Abstract

Objective: To determine prognostic indicators for the surgical treatment of brachycephalic obstructive airway syndrome (BOAS) and to compare the prognosis of two different multilevel surgical procedures.

Study Design: Prospective clinical study

Sample Population: Client-owned pugs, French bulldogs, and bulldogs (n=50)

Methods: Non-invasive whole-body barometric plethysmography (WBBP) was used to assess respiratory function before and 1-6 months after upper airway corrective surgery. Post-operatively, BOAS indices (i.e. ascending severity score generated from WBBP data, 0-100%) that equaled to or exceeded the cut-off values of BOAS in the diagnostic models were considered to have a “poor prognosis”. A multivariate logistic regression was used to assess predictors for prognosis.

Results: Overall the median BOAS indices decreased significantly after surgery (from 76% to 63%, p<0.0001), however, dogs with indices in this range would still be considered clinically affected. Age (Odds ratios [OR] =0.96, 95% confidence interval [CI]: 0.93-0.99, p<0.05), body condition (OR=0.06, 95%CI: 0.01-0.39, p<0.01), laryngeal collapse (OR=6.1, 95%CI: 1-37.22, p<0.05), and surgical techniques (OR=7.94, 95%CI: 1.17-54.01, p<0.05) were significantly associated with post-operative prognosis. The multivariate model suggests modified multilevel surgery may have a better outcome than traditional multilevel surgery (p=0.034). The positive predictive value of the logistic model was 84% (95%CI: 68-94%) and the area under the receiver operating characteristic (ROC) curve was 89% (95%CI: 78-99%, p<0.0001).
Conclusions: Age, body condition, laryngeal collapse, and surgical techniques are the main prognostic factors for BOAS surgery. Modified multilevel surgery is recommended, particularly for dogs that have a higher probability of having a poor prognosis.
Introduction

Brachycephalic obstructive airway syndrome (BOAS) is a respiratory disease in dogs that often requires surgical treatment to alleviate clinical signs. A variety of surgical techniques have been described to correct the anatomical lesions that contribute to BOAS. Conventionally, wedge resection of ala nasi\textsuperscript{1-5}, staphylectomies with different resection techniques\textsuperscript{1,2,6-8}, partial tonsillectomy\textsuperscript{9}, and ventriculectomy\textsuperscript{1,2,7} are the most commonly performed procedures for BOAS. More recently, modified and advanced techniques such as folded flap palatoplasty (FFP)\textsuperscript{10}, nasal vestibuloplasty\textsuperscript{11} and laser-assisted turbinectomy (LATE)\textsuperscript{12} have been reported.

Assessing the prognosis following surgical treatment of BOAS has several difficulties. The lack of objective respiratory function assessment was traditionally the major obstacle. Most of the studies determining surgical effectiveness were based on subjective evaluation such as history (e.g. phone interview, questionnaire)\textsuperscript{10,13,14} or both physical examination and history\textsuperscript{15-18}. The subjectivity makes it difficult to compare the pre- and post-operative clinical signs consistently as well as to compare the outcome of different surgical techniques.

Several prognostic factors for BOAS surgery have been evaluated and discussed. Laryngeal collapse is controversial in terms of its effect on prognosis. Although traditionally associated with a worse prognosis, more recent studies showed that the grade of laryngeal collapse did not affect the surgical outcome\textsuperscript{16,19}. Obesity has been shown to compromise respiratory function\textsuperscript{20-22} as well as to be related to BOAS\textsuperscript{19,22,23}. 
Similar findings have been reported in human sleep apnea patients. We therefore hypothesized that these non- or minimally operable lesions and conditions are key prognostic factors for BOAS surgery. One recent review suggested that the current surgical techniques and post-operative care have resulted in significant improvements in the prognosis even in middle-aged dogs. Some have suggested prophylactic surgery at a young age is likely to benefit the dog’s breathing as it matures. However, the association between the age when presented for surgery and surgical outcome has not as yet been investigated with other prognostic factors.

