–5 fractions, 5–9 Gy/fx prescribed to the margin and defined as hypofractionated stereotactic radiotherapy by the on-site radiation oncologist), or stereotactic radiosurgery (1 fraction, 12–15 Gy/fx).

We recognize, bearing in mind the recommendations for reporting of radiation therapy [33, 34], that our categorization omits detail that will be important for analysis of optimal application of radiation for brain tumor treatment in dogs. However, the aim of this study was to provide an overview analysis of what can generally be expected when radiation or surgery is applied to meningiomas in dogs, rather than to define the optimal radiation dosing recommendations or specific surgical techniques. This pragmatic approach has the merit of greater generalizability and more reliable estimation of effectiveness, that is, outcomes when treatment is applied in real-life conditions, but requires future complementary investigation of differences in detail of treatment application.

The primary outcome in this study was all-cause death. This outcome was chosen: (i) to avoid difficulties in determining cause of death. Death in these cases is usually euthanasia at a time decided in consultation between veterinarian and owner and so the relative importance of the clinical signs of brain disease, compared to clinical signs relating to other body systems, varies considerably from case to case; and, (ii) because of its pragmatic importance to owners when making treatment choices: the most pertinent question that owners want answered is how long their dog will be likely to live (rather than how long it will live if it dies from its brain tumor). For survival analysis (see below) we recorded the interval from date of first diagnosis till death or euthanasia or the interval from first diagnosis till the last date at which the dog was known to be alive (for dogs for which a date of death was not known). All follow-up was obtained from the relevant referral clinic or from the referring veterinarian; owners were not directly contacted.

In addition to recording treatment by surgery or radiation (and the radiation protocol) we also extracted relevant information that might contribute to treatment allocation (such as tumor location and size), survival (such as age at diagnosis, weight, history of tumor-associated seizures), or both. Brain weight was estimated from the weight of the dog using Bronson's equation [35]:

$$y = 0.39 \times x^{0.27},$$

where y is brain weight (kg) and x is body weight (kg).

Lesion size and location was determined from T1W post-contrast images obtained at first diagnosis that were sent to Texas A&M University from each institution, using methods similar to those reported before for measuring intracranial lesions in dogs [36]. Lesion size was measured by the same investigator (RG) using Horos software (Horos Project, Purview, Annapolis, MD; Figure 1). Tumor volume (mm^3) was calculated using the measured tumor area on each slice on which it was visible and then multiplied by the individual MRI slice thickness. Lesion size was expressed as a ratio to brain size for each individual, that is, total calculated tumor volume (mm^3)/estimated brain weight (kg).

2.1 | Statistical Analysis

Summary statistics were derived from the raw data and tabulated. Data showing a normal distribution on histograms were summarized as mean and standard deviation (SD), while non-normal distributions were summarized with median and inter-quartile range (IQR). Cox proportional hazards provided a summary unadjusted comparison of survival between radiotherapy and surgery treatment groups. Exploratory univariable analysis of the other recorded data, including different

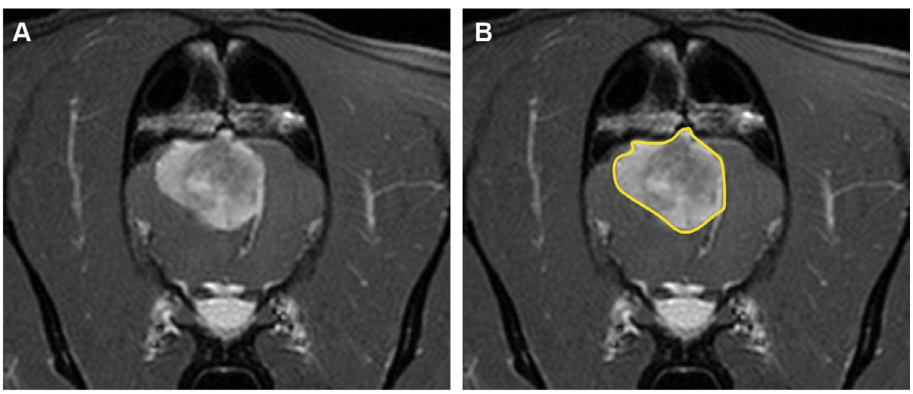


FIGURE 1 | Post-contrast T1-weighted MR images illustrating the method to measure lesion volume. (A) “Raw” image; (B) Image with traced lesion outline to determine area. All images showing the lesion were traced and summed to produce an estimate of lesion volume.

radiotherapy regimens, was examined to investigate their relationship with overall survival. Variables to include in the optimal multivariable model of survival were selected by minimizing the Bayesian information criterion associated with the least absolute shrinkage and selection operator (lasso).

