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ORIGINAL ARTICLE

Complications and outcomes of temporary tracheostomy in 24 cats

K. Elmenhorst *,[1], E. J. A. Villedieu*, M. Cantatore†, M. Rossanese‡ and S. J. Baines *

*Willows Veterinary Centre and Referral Service, Solihull, UK
†Lumbry Park Veterinary Specialist, Alton, UK
‡Department of Clinical Science and Services, The Royal Veterinary College, Hatfield, UK

[1]Corresponding author email: kine.elmenhorst@gmail.com

Objectives: To report complications and outcomes associated with the use of temporary tracheostomy tubes in cats. We hypothesised that a temporary tracheostomy tube in cats would be associated with lower complication rates and better outcomes than previously reported.

Materials and Methods: This retrospective descriptive study reviewed medical records from three referral centres to identify cats that underwent temporary tracheostomy between January 2004 and December 2020. Inclusion criteria included complete medical records with documentation of complications and short-term outcome of tracheostomy site healing.

Results: Twenty-four cats were included. Inflammatory or infectious laryngitis (8/24; 33%) and laryngeal neoplasia (6/24; 25%) were the most common underlying diseases. Other indications included upper airway obstruction after ventral bulla osteotomy (2/24; 8%); trauma (2/24; 8%); and one of each of laryngeal paralysis, oral mass biopsy and after arytenoid lateralisation. Three cats (13%) had an elective tracheostomy tube placed. 14/24 (58%) cats survived to discharge and 7/24 (29%) were euthanised due to the underlying disease process or complications unrelated to the tracheostomy. Tracheostomy-related complications occurred in 13/24 (54%) cats, of which 9/13 (69%) survived to discharge. Complete tube obstruction (7/24; 29%), partial tube obstruction (6/24; 25%) and tube dislodgement (2/24; 8%) were the most common complications. No cats were euthanised due to tracheostomy tube complications. Management was successful in 21/24 cats (87%). 3/24 (13%) cats died due to cardiopulmonary arrest.

Clinical Significance: Complications following temporary tracheostomy in cats were common (54%). However, successful management was possible in most cats (87%) with mortality mainly related to the underlying disease process rather than the tracheostomy tube itself.

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INTRODUCTION

Upper airway obstruction in small animals is a potentially life-threatening condition due to a variety of causes. A temporary tracheostomy provides a means of bypassing the upper airway, helping to stabilise patients prior to further investigation or definitive treatment (Mazzaferro, 2013). The use of temporary tracheostomy has been described in dogs and cats with conditions such as laryngeal neoplasia, laryngeal paralysis, inflammatory laryngeal disease, severe laryngeal swelling or trauma and laryngeal collapse (Guenther-Yenke & Rozanski, 2007; Hedlund, 1994).

In dogs, mortality rates following temporary tracheostomy tube placement range from 5% to 40%, depending on the underlying aetiology (Bird et al., 2018; Nicholson & Baines, 2012; Stordalen et al., 2020). Nicholson and Baines (2012) distinguished between successful tracheostomy tube management and

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patient outcome, classifying tracheostomy tube success as the ability to maintain the tracheostomy tube without complications leading to death, or the ability to wean the patient off the tracheostomy tube. When this classification system was applied and patients euthanised due to underlying disease process were excluded, a successful outcome of tracheostomy tube placement was reported in 81% to 97% of dogs (Bird et al., 2018; Nicholson & Baines, 2012; Stordalen et al., 2020). This is despite high complication rates, ranging from 38% to 95%, reported in dogs with tracheostomy tubes (Bird et al., 2018; Hedlund, 1994; Nicholson & Baines, 2012; Stordalen et al., 2020).

In contrast, information regarding outcomes following tracheostomy tube placement in cats is more limited. Guenther-Yenke and Rozanski (2007) reported a complication rate of 87% in 23 cats following temporary tracheostomy tube placement, including major complications in ten cats (44%) and the need for conversion to a permanent tracheostomy in six cats (26%). Only ten out of 23 (44%) cats were successfully managed with temporary tracheostomy. The reported mortality rate for cats with temporary tracheostomy was 26%, with six out of 23 cats dying. Of these, four cats were euthanised due to an underlying neoplastic process, one cat died following cardiopulmonary arrest due to complications from bite wounds and one cat was found dead due to an unknown cause. Similarly, Stepnik et al. (2009) reported a complication rate of 66% following permanent tracheostomy in 21 cats, with a mortality rate of 29% (six cats) prior to discharge. Five of these deaths were due to asphyxiation caused by mucus plugs, confirmed on necropsy and one cat died from pulmonary oedema and pneumonia. Of the 15 cats that were discharged from the hospital, another five cats died within a few weeks due to upper airway obstruction. Therefore, the overall mortality rate related to permanent tracheostomy in the immediate postoperative period was 52% (Stepnik et al., 2009).