Whole-body barometric plethysmography (WBBP) is a non-invasive clinical tool which measures respiratory function in dogs objectively. Previously, we modeled the WBBP data and established 3 breed-specific classifiers (for the pug, the French bulldog, and the bulldog) to generate a numeric scoring system, the BOAS index, which indicates the severity of the disease and can be used to assess the outcome of BOAS surgery. A pilot study showed that more severely affected French bulldogs had a poorer response to traditional multilevel BOAS surgery (i.e. post-operative BOAS indices were still considered clinically affected) when compared to moderately affected French bulldogs. Since the surgical techniques for treating BOAS have recently been modified to increase effectiveness, we here proposed and evaluated a modified multilevel surgery, which combined a number of relatively novel procedures.

The objectives of this study were to determine the prognostic factors for BOAS surgical treatment and to compare the outcome of two different multilevel surgeries.
Material and Methods

Subjects

Pugs, French bulldogs, and bulldogs that were referred for BOAS consultation from May 2010 to Jan 2016 and underwent WBBP test both before and 1-6 months after surgery were included in this study. Dogs that had upper airway corrective surgery previously and were referred for revision surgery were excluded in this study.

On the day of admission, each dog underwent physical examination, a 3-minute exercise tolerance test and a 20-minute WBBP test. Laryngoscopy and imaging (radiographs or computed tomography) were performed prior to surgery under the same general anesthesia to confirm the lesion sites and severity. Body condition score (BCS) and stage of laryngeal collapse were recorded. Post-operatively, each dog was observed in the intensive care unit for at least 12 hours to monitor for post-operative airway swelling, airway obstruction and aspiration pneumonia, particularly in dogs that had a history of frequent regurgitation. Each dog was rechecked 1-6 months after surgery. On the day of reassessment, physical examination, exercise tolerance test and WBBP test were performed.

Whole-body barometric plethysmography (WBBP): non-invasive respiratory function assessment
The detailed protocol for WBBP measurements and data analysis has been reported in a previous study. Briefly, WBBP measurements were performed using a barometric chamber EMMS (Electro-Medical Measurement Systems, Bordon, UK) model PLY370 with inner volume of 175 L for small dog breeds and model PL360 with inner volume of 280 L for middle-sized breeds. One port of a pressure transducer (TRD5701, EMMS) was attached to the main chamber and the other pole was open to a reference chamber. The pressure signals were amplified and sampled by commercial software (ESS-102 EMMS Data Acquisition, eDacq, for Microsoft Windows XP). A balanced bias airflow of room air (bias flow regulator BFL0404, EMMS, 20 L/min) was supplied.

At each appointment, after a clinical assessment the dog was placed in the chamber, given an acclimatization period (5-10 minutes) before recording for a period of 20 minutes. Time segments of body movement, sniffing, or vocalization that caused artefacts were identified using the recorded surveillance video and eliminated manually. Twenty consecutive constant breaths during wakefulness were selected for further data analysis. Means and standard deviations of ratio of peak expiratory flow rate to peak inspiratory flow rate, ratio of expiratory time to inspiratory time, and minute volume per kilogram of body weight were calculated. BOAS index was generated by means of user-friendly breed-specific calculators available on our research website.

Surgical techniques: traditional multilevel surgery (TMS) and modified multilevel surgery (MMS)
Dogs that were referred for BOAS between May 2010 and June 2014 had TMS procedures; between June 2014 and Jan 2016 underwent MMS.

Traditional multilevel surgery (TMS) consisted of alaplasty using a vertical wedge resection technique, cut-and-suture staphylectomy, removal of everted saccules when needed and partial removal of the tonsils (using harmonic scalpel or bipolar forceps with metzenbaum scissors for resection) if they were extruded.