Hazard ratios provide estimation of relative likelihood of death within any specified period (or "instant") between the two treatment modalities but do not provide a result that is intuitive for owners. Therefore, using a counterfactual analysis method we also estimated mean survival under 1 treatment and the estimated overall difference in survival if the alternative treatment were to have been used instead, while taking account of variables that might influence treatment selection and variables associated with survival. This method is designed to generate results in which the bias introduced by treatment selection by clinicians can be minimized and provides a more intuitive answer for owners regarding overall survival. This analysis was implemented using survival time inverse-probability weighting estimation (Stata *stteffects ipw* command) and provided summary comparisons of overall survival between the two methods, by including weighting for the data "missing" in the counterfactual analysis because of non-random treatment allocation. Variables associated with survival in the lasso-selected multivariable model were incorporated into this treatment effects analysis. Stata 18 (StataCorp, College Station, TX) was used for all statistical analyses.

3 | Results

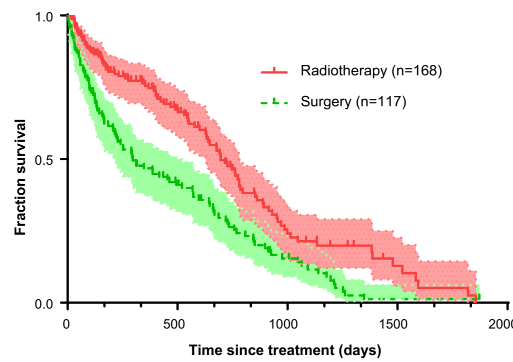
Information regarding 393 dogs with meningiomas was available for consideration for inclusion in this study. However, 108 dogs were excluded from further analysis because of incomplete data availability, treatment with both modalities, incomplete imaging series or lack of recording of dog weight. Of the 285 dogs that remained, the most common types were mixed breed dogs ($n=37$), Labrador retriever ($n=28$), German shepherd dog ($n=23$), golden retriever ($n=23$), boxer ($n=15$), bull terrier ($n=7$), Weimaraner ($n=6$) and West Highland white terrier ($n=5$). There were 143 females (of which 126 were spayed) and 142 males (of which 108 were neutered). Some ($n=56$) of the dogs included in this current analysis were also included in a previously published report on surgical treatment of meningiomas [37]. Histopathology results, confirming the suspicion of meningioma, were available for all except 13 of the surgery group; in 2 additional dogs the diagnosis was of another lesion (in 1 dog the egg of a capillarid worm was found in the excised lesion and in 1 the final diagnosis was lymphocytic encephalitis). Meningioma was confirmed on histopathological examination in five dogs in the radiotherapy group.

Although the age and weight of treated dogs were similar there were a few differences in summary statistics between the groups (Table 1). A greater proportion of surgical cases had rostrotentorial lesions and pre-operative seizures compared with radiotherapy cases. Lesion size, expressed as a ratio of volume (mm^3) to brain size (in kg, estimated from body weight) was similar between groups.

At the time of data collection 93 of the 168 dogs receiving radiotherapy and 101 of the 117 receiving surgery were known to be dead (euthanasia or natural death). Plotting of survival on a Kaplan–Meier graph showed longer overall survival in the radiotherapy group (Figure 2), including longer median survival time (696 days for radiotherapy versus 297 days for surgical excision, see Table 2). This difference was supported by the unadjusted hazard ratio (HR; for death of surgical versus radiotherapy cases) of 1.802 (95% confidence interval [CI]: 1.357–2.394; Table 3). Exploratory univariable analysis of the other putative prognostic factors suggests that only increasing age and weight were associated with increased hazard of death; notably there was no apparent association of larger lesion size with increased hazard (Table 3). Selection for the optimal multivariable survival model using lasso included only treatment modality (surgery vs. radiotherapy), weight and age (Table 4).

TABLE 1 | Summary of demographic characteristics of treatment groups.