The aim of this retrospective study was to report the complications and outcomes associated with the use of temporary tracheostomy tubes in cats from January 2004 to December 2020, and to compare these results with previous reports. Our hypothesis is that the use of temporary tracheostomy tubes in cats is associated with lower complication rates and better outcomes than previously reported.

MATERIALS AND METHODS

Ethical approval for the study was obtained from the Animal Health Trust's Animal Welfare and Ethical Review Board. Medical patient records of cats that underwent temporary tracheostomy between January 2004 and December 2020 were retrospectively reviewed. Cats were recruited from three veterinary academic or private practice referral hospitals. Cats were included if they had a temporary tracheostomy placed and had a comprehensive medical record, including documentation of complications and outcome. A minimum follow-up period until healing of the tracheostomy site was required. Three investigators independently searched the database using the search engine available in the practice management systems (Jupiter, Animana and CRIS), using the key words "cat", "cats", "feline", "temporary tracheostomy", "temp trach" and "trach tube".

Data were extracted between February 2021 and June 2021 across the three hospitals. The cases retrieved were imported into a Microsoft Excel spreadsheet. Data retrieved from the medical records included signalment, previous general medical history, reason for temporary tracheostomy, pre-existing respiratory disease, previous general medical or surgical treatment, laryngoscopy findings, presence or absence of neurological signs (including megaoesophagus), date of temporary tracheostomy, surgical procedure, intraoperative complications, maintenance regime for the temporary tracheostomy (cleaning intervals, pre-oxygenation and nebulisation), postoperative complications, duration of hospitalisation, duration of temporary tracheostomy use and short-term outcome up until the time of tracheostomy wound closure. Follow-up until tracheostomy site healing was obtained via clinical records and telephone interviews with referring veterinarians.

A temporary tracheostomy tube was placed in a routine manner as described by Mazzaferro (2013, pp. 74–78). Briefly, the cat was positioned in dorsal recumbency with the neck extended. A ventral midline incision was made through the skin and subcutaneous tissues overlying the cranial trachea. The sternohyoid muscles were separated in the midline, stay sutures were placed around the cranial and caudal tracheal rings, and a horizontal stab incision was made in the annular ligament between tracheal rings three and four or four and five to enter the tracheal lumen. The incision was extended to involve no more than 50% of the circumference of the trachea and a tracheostomy tube approximately 60% to 70% of the diameter of the tracheal lumen was placed. After tracheostomy tube removal, the wound was left to heal by secondary intention.

All complications were classified as either "minor" or "major". Minor complications included self-limiting issues (like cough), partial tube obstruction, or complications requiring medical intervention. Major complications included complete tube obstruction or tube dislodgement that required immediate intervention due to life-threatening circumstances or necessitated further surgical procedures. Each type of complication was only recorded once per cat.

The outcome for each case was classified as previously described by Nicholson and Baines (2012). In brief, the outcome of each cat was recorded as follows:

1. *Survived*: Cats survived until the tracheostomy tube was removed.
2. *Euthanised (underlying disease)*: Cats were euthanised with a tracheostomy tube in place due to an underlying disease deemed untreatable by the veterinarian, the owner or both, with no recorded influence of any tracheostomy tube complications.
3. *Euthanised (complications)*: Cats were euthanised with a tracheostomy tube in place due to a combination of the underlying disease, with recorded influence of one or more tracheostomy complications arising in hospital, where the resulting situation was deemed untreatable by the veterinarian, the owner or both.

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4. *Died*: Cats died while in hospital with a tracheostomy tube in place.

Tracheostomy tubes were termed "successful" if outcome 1 or 2 occurred, or "failed" if outcome 3 or 4 occurred.

RESULTS

Twenty-four cats met the inclusion criteria. A summary of the signalment, reason for temporary tracheostomy tube placement and postoperative complications can be found in Table 1.

