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Long-term clinical outcomes following surgery for spontaneous pneumothorax caused by pulmonary blebs and bullae in dogs – a multicentre (AVSTS Research Cooperative) retrospective study

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OBJECTIVES: To report the clinical characteristics and recurrence rate of spontaneous pneumothorax secondary to pulmonary blebs and bullae following surgical management in a large cohort of dogs. To explore potential risk factors for recurrence and describe outcome.

MATERIALS AND METHODS: Medical records were retrospectively reviewed for cases with spontaneous pneumothorax managed surgically between 2000 and 2017. Signalment, clinical presentation, diagnostic imaging, surgery, histopathology findings and patient outcomes were recorded. Follow-up was performed *via* patient records and telephone contact.

RESULTS: Records of 120 dogs with surgically treated pneumothorax were identified and reviewed, with 99 cases appropriate for exploratory statistical analysis. Median follow-up was 850 days (range: 9–5105 days). Two- and 5-year survival rates were 88.4% and 83.5%, respectively. There was recurrence in 14 of 99 dogs (14.1%) with adequate follow-up, with a median time to recurrence of 25 days (1–1719 days). Univariable Cox regression analysis suggested increased risk for recurrence in giant breeds (hazard ratio = 11.05, 95% confidence interval: 2.82–43.35) and with increasing bodyweight (HR = 1.04, 95% confidence interval: 1.00–1.09). Of 14 dogs with recurrence, six were euthanased, two died of causes related to pneumothorax and six underwent further treatment, of which five were resolved.

CLINICAL SIGNIFICANCE: Long-term survival for dogs with surgically managed spontaneous pneumothorax was good and associated with a low risk of recurrence. Giant breed dogs and increased bodyweight were the only variables identified as possible risk factors for recurrence. The outcome for dogs with recurrence undergoing a second intervention was also favourable.

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INTRODUCTION

Spontaneous pneumothorax is the accumulation of air within the pleural space in the absence of trauma. In dogs, it most commonly occurs secondary to rupture of pulmonary blebs and bullae. Pulmonary blebs are accumulations of air within the visceral pleura, and pulmonary bullae arise following destruction, dilation and confluence of adjacent alveoli within the lung parenchyma (Lipscomb *et al.* 2003). In one study, medium to large breed dogs appeared to be at an increased risk for spontaneous pneumothorax and Siberian huskies were overrepresented (Puerto *et al.* 2002).

Surgical management is advocated as the treatment of choice for spontaneous pneumothorax in dogs (Puerto *et al.* 2002). Median sternotomy is the most common approach and facilitates exploration of both sides of the thoracic cavity. The thoracoscopic approach has been described (Brissot *et al.* 2003), but appears to be associated with a high rate of conversion to open surgery if a pulmonary lesion cannot be identified (Case *et al.* 2015). Surgical treatment is associated with lower recurrence and mortality rates than non-surgical treatment (Puerto *et al.* 2002). Recurrence rates of 0 to 25% (0% (Lipscomb *et al.* 2003), 3% (Puerto *et al.* 2002), 17% (Case *et al.* 2015), 25% (Holtzinger *et al.* 1993)) for surgically treated cases are reported, compared with 50% for non-surgical treatment of spontaneous pneumothorax (Puerto *et al.* 2002). However, many of the current published studies have relatively small case numbers and include cases of pneumothorax secondary to disease other than pulmonary blebs and bullae (such as neoplasia, pneumonia and migrating foreign bodies), which may impact on these reported recurrence rates (Holtzinger *et al.* 1993, Puerto *et al.* 2002).

Of dogs with documented pneumothorax recurrence, the majority are reported to recur within 2 weeks of surgery (Holtzinger *et al.* 1993, Puerto *et al.* 2002, Case *et al.* 2015). However, there is scant information on the outcome of dogs with recurrent pneumothorax following further surgical management. In two retrospective studies in which recurrence was suspected or identified, all dogs were euthanased or died (Holtzinger *et al.* 1993, Puerto *et al.* 2002). To our knowledge, there are no reports of outcome of dogs undergoing further surgical management following pneumothorax recurrence.