	Surgery ($n=117$)	RT ($n=168$)
Pre-treatment seizures	107 (91%)	83 (49%)
Rostrotentorial	108 (92%)	99 (59%)
Weight (kg)	26.5 ± 12.6	21.0 ± 12.6
Lesion size (ratio)	2561 IQR: 1210–4125	2051 (IQR: 820–3796)
Age (yrs)	9.9 ± 2.1	10.2 ± 2.6



		Years after diagnosis		
		1	2	3
Number surviving	RT	88	45	16
	Surgery	50	27	10

FIGURE 2 | Kaplan–Meier curve illustrating the survival of dogs that underwent surgical excision (green, dashed line) or radiation therapy (red) for a single (presumed) intracranial meningioma. The wider shaded areas correspond to 95% confidence intervals.

TABLE 2 | Summary of survival in radiotherapy and surgery groups.

		Survival time (days)		
Treatment	Case number	25%	50%	75%
Radiotherapy	168	368	696	999
Surgery	117	99	297	768
Total	285	165	596	925

TABLE 3 | Univariable analysis of recorded possible risk factors for death.

Variable	Hazard ratio	95% confidence interval	
Weight (kg) (increase)	1.019	1.008	1.031
Age (yr) (increase)	1.074	1.015	1.137
Seizures	1.358	0.996	1.852
Rostrotentorial	1.367	0.968	1.929
Lesion size	1.000	1.000	1.000
Gender/neutering	1.027	0.924	1.141
Surgery (vs. RT)	1.802	1.357	2.394

Note: hazard ratios are described for one unit change. For instance, for weight the increased hazard of death for a dog that is 10 kg heavier than another is $1.019^{10} = 1.21$ (i.e., ~20% increase); "lesion size" in this analysis is ratio of tumor volume (mm^3) to estimated brain weight (kg).

TABLE 4 | Optimal multivariable model after variable selection using lasso.

Variable	Hazard ratio	95% confidence interval	
Surgery (vs. RT)	1.755	1.315	2.343
Body weight (increase)	1.023	1.011	1.036
Age (increase)	1.130	1.060	1.204

TABLE 5 | Comparative estimated survival times for dogs treated by radiotherapy or surgery.

Variable	Mean survival (days)	95% confidence interval
Radiotherapy	673	565–782
Surgery	480	395–564
Effect of surgery (compared to RT)	−194	−48 to −339

Survival time, for the study sample as a whole, analyzed using the counterfactual modeling inverse-probability weighting estimator, including and weighting prognostic factors identified as important through lasso analysis as above, was estimated as 673 (95% CI: 565–782) days for dogs with intracranial meningioma treated with radiotherapy and 480 (95% CI: 395–564) days for dogs treated by surgery. Thus, there is a mean reduction in survival time of 193 (95% CI: 48–339) days associated with surgery compared with radiotherapy (a 29% decrease; Table 5).

Analysis of interactions amongst various covariables was explored for their potential as further research avenues. Interaction between surgery and lesion location (i.e., rostro- versus caudotentorial) did not suggest a meaningful association (HR = 0.493; 95% CI: 0.213–1.145) nor between surgery and lesion size (HR: 1.000; 95% CI: 1.000–1.000). Of the 168 dogs receiving radiotherapy, 86 received conventionally fractionated protocols, 74 received hypofractionated stereotactic radiotherapy protocols, 8 received hypofractionated protocols, and none received a stereotactic radiosurgery protocol. Analysis suggested that these broad categories of radiation therapy were not associated with differing survival (HR = 0.971; 95% CI: 0.708–1.331; Table 6).

TABLE 6 | Summary of survival for dogs treated with different radiotherapy regimens.

Treatment	Case number	Survival time (days)		
		25%	50%	75%
Conventional fractionation	86	339	647	1046
Hypofractionated stereotactic	74	368	695	970
Hypofractionated	8	696	951	1134
Total	168	165	596	999

4 | Discussion

The results of this study strongly suggest that radiotherapy is associated with longer survival than surgery when treating dogs with single intracranial meningiomas. Moreover, the magnitude of effect is large: a mean decrease in survival time of ~29% associated with opting for surgery compared to radiotherapy, and the lower bound of the confidence interval indicates a minimum decrease in survival of ~7 weeks. The analytical method used here takes account of clinician decisions relating to treatment allocation (such as, in this dataset, tumor size, tumor location, and dog age and weight), so strengthening the reliability of the comparative outcomes we report here.