The most common indication for temporary tracheostomy tube placement was upper airway obstruction due to inflammatory or infectious laryngitis (8/24; 33%), followed by laryngeal neoplasia (6/24; 25%). Other causes for placement due to upper airway obstruction included after ventral bulla osteotomy (2/24; 8%, one unilateral [left] and one bilateral); trauma (2/24; 8%); and one of each of the following: laryngeal paralysis, biopsy (mass at the base of tongue and excisional biopsy of retropharyngeal lymph nodes) and postoperative obstruction following arytenoid lateralisation. Three out of the 24 cats (13%) underwent elective tracheostomy tube placement. These included two cats following removal of a mass from the base of the tongue and larynx, and one following enucleation in a cat with redundant arytenoid mucosa causing partial obstruction at the time of anaesthesia induction.

No intraoperative complications were recorded during the tracheostomy tube placement. The experience level of the surgeon was recorded for 23 of 24 cases. In 21 of 23 cats (91%), a Diplomate in small animal surgery placed the tracheostomy tube while a resident in surgery under the guidance of a Diplomate in surgery or a residency-trained surgeon performed the remaining procedures.

The type and size of tracheostomy tube were determined in 17 cases. The most common was a 3.5 mm Shiley paediatric tube (10/17), followed by 3.0 mm (3/17), 4.0 mm (3/17) and 5.0 mm (1/17). Further information regarding the tubes was not provided.

No stoma dressings were used. Postoperative antibiotics were prescribed in ten of 24 cats (42%) with a variety of underlying disorders (see Table 1). All ten cats received amoxicillin-clavulanic acid, with one also receiving marbofloxacin. Additional medication included dexamethasone (6/24; 25%), prednisolone (5/24; 21%), vincristine (2/24; 8%) for cats with lymphoma, and acetylcysteine (2/24; 8%). Both cats prescribed acetylcysteine were diagnosed with obstructive laryngitis and experienced complete tube obstruction with mucus (one episode each). It was unclear from the records whether the acetylcysteine was started before or after these episodes.

Additional postoperative management included tracheostomy tube cleaning at regular intervals in 15 of 24 cats (62%), either every 2 hours (five cats) or 4 hours (ten cats), and nebulisation with saline for 5 to 10 minutes in nine of 24 cats (37%), either 2 hours (six cats) or every 4 hours (six cats). The median time from temporary tracheostomy tube placement to removal was 60 hours (range 12 to 168 hours). For cats that were euthanised or that died prior to discharge, successful management of the tracheostomy tube had been performed for a median of 96 hours (range 72 to 360 hours).

COMPLICATIONS

Complications occurred in 13 of 24 (54%) cats, with a total of 20 complications recorded. Six cats experienced more than one complication. Eight cats experienced major complications, including tube obstruction in seven of 24 cats (29%) and tube dislodgement in two of 24 cats (8%), with one cat having both complications. Eight cats experienced minor complications, including partial tube obstruction in six cats, and postoperative Horner's syndrome, cough, surgical site infection and pyrexia in the same cat following a ventral bulla osteotomy. Three cats (12%) experienced both a minor and major complications.

Of the 13 cats that experienced complications, nine cases (69%) survived to discharge. Of the four cats that did not survive to discharge, three were euthanised due to the underlying disease (squamous cell carcinoma and poorly differentiated carcinoma in two cats, and laryngeal paralysis with aspiration pneumonia in one) and one cat died from cardiopulmonary arrest of unknown cause 3 days following temporary tracheostomy tube placement.

OUTCOME

Using the classification system described by Nicholson and Baines (2012), temporary tracheostomy tube management was considered successful in 21 out of 24 cats (87%). This included 14 cats (58%) that survived to discharge and seven cats (29%) that were euthanised due to underlying disease processes, without any documented influence of tracheostomy-related complications. These cases were classified as outcome Groups 1 and 2, respectively.

The remaining three cats (12%) were classified as unsuccessful outcomes, in accordance with Groups 3 and 4. None of the cats were euthanised as a direct result of tracheostomy tube complications, meaning there were no cases in Group 3. However, three cats died while hospitalised with a tracheostomy tube in place and were classified as Group 4. One of these deaths occurred following conversion to a permanent tracheostomy and was attributed to airway obstruction. The other two cats suffered cardiopulmonary arrest, one in association with suspected complications of lymphoma treatment and the other following trauma with no identifiable cause of death.

