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Bacterial infection before and after stent placement in dogs with tracheal collapse syndrome

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Abstract

Background: Dogs with tracheal stents often have positive airway bacterial cultures. The pathogenicity of these organisms and risk factors for infection have not been investigated.

Objective: Describe bacterial infection in dogs with tracheal collapse before and after tracheal stent placement.

Animals: Fifty-three client-owned dogs.

Methods: Retrospective review of medical records of dogs receiving tracheal stents with thoracic radiographs, tracheoscopy, and endotracheal lavage.

Results: There was no difference between the overall prevalence of dogs with positive bacterial cultures before (31/38; 82%) or after stent placement (24/31; 77%) (P = .67). An increased number of geriatric (17/28; 61%) and traditional-type collapse (TTC) (16/26; 62%) dogs had positive pathogenic airway infections before stent placement, compared to young (8/25; 32%; P = .04) and malformation-type collapse (MTC) dogs (9/27; 33%; P = .04). After tracheal stent placement, geriatric dogs had a 52% reduction in pathogenic bacteria infection frequency (P = .02) and dogs with TTC had a 56% reduction in pathogenic bacteria infection frequency (P = .01). Significant risk factors for pathogenic infection included a history of pneumonia (OR = 3.6; 95% CI, 0.28-43.36) and cardiac disease (OR = 1.25; 95% CI, 0.16-9.92) in geriatric dogs, and hepatomegaly in young dogs (OR = 1.5; 95% CI, 0.12-19.44).

Conclusions and Clinical Importance: Tracheal stent placement does not increase the overall rate of pathogenic bacterial infection in dogs with tracheal collapse and can decrease the rate of subsequent pathogenic infections in geriatric dogs and dogs with TTC that require tracheal stenting. Airway culture and cytology should be performed in all dogs undergoing tracheal stent placement.

KEYWORDS

airway culture, interventional radiology, tracheal collapse, tracheal stent, tracheal wash

Abbreviations: IR, interventional radiology; MTC, malformation-type tracheal collapse; TC, tracheal collapse; TTC, traditional-type tracheal collapse.

1 | INTRODUCTION

Dogs with tracheal collapse (TC) often receive antibiotics. However, the role of bacterial infection in these dogs is unknown. In dogs with TC, 83% have positive cultures, with *Pseudomonas* species identified most frequently (58%).[1] Despite the high frequency of positive cultures, an association between bacterial infection and TC is not ultimately established because of the absence of cytological evidence supporting an infection.[1]

Infection and pneumonia have been associated with tracheal stent placement in dogs, and might develop because of decreased mucociliary clearance, stent-induced inflammation, failure of the stent to become embedded within the tracheal mucosa, or oropharyngeal colonization.[2,3] The presence of bacterial tracheitis might further decrease mucosal integration of the stent, resulting in progressive coughing or stent migration.[3] Tracheoscopic examination after tracheal stent placement reveals gaps (between the trachea and stent) filled with mucous plugs in 10/18 (56%) of dogs, although bacterial cultures are not reported.[4] Bacterial tracheitis is confirmed in cultures obtained via tracheoscopy in 5/12 (42%) of dogs after placement of nitinol stents, but follow-up was not available for 4/5 (80%) of dogs with confirmed bacterial tracheitis.[3]

Although bacterial populations in dogs with TC and tracheal stent placement are described, little is known about the pathogenicity of these organisms and the clinical factors that predispose dogs with tracheal stents to bacterial infection. The purpose of this study was to determine the frequency of bacterial infection in a population of dogs with tracheal collapse syndrome (TCS) before, and after, tracheal stent placement using microbiological results as well as concurrent cytologic and radiographic findings in support of pathogenicity. Additional aims of this study included identifying risk factors for infection as well as the most common bacterial isolates and sensitivities in dogs with TCS receiving tracheal stents. The authors hypothesized that tracheal stent placement would decrease the risk of pathogenic infection in geriatric dogs and dogs with traditional-type (TTC) TCS; however, younger dogs and those with malformation-type (MTC) TC would have higher rates of infection after tracheal stent placement.

2 | MATERIALS AND METHODS

2.1 | Medical records

A retrospective review of medical records and imaging findings of dogs with tracheal stent placement examined by the interventional radiology (IR) Service between September 2009 and November 2015 was performed. Only dogs with thoracic radiography, tracheoscopy, and endotracheal lavage culture results were included. Data collected from the medical records included age, sex, breed, prior medical management, radiographic results, tracheoscopic findings, TC type, endotracheal lavage culture/cytology, ancillary procedures, and comorbidities. Comorbidities recorded were: history of pneumonia, cardiac disease, hepatomegaly, thoracic skeletal disease (sternal abnormality or rib fractures), cystolithiasis, chronic nephropathy, diabetes mellitus, hyperadrenocorticism, and hypothyroidism. Both IR and referring veterinarian records (when available) were evaluated to see if animals were administered antimicrobials alone, steroids alone, or both antimicrobials and steroids at the time of stent placement. "Before-stent" dogs included those dogs with endotracheal lavage bacteriological cultures obtained at the time of initial stent placement, whereas "after-stent" dogs had endotracheal lavage bacteriological cultures obtained at any point at least 1 week after stent placement. All dogs had aerobic cultures with antimicrobial sensitivity performed. Anaerobic and *Mycoplasma* cultures were obtained at the discretion of the clinician. A "positive culture" was defined as any endotracheal lavage culture positive for bacteriologic growth. A "positive pathogenic culture" contained compatible cytological evidence (septic intracellular suppurative, septic extracellular suppurative, or nonseptic suppurative with supportive overall impression of the clinical pathologist for septic process such as neutrophil pathology or excessive degree of neutrophilic inflammatory process), radiographic findings consistent with pneumonia 72 hours before or after culture acquisition, or both compatible cytological and radiographic findings.