The objectives of this study were to describe the clinical characteristics and report the recurrence rate of spontaneous pneumothorax secondary to pulmonary blebs and bullae following surgical management on a large cohort of dogs, explore potential risk factors for recurrence of spontaneous pneumothorax and to describe the outcome of dogs with recurrence. Based on previous studies, we hypothesised that: (1) multiple blebs or bullae; and, (2) high bodyweight might be potential risk factors for recurrence.

MATERIALS AND METHODS

All dogs that underwent surgical management for spontaneous pneumothorax over a 17-year period (January 1, 2000 to December 31, 2017) were included. The study was designed in conjunction with the Association of Veterinary Soft Tissue Surgeons (AVSTS) Research Cooperative (ARC) and ethical approval was granted by the University of Bristol Animal Welfare and Ethics Review Board (VIN 15/045). Centres were invited to participate *via* the ARC list server and by direct contact with authors. Cases were recruited from 11 veterinary referral hospitals (Small Animal Referral Hospital of the University of Bristol, School of Veterinary Medicine of the University of Wisconsin, Hospital for Small Animals of the University of Edinburgh, Hospital for Small Animals of the University of Vienna, Cornell University Veterinary Specialists, Anderson Moores Veterinary Specialists, Southfields Veterinary Specialists, North Downs Specialist Referrals, Pride Veterinary Centre, Clinic for Small Animal Surgery and Reproduction of Ludwig Maximilian University, Animal Emergency Centre Veterinary Referral Hospital, Victoria, Australia). Case records were reviewed for information regarding signalment (age, sex and breed), clinical presentation, diagnostic imaging modalities used, details of surgery, location and number of blebs or bullae identified at surgery, lung lobectomy technique, intraoperative and postoperative complications and histopathological findings. All surgeries were performed by either a supervised surgery resident or board-certified surgeon. Long-term follow-up information was obtained from medical records if available and through telephone communications with primary care veterinarians and owners when necessary. Information on whether the dog was alive or dead at the time of follow-up was acquired.

Cases were excluded if pulmonary blebs or bullae were not identified at surgery or on histopathological analysis, or if additional pulmonary disease (for example neoplasia, pyothorax or lung lobe torsion) was confirmed.

Cases with more than 4 weeks follow-up or cases with a known outcome (*e.g.* dogs that had died or been euthanased within 4 weeks of surgery) were included in the risk factor analysis. The data pertaining to all cases with surgically managed pulmonary blebs or bullae were summarised by descriptive statistics. For each dog, disease-free time was determined as the time elapsed from the date of surgery to the date of pneumothorax recurrence or censorship. Cases were then assigned to recurrence and non-recurrence groups and the Kaplan-Meier method and univariable Cox proportional hazards analysis were used to explore the association of a range of variables with time to recurrence: weight, breed, surgical approach, blebs or bullae in cranial lung lobes, blebs or bullae in more than one lung lobe and the presence of suspicious unoperated pulmonary lesions. A multivariable model was constructed using all variables that had

a univariable $P < 0.2$ (without including weight and giant breed together [which cannot be included together because of collinearity]) and then modified using likelihood ratio tests to compare models and guide elimination of variables. Dogs were censored from the disease-free analysis if they were alive at the time of analysis, lost to follow-up or died for a reason unrelated to the disease. All statistical testing used commercial software (Graph-Pad Prism 7.0 for Windows and Stata 14, StataCorp, College Station, TX).

RESULTS

One hundred and twenty surgically managed cases of spontaneous pneumothorax were reviewed. Nine cases without a definitive diagnosis of pulmonary blebs or bullae, or with a diagnosis of other pulmonary disease, were excluded, leaving a total of 111 cases for descriptive statistical analysis. Twelve cases were excluded from risk factor analysis due to insufficient follow-up, leaving a total 99 cases for inferential statistical exploration (Fig. 1).

Signalment

The mean age at initial presentation was 6 years 8 months (± 2 years 9 months). There were 66 males (55 castrated and 11 intact) and 45 females (30 spayed and 15 intact). Breeds represented were; Labrador retriever ($n = 17$), Siberian husky ($n = 12$), German shepherd dog ($n = 10$), lurcher ($n = 8$), golden retriever ($n = 8$), cross breed ($n = 7$), Samoyed ($n = 5$), English springer spaniel ($n = 5$), great Dane ($n = 4$), Border collie ($n = 3$), Jack Russell terrier ($n = 3$), German short-haired pointer ($n = 3$), Gordon setter ($n = 3$), Irish wolfhound ($n = 2$), Staffordshire bull terrier ($n = 2$), Rottweiler ($n = 2$), cocker spaniel ($n = 2$), Pomeranian ($n = 2$) and whippet ($n = 2$). Breeds represented by one dog include greyhound, Alaskan Malamute, Doberman pinscher, English setter, Irish setter, American bulldog, standard poodle, boxer, Akita, deerhound and basset hound.