Additional details regarding each outcome group are provided below.

Survived – 14/24 (58%)

Fourteen of 24 (58%) cats survived to discharge. These included seven of eight cats treated for obstructive laryngitis, two of six cats treated for neoplasia (both lymphoma), two of three cats treated with an elective tracheostomy tube, one of two cats treated due

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Table 1. Clinical summary of all cases

Case number	Breed	Sex	Age (months)	Reason for tracheostomy	Perioperative medications	Minor complication	Major complication	Death/Euthanasia	Survival to discharge
1	DSH	MN	92	Pharyngeal abscess due to FB	Amoxicillin-clavulanic acid	NA	NA	NA	Yes
2	Burmese	FN	134	Upper airway obstruction following VBO	Amoxicillin-clavulanic acid	NA	NA	Euthanasia – cholangiohepatitis and septic peritonitis	No
3	DSH	FN	186	Laryngeal SCC	NA	NA	NA	Euthanasia – poor prognosis	No
4	DSH	MN	216	Laryngeal SCC	NA	NA	Tube obstruction with mucus plug ×4 episodes	Euthanasia – poor prognosis	No
5	DSH	MN	156	Laryngeal adenocarcinoma	Amoxicillin-clavulanic acid dexamethasone	NA	NA	Euthanasia – poor prognosis	No
6	DSH	FN	132	Ulcerated, inflammatory (neutrophilic) mass	Amoxicillin-clavulanic acid, dexamethasone	NA	NA	Euthanasia – deterioration with aspiration pneumonia (present pre-operatively)	No
7	DSH	FN	156	Obstructive laryngitis	Prednisolone	NA	NA	NA	Yes
8	DSH	MN	132	Laryngeal lymphoma	Amoxicillin-clavulanic acid, dexamethasone and prednisolone	Surgical site infection, pyrexia	NA	NA	Yes
9	DSH	MN	60	RTA tongue laceration and multiple fractures to head	Amoxicillin-clavulanic acid	NA	Tube obstruction with mucus plug ×3 episodes	CPA – no obstruction found	No
10	Main Coon	MN	128	Laryngeal lymphoma	Vincristine and prednisolone	NA	NA	CPA – hypoperfusion and neutropenia, suspected due to vincristine toxicity	No
11	DSH	FN	132	Obstructive laryngitis	Amoxicillin-clavulanic acid, prednisolone	NA	NA	NA	Yes
12	Burmese	FN	55	Obstructive laryngitis	Acetylcysteine	Partial tube obstruction with blood	Tube obstruction with mucus plug	NA	Yes
13	Burmese	FN	32	Obstructive laryngitis	Amoxicillin-clavulanic acid, dexamethasone, acetylcysteine	NA	Tube obstruction with mucus plug	NA	Yes
14	DSH	MN	66	Trauma laryngeal fracture	NA	NA	NA	NA	Yes
15	DSH	FN	66	Obstructive laryngitis – managed 15 days with temporary tracheostomy before conversion to permanent tracheostomy	NA	NA	NA	CPA – airway obstruction 6 days post conversation to permanent tracheostomy	No
16	DSH	MN	132	Laryngeal lymphoma	Vincristine and prednisolone	NA	NA	NA	Yes
17	DSH	FN	122	Left laryngeal paralysis following cervical surgery	NA	Partial tube obstruction with mucus, laryngeal paralysis	Tube obstruction with mucus plug ×2	NA	Yes
18	Burmese	MN	72	Obstructive laryngitis	Dexamethasone	Partial tube obstruction with mucus	Tube obstruction with mucus plug	NA	Yes
19	DSH	MN	169	Obstructive laryngitis	Amoxicillin-clavulanic acid	NA	Tube dislodgement, not replaced as breathing well	NA	Yes

(Continues)

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Table 1. (Continued)