2.2 | Imaging studies

All dogs had 3-view thoracic radiography performed within 72 hours of tracheal stent placement that were reviewed for the presence of pneumonia by a board-certified radiologist.

Tracheoscopic examination was performed before and after tracheal stent placement under general anesthesia with the dog in sternal recumbency. All tracheoscopic exams were performed by or under the supervision of a board-certified surgeon or board-certified internist. The presence of TC and determination of collapse type was based on subjective appearance during tracheoscopy. Diagnosis of TTC was based on the finding of weakened tracheal cartilage rings with flattened tracheal lumen. Diagnosis of MTC was based on the appearance of firm but abnormally developed tracheal cartilage. Contact of the expanded stent was assessed via presence or absence of an area lacking contact between the stent and tracheal wall ("gutter"; Figure 1). If gutters existed, balloon dilation of the stent was routinely performed. After tracheal stent placement and tracheoscopic evaluation, an endotracheal wash was performed through a sterile endotracheal tube to obtain samples for bacterial culture and, if sufficient sample, cytological evaluation. An upper airway exam was performed or supervised by a board-certified surgeon for presence of an elongated soft palate, laryngeal collapse, laryngeal paralysis, everted laryngeal saccules, or epiglottic retroversion, and repair was performed if indicated.

2.3 | Statistical analysis

Baseline descriptive statistics are presented as mean and SD for normally distributed variables. Between groups, analyses of baseline

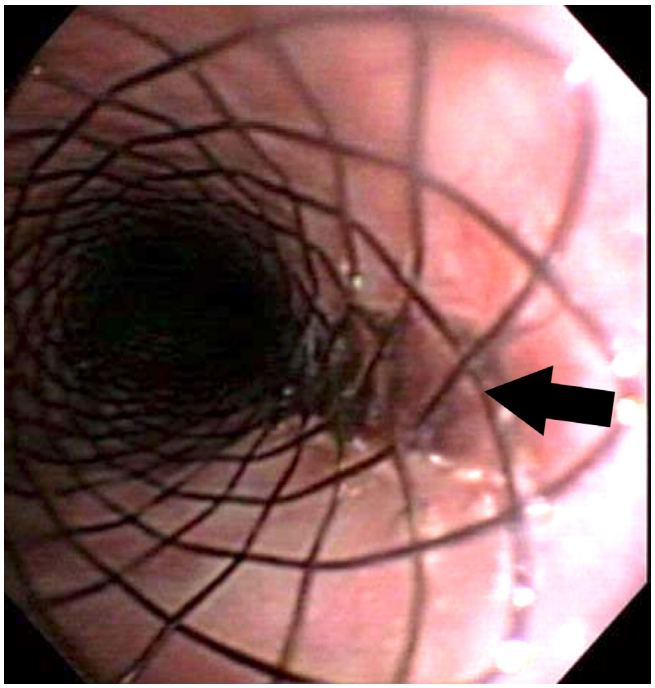

FIGURE 1 A tracheoscopic image of a malformation-type trachea after stent placement. An incompletely filled area ("gutter") lacking contact between the stent and tracheal wall is visible at the 4 o'clock position (arrow). This gutter can result in accumulation of mucus, fluid, and tissue

variables were performed using analysis of variance (ANOVA). The normality of the error residuals was analyzed by the Kolmogorov-Smirnoff analyses and deemed normal. Analysis for proportions of categorical variables was performed using Chi-square analysis or Fisher's exact test where appropriate. All analyses were considered significant if $P < .05$ and were carried out using a commercially available statistical software (SAS 9.4, SAS Institute Inc, Cary, North Carolina).

3 | RESULTS

3.1 | Animal population

Review of medical records identified 84 dogs that had tracheal stent placement during the study time period. Of these dogs, 53 had thoracic radiography, tracheoscopy studies, and endotracheal lavage cultures available for review, satisfying criteria for inclusion in the study.

Of the 53 dogs, 33 were male (62%) and 20 were female (38%). Thirty-one dogs were male neutered, 2 male intact, 17 female spayed, and 3 female intact. Yorkshire Terriers (n = 37/53; 70%) were the most common breed affected, followed by Pomeranians (n = 9/53; 17%), Maltese (n = 3/53; 6%), Yorkshire crosses (n = 2/53; 4%), Pug (n = 1/53; 2%), and Japanese Chin (n = 1/53; 2%). The age at time of first tracheal stent placement ranged between 2 and 16 years (mean 8 ± 3.4 years).