Clinical findings and diagnosis

The clinical signs most frequently reported at presentation included dyspnoea (74, 67%), tachypnoea (60, 54%), lethargy (29, 26%), coughing (23, 21%), inappetence (20, 18%), cyanosis (13, 12%) and exercise intolerance (11, 10%). Imaging modalities used included radiographs in 21 (19%) cases and a combination of radiographs and CT or CT alone in 90 (81%) cases.

Surgery

The surgical approach was made *via* median sternotomy in 86 cases, lateral thoracotomy in 25, and thoracoscopic exploration was performed in four cases. A conversion to median sternotomy was required for one of 25 cases undergoing lateral thoracotomy and three of four cases undergoing thoracoscopy. Of the three thoracoscopic procedures converted to median sternotomy, all conversions were due to an inability to identify a pulmonary bleb or bulla thoracoscopically. Bullae were identified in all four cases following conversion to median sternotomy. The median number of pulmonary blebs and bullae identified at surgery for dogs undergoing median sternotomy and lateral thoracotomy were 1 (range: 1–6) and 1 (range: 1–2) respectively. An automatic stapling device was used for lung lobectomy in 97 cases; sutures ($n = 10$), a combination of sutures and staples ($n = 2$), and a vessel sealing device ($n = 2$) were also used.

Distribution of blebs and bullae

The majority of pulmonary blebs and bullae were located in the cranial lung lobes (96 of 182, 52.7%) (Table 1) and 41% (46 of 111) of dogs had blebs or bullae identified within more than one lung lobe during surgery.

Histopathological findings

Histopathology reports were available for 95 of 111 (86%) cases and pulmonary blebs or bullae were confirmed on histopathology in 47 of these 95 (49%). Additional histological findings

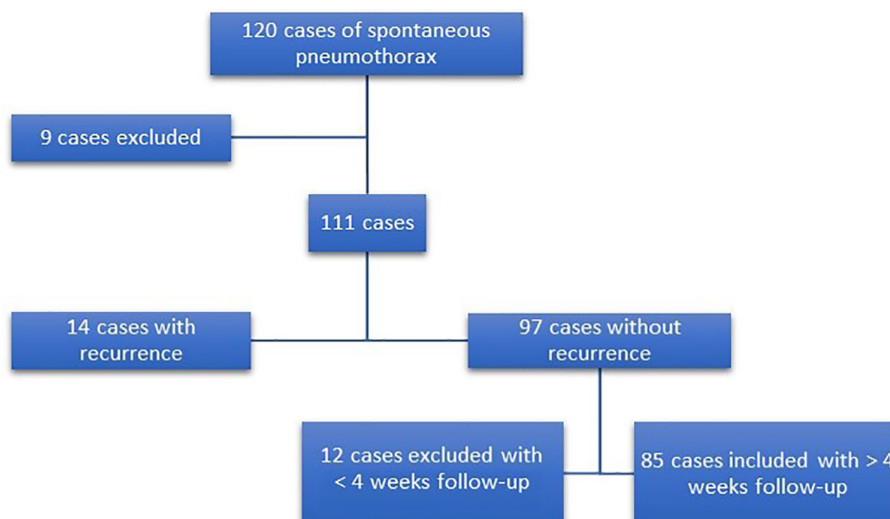


FIG 1. Flowchart illustrating case recruitment

Table 1. Lung lobe location of blebs and bullae identified at surgery

Lung lobe	Number	Percentage (%)
Right cranial	53	29.1
Left cranial	43	23.6
Right middle	29	15.9
Left caudal	22	12.1
Right caudal	19	10.4
Accessory	16	8.7