Modified multilevel surgery (MMS) has been described and was slightly adjusted in this study. Prior to the surgery, we routinely sprayed nasal decongestant (xylometazoline hydrochloride 0.1% w/v, 0.2 ml in each side of nasal cavity) into both sides of the nasal cavity before performing rhinoplasty. MMS procedures included a modified rhinoplasty technique combining a Trader’s alaplasty and nasal vestibuloplasty (The dorsal part of the alar fold was grasped by a pair of curved hemostats. The first incision was made by a #11 blade horizontally to dissect the ventral connection of the alar fold to the vestibule. The dorsal part of the alar fold was then gently rotated with the hemostats laterally enabling the blade to be placed between the alar fold and the lateral vestibule wall, thus resecting the dorso-medial and caudal portion of the alar fold.) to create a wider nasal vestibule and release both the external and the inner stenosis of the nares; folded flap palatoplasty for shortening and thinning the oversized soft palate; bilateral ventriculectomy for dogs with everted laryngeal saccules (similar to TMS but using endoscopic scissors); partial cuneiformectomy for dogs with Grade II or III laryngeal collapse; and partial tonsillectomy if extruded (same techniques as TMS).
Statistical analyses

(1) Subject characteristics

The Kolmogorov-Smirnov test and frequency histogram were used to examine continuous variables for normality (age, pre- and post-operative BOAS indices, and the time between surgery and the post-operative reassessment), and results are presented as mean ± standard deviation for normally distributed data or median (quartiles) for non-normally distributed data. Categorical variables are reported as numbers and percentages. Paired-samples t-tests or Wilcoxon signed ranks tests were used to compare BOAS indices pre- and post-operatively, both among breeds and for each breed; independent-samples t-test or Mann-Whitney non-parametric tests were used to test the hypothesis that dogs with laryngeal collapse had a higher pre-operative BOAS index as well as to test whether the time between the surgery the post-operative reassessment are different between the good prognosis group and poor prognosis group.

(2) Developing prognostic scores

A binary outcome for prognosis was defined and coded as follows: 0=good prognosis, post-operative BOAS index below the breed specific cut-off diagnostic values (BOAS index of 55.4% for pugs, 49.41% for French bulldogs, and 43.53% for bulldogs); 1=poor prognosis, post-operative BOAS index equal to or exceeding the breed specific cut-off diagnostic values. The explanatory variables and coding were as follows: breed (1=pug; 2=French bulldog; 3=bulldog), patient age in months, gender (0=female;
169 1=male), neuter status (0=entire; 1=neutered), body condition (0=BCS<7; 1=BCS≥7),
170 laryngeal collapse (0=normal larynx or had everted laryngeal saccules; 1=Grade II or III
171 laryngeal collapse), surgical techniques (0=TMS; 1=MMS).
172
173 Variables that had a Wald test p-value of <0.25 on univariate logistic regression were
174 selected as candidates for the multivariate analysis using method of purposeful
175 selection\textsuperscript{37-39}. The selected candidate variables were used in multiple logistic regression
176 to identify factors associated with prognosis. In the final model, variables that were not
177 statistically significant at p<0.05 were excluded using backwards elimination. Odds ratios
178 (ORs) with 95% confidence intervals (CIs) were estimated using the predictive
179 probabilities of having a poor prognosis based on the regression coefficients of the
180 significant variables. Hosmer and Lemeshow goodness of fit (GOF) test was used to test
181 the model fit. Cross-tabulation with Chi-square or Fisher’s exact tests were used to
182 compare proportions and traditional formulas were used to calculate sensitivity,
183 specificity, positive predictive value and negative predictive value of the predictive rule.
184 The receiver operating characteristic (ROC) curve was used to demonstrate the
185 discriminant ability of the model. The results were considered significant when the p-
186 value was <0.05. Commercial statistics software SPSS v23.0 (IBM) was used for all the
187 analyses in this study.
Results