3.2 | Tracheal collapse type

Of the 53 dogs with TCS requiring stent placement, 26 dogs had TTC (49%) and 27 dogs had MTC (51%). The mean age for dogs with MTC was 6.8 ± 0.62 years versus 9.2 ± 0.63 years for dogs with TTC ($P = .01$). For dogs with MTC, 16/27 (59%) were less than the mean age (8 years), and classified into a young cohort, whereas 11/27 (41%) were greater than or equal to 8 years of age and classified into a geriatric cohort ($P = .17$). For dogs with TTC, 9/26 were young (35%) and 17/26 (65%) were geriatric ($P = .02$). Yorkshire Terriers comprised the majority of dogs with MTC (24/27; 89%), followed by Pomeranians (2/27; 7%) and Pug (1/27; 4%) ($P \leq .01$). Half of the dogs with TTC were Yorkshire Terriers (13/26; 50%), followed by Pomeranians (7/26; 27%), Maltese (3/26; 12%), Yorkshire crosses (2/26; 8%), and Japanese Chin (1/26; 4%). A majority of Yorkshire terriers (24/37; 65%) had MTC, whereas 13/37 (35%) had TTC ($P = .01$). For the 27 dogs with MTC, 17 dogs (63%) had presence of a visible gutter, 4 dogs (15%) did not have a gutter, and in 6 dogs (22%) gutter evaluation was not recorded.

3.3 | Culture and cytology results

A total of 81 bacteriological culture results were available from 53 dogs (Table 1). Thirty-one of 38 dogs with cultures taken at initial stent placement (before-stent cultures) had positive bacteriological cultures (31/38; 82%). Of the 38 dogs with before-stent cultures, 25 had positive pathogenic bacteriologic cultures (25/38; 66%). Of the 31 positive before-stent cultures, 25 (25/31; 81%) were pathogenic, with compatible cytological (n = 10), radiographic (n = 6), or both cytological and radiographic findings (n = 9). For 19 dogs with compatible cytology, 9 were septic intracellular suppurative, 4 were septic extracellular suppurative, and 6 were nonseptic suppurative. Of the 38 before-stent cultures, 18 (18/38; 47%) cultures were positive with radiographic evidence of pneumonia, intracellular septic cytology, or both; 7/38 (18%) cultures were positive with extracellular suppurative or nonseptic suppurative cytology, 6/38 (16%) cultures were positive without radiographic or cytological evidence of pathogenicity, and the remaining 7/38 (18%) cultures were negative.

Thirty-one dogs had 43 after-stent cultures performed after initial stent placement. After-stent cultures were obtained from 8 to 1602 days after initial stent culture (mean 585 ± 416 days). Cultures were obtained in dogs with clinical deterioration by clinician discretion via endotracheal wash during re-stenting procedure (37/43; 86%) or tracheoscopy (6/43; 14%). Of the 31 dogs that required a second stent, 9/31 (29%) were because of stent fracture, 14/31 (45%) were because of tissue ingrowth, and 8/31 (26%) were because of progressive TC. Five dogs required placement of a third stent (3 for tissue ingrowth, 1 for stent fracture, and 1 for progressive collapse). One dog had a fourth stent placed for progressive TC.

Twenty-four of 31 dogs with after-stent cultures had positive bacteriologic cultures (24/31; 77%). Of the 31 dogs with after-stent

TABLE 1 Airway cultures and cytology in dogs with tracheal collapse syndrome (TCS). The number of dogs with "before-stent" cultures (endotracheal lavage bacteriological cultures obtained during initial stent placement), "after-stent" cultures (endotracheal lavage bacteriological cultures obtained at any point at least 1 week after stent placement), both "before-stent" and "after-stent" cultures, and airway cytology performed

	Before-stent cultures	After-stent cultures	Both before- and after-stent cultures	Airway cytology
Number of dogs (N = 53)	38/53 (72%)	31/53 (58%)	16/53 (30%)	37/53 (70%)
Number of cultures (N = 81)	38/81 (47%)	43/81 (53%)	37/81 (46%)	50/81 (64%)

cultures, 20 had positive pathogenic bacteriologic cultures (20/31; 65%). Of the 24 positive after-stent cultures, 20 (20/24; 83%) were pathogenic, with compatible cytological (n = 10), radiographic (n = 4), or both cytological and radiographic findings (n = 6). For the 16 dogs with compatible cytology, 12 had septic intracellular suppurative and 4 had nonseptic suppurative cytology. For these 31 dogs with after-stent cultures, 17/31 (55%) had positive cultures with radiographic evidence of pneumonia, intracellular septic cytology, or both; 3/31 (10%) had positive cultures with extracellular suppurative or nonseptic suppurative cytology, 4/31 (13%) had positive cultures without radiographic or cytological evidence of pathogenicity, and the remaining 7/31 (23%) had negative cultures. Of the 20 dogs with positive pathogenic after-stent cultures, 13 dogs had 1 positive pathogenic after-stent culture, 3 dogs had 2 positive pathogenic after-stent cultures, 3 dogs had 3 positive pathogenic after-stent cultures, and 1 dog had 4 positive pathogenic after-stent cultures.