Case number	Breed	Sex	Age (months)	Reason for tracheostomy	Perioperative medications	Minor complication	Major complication	Death/Euthanasia	Survival to discharge
20	Siamese	MN	144	Chronic otitis interna with development of laryngeal paralysis and aspiration pneumonia. Upper airway obstruction following left unilateral arytenoid lateralisation	Amoxicillin-clavulanic acid, marbofloxacin and dexamethasone	Partial tube obstruction with mucous	NA	Euthanasia – progression of aspiration pneumonia	No
21	Burmese	MN	68	Elective following removal of perilaryngeal submucosa mass (chronic active pyogranulomatous inflammation)	NA	Partial tube obstruction with mucus and blood	NA	NA	Yes
22	DSH	FN	123	Elective following biopsy of laryngeal mass (poorly differentiated carcinoma)	NA	Tube dislodgement and, tube obstruction with mucus	NA	Euthanasia – poor prognosis	No
23	DSH	FN	60	Upper airway obstruction following left VBO	Horner's syndrome, coughing and left-sided head tilt (resolved 2 weeks post op)	NA	NA	NA	Yes
24	Burmese	FN	98	Elective following enucleation. History of chronic inspiratory effort, redundant arytenoid mucosa causing partial airway obstruction	Partial tube obstruction ×4 episodes	NA	NA	NA	Yes

CPA Cardiopulmonary arrest, DSH Domestic short hair, EUA Examination upper airways, FN Female neutered, MN Male neutered, NA Not applicable, RTA Road traffic accident, SCC Squamous cell carcinoma, VBO Ventral bulla osteotomy

to airway swelling following ventral bulla osteotomy, one of two cats treated for trauma and one cat treated for laryngeal paralysis.

Euthanised (underlying cases) – 7/24 (29%)

Four of seven (57%) cats were euthanised following histological confirmation of neoplasia (two of each of squamous cell carcinoma and adenocarcinoma). Two of seven cats (29%), one with laryngeal paralysis and one with an ulcerated oral lesion (neutrophilic inflammation), were euthanised due to deterioration in clinical status, due to aspiration pneumonia diagnosed prior to tracheostomy tube placement. The last cat developed cholangiohepatitis and septic peritonitis following surgery for a ventral bulla osteotomy, and the owners declined further treatment.

Euthanised (complications) – 0/24 (0%)

No cats were euthanised due to tracheostomy tube complications.

Death – 3/24 (12%)

Three out of 24 (12%) cats died during hospitalisation while the tracheostomy tube was still in place. One cat, diagnosed with inflammatory laryngitis, experienced cardiopulmonary arrest following airway obstruction 6 days after conversion to a permanent tracheostomy. This conversion was performed on postoperative day 15, after several unsuccessful attempts to remove the temporary tracheostomy tube. The cat was successfully managed for 6 days post-conversion before suffering an acute and fatal cardiopulmonary arrest. The remaining two cats died from cardiopulmonary arrest without confirmed tracheostomy-related complications. One of these cats had been diagnosed with lymphoma and had initiated treatment with prednisone and vincristine, but subsequently developed hypovolaemia and neutropenia prior to death. The second cat was presented following a suspected road traffic accident, sustaining a partial tongue laceration and multiple skull fractures. A tracheostomy tube was placed to manage progressive upper airway swelling and airway obstruction. The cat was hospitalised for 3 days prior to a sudden cardiopulmonary arrest. No underlying cause was identified during resuscitation, and no airway obstruction was noted.

DISCUSSION

This multicentre retrospective study described the outcomes and complications associated with temporary tracheostomy tube

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placement in 24 cats. The most common indication for temporary tracheostomy was upper airway obstruction secondary to inflammatory or infectious laryngitis, followed by laryngeal neoplasia. Despite the high overall complication rate (54%), successful tracheostomy tube management, as defined by Nicholson and Baines (2012), was achieved in 87% of cases. These findings suggest that, although complications are common, temporary tracheostomy tubes can be successfully managed in most cats, and mortality is more often associated with the severity of the underlying disease process than with tracheostomy-related issues.

The complication rate (13/24, 54%) observed in this study is lower than that previously reported. Guenther-Yenke and Rozanski (2007) found an overall complication rate of 87% in 23 cats with temporary tracheostomy tubes, while Stepnik et al. (2009) reported a 66% complication rate following permanent tracheostomy in 21 cats. In our cohort, major complications occurred in 42% (10/24) of cats, most commonly due to complete tube obstruction (7/13, 54%). This finding aligns with both feline and canine literature, where tube obstruction is consistently the most frequently reported complication (Bird et al., 2018; Guenther-Yenke & Rozanski, 2007; Nicholson & Baines, 2012; Stepnik et al., 2009; Stordalen et al., 2020).