Fifty brachycephalic dogs met the inclusion criteria for the study, including 21 pugs, 21 French bulldogs, and 8 bulldogs. The median time from surgery to the post-op reassessment was 42 days (quartile: 31-69 days) and was not significantly different between the good prognosis group and poor prognosis group (p=0.058). The binary variables, gender, neuter status, body condition, laryngeal collapse and surgical procedure all had nearly equal proportions for each category (Table 1). Overall, upper airway corrective surgery significantly improved respiratory function among all 3 breeds (median BOAS index from 75.8% before surgery to 63.2% after surgery, p<0.0001) and within each breed (Pugs, p<0.0001; French bulldogs, p<0.0001; bulldogs, p=0.008) (Fig 1). However, the median post-operative BOAS indices for each breed were within the range that would suggest that these dogs still would be considered clinically affected (above the breed-specific cut-off value\textsuperscript{22}). Of the 50 dogs, 16 (32%, 95%CI: 20-47%) had a satisfactory outcome post-surgery while 34 (68%, 95%CI: 53-80%) of the dogs had poor surgical outcome based on the post-operative BOAS indices.

Dogs that had laryngeal collapse had significantly higher pre-operative BOAS indices (mean=84%) than dogs that had no collapse or only saccule eversion (mean=70%), p=0.005. However, the differences in post-operative BOAS indices between dogs that had laryngeal collapse and dogs that did not were marginally non-significant (p=0.058).

Two subsets were made to separate dogs with and without advanced laryngeal collapse. The median post-operative BOAS index of dogs with advanced laryngeal collapse was 66.1% while the median post-operative BOAS index of dogs without advanced laryngeal
collapse was 54.2%. However, the difference was marginally not significant (p=0.08).

The median post-operative BOAS index was not statistically significantly different (p=0.65) between dogs that underwent TMS (median post-operative BOAS index=62%) and MMS (median post-operative BOAS index=66.7%). For dogs without advanced laryngeal collapse, the median post-operative BOAS index was 60.8% in dogs that underwent TMS, and 44.5% in dogs that underwent MMS. However, the difference was not statistically significantly (p=0.23).

Purposeful selection of variables for the multiple logistic regression model was performed with a preliminary univariate logistic regression analysis (Table 1). Five variables were chosen as potential candidates for the multiple logistic regression: age, body condition, laryngeal collapse, pre-operative BOAS index, and surgical techniques. Pre-operative BOAS index was further removed from the final model (p=0.8), leaving 4 significant variables (Table 2). The final model was statistically significant, $X^2(4)=22.47$, $p<0.0001$. The pseudo-$R^2$ statistics was 0.51 (Nagelkerke $R^2$) and correctly classified 82% of cases. According to the Hosmer and Lemeshow goodness of fit (GOF) test, there was no significant difference between observed and predicted values (p=0.326). The final model showed that, while controlling for the other independent variables, younger age was associated with an increased likelihood of having a poor prognosis; dogs that were not obese but presented with BOAS were 17 times more likely to have a poor prognosis after surgery than dog that were obese and presented with BOAS; dogs with laryngeal collapse were more likely to have poor prognosis although it was only marginally statistically significantly; MMS provided a better surgical outcome compared to TMS, as dogs that underwent TMS had an 8-fold increased risk of a poor prognosis post-surgery.
than dogs that underwent MMS. However, the wide 95% CIs reflect the relatively small number of cases in some of the subgroups.

The estimated probability of having a poor prognosis for each dog was calculated based on the constant and coefficients listed in Table 2. Sensitivity of the logistic model was 91% (95%CI: 76% to 98%), specificity was lower at 63% (95%CI: 35% to 85%), positive predictive value was 84% (95%CI: 68% to 94%), and negative predictive value was 77% (95%CI: 46% to 95%). Area under the ROC curve (AUC) was 0.89 (95%CI: 0.78 to 0.99, p<0.0001) (Fig 2), which is at the high end of what is considered to be a moderate discriminating test (0.7<AUC≤0.9).
Discussion

To the authors’ knowledge, this is the first study that uses an objective method to evaluate the outcome of BOAS surgery. Age, body condition, laryngeal collapse, and surgical technique were significant prognostic factors.