There was no significant difference between the prevalence of dogs with positive bacterial cultures before stent placement (31/38; 82%) or after stent placement (24/31; 77%) (P = .67). There was no significant difference between the prevalence of dogs with positive pathogenic cultures before stent placement (25/38; 66%) or after stent placement (20/31; 65%) (P = .91). When evaluating dogs with radiographic evidence of pneumonia, intracellular septic cytology, or both radiographic evidence of pneumonia and intracellular septic cytology, there was no significant difference between the prevalence of positive cultures in dogs before stent placement (18/38; 47%) or after stent placement (17/31; 55%) (P = .54).

3.4 | Ancillary medical management

Medical records were reviewed for the use of antibiotics and steroids at time of stent placement. Information regarding recent antibiotic use was available for review in 66/81 (81%) of cultures, and 53/81 (65%) of cultures had information regarding recent steroid use.

Of the 66 cultures with antibiotic information available, 27/66 (41%) were obtained during antibiotic use, and 39/66 (59%) were obtained in the absence of antibiotic use. Approximately half of cultures with antibiotic information available were obtained from dogs in the before-stent group (34/66; 52%), and the remainder were obtained from dogs in the after-stent group (32/66; 48%). There was no significant difference in the frequency of positive cultures obtained during antibiotic use before stent placement (12/34; 35%) compared to cultures obtained after stent placement (8/32; 25%) (P = .36).

Of the 53 cultures with steroid information available, 39/53 (68%) were obtained during steroid use and 14/53 (32%) were obtained in the absence of steroid use. Thirty of 53 (30/53; 57%) cultures with steroid information available were obtained from dogs in the before-stent group, and the remainder were obtained from the after-stent group (23/53; 43%). There was no significant difference in the frequency of positive cultures obtained during steroid use before stent placement (16/30; 53%) compared to cultures obtained after stent placement (17/23; 74%) (P = .13).

A majority of cultures (61/81; 75%) had information regarding antibiotics that dogs were prescribed after culture acquisition. Of these cultures, 12/61 (20%) were negative and 49/61 (80%) were positive for bacteriologic growth. For negative cultures, 7/12 (58%) were taken from dogs that were on antibiotics at time of culture acquisition, whereas 5/12 (42%) were not receiving antibiotics. Of the 49 positive cultures, antimicrobial sensitivity testing suggested empirically prescribed antibiotics were correct for 31/49 (63%) and incorrect for 18/49 (37%) of cultures. Combination treatment with amoxicillin-clavulanate/enrofloxacin was correct for 17/19 (89%) of cultures. Monotherapy with amoxicillin-clavulanate was correct for 10/19 (53%) of cultures, marbofloxacin was correct for 1/4 (25%), enrofloxacin was correct for 2/3 (66%), and cefpodoxime was correct for 1/1 (100%).

3.5 | Bacterial isolates

The most common bacterial isolates for all bacteriological cultures included *Escherichia coli* (23%) and *Pseudomonas* species (15%) (Table 2). The most frequently isolated organisms at the time of initial stent placement (before-stent group) included *E. coli* (6/38; 16%), *Pseudomonas* species (6/38; 16%), and *Staphylococcus* species (6/38; 16%). The most frequently isolated organisms at least 1 week after initial stent placement (after-stent group) included *E. coli* (13/43; 30%) and *Pseudomonas* species (6/43; 14%). A majority of the most frequently isolated pathogens had compatible cytological, radiographic, or both cytological and radiographic signs of pathogenicity, including *E. coli* (84%), *Klebsiella pneumoniae* (83%), *Streptococcus* spp. (75%), *Pseudomonas* spp. (67%), and *Staphyloccocus* spp. (67%).

3.6 | Risk factors for infection

A significantly higher percentage of geriatric dogs (≥8 years of age) had positive before-stent pathogenic cultures (17/28; 61%), compared

