TITLE: Complications following laryngeal sacculectomy in brachycephalic dogs

AUTHORS: J. R. Hughes, B. M. Kaye, A. R. Beswick, G. Ter Haar

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Complications following laryngeal sacculectomy in brachycephalic dogs

Abstract:

Objectives: Evaluate the effect of sacculectomy on the immediate postoperative complication rate in dogs affected with brachycephalic obstructive airway syndrome (BOAS)

Methods: Clinical records for brachycephalic dogs with everted saccules who underwent surgery for BOAS between 2009 and 2014 were reviewed retrospectively for type and severity of complications. Dogs were grouped as those having nares resection and staphylectomy only (S^0) and those having nares resection, staphylectomy and laryngeal sacculectomy performed (S^1). Complications were scored as mild (< 48 hours regurgitation and\or mild stertor/stridor), moderate (> 48 hours regurgitation and/or mild coughs and short term spontaneous resolving dyspnoea) or severe (dyspnoea that required intervention including tracheotomy or assisted ventilation and euthanasia/death).

Results: 37 dogs were included in S^1 and 44 in S^0. Dogs in S^1 were more likely to develop post-operative complications (P<0.05), with 48.6% developing complications, 50% (n=9) of which were moderate to severe. In S^0, 20.5% of dogs developed complications, of which 11.1% (n=1) were severe.

Clinical Significance: Brachycephalic dogs undergoing a sacculectomy procedure, in addition to nares resection and staphylectomy, had significantly higher post-

operative complication rates. This study suggests that additional studies are needed to assess differences in long term outcome of dogs undergoing or not undergoing laryngeal sacculectomy.

Keywords: Brachycephalic airway syndrome, BOAS, sacculectomy

Introduction

Brachycephalic obstructive airway syndrome (BOAS) is characterised by the primary morphological abnormalities of stenotic nares, aberrant nasal turbinates with increased mucosal contact points, an elongated soft palate, and tracheal hypoplasia (Koch et al., 2003, Pink et al., 2006, Torrez and Hunt, 2006, Oechtering et al., 2007, Bernaerts et al., 2010, Fasanella et al., 2010, Cantatore et al., 2012, Riecks et al., 2007). Breeds affected by BOAS include Pugs, British bulldogs, French bulldogs, Cavalier King Charles spaniels and Staffordshire bull terriers among others (Torrez and Hunt, 2006). Reported clinical signs of BOAS include stertor, stridor, coughing, dyspnoea, tachypnoea, gagging, regurgitation, vomiting and syncope and/or collapse (Koch et al., 2003, Torrez and Hunt, 2006, Riecks et al., 2007, Bernaerts et al., 2010, Mercurio, 2011, Furtado, 2014).

Everted laryngeal saccules are a well-documented finding in dogs suffering from BOAS. Previous studies report incidences of 54.1% to 66% of saccular eversion alongside the primary abnormalities of BOAS (Poncet et al., 2006, Torrez and Hunt, 2006, Riecks et al., 2007, Fasanella et al., 2010). Everted saccules are considered to be the first degree of laryngeal collapse, categorised as grade I. Grade II consists of medial displacement, and sometimes overlap, of the cuneiform processes due to a loss of rigidity, and grade III is the collapse of the corniculate processes (Leonard, 1960, Monnet, 2003). Everted saccules are most often seen with at least 2-3 other criteria defining BOAS, and are considered to be a secondary physical change to the laryngeal soft tissues as a result of increased airway resistance, negative intraluminal pressure, and a turbulent airflow (Bernaerts et al., 2010, Lodato and Hedlund, 2012, Riecks et al., 2007). The clinical relevance of saccule eversion is currently unknown and there is no standardised way of measuring the level of upper airway obstruction that they cause.