Our determination of “good prognosis” and “poor prognosis” of BOAS surgery was based on objective measurement of respiratory function using WBBP rather than a subjective history or clinical examination. Recognition of BOAS clinical signs by owners was reportedly low at only about 40%. A considerable proportion of owners are not able to identify clinical signs, and respiratory noise in brachycephalic breeds is often interpreted as normal for the breeds. Moreover, the frequency of different types of clinical signs, which was the criterion of a widely used BOAS clinical sign grading system, is highly dependent on intensity and proportions of activity status (i.e. exercising, resting, and sleeping) during the day. In the clinic, it is not uncommon to come across an ambiguous owner description about the dog’s clinical signs. The objective respiratory function assessment used in this study has the advantage of avoiding bias when comparing pre- and post-surgery.

Whole-body barometric plethysmography (WBBP) is a non-invasive clinical tool that can quantify respiratory function. We routinely test the patients the day before surgery, and 1-6 months after the surgery when post-operative airway swelling has resolved and the wounds have healed. Whole-body barometric plethysmography is a very useful clinical assessment as it is non-invasive and does not require sedation or general
anesthesia. Moreover, its short operating time (about 20 minutes) is reasonable for a clinical diagnostic test. As WBBP is non-invasive, it is ideal for repeated monitoring of disease progression. In the present study, we only included short-term follow-up data as unfortunately there was an insufficient sample size available for longer-term follow-up. Even though 32% of dogs in this study had good short-term surgical outcome, it would be useful to have longer-term follow-up to ensure that the improvement was maintained.

The prognosis following BOAS surgery has been controversial. Reported improvement in clinical signs post-operatively ranges from 30.4% to 58.3%. However, a precise comparison among studies is not feasible since the assessment criteria vary substantially. In our study, although overall respiratory function in the affected dogs improved significantly after surgery, 68% of dogs still had compromised respiratory function and required regular follow-ups. Considering the severity of airway obstruction seen in some of our cases it is perhaps overly optimistic to expect these dogs to have a normal respiratory function post-surgery. Comparing the effectiveness of TMS and MMS while taking other factors into account, dogs that underwent MMS had lower probability of having poor prognosis after surgical treatment. Modified multilevel surgery is a combination of a number of newly introduced surgical techniques that theoretically provide better nasal flow by partially resecting the alar folds at the nasal vestibule; thin the soft palate by removing some of the hypertrophic tissues; and reduce the collapsible structure at the rima glottidis area by trimming the malformed cuneiform process. It was not possible to separate the surgical procedures to identify which was the most effective but the overall surgical results of MMS were encouraging. Further objective evidence of anatomical changes as to whether the soft palate thickness is
reduced effectively by a folded flap palatoplasty is needed. Nasal vestibuloplasty is a newly developed technique to address the obstruction at the nasal entrance. Combined with the Trader’s technique, this novel method of rhinoplasty provides a wider opening of the nostrils both externally and internally. The immediate appearance of the wounds post-operatively is less cosmetic than the method of wedge resection but over 2-3 weeks the wounds heal well with a satisfactory outcome of wide-opened nostrils.

Even though the MMS had a better prognosis, 60% of dogs still had compromised respiratory function post-surgery. The untreated lesions in these patients such as the aberrant and hypertrophic nasal turbinates, hypoplastic trachea or the relatively large tongue base might contribute to the poor prognosis. Our previous pilot study on 8 pugs that underwent selective LATE surgery showed that pugs that had an unsatisfactory result after MMS had improved respiratory function after LATE in the short and long-term.

Seven out of the 8 pugs had a good outcome based on BOAS indices (i.e. the short-term post-operative median BOAS index was 46%) with follow-up periods from 2 months to 15 months. Interestingly, there was a trend in those dogs for their respiratory function to gradually improve with time on each post-operative follow-up appointment. This could be as a result of reduction of soft tissue swelling and inflammation as the previously high negative pressure within the airway is reduced. BOAS index is a useful criterion for determining if further surgery such as LATE is indicated after MMS. A broader validation study will be required to establish the standard treatment strategies.