TABLE 2 Bacterial isolates from 53 dogs with tracheal stent placement

Bacterial organism	Total # of specimens	# of specimens with isolate (before-stent)	# of specimens with isolate (after-stent)	# of pathogenic cultures
Escherichia coli	19/81 (23%)	6/19 (32%)	13/19 (68%)	16/19 (84%)
Pseudomonas	12/81 (15%)	6/12 (50%)	6/12 (50%)	8/12 (67%)
Pseudomonas aeruginosa	8/81 (10%)	3/8 (38%)	5/8 (63%)	6/8 (75%)
Pseudomonas stutzeri (2 biotypes)	1/81 (1%)	1/1 (100%)	0	0
Other *Pseudomonas* spp.	3/81 (4%)	2/3 (67%)	1/3 (33%)	2/3 (67%)
Normal naso-oropharyngeal spp.	10/81 (12%)	5/10 (50%)	5/10 (50%)	10/10[a] (100%)
Staphylococcus	9/81 (11%)	6/9 (67%)	3/9 (33%)	6/9 (67%)
Staphylococcus pseudointermedius	4/81 (5%)	2/4 (50%)	2/4 (50%)	¾ (75%)
Staphylococcus intermedius	3/81 (4%)	2/3 (67%)	1/3 (33%)	1/3 (33%)
Staphylococcus coagulase negative	2/81 (2%)	2 (100%)	0	2/2 (100%)
Streptococcus	8/81 (10%)	4/8 (50%)	4/8 (50%)	6/8 (75%)
Beta-hemolytic streptococcus	6/81 (7%)	2/6 (33%)	4/6 (67%)	5/6 (83%)
Alpha-hemolytic streptococcus	1/81 (1%)	1 (100%)	0	0
Gamma-hemolytic streptococcus	1/81 (1%)	1 (100%)	0	1/1 (100%)
Pasteurella spp.	8/81 (10%)	3/8 (38%)	5/8 (63%)	5/8 (63%)
Non-enteric gram-negative rod (unable to speciate)	7/81 (9%)	3/7 (43%)	4/7 (57%)	4/7 (57%)
Klebsiella pneumoniae	6/81 (7%)	3/6 (50%)	3/6 (50%)	5/6 (83%)
Enterobacter cloacae	6/81 (7%)	3/6 (50%)	3/6 (50%)	5/6 (83%)
Stenotrophomonas maltophilla	5/81 (6%)	3/5 (60%)	2 (40%)	3/5 (60%)
Enterococcus	3/81 (4%)	1/3 (33%)	2/3 (67%)	3/3 (100%)
Bacillus	1/81 (1%)	1/1 (100%)	0	1/1 (100%)
Corynebacterium	1/81 (1%)	0	1 (100%)	0
Mycoplasma	1/81 (1%)	0	1/1 (100%)	1/1 (100%)
Serratia marcesens	1/81 (1%)	1/1 (100%)	0	1/1 (100%)
Morganella morganii	1/81 (1%)	0	1/1 (100%)	1/1 (100%)
Ralsotonia picketti	1/81 (1%)	1/1 (100%)	0	1/1 (100%)
Raoultella (Klebsiella) planticola	1/81 (1%)	0	1/1 (100%)	0/1
Enterobacter aerogenes	1/81 (1%)	1/1 (100%)	0	1/1 (100%)
Acinetobacter baumannii	1/81 (1%)	0	1/1 (100%)	1/1 (100%)
Sphingomonas paucimobilis	1/81 (1%)	1/1 (100%)	0	1/1 (100%)
Unidentified gram-positive organisms	1/81 (1%)	0	1/1 (100%)	0
Proteus mirabilis	1/81 (1%)	0	1 (100%)	1/1 (100%)

[a]Nine of 10 were in combination with other growths, including *Escherichia coli* (3), *Pseudomonas aeruginosa* (2), *Stenotrophomonas maltophilia* (2), *Klebsiella*, *Beta-hemolytic streptococcus*, non-enteric gram-negative rod (unable to speciate), and *Enterobacter cloacae*.

TABLE 3 Frequency of positive pathogenic infections in young dogs compared to geriatric dogs

Positive pathogenic cultures (PPC)	Young dogs (<8 years) (n = 25 dogs)	Geriatric dogs (≥8 years) (n = 28 dogs)	Change in positive pathogenic culture frequency in geriatric dogs	*P* value
Dogs with before-stent PPC	8/25 (32%)	17/28 (61%)	91% increase in infection frequency	.04*
Dogs with after-stent PPC	12/25 (48%)	8/28 (29%)	40% reduction in infection frequency	.15
Change in positive culture frequency after stent placement	50% increase in infection frequency	52% reduction in infection frequency		
P value	.25	.02*		

*$P < 0.05$.

TABLE 4 Frequency of positive pathogenic infections in dogs with traditional-type TC compared to malformation-type TC

Positive pathogenic cultures (PPC)	Malformation-type TC (n = 27 dogs)	Traditional-type TC (n = 26 dogs)	Change in positive pathogenic culture frequency in traditional-type dogs	*P* value
Dogs with before-stent PPC	9/27 (33%)	16/26 (62%)	88% increase in infection frequency	.04*
Dogs with after-stent PPC	13/27 (48%)	7/26 (27%)	44% reduction in infection frequency	.11
Change in positive culture frequency after stent placement	45% increase in infection frequency	56% reduction in infection frequency		
P value	.27	.01*		

*$P < 0.05$.

TABLE 5 Odds ratios for risk of positive pathogenic cultures associated with comorbidities

	Before-stent pathogenic cultures		After-stent pathogenic cultures	
Comorbidity	Young dogs (<8 years)	Geriatric dogs (≥8 years)	Young dogs (<8 years)	Geriatric dogs (≥8 years)
History of pneumonia	0.85	0.67	N/A	**3.6**
Cardiac disease	N/A	0.14	0.71	**1.25**
Hepatomegaly	N/A	0.27	**1.5**	0.19
Skeletal abnormalities	N/A	**1.07**	0.27	0.35
Cystolithiasis	N/A	0.31	N/A	N/A
Chronic kidney disease	N/A	N/A	N/A	N/A
Diabetes mellitus	N/A	N/A	N/A	N/A
Hyperadrenocorticism	N/A	N/A	N/A	N/A
Hypothyroidism	N/A	N/A	N/A	N/A

Abbreviation: N/A, no dogs with pathogenic infection had the comorbidity.
Bold values indicate significant (positive) odds ratio.

to younger dogs (<8 years of age) (8/25; 32%) (*P* = .04). In the young cohort, 32% (8/25) had positive before-stent pathogenic cultures, compared to 48% (12/25) after stent placement (*P* = .25). In the geriatric cohort, 61% (17/28) had positive before-stent pathogenic cultures that decreased to 29% (8/28) of dogs after stent placement (*P* = .02) (Table 3).