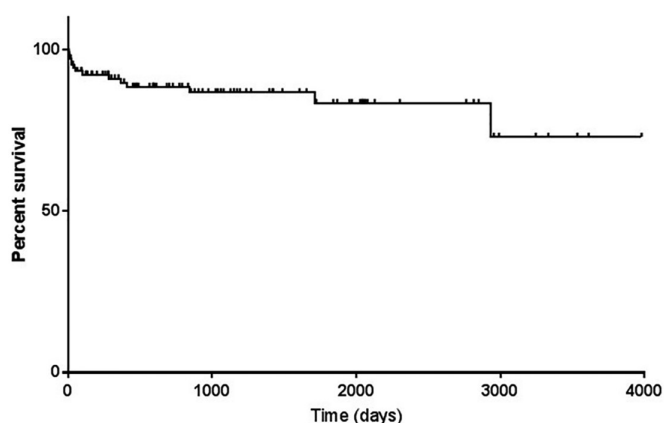


FIG 2. Kaplan-Meier survival curve for dogs with surgically treated spontaneous pneumothorax. Dogs were censored from the disease-free analysis if they were alive at the time of analysis, lost to follow-up or died for a reason unrelated to the presence of the disease. The median survival rate was not reached.

included atelectasis (45, 47%), fibrosis (27, 28%), haemorrhage (15, 16%), smooth muscle hypertrophy (15, 16%) and pulmonary congestion (6, 6%).

Outcome

Follow-up was obtained at a median of 850 days (range: 9–5105 days) post-operatively. The median period in which each dog was disease-free following surgery was 637 days (range: 9–3963 days). A median disease-free period for the study population could not be calculated because more than 50% of dogs were disease-free for the whole period of analysis (Fig. 2). The 2- and 5-year survival rates were 88.4% and 83.5%, respectively, with 55 and 25 dogs at risk respectively at these time points. Of the dogs with adequate follow-up ($n = 99$), recurrence of spontaneous pneumothorax was reported in 14 dogs (14.1%). The median time to recurrence was 25 days (range: 1–1719 days).

Initial statistical exploration included univariable Cox regression analysis of the relationship between various putative explanatory variables and the time to recurrence of pneumothorax. Of the six variables examined in our univariable analysis, only “giant breed” was conventionally statistically significant (“giant breeds,” hazard ratio [HR] = 11.05, 95% CI: 2.82–43.35, $P = 0.001$; “sternotomy versus thoracotomy,” HR = 0.56, 95% CI: 0.13–2.42, $P = 0.44$; “location of the bulla in cranial lung lobes,” HR = 2.49, 95% CI: 0.69–9.03, $P = 0.16$; “multiple bullae,” HR = 2.19, 95% CI: 0.73–6.58, $P = 0.16$; “unoperated lung lesions,” HR = 2.01, 95% CI: 0.56–7.26, $P = 0.29$; “dog

bodyweight,” HR = 1.04, 95% CI: 1.00–1.09, $P = 0.06$). In multivariable analysis only “giant breed” remained as a suggested risk factor. When weight was included in the multivariable model instead of giant breed the associated HR was 1.04 (95% CI: 1.00–1.09; $P = 0.08$). Extrapolation of these 95% CI implies the possibility of quite strong effects of increasing bodyweight on the rate of recurrence: assuming that all other factors are held constant, for each increase of 10 kg the hazard of recurrence may increase by as much as 232% from baseline or, alternatively, decrease by as much as 5% from baseline (although the lower bound HR is reported as 1.00 to two decimal places above, it was slightly below 1).

Twelve of 14 dogs with pneumothorax recurrence were dead at the time of follow-up; nine of 12 deaths were related to recurrence (Table 2). Six dogs were euthanased, and two dogs died following recurrence. Of the two dogs that died, the owners described an acute onset episode of severe dyspnoea consistent with tension pneumothorax. One dog was euthanased for persistent pneumothorax following a second surgery.

Six dogs underwent further management for recurrence, of which two dogs were successfully treated by continuous suction drainage for 3 days, at which point the pneumothorax resolved. The remaining four dogs underwent further surgery, during which bullae were identified within lung lobes reported as normal during the first surgery. Of those four dogs, one was still alive at the time of follow-up, two dogs died for reasons unrelated to the pneumothorax and the fourth dog was euthanased for pneumothorax recurrence 6 days after the second surgery (same dog as listed in previous paragraph) (Table 3). For the three dogs with pneumothorax resolution, no intra-operative or post-operative complications were reported. Median survival time was 38 (9- >1720) days for dogs with recurrence ($n = 14$) and 710 (34- >3963) days for dogs without recurrence ($n = 85$).