The proposed prognostic factors in this study are all easily assessed at a general clinical setting. Advanced stages of laryngeal collapse (Grade II and III) have traditionally been
associated with a poorer prognosis\textsuperscript{1,5,23,47-49} whereas a recent study on pugs and French bulldogs showed that the grade of laryngeal collapse did not affect the grade of respiratory signs before surgery or the surgical outcome\textsuperscript{16}. In our study, 52\% of dogs had Grade II or III laryngeal collapse, which is similar to other studies at 50\%-63.9\%\textsuperscript{16,18,19}.

In the remainder of the dogs, 22/24 had Grade I laryngeal collapse (everted laryngeal saccules) and only 2/24 had completely normal laryngeal conformation. Everted laryngeal saccules were common in brachycephalic dogs and the associated laryngeal clinical signs were often mild. The decision to use a binary definition in the final analysis was due to the clinical relevance mentioned above. Another reason was that there were only 2 dogs that did not have laryngeal collapse in our study population.

Judgment of whether the everted saccules actually caused WBBP waveforms changes requires further recruitment of BOAS affected brachycephalic dogs that have a completely normal larynx. For dogs with advanced laryngeal collapse, the pre-operative BOAS indices were significantly higher than dogs with no collapse or only everted saccules. Partial resection of the cuneiform process\textsuperscript{11} was used as part of the MMS procedures in this study to address the collapsed laryngeal cartilages. Long-term reassessments of the larynx under light general anesthesia in some cases revealed that the lesion site healed well with no stenosis at the larynx. The procedure produces a wider glottidis opening as well as preventing dynamic obstruction when the collapsed cuneiform process is drawn into the rima glottidis. However, post-operative BOAS indices in dogs with advanced laryngeal collapse were not significantly different between TMS and MMS. It could be argued that cuneiformectomy might not be effective to address the problem of laryngeal collapse. However, the study design as well as our
sample size was not sufficient to determine the effect of partial cuneiformectomy in dogs with laryngeal collapse.

Age was also found to be associated with the surgical prognosis. Dogs that have developed moderate or severe BOAS at young age were prone to have a poor prognosis. These dogs were likely to have severe congenital malformations of the upper airway which contributed to early onset of BOAS and also resulted in a poor outcome after surgical intervention. This finding is in contrast to the commonly held belief that surgery performed at older age would have guarded outcome due to chronic secondary changes such as laryngeal collapse\textsuperscript{5,31}. One study however, reported that 5/7 brachycephalic puppies (i.e. age between 4 and 6 months) were diagnosed with grade II or grade III laryngeal collapse\textsuperscript{50}. In the present study, 46\% of the dogs with laryngeal collapse were younger than 2 years of age. Some of our younger patients had a malformed larynx similar to congenital laryngomalacia in humans, which is a dynamic lesion where the immature and softened cartilage of larynx collapses inward during inspiration\textsuperscript{51}. The laryngeal dynamic obstructions might be underestimated when evaluated under general anesthesia. Further investigations to compare the etiology of laryngeal collapse at different ages in BOAS-affected dogs are needed. Another possible explanation could be that the continuous growth of tissues in young dogs may result in further airway obstructions. Whether or not performing prophylactic surgery on young dogs that present with mild clinical signs of BOAS is of benefit is still unknown and requires a longitudinal study or a case-matched study to determine.
We have previously demonstrated that obese dogs are 1.9-fold more likely to be BOAS affected than dogs with normal body condition\textsuperscript{22}. Interestingly, it was highly significant that non-obese dogs that developed severe BOAS were more likely to have a poor prognosis after surgery. This does not support dogs remaining overweight or obese when they have a compromised airway. Rather it suggests that the slim dogs that have BOAS have more severe obstructions that are not so easily alleviated by surgery. There is currently no longitudinal study following respiratory function in BOAS-affected dogs on a weight-control program. Nonetheless, in human obstructive sleep apnea patients, it is widely known that obesity is one of the main factors contributing to the disease\textsuperscript{24,52,53}. The bulldog has been used as a natural-occurring animal model for human sleep apnea studies since the lesions that cause respiratory obstructions are comparable\textsuperscript{54}. Therefore, weight control before and after the BOAS surgery is still recommended. Another possible explanation to our findings could be that the severely affected dogs tend to have chronic and frequent regurgitation\textsuperscript{55} as well as be more likely to have eating difficulties. The consequences of gastrointestinal signs may interfere with nutrition intake and lead to slimmer body condition.