A significantly higher percentage of dogs with TTC had positive before-stent pathogenic cultures (16/26; 62%), compared to dogs with MTC (9/27; 33%) (*P* = .04). For dogs with MTC, 9/27 (33%) had positive pathogenic before-stent cultures, compared to 13/27 (48%) with positive pathogenic after-stent cultures (*P* = .27). For dogs with TTC, 16/26 (62%) had positive pathogenic before-stent cultures, compared to 7/26 (27%) with positive pathogenic after-stent cultures (*P* = .01) (Table 4).

A majority (39/53; 74%) of dogs had comorbidities. Nineteen dogs had 1 comorbidity, 16 dogs had 2 comorbidities, and 4 dogs had 3 comorbidities. Comorbidities included cardiac disease (n = 22), hepatomegaly (n = 16), thoracic skeletal disease (n = 10), history of pneumonia (n = 6), hypothyroidism (n = 3), cystolithiasis (n = 2), chronic kidney disease (n = 2), diabetes mellitus (n = 1), and hyperadrenocorticism (n = 1). Dogs with comorbidities were 5.6 times more likely to have positive pathogenic before-stent cultures and 2.8 times more likely to have positive pathogenic after-stent cultures. For dogs with positive before-stent pathogenic cultures, 50% (4/8) of young dogs had comorbidities present, versus 88% (15/17) of geriatric dogs (*P* = .04). Geriatric dogs were more likely to have positive before-stent pathogenic cultures (OR = 1.9; 95% CI, 1.06-10.19), compared to younger dogs. Among geriatric dogs, those with a history of pneumonia (OR = 3.6; 95% CI, 0.28-43.36) and cardiac disease (OR = 1.25; 95% CI, 0.16-9.92) were more likely to have positive after-stent pathogenic cultures. Young dogs with a history of hepatomegaly were more likely (OR = 1.5; 95% CI, 0.12-19.44) to have positive after-stent pathogenic cultures (Table 5).

3.7 | Ancillary procedures

Information regarding dogs that received ancillary procedures is in the Supporting Information document.

4 | DISCUSSION

In this study, a majority of dogs with TC had evidence of pathogenic infection before, and after, tracheal stent placement. In dogs with TC, 83% (24/29) have positive bacteriologic cultures. Those results are similar to findings from this study, where 81% (31/38) of dogs with TC had positive bacteriologic cultures. In contrast to previous studies, however, we conclude that a majority of these cultures (66% of before-stent dogs and 61% of after-stent dogs) represented pathogenic infections, with compatible airway cytologic, radiographic, or both cytologic and radiographic findings.[1,5] Our findings are

compatible with what is found in human patients, where 78% of people had airway colonization after airway stenting, with 55% of these microorganisms suspected to be pathogenic (such as *Pseudomonas* and *Klebsiella* spp.).[6]

Radiographic evidence of pneumonia, cytological findings (septic intracellular suppurative, septic extracellular suppurative, or nonseptic suppurative inflammation with supportive overall impression of the clinical pathologist), or the presence of both compatible radiographic and cytological findings were considered evidence for pathogenicity. Samples with suppurative cytology were ultimately included because the identification of intracellular bacteria in airway samples has a low sensitivity for infection. Intracellular organisms on transtracheal cytology are found in only one-third of dogs with lower respiratory tract infection, and observed on bronchoalveolar lavage cytology in 54% of dogs with bacterial pneumonia.[7] Because of the low sensitivity of identifying intracellular bacteria on airway cytology, it is recommended to interpret culture and sensitivity results along with neutrophilic inflammation or clinical evidence of pneumonia.[8] Neutrophilic or mixed neutrophilic/macrophagic inflammation is supportive of a diagnosis of bacterial infection in bronchoalveolar lavage fluid cytology of dogs.[9] A clinical diagnosis of canine lower respiratory tract infection can also be based on overall review of the case history, which includes physical examination, CBC, thoracic radiography, and gross bronchoscopic findings.[10] Therefore, the authors chose similar principles to guide inclusion criteria for dogs with clinical evidence of pathogenic infection. The same principles were used for both before- and after-stent dogs, so both groups should have been similarly affected by these inclusion criteria. Moreover, there was no significant difference between the prevalence of dogs with radiographic findings compatible with pathogenic infection or cytology limited to only intracellular bacteria before stent placement (18/38; 47%) or after stent placement (17/31; 55%) (P = .54). In other words, similar findings were present when excluding dogs with extracellular septic or suppurative cytology and only including dogs with intracellular septic cytology.

The dogs in this study demonstrated dramatically different airway cytology from what has been previously reported for dogs with TC. Cytology from the airway of 13 TC dogs with positive bacterial cultures reveals epithelial cells in 10 of 13 samples, and the remaining 3 samples have eosinophils, red blood cells, and histiocytes.[1] In these 13 dogs, bacteria are identified in only 2/5 samples that contain neutrophils, and intracellular bacteria are not seen in any samples.[1] Our study demonstrated a majority of cultures with cytology performed (35/50; 70%) had cytology supportive of a diagnosis of bacterial infection; 21 were septic intracellular suppurative, 4 were septic extracellular suppurative, and 10 were nonseptic suppurative. The dogs in the current study were receiving tracheal stents and were therefore likely more clinically affected than the previous study on dogs with TC having tracheobronchoscopy alone.