54 The treatment for BOAS has been well described and combines both medical and
55 surgical management. Standard surgical management options for BOAS include nares
56 resection¸ staphylectomy and resection of the everted laryngeal saccules, and reportedly
57 have a favourable outcome (Riecks et al., 2007). Few studies have documented the
58 effects of the individual procedures of BOAS surgery on outcome and the complication
59 rate of the individual procedures (Harvey, 1982a, Harvey, 1982b, Harvey, 1982c).
60 While most surgeons consider nares resection and staphylectomy indicated in patients
61 suffering from BOAS, there is no consensus to the necessity of sacculectomy (Pink et
62 al., 2006, Poncet et al., 2006). The procedure is currently performed based on the
63 individual surgeon's preference depending on a subjective assessment of the level of
64 obstruction to the laryngeal lumen they cause. Reported post-operative complications
65 of BOAS surgery include regurgitation, coughing, dyspnoea, cyanosis, airway oedema
66 and swelling, respiratory tract obstruction and aspiration pneumonia (Torrez and Hunt,
67 2006). It is currently unknown if the complications reported are due to the disease
68 process or general anaesthesia with intubation itself, primary healing of the incision
69 sites of the pharyngeal component (staphylectomy), the laryngeal component
70 (sacculectomy) or all of the above. To the authors' knowledge, complications
71 associated with sacculectomy specifically in the immediate post-operative period have
72 not been reported but are hypothesised to include local haematoma formation, oedema
73 and swelling of the laryngeal mucosa leading to further luminal obstruction (Cantatore
74 et al., 2012). By increasing the negative intrathoracic pressure, the latter could lead to
75 an increased risk of regurgitation and subsequent aspiration pneumonia (Griffon, 2016,
76 Poncet et al., 2006).

77 The aims of this study were to document the incidence and severity of immediate
78 complications following BOAS surgery, and to examine differences in risks between

79 animals elected to have nares resection and staphylectomy alone versus those elected
80 to have additional sacculectomy.
81

Materials and Methods

Dogs and Clinical Data:

Records of client-owned dogs that presented at the XXXX, for investigation of BOAS were retrospectively reviewed (2009 to 2014). Dogs were eligible for inclusion if they (1) were a Pug, British Bulldog, or a French bulldog, (2) had a history and clinical examination, by a board certified surgeon, consistent with BOAS, (3) had laryngoscopic evidence of saccule eversion, (4) had either a surgical procedure including nares resection and staphylectomy only, or nares resection, staphylectomy and laryngeal sacculectomy, and (5) had no other significant respiratory pathology diagnosed on thoracic imaging prior to surgery. Dogs were excluded from the study if they had additional procedures performed, had previous upper airway surgery, had a prophylactic temporary tracheostomy performed during the surgery for BOAS, or did not receive perioperative steroids.

Baseline clinical details obtained from medical records at the time of surgery included breed, sex, age, weight, presenting clinical signs, pharyngolaryngoscopic findings including grade of laryngeal collapse, the results of pre-operative head and thoracic imaging, peri-operative medical protocols, surgical procedures performed, and post-operative complications. Grade of laryngeal collapse was scored between 1-3 according to Leonard et al 1960; Stage 1 - laryngeal saccule eversion, Stage 2 – medially displaced cuneiform processes, stage 3 – collapse of the corniculate processes.

The patient population was divided into two groups according to the aforementioned inclusion criteria. The control group (S^0) consisted of dogs that had nares resection and staphylectomy only. The sacculectomy group (S^1) had nares resection, staphylectomy and bilateral laryngeal sacculectomy performed. Both groups of

patients had laryngoscopic evidence of laryngeal saccule eversion but the decision whether or not to perform sacculectomy was solely based on the preference of the surgeon. The post-operative period was defined as the post-operative anaesthesia time (from time of extubation) and subsequent post-operative period until discharge. All upper airway or upper gastrointestinal complications were recorded to be significant. Post-operative complications were defined as mild, moderate or severe.

Mild complications were defined as dogs who had <48 hours of post-operative regurgitation and/or mild stertor/stridor without dyspnoea and normal exercise tolerance. Moderate complications were those who had > 48 hours of regurgitation, mild coughs post-operatively and/or any episode of spontaneously resolving dyspnoea. Severe complications included any worsening dyspnoea requiring intervention, including temporary tracheostomy tube placement for severe upper airway obstruction, medical treatment for aspiration pneumonia, or the need for mechanical ventilation, or complications resulting in euthanasia or death.