This finding is different from that found in an analysis of previously published data on meningioma treatment that suggested little difference in survival between these treatment modalities [22]. There are many possible reasons for this discrepancy, for instance that review was susceptible to various biases (such as selection bias and reporting bias) that will inevitably occur when summarizing small-scale non-randomized reports. Our dataset is much larger than those in previous reports and we have made attempts to account for other variables that might influence survival and so it is likely to be more reliable. Nevertheless, any observational dataset will contain biases, and it is possible that unmeasured variables could have contributed to the differential outcome we report here. The most obvious source of possible residual bias to account for our finding of superiority of radiotherapy is that clinicians might have deliberately or incidentally allocated to radiotherapy cases that were inherently more likely to survive. In this type of study, it is not possible to know whether this might have occurred, although it is unlikely, across all the collaborating clinics, that treatments were systematically allocated in such a way. There are possible reasons for positive allocation of more severely affected cases to radiotherapy, such as the shorter episodes of anesthesia and generally lower expected exacerbation of morbidity in animals that are comatose, continuously seizuring or unable to eat or drink. On the other hand, more severely affected dogs might be more likely to have surgery recommended as a means to rapidly reduce intracranial pressure. Although we did not request information regarding pre-treatment morbidity of the dogs (because it is difficult to categorize for this disease with such heterogenous presentation) the general experience with dogs with meningioma is that most do not present as life-threatening emergencies and so the overall effect of a small proportion of severely affected individuals is likely to be minimal. Furthermore, the Kaplan–Meier plot indicates that the difference between treatment modalities begins to become apparent at around 100 days after treatment initiation, suggesting that there is not a large or systematic difference in allocation of overtly poor-prognosis individuals to either treatment arm. Nevertheless, we cannot totally exclude the possibility of this bias without random treatment allocation. On the other hand, the magnitude of effect of different treatment in this study is large and the data were collected on a relatively large number of dogs in many different clinics, meaning that biased treatment allocation (unless systematic at all clinics) of a few dogs is unlikely to substantially affect the overall conclusion.

There are other potential sources of bias in this dataset, such as the non-inclusion of dogs for which we had missing information, because their systematic omission could imply that the treated sample of dogs with meningioma that we investigated might not be representative of the entire population of dogs with meningioma. However, there is no specific reason to suppose that the omissions would favor either treatment arm in this study. It is important to note that our designation of therapies as "black box" treatments means that there could be differences in outcome associated with different forms of "definitive-treatment radiotherapy." Our initial exploratory analysis does not support this hypothesis but there are relatively small numbers of animals in each sub-category meaning that further investigation is required. A further potential source of bias is disproportionate inclusion of non-meningioma cases between groups. We aimed to mitigate this possibility by including in the surgical group individuals that were thought to have a meningioma at the commencement of surgery (because the radiotherapy group would include similar cases).

Some of our secondary analyses provide results that seem unexpected, for instance that site of the lesion does not seem to be important (overall) in prognosis. There is some evidence that rostrotentorial lesions have a better prognosis [9, 10], but this is not supported by our analysis, nor by some previous publications [12]. Furthermore, our analyses do not support an interaction between site and surgery (i.e., that there is a differential effect between radiotherapy and surgery in the different sites [as might be expected if caudal cranial fossa lesions are more difficult to operate]), although this conclusion is susceptible to type II error because of the low power of this type of exploratory analysis.