The findings of this study point to the importance of signalment when evaluating dogs with TC. Overall, 2 populations of dogs that necessitated tracheal stent placement emerged in this study. Dogs with MTC were significantly younger (mean age 6.8 years) than those with TTC (mean age 9.2 years) (P = .01). Moreover, a majority of Yorkshire Terriers (24/37; 65%) had MTC, whereas 13/37 (35%) had TTC. This difference in signalment could help guide clinical decisions and prognostic information about stent placement.

This study identified a number of risk factors for infection. Geriatric dogs (≥8 years of age) presenting for tracheal stent placement were more likely to have positive before-stent pathogenic cultures (OR = 1.9; 95% CI, 1.06-10.19), compared to younger dogs (<8 years of age). This might reflect the higher prevalence of comorbidities in the geriatric population. Although 88% of geriatric dogs with positive pathogenic cultures had comorbidities, only 50% of dogs less than 8 years of age had comorbidities present (P = .04). Furthermore, dogs with comorbidities were 5.6 times more likely to have positive pathogenic before-stent cultures and 2.8 times more likely to have positive pathogenic after-stent cultures.

In geriatric dogs, significant risk factors for pathogenic infection included a history of pneumonia (OR = 3.6; 95% CI, 0.28-43.36) and cardiac disease (OR = 1.25; 95% CI, 0.16-9.92). The history of pneumonia might suggest a more severe and chronic TC subpopulation, because these dogs could have mucociliary apparatus dysfunction, oropharyngeal colonization, and chronic medical management (including empirical antibiotic and glucocorticoid treatment) that can predispose to infection and pneumonia. Cardiac disease is known to be present in some dogs with airway collapse.[1,11-13] Airway resistance caused by TC can induce pulmonary hypertension and right-sided heart failure.[11,12] In dogs with airway collapse, 17% have mitral regurgitation, and it is hypothesized that the space-occupying effects of cardiomegaly might play a role in airway collapse.[1] In people, left atrial enlargement and compression from the left pulmonary artery can lead to narrowing of the left principal bronchus.13 Although bronchoscopy was not the focus of this study, many dogs with TC have concurrent bronchial collapse.[5] Therefore, these factors are suspected to be applicable to this population.

Younger dogs (<8 years of age) with hepatomegaly were more likely to have positive after-stent pathogenic cultures (OR = 1.5). Hepatopathy and hepatomegaly are common in dogs with TC, with suspected causes including hypoxic hepatitis, steroid hepatopathy, hepatic lipidosis, and hepatic congestion secondary to chronic right-sided congestive heart failure induced by high airway resistance.[11,12,14] In our population, hepatomegaly could suggest more chronic TC, although this was not evaluated specifically.

Placement of a tracheal stent did not lead to a higher incidence of infection. The rate of positive cultures and positive pathogenic cultures after stent placement (77 and 65%, respectively, compared to 82 and 66% before stent placement), was not significantly different (P = .67 for overall culture frequency, and P = .91 for pathogenic cultures). This is particularly interesting because after-stent cultures were only obtained in dogs with complications requiring additional procedures, such as stent fracture and tissue ingrowth, likely increasing the risk of obtaining a positive bacterial culture. Obtaining cultures and cytology in after-stent dogs without clinical signs or complications would help demonstrate if some of these dogs are truly at a lower risk of infection after stent placement.

Geriatric dogs had significantly fewer positive pathogenic cultures after stent placement (8/28; 29%) compared to before stent

placement (17/28; 61%) (P = .02). Additionally, 62% (16/26) of dogs with TTC had positive pathogenic cultures before stent placement, compared to 27% (7/26) of dogs with TTC after stent placement (P = .01). The authors suspect that the high rates of infection in these dogs before stent placement are related not only to TC and loss of mucociliary clearance function, but also to comorbidities present in TTC dogs that tend to occur in older dogs. Therefore, we suspect that tracheal stents can protect against airway infection in dogs with advanced age and TTC through reduced airway inflammation, protection against oropharyngeal contamination, and restored mucociliary apparatus and clearance function. The dynamic TC associated with TTC damages the mucociliary apparatus perhaps to a greater degree than occurs in MTC dogs with more rigid, static narrowing of the tracheal lumen.

Although it has been previously reported that infections in dogs with gaps between the trachea and stent tend to be responsive to antibiotic treatment, bacterial cultures have not been previously reported.[4] Therefore, it may be prudent to recommend early endotracheal fluid and culture evaluation in younger dogs and dogs with MTC presenting with respiratory signs after tracheal stent placement, as the presence of gutters may potentiate bacterial infection. The authors have been increasingly careful to avoid the presence of gutters in MTC dogs via appropriate stent sizing and dilatation of the stents immediately after placement to improve stent-to-wall contact.

