CLINICAL AND LARYNGOSCOPIC CHARACTERIZATION OF NORWICH TERRIER UPPER AIRWAY SYNDROME (NTUAS): PRELIMINARY RESULTS

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Norwich Terrier Upper Airway Syndrome

INTRODUCTION

Upper airway issues in Norwich Terriers (NT) has been long recognized among breeders, but only recently reported by veterinarians. Clinical signs of NTUAS range from intermittent stridor to severe respiratory distress, collapse and asphyxiation (Figure 1). It has been hypothesized that the NT are tending toward brachycephaly, but the association is weak and anatomic changes are not consistent with brachycephalism. Preliminary studies reveal pathology similar to a primary laryngeal anomaly, such as laryngomalacia.

***Figure 1**: NT will often present as emergencies, and require oxygen supplementation.*

The most commonly reported anomaly in NTUAS is fleshy, everted tissue from the laryngeal ventricles (Figure 3D). Redundant supra-arytenoid mucosa and a narrowed infraglottic laryngeal lumen have recently been described. Unlike brachycephalic airway syndrome, structures rostral to the larynx are typically normal in NT (Figure 2). Ventriculectomy may improve respiratory signs, but recurrence or persistence of signs is common. Despite its high prevalence, the etiology and pathology of the condition is unknown, and its progressive nature uncharacterized.

OBJECTIVES

This study aims to undertake a detailed characterization of the upper airway in a large cross-section NT (n=150), using questionnaire and videoendoscopy. A subset of these NT will undergo additional testing to determine intranasal airway resistance. Results will be compared to age-matched Norfolk terriers, brachycephalic and mesaticephalic dogs. A scoring system for NTUAS will be developed from findings. NT can then be scored by veterinarians and their score used to guide breeders.

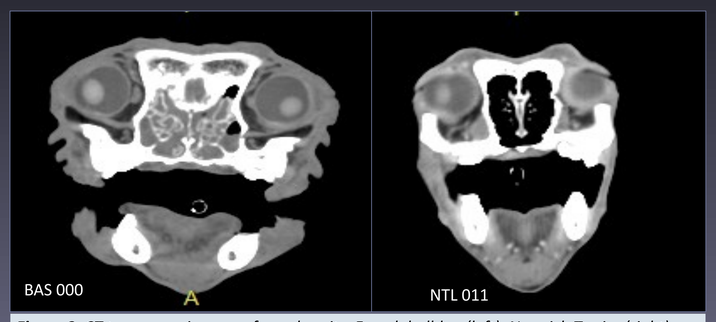

***Figure 2**: CT transverse images of nasal cavity. French bulldog (left), Norwich Terrier (right). The NT nares and intranasal components are similar to mesaticephalic breeds.*

MATERIALS AND METHODS

150 NT and 25 dogs of different muzzle conformation are recruited into stratified age groups (Table 1). Each dog owner completes a detailed history questionnaire via REDCap online clinical database.* Enrolled dogs then undergo blood work, thoracic radiographs, physical examination and upper airway videoendoscopic examination. Results are entered into REDCap by each institutional investigator. Dog identity will be masked and each institutional investigator will review all endoscopic studies. Agreement between observers will be evaluated by a Light's weighted kappa statistic. Based on which endoscopic variables correlate consistently with clinical and historical status, an NTUAS Score will be developed. NTUAS Scores will be compared for each age group, to determine effect of age on NTUAS.

NT (N=5) will be randomly selected from each age group, and all brachycephalic, mesaticephalic and Norfolk terriers will additionally undergo rhinomanometry and CT (Figures 2&3). Univariate followed by multivariate analysis will be used to determine the influence of CT characteristics on measured airflow impedance, separately for each group. Eight explanatory variables will be age, weight, sex, presence of septal deviation, and presence of aberrant turbinates, nasal volume, turbinate density and principal component 1 eigenvalue. The response variable will be the measured airflow impedance through the nose. The nature of the explanatory variables (continuous, binary and categorical) will be determined and univariate analysis will be used to determine significant relations between variables. Univariate tests will be chosen based on the explanatory variable type: unpaired t-test, chi square (or Fisher's exact test when number <5), one-way-analysis of variance, and regression-analysis. Only variables showing a potential $p<0.30$ association will be included in the multivariate analysis and entered into the regression equation, presenting any variable with $p<0.05$. Multicollinearity will be assessed by means of the variance-inflation-factor (VIF), where VIF <2.5 is acceptable.

***Table 1**: Planned enrollment data and enrolled cases to date – 61 NT of proposed 225 dogs have been enrolled.*

Age	NT	Norfolk	Brachycephalic	Mesaticephalic	Enrolled:
< 1 yr	30	5	5	5	8NT
1-2 yrs	30	5	5	5	16NT
3-4 yrs	30	5	5	5	12NT
5-7 yrs	30	5	5	5	15NT
> 8 yrs	30	5	5	5	12NT

Histopathology of any resected airway tissue will also be examined, and DNA extracted from each subject for genetic investigations. This multi-site study will provide a standard baseline for NTUAS. NT less than 1 year of age in this study will form a cohort for a future longitudinal study.