Despite the incidence of complications, 87% of cats had a successful tracheostomy tube outcome, and 58% survived to discharge. These results are consistent with findings in dogs, where successful tube management has been reported in 81% to 100% of cases, even with complication rates up to 95% (Bird et al., 2018; Nicholson & Baines, 2012; Stordalen et al., 2020). This highlights the importance of vigilant postoperative monitoring to identify and manage complications early, rather than viewing their occurrence as a predictor of poor outcome.

The pathophysiology of tube obstruction in cats may be multifactorial. Cats have a narrower tracheal lumen and are thought to produce more viscous tracheal secretions than dogs, potentially predisposing them to mucus plug formation (Guenther-Yenke & Rozanski, 2007; Stepnik et al., 2009). In this study, two cats received the mucolytic agent N-acetylcysteine as part of their postoperative management. However, due to the retrospective nature of this study, it was unclear whether treatment began before or after temporary tracheostomy tube obstruction. N-acetylcysteine is thought to reduce mucus viscosity by breaking disulphide bonds in mucoproteins and enhancing ciliary clearance (Patel & Theokli, 2014; Sadowska et al., 2006). In humans, mucolytics are typically reserved for severe cases with temporary tracheostomy tubes, with emphasis instead placed on systemic hydration, humidification and airway protection to prevent secretion thickening. Further research is needed to evaluate the efficacy of N-acetylcysteine as a mucolytic agent in veterinary patients and its potential to reduce the incidence of tube obstructions.

Previous studies on temporary tracheostomy tubes in cats have reported high mortality rates and poor outcomes (Guenther-Yenke & Rozanski, 2007; Stepnik et al., 2009), which, in the authors' opinion, may contribute to reluctance among clinicians to perform this procedure in cats. In contrast, the current study focused specifically on the outcome of tracheostomy tube management, rather than overall survival rates and reported successful management of temporary tracheostomy tubes in 87% of the cats, with 58% of all cats surviving to discharge. Euthanasia due to the underlying disease process was the most common cause of mortality in this study, accounting for 29% (7/24) of cases. These results are comparable to those reported in dogs, where Nicholson and Baines (2012) documented successful tube management in 81% of cases and a 60% survival to discharge. It is important to note that the high mortality rate in previous studies looking at temporary tracheostomy tubes in cats was often associated with euthanasia during treatment, although it remains unclear whether this decision was primarily influenced by poor prognosis from the underlying disease or complications related directly to the tracheostomy tube.

The indications for temporary tracheostomy tube placement differ between cats and dogs. In dogs, the most common reason for temporary tracheostomy tube placement is postoperative airway swelling following multilevel airway surgery for brachycephalic obstructive airway syndrome (Bird et al., 2018; Nicholson & Baines, 2012; Stordalen et al., 2020). In contrast, cats typically require temporary tracheostomy tubes due to primary inflammatory or neoplastic swelling of the upper airway (Guenther-Yenke & Rozanski, 2007). Notably, even in cases involving neoplasia, successful tube management is achievable, as demonstrated by the 87% success rate in this study, allowing valuable time for definitive diagnosis and treatment planning.

Three cats (12%) in this study had an unsuccessful outcome. One cat died following conversion to permanent tracheostomy due to a mucus plug, while the other two suffered cardiopulmonary arrest with no evidence of tracheostomy-related obstruction at the time of death. No *post mortem* examinations were performed, limiting the ability to fully exclude tracheostomy-related complications as a contributing factor.

Several limitations should be acknowledged. The retrospective design introduces variability in surgical technique, postoperative management and medical record quality. Additionally, the small sample size, despite data from three referral centres, limits the generalisability of the observations.

In conclusion, temporary tracheostomy tube placement, although infrequently performed in cats, can be successfully managed in the majority of cases. While associated with a high complication rate, these complications are often manageable and do not necessarily preclude a positive outcome. The clinical outcome of these cats was primarily dependent on the underlying disease process rather than complications related to temporary tracheostomy tube placement. The results of this study support the role of this procedure as a viable and often life-saving intervention, provided appropriate postoperative monitoring is in place.

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Author contributions

K. Elmenhorst: Writing – review and editing; writing – original draft; investigation. **S. J. Baines:** Writing – review and editing; data curation; supervision. E. Villedieu has provided ethical approval and helped with editing and reviewing data. Cantatore

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and Rossanese has both helped with data collection, and review of the paper.

Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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