In this dataset, as in others [15], there is a lack of evidence that lesion size influences survival. One possibility is that there might have been excessive errors in measurement of lesion size or the estimation of brain weight, but this seems an unlikely explanation, for two reasons. First, the volumetric method used for measuring lesion size has been evaluated previously and considered to be reliable and reproducible [38]. Second, the method for estimating brain weight from bodyweight [35] was derived from a large study ($n = 2100$) of many different dog breeds (and mixed breed dogs) suggesting that, in a large sample like ours, any imprecision will tend to "average out." In addition, there is no reason to think that there will be a systematic difference in measurement error between the treatment groups. A possible interpretation is that the size does not influence the outcome as much as other factors, for instance the impact of the treatment modality on lesion growth. This could be a reason why radiotherapy is associated with superior survival because it can treat every part of the tumor, whereas surgery will only be effective at removing what can be detected at surgery (and so might be incomplete). The Kaplan–Meier plot provides some support for this interpretation because the lines for surgery and radiotherapy begin to deviate at around 100 days after initiation of treatment, which is when it might be expected that the remnants of a slow-growing tumor might begin to cause recurrence of clinical signs. Lastly, pre-treatment seizures do not seem to be associated with overall survival, which is surprising considering that persistent seizures are a common reason for owners to euthanize dogs [39]. One explanation might be that both treatment strategies deal with the seizures similarly well (or poorly; although Monforte Monteiro et al. [40] specifically reported good success with radiotherapy in reducing seizures in dogs with brain tumors). Increasing dog weight appears to be associated with reduction in survival time. This might perhaps be best explained by the difficulties that owners have in dealing with larger dogs that are having seizures or becoming progressively less able to ambulate without assistance, but these interpretations cannot be supported or refuted by the data we have available at the current time.

One difficulty in interpreting these results is that although we included "site" as a possible prognostic factor it was simply dichotomized to rostro- versus caudo-tentorial and this is a relatively crude differentiation. We chose this method because it is difficult to completely classify the lesions into groups in a meaningful way without fragmentation of the data into tiny sub-categories of (almost) unique lesions, which would preclude meaningful statistical analysis, but there was a previous perception that there was a difference in outcome associated with rostro- versus caudo-tentorial lesions. A previous publication [37] suggested a worse prognosis for meningiomas resected from the pre-frontal region. We did not re-examine prognostic effects of lesions at this specific location because we have included some of those previously published cases in this study and reanalysis of overlapping datasets can generate misleading interpretations. A more generally relevant clinical question might be whether the tumors were "operable" or not, but this is highly subjective (although meningiomas are almost always located on the brain surface and so often relatively accessible) and a question that would not translate well from 1 set of observers to another and so we did not include it. Nevertheless, this could be relevant to the outcome we report here, because at least some of the cases treated by radiotherapy might not have been reasonable candidates for surgery.

It is sometimes suggested, without strong evidence, that the combination of RT and surgery might be the most preferred option [20, 21]. However, not only is this not a realistic option for many dog owners because of cost, but the cases that have been treated in this way form a biased sub-group, because they would have had to have survived for a certain period after the first treatment (usually surgery) before being available to undergo the second therapy. This type of "survivorship bias" [30, 31] carries the implication that such individuals are inherently likely to have a more favorable prognosis.

The most prominent limitations of this study are those associated with retrospective data accrual as outlined above. We also acknowledge that, because of the pragmatic objectives and breadth of this study, we did not collect nor report radiation equipment, treatment planning data, dose delivery, or adverse effects according to published guidelines [33, 34, 41]. Instead, the radiation oncologist at each institution defined "definitive intent" for each case and all types of external beam radiotherapy were included regardless of technology. The lack of detailed radiation dosimetry reporting, surgical technique, level of post-operative and anesthetic care, implies that we cannot recommend specific regimens for successful therapy. Radiation dosimetry, surgical technique and anesthetic protocols could all affect overall survival but might also influence cause of death (e.g., tumor progression versus late radiation adverse effects). In our pragmatic study design, we realized that the study design would inevitably omit much to this detail, but the trade-off benefit was a detailed highly generalizable analysis of comparative effectiveness (i.e., comparison of summary outcomes after application of the two therapies as currently used in everyday veterinary practice) because of our ability to include a large number of cases.

5 | Conclusion

This investigation that uses statistical methods to mitigate the bias associated with treatment allocation and controls for multiple factors that might influence survival, is likely to be the best evidence we can use to decide what treatment modality to recommend to owners of dogs with intracranial meningioma. The clear conclusion from this study is that radiotherapy should be recommended in preference to surgery no matter the size or location of the meningioma within the calvarium. The caveats we outline above regarding the possible residual confounding effects of treatment allocation according to severity of clinical signs at presentation should also be considered.

Disclosure

Authors declare no off-label use of antimicrobials.

Ethics Statement

Authors declare no Institutional Animal Care and Use Committee (IACUC) or other approval was needed. Authors declare human ethics approval was not needed.

Conflicts of Interest

The authors declare no conflicts of interest.

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