DISCUSSION

The recurrence rate for surgically managed cases of spontaneous pneumothorax secondary to pulmonary blebs and bullae was 14% in this study, which is comparable with previously reported data (0–25%) (Lipscomb *et al.* 2003, Puerto *et al.* 2002, Case *et al.* 2015, Holtsinger *et al.* 1993). This rate is considerably lower than the reported recurrence rate following medical management (50%) (Puerto *et al.* 2002). This study therefore supports the notion that surgical management is preferable for dogs with spontaneous pneumothorax. Because our study focused on a large cohort consisting solely of dogs with spontaneous pneumothorax secondary to pulmonary blebs and bullae it provides a more accurate representation of the results of surgical treatment of this condition than previous reports.

CT was the most frequently used imaging modality for investigation of spontaneous pneumothorax in this study. Previous studies have demonstrated the superiority of CT over radiographs to identify pulmonary blebs and bullae (Lipscomb *et al.* 2004), with reported accuracies of 76% for CT compared with

Table 2. Outcome of 14 dogs with spontaneous pneumothorax recurrence; including signalment, further medical or surgical management and cause of death

Case	Breed	Treatment	Cause of death
1	English springer spaniel	Second surgery Euthanased	Related
2	English setter	Second surgery	Unrelated
3	Irish wolfhound	Resolution with continuous chest drainage	Unrelated
4	German short-haired pointer	Euthanased	Related
5	Great Dane	Euthanased	Related
6	Siberian husky	Died	Related
7	Standard poodle	Euthanased	Related
8	German shepherd dog	Euthanased	Related
9	Labrador retriever	Second surgery	Unrelated
10	German shepherd dog	Second surgery	Alive
11	Deerhound	Euthanased	Related
12	Labrador retriever	Resolution with continuous chest drainage	Alive
13	Golden retriever	Euthanased	Related
14	Lurcher	Died	Related

Table 3. Outcome of four dogs with spontaneous pneumothorax recurrence that underwent further surgical management; including additional bleb/bulla location noted at surgery

Case	Outcome following second surgery	Reason for death	Notes
1	Recurrence	Related	Identified bulla within the left cranial lung lobe not previously noted at first surgery. Euthanased following second recurrence
2	Resolution	Unrelated	Identified bulla within the left cranial lung lobe not previously noted at first surgery
9	Resolution	Unrelated	Identified bulla within the right caudal lung lobe not previously noted at first surgery
10	Resolution	Alive	Identified multifocal emphysema but no discrete bullae. Histopathology report suggestive of multiple arterial thromboemboli

23% for radiographs (Au *et al.* 2006). Details of the individual CT findings were not available for this study, nor was the number of CT scans that were diagnostic for ruptured blebs or bullae, as this was not the purpose of the study. Interestingly, despite the wide use of CT in this study, median sternotomy was the most common approach (81% cases) for exploration of the thoracic cavity. Median sternotomy is largely preferred as it provides better access to both sides of the thoracic cavity. Our interpretation of this finding is that although CT is the favoured imaging modality to diagnose spontaneous pneumothorax and exclude other pulmonary disease, it does not influence the decision on surgical approach.

In humans, video-assisted thoracoscopic surgery (VATS) is the favoured approach over open thoracotomy for management of persistent or recurrent spontaneous pneumothorax. VATS is associated with decreased chronic pain and requirement for long-term analgesics (Chee *et al.* 1998). Human studies initially demonstrated a higher risk of recurrence following VATS when compared with open thoracotomy but it has since been shown that recurrence rates decline with surgeon experience (Ben-Nun *et al.* 2006). A high conversion rate (58%) has previously been reported in a study evaluating VATS for management of spontaneous pneumothorax in dogs (Case *et al.* 2015). This finding was replicated in the small number of cases in our study that underwent VATS, with three of four cases requiring conversion due to an inability to identify a lesion. This may be due to the difficulty in examining the entirety of the lung parenchyma dur-

ing thoracoscopic examination and the challenges of performing saline submersion during VATS. Further research into techniques for intraoperative identification of pulmonary lesions in dogs are required to increase our ability to diagnose lesions, reduce the requirement to convert to open techniques and reduce the risk of recurrence.