A number of limitations in this study have been discussed above. A major limitation was that randomization of TMS and MMS was not performed. Instead, all animals in the initial period of study were operated using TMS and all animals in the latter period of study had MMS. Several possible factors might cause potential bias in the outcomes such as improved experience of surgeon, level of post-operative care, and patient populations. Additionally, the logistic model might be improved by increasing the sample size. More advanced predictors, such as airway dimensional parameters, may be included into the
model in the future and this may help to explain more variance within the population.

Subjects included in this study were all referral cases and, as such are likely to have more severe clinical signs than cases that stay within general practice. Whether the proposed prognostic model can be used on different clinical populations also requires further validation.

To conclude, age, body condition, and laryngeal collapse are the main prognostic factors for BOAS surgery. Modified multilevel surgery\textsuperscript{11,35,36} may have a better outcome than TMS. The proposed prognostic model can be used to predict the outcome of surgery with factors that are easily accessible.
Acknowledgement

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Disclosure Statement

The authors declare no conflict of interest related to this report.
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Figure Legends

Figure 1. Box and whisker plots showing BOAS index before and after upper airway corrective surgery and results of Wilcoxon signed ranks tests to compare among all dogs and also with in each breed. The box contains the middle 50% of data with the upper and lower edges representing the 75th and 25th percentiles, respectively. The bold line in the box represents the median value of the data. The ends of the vertical line represent minimum and maximum data values. Outliers are presented as circles. ** statistically significant different from pre-operative BOAS index at p<0.001, *** p<0.0001

Figure 2. Receiver operating characteristic (ROC) curve of the prognostic model for brachycephalic obstructive airway syndrome (BOAS) surgery. The ROC curve shows the discriminatory ability of the logistic model to predict between good prognosis and poor prognosis after upper airway corrective surgery for BOAS. The test was considered to be a moderate discriminating test based on the area under the ROC curve (AUC).
Table 1. Patient characteristics and results of univariate logistic regression in 50 dogs that had good prognosis or poor prognosis after upper airway corrective surgery for brachycephalic obstructive airway syndrome (BOAS).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total (N=50)</th>
<th>Patients with good prognosis ‡ (n=16)</th>
<th>Patients with poor prognosis § (n=34)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) pugs, n (% of N)</td>
<td>(1) 21 (42)</td>
<td>(1) 5 (31.25)</td>
<td>(1) 16 (47.06)</td>
<td></td>
</tr>
<tr>
<td>(2) French bulldogs, n (% of N)</td>
<td>(2) 21 (42)</td>
<td>(2) 8 (50)</td>
<td>(2) 13 (38.24)</td>
<td></td>
</tr>
<tr>
<td>(3) bulldogs, n (% of N)</td>
<td>(3) 8 (16)</td>
<td>(3) 3 (18.75)</td>
<td>(3) 5 (14.71)</td>
<td></td>
</tr>
<tr>
<td>Age, months†</td>
<td>26.46 (12-48)</td>
<td>38.5 (9.51-73.77)</td>
<td>17.52 (12-48)</td>
<td>0.126*</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>24 (48)</td>
<td>7 (43.75)</td>
<td>17 (50)</td>
<td>0.68</td>
</tr>
<tr>
<td>Neutered, n (%)</td>
<td>21 (42)</td>
<td>8 (50)</td>
<td>13 (38.24)</td>
<td>0.433</td>
</tr>
<tr>
<td>Body condition score ≥7, n (%)</td>
<td>26 (52)</td>
<td>14 (87.5)</td>
<td>12 (35.29)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Grade II-III Laryngeal collapse, n (%)</td>
<td>26 (52)</td>
<td>6 (37.5)</td>
<td>20 (58.82)</td>
<td>0.164*</td>
</tr>
<tr>
<td>Surgical procedures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) TMS, n (%)</td>
<td>(1) 25 (50)</td>
<td>(1) 6 (37.5)</td>
<td>(1) 19 (55.88)</td>
<td>0.229*</td>
</tr>
<tr>
<td>(2) MMS, n (%)</td>
<td>(2) 25 (50)</td>
<td>(2) 10 (62.5)</td>
<td>(2) 15 (44.12)</td>
<td></td>
</tr>
<tr>
<td>Pre-operative BOAS index, ‡ (%)</td>
<td>75.79 (66.69-94.21)</td>
<td>73.4 (55.56-94.61)</td>
<td>75.79 (68.92-94.21)</td>
<td>0.12*</td>
</tr>
<tr>
<td>Post-operative BOAS index, ‡ (%)</td>
<td>63.22 (40.44-68.55)</td>
<td>35.38 (25.54-40.44)</td>
<td>66.67 (61.08-70)</td>
<td>N/A‡</td>
</tr>
</tbody>
</table>