Bacterial populations found in this population of dogs with TC reflect poor clearance of pharyngeal and enteric organisms. The most common bacterial isolates for all bacteriologic cultures in this study included *E. coli* (23%), followed by *Pseudomonas* species (15%). *Pseudomonas* is isolated most frequently in dogs with TC without stent placement.[1] The most common isolates among 7/12 dogs after stent placement include *Pasteurella multocida*, alpha-hemolytic *Streptococcus*, and non-fermentative gram-negative rods.[15] These findings contrast to our population in which *E. coli* was isolated most frequently. *Escherichia coli* is the most frequent organism isolated from the airway cultures of 156 animals with respiratory failure, which likely represents aspiration, whereas gram negative non-enteric organisms (such as *Pseudomonas*) are more commonly found in dogs that have respiratory disease and infection.[16] Therefore, the high prevalence of *E. coli* in this population may highlight the severity of infection and inability to clear enteric organisms. Dogs with brachycephalic airway syndrome may be predisposed to gastroesophageal reflux because of high negative intrathoracic pressures.[17] Similarly, the high presence of *E. coli* in this population may suggest reflux as a possible etiologic component secondary to increased intrathoracic pressures, although esophageal pH or other techniques would be required to conclusively demonstrate a link.

Of the 49 positive cultures with complete medical records, empirical antibiotics were correct for 31/49 (63%). in vitro airway bacterial resistance to empiric antimicrobials can often exist. In canine ICU dogs, the selected antibiotic is reported to be correct in only 30% of cases.[18] In dogs with bacterial pneumonia, 26% of dogs have at least 1 bacterial isolate that is resistant to empirically selected antimicrobials.[19] This highlights the importance of airway sampling for bacterial culture and cytology. Of the 31 cultures with appropriately selected empirical antibiotics, amoxicillin-clavulanate/enrofloxacin was the most commonly correct choice. This is in line with the recommendation made for human patients with tracheal stents, where a combination of amoxicillin-clavulanate and fluoroquinolone (Ofloxacin) was deemed the most effective antibiotic treatment.[20] Based on this information, we recommend empirical treatment with amoxicillin-clavulanate/enrofloxacin pending results of culture and sensitivity results.

This study likely overestimated the prevalence of after-stent positive cultures. This population of after-stent dogs had tracheal stent and TC complications requiring additional procedures, therefore selecting for a population of dogs presumably more likely to demonstrate positive cultures. This biased population may demonstrate higher infection rates compared to after-stent dogs that are well-controlled with few clinical signs. In order to answer this question, well-controlled after-stent dogs would need to receive endotracheal lavages to determine if subclinical infections were present or absent. Despite the severity of disease in this after-stent group, the placement of tracheal stents did not lead to increased rates of infection. This seems counterintuitive as stents have historically been associated with inflammation, decreased mucociliary clearance, mucus secretion, oropharyngeal colonization, stent colonization, bacterial biofilms, and bacterial tracheitis.[2,3,7,19,21,22] These findings suggest that tracheal stents reduce subsequent infection in certain subsets of dogs with severe canine TC syndrome; however, the risks associated with airway stenting must also be considered.

This study had important limitations. Although the authors attempted to limit false-positive results by defining pathogenicity with ancillary evidence of cytological or radiographic evidence, dogs with positive infections may have had bacterial stent colonization without a clinically significant infection. Moreover, dogs with suppurative cytology were considered as having evidence of infection; however, inflammation may have been secondary to stent placement, TC, and airway reactivity, rather than an active infection. The same criteria were used in before- and after-stent culture evaluations in order to minimize the effects these limitations could have on post hoc comparisons.

The use of ancillary medication use in these dogs was not controlled because of the retrospective nature of this study, client finances, and case management by varying referral veterinarians. Moreover, because of incomplete referral records, information regarding ancillary medical management was not available for all dogs. Interestingly, despite these limitations, peri-procedural antibiotic and steroid use did not affect overall infection rates, because there was no significant difference in the frequency of positive cultures obtained during antibiotic and steroid use before stent placement compared to after stent placement.

The retrospective design of this study further limited the findings of this investigation. All dogs had aerobic cultures performed; however, anaerobic and *Mycoplasma* cultures were not routinely performed. Some dogs only had cultures available at time of stent placement or post stent placement, but not both. These differences in

case management are reflective of clinician preference, client financial limitations, and the retrospective design of this study. The use of endotracheal wash may have yielded different organisms, compared to other studies, where bronchoscopy with bronchoalveolar lavage was performed.[1] A number of dogs in this study had ancillary procedures (staphylectomy and epiglottic tacking) concurrently performed; therefore, the effect of these procedures may confound the effect of tracheal stent placement on future infection prevalence. Lastly, the small sample size may have precluded some findings from reaching statistical significance.

This is the first known study describing the pathogenicity of bacterial infections in dogs before, and after, tracheal stent placement. Placement of a tracheal stent did not increase the overall rate of bacterial infection in this population of dogs with TCS. Subsequent airway infections were significantly reduced after stent placement in geriatric TC dogs and dogs with TTC. Because of the high number of pathogenic infections identified, the authors recommend performing airway culture and cytology in all dogs undergoing tracheal stent placement, as well as evaluating signalment and comorbidities to ascertain the risk of airway infection.

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CONFLICT OF INTEREST DECLARATION

Dr. Weisse is a minority shareholder in Infiniti Medical, LLC. Dr. Berent and Dr. Weisse are consultants for Infiniti Medical, LLC.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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