Pulmonary blebs and bullae were most commonly located in the cranial lung lobes and multiple lesions were commonly identified at surgery (41%). These findings are in agreement with previously published data and highlight the importance of thorough inspection of the entire lung parenchyma during surgery (Lipscomb *et al.* 2003). Of those cases with recurrence that underwent a second surgery, bullae were identified within lung lobes reported as normal during the first surgery. Whether these cases reflect a recurrence of spontaneous pneumothorax following rupture of a newly formed bleb or bulla, or whether these reflect lesions that were overlooked during the first surgery is not known. However, with a median time to recurrence of 25 days, it seems plausible that the majority of cases of recurrence are secondary to missed lesions. Histopathology confirmed pulmonary blebs or bullae in only 49% of tissue submitted for analysis. Interestingly, the previously reported pulmonary bleb and bullae classification system was not widely used, indicating that its clinical use may be limited (Lipscomb *et al.* 2003). However, histopathology plays an important role in excluding additional underlying disease processes that may alter prognosis, for example neoplasia.

Our study did not suggest increased risk of recurrence associated with the location or number of blebs or bullae identified at surgery, nor was there an apparent increased risk of recurrence associated with unoperated pulmonary lesions. We did identify a possible increased risk of recurrence for giant breed dogs (great Danes, wolfhounds and deerhounds), albeit with a small number of patients in this category. Human patients diagnosed with primary spontaneous pneumothorax tend to be taller than control patients (MacDuff *et al.*, 2010). Interestingly, it has been suggested that taller individuals subject the alveoli at the lung apices to significantly greater forces due to the gradient of negative pleural pressure which increases from the lung base to apex, which may also be applicable to giant breed dogs with deep chest conformation. Another explanation for this finding is the increased challenge that comes with examining the entire thoracic cavity of a giant breed dog. A possible association between patient weight and recurrence was also identified. It is therefore possible that the larger the dog (irrespective of conformation), the more likely they are to suffer recurrence. It is also important to note that all these analyses (both univariable and multivariable) include very wide confidence intervals, in keeping with the low statistical power resulting from the small number of recurrences; therefore, further data are required to confirm these exploratory findings.

Of the cases with pneumothorax recurrence, the majority died for reasons relating to recurrence, and the prognosis was therefore considered guarded. However, this outcome is likely skewed by the decision of owners to euthanase patients following diagnosis of recurrence. This may be due to the assumption that recurrence is associated with poor outcome or due to financial constraints. However, of the dogs that underwent further management (continuous chest drainage or further surgical management), resolution was achieved in the majority of cases. This should therefore encourage surgeons to consider further treatment for cases of recurrent spontaneous pneumothorax where possible. The use of pleural access ports for continued drainage has also been described in dogs managed for recurrent pneumothorax following surgery (Cahalane & Flanders 2012). This method was not reported in the current study but could be considered where appropriate.

One of the main limitations of this study was the relatively low rate of recurrence which, although it suggests a favourable outcome for patients following surgical management of spontaneous pneumothorax, limits the ability to analyse multiple risk factors for recurrence. The multicentre, retrospective nature of the study is also a limiting factor, as there will be inevitable differences between treatment protocols at different centres and complete data acquisition relies on medical documentation made at the time of treatment. Furthermore, our clinical impression is

that pneumothorax recurrence most commonly occurs within 4 weeks of surgery and a minimum of 4 weeks follow-up was therefore required for inclusion into risk factor analysis. This suspicion was confirmed with a median time to recurrence of 25 days. However, a small number of cases recurred outside of this time frame, and it is therefore possible that cases of recurrence were missed, and our reported recurrence rate is falsely low.

In conclusion, the long-term survival rate of dogs undergoing surgical treatment of spontaneous pneumothorax is good and the recurrence rate is relatively low. These findings support the current preference for surgical management of spontaneous pneumothorax secondary to pulmonary blebs or bullae in dogs. Statistical analysis was suggestive of an increased risk of recurrence in giant breed dogs and with increased bodyweight, but these findings should be interpreted with care due to the small numbers of such dogs included in the study. For dogs with recurrence, most died or were euthanased at the time of follow-up, although the outcome for dogs undergoing further medical or surgical management of recurrent pneumothorax was favourable and should therefore be considered for cases of recurrent spontaneous pneumothorax where possible.

Conflict of interest

The authors declare no conflicts of interest.

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