TMS, traditional multilevel surgery; MMS, modified multilevel surgery; BOAS, brachycephalic obstructive airway syndrome

* Variables with p<0.25 in univariate logistic regression based on the Wald test were included in multiple logistic regression (Table 2).
† Continuous variables reported as median (quartiles).
‡ Post-operative BOAS index was not included in the variables selection process. It was used for determining the prognostic status.
§ Good prognosis was defined as post-operative BOAS index below the breed specific cut-off diagnostic values (55.4% for pugs, 49.41% for French bulldogs, 43.53% for bulldogs); poor prognosis was defined as post-operative BOAS index equal to or exceeding the breed specific cut-off diagnostic values.
Table 2. Multivariate logistic regression model of factors associated with poor prognosis after upper airway corrective surgery for brachycephalic obstructive airway syndrome (BOAS)

<table>
<thead>
<tr>
<th>Variable</th>
<th>B (SE)</th>
<th>Wald test statistic</th>
<th>p-value</th>
<th>Estimated OR</th>
<th>95% CI for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>4.253 (1.374)</td>
<td>9.578</td>
<td>0.002</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Age (months)</td>
<td>-0.039 (0.018)</td>
<td>4.641</td>
<td>0.031</td>
<td>0.962</td>
<td>0.928-0.996</td>
</tr>
<tr>
<td>Body condition score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7 (Reference)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≥7</td>
<td>-2.846 (0.976)</td>
<td>8.497</td>
<td>0.004</td>
<td>0.058</td>
<td>0.009-0.394</td>
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<tr>
<td>Grade of laryngeal collapse</td>
<td></td>
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<td></td>
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<tr>
<td>0-I (Reference)</td>
<td></td>
<td></td>
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<tr>
<td>II-III</td>
<td>1.809 (0.923)</td>
<td>3.843</td>
<td>0.05*</td>
<td>6.102</td>
<td>1-37.222</td>
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<tr>
<td>Surgical technique</td>
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<tr>
<td>TMS (Reference)</td>
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<tr>
<td>MMS</td>
<td>-2.072 (0.978)</td>
<td>4.486</td>
<td>0.034</td>
<td>0.126</td>
<td>0.019-0.857</td>
</tr>
</tbody>
</table>

B, regression coefficient; SE, standard error; OR, odds ratio; CI, confidence interval; TMS, traditional multilevel surgery; MMS, modified multilevel surgery

Poor prognosis was defined as post-operative BOAS index equal to or exceeding the breed specific cut-off diagnostic values (55.4% for pugs, 49.41% for French bulldogs, 43.53% for bulldogs²²).

Pre-operative BOAS index was removed from the final model as it was not statistically significant (p=0.8).

* The exact p-value was 0.04997 and was rounded to be 0.05.