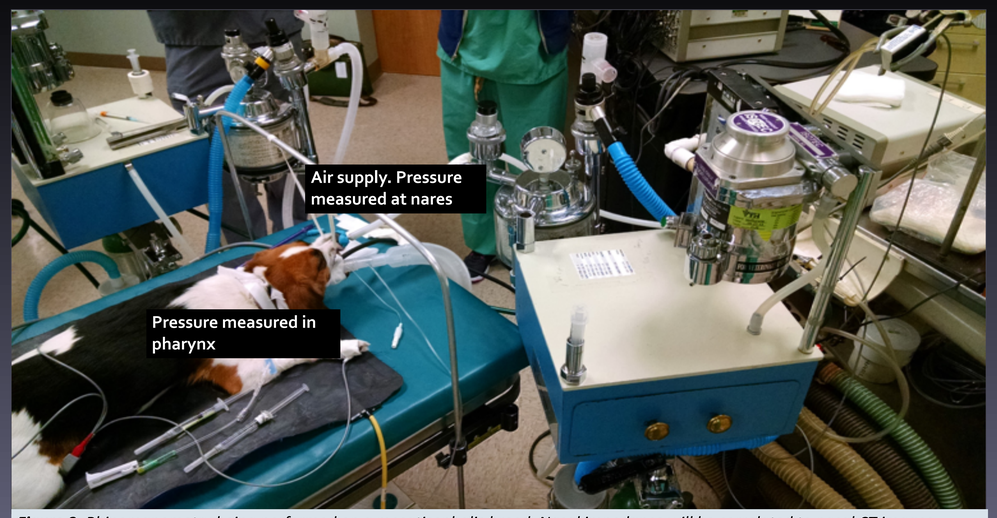

***Figure 3**: Rhinomanometry being performed on a mesaticephalic breed. Nasal impedance will be correlated to nasal CT images. These data will be compared between NT, Norfolk terriers, brachycephalic breeds and mesaticephalic breeds.*

RESULTS to date (Aug 2016):

Of the 61 NT currently evaluated, 29 (47.5%) were considered unaffected by their owners, with the remaining 32 dogs being evenly distributed as mildly, moderately and severely affected. For 20/32 (62%) of the clinically affected dogs, the age of onset of signs was < 1yr old. All dogs had normal nares and choanae; abnormalities found on endoscopic examination are displayed in Table 2 (Figure 4). Additionally, 8 of the 61 (13%) dogs had decreased laryngeal abduction upon inspiration. Only one NT was considered to be anatomically normal. Histology was performed on 22 samples of excised ventricles. A wide variety of inflammation was reported, with no consistent pattern in cell types. Interestingly, 35/61 dogs showed periodontal disease with enlarged and hyperemic tonsils.

***Table 2**: Preliminary results of abnormal changes seen in NTUAS.*

Anatomic Abnormality	N (61)	%
Mildly Elongated Soft Palates (5-8mm)	39	63.9
Redundant Dorsal Pharyngeal Wall	41	67.2
Redundant Laryngeal Mucosa	37	60.6
Abnormal Cuneiform Processes	25	40.9
Abnormal Corniculate Processes	18	29.5
Partially/ Fully Everted Ventricles	48	78.6
Abnormally Narrowed Infraglottic Lumen	53	86.8
Periodontal Disease, Enlarged & Hyperemic Tonsils	35	57.3

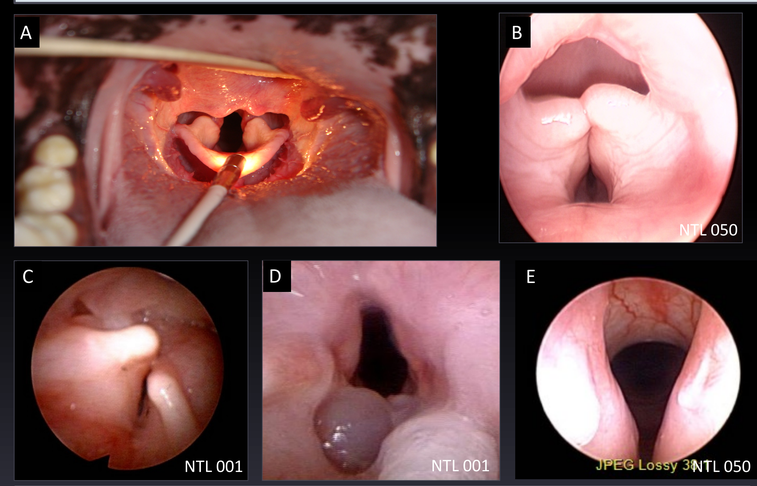

***Figure 4**: Endoscopic examination images. A. Normal larynx. B, C, D. Abnormal larynges, showing thickened, redundant mucosa, medial displacement, everted ventricles. E. Keyhole infraglottic lumen*

CONCLUSIONS

Although only half of the NT were considered to be clinically affected, 60/61 dogs showed laryngeal and pharyngeal abnormalities. The abnormalities documented so far are not consistent with brachycephalism, but rather appear to be primarily pharyngeal and laryngeal in origin. The small amount of soft palate elongation does not warrant the severity of changes seen in the larynx. Redundant dorsal pharyngeal wall may play a role in the laryngeal abnormalities, or this may be a primary laryngeal condition. The gross appearance has similarities with laryngomalacia in children.

* Vanderbilt University. https://redcap.bric.msu.edu

***Funding** : American Kennel Club, Canine Health Foundation & Norwich Terrier Club of America*