Statistical analysis:

Statistical analysis was performed using commercially available statistical software (IBM SPSS Statistics 22). Histograms were used to assess the distribution of any continuous variables. Normally distributed data was displayed as mean (± standard deviation), whilst non-normally distributed data was displayed as median (range). Chi squared association was used to assess the difference between categorical variables. An Independent samples T test was used to assess the difference between the two surgical groups of any parametric continuous data. A Mann-Whitney U test was used to assess the difference between the two surgical groups of any non-parametric continuous

130 variables. Ordinal logistic regression was used to assess the effect of surgical group on
131 the occurrence of complications with a specified odds ratio (OR). A P value of <0.05
132 was considered significant. between the two surgical groups.

133

Results

One hundred and fifty-one brachycephalic dogs were assessed during the study period. Seventy dogs did not meet the inclusion criteria and were excluded. Breed distribution is presented in table 1. Forty-four of 81 dogs (54.3%) had nares resection and staphylectomy only (S^0) and 37/81 dogs (45.7%) had nares resection, staphylectomy and laryngeal sacculectomy performed (S^1). In S^1, French bulldogs were underrepresented whilst British bulldogs were overrepresented ($P<0.05$). Of the 81 dogs included, 32/81 (39.5%) dogs were female (of which 15, 18.5% were neutered) and 49/81 (60.5%) dogs were male (of which 13, 16% were neutered). The median age at time of surgery was 25 months (range 4 - 132 months). There was no difference in median age between the two surgical groups ($P=0.429$). Median weight was 10.6 kg (range 4.8 – 36). There was no difference in median weight between the two surgical groups ($P=0.919$). Distribution of presenting clinical signs is shown in Table 2.

All dogs underwent routine general anaesthesia according to institutional protocols. Peri-operative antibiotic and corticosteroid, anti-emetic and gastroprotectant use consisted of either potentiated amoxicillin (Augmentin, GSK) or cephalosporins (Zinacef, GSK) (20 mg\kg IV every 2 hours intra-operatively and every 8 hours post-operatively if necessary) and dexamethasone sodium phosphate (Colvasone, Norbrook) (0.1-0.2 mg/kg, IV) at induction, omeprazole (Losec, AstraZeneca) (1 mg/kg orally, once daily, 6-12 hours before surgery) and maropitant citrate (Cerenia, Zoetis) (2mg/kg orally, once daily, 6-12 hours before surgery).

Inspection of the nares and pharyngolaryngoscopic examination revealed brachycephaly related abnormalities including stenotic nares, elongated soft palate and

158 eversion of the saccules in all dogs. The degree of laryngeal collapse was scored as
159 previously described, (Leonard et al 1960) with results listed in Table 3, but no
160 objective assessment of degree of airway obstruction was made. No other significant
161 findings were reported in the pharyngolaryngeal region than those described. There was
162 no significant difference in grading of laryngeal collapse between the two surgical
163 groups (P=0.191). No other significant findings were identified on CT or radiography.

164 Nares resection using a wide horizontal or vertical wedge resection technique with
165 scalpel blades and a staphylectomy with scissors were carried out by a board certified
166 specialist surgeon or resident under direct supervision of a specialist surgeon (Tobias
167 and Johnston, 2012). All wedge resections of the nares were closed using interrupted
168 absorbable suture material. Staphylectomy resection sites were closed either in a
169 continuous or interrupted pattern using absorbable suture material. Sacculectomy, if
170 performed, was carried out after temporary extubation at the end of the procedure by
171 placing Allis forceps on the everted saccule and amputation at the base using
172 Metzenbaum scissors.

173 All dogs were recovered from general anaesthesia, extubated and returned to surgical
174 wards or the intensive care unit dependent on the nature of their recovery. Generally
175 antibiotics were not given in the postoperative period unless aspiration pneumonia was
176 suspected. Postoperative analgesia was provided with varying opioid analgesics but
177 generally consisted of buprenorphine (Buprecare, Animalcare) (0.02mg/kg
178 intravenously). Anti-emetic and gastroprotectant medication was prescribed for those
179 patients that experienced postoperative nausea and regurgitation respectively in the
180 same doses as described above. Patients were discharged when they were clinically
181 stable and adequately analgised on oral medication.

Immediate post-operative complications experienced in S^0 and S^1 are summarized in Table 4. All of the dogs that were categorised as having mild complications had less than 48 hours of regurgitation. Overall, there were 10 dogs (12.3%) that experienced moderate or severe complications, all of which were respiratory or respiratory and upper gastro-intestinal. Three dogs (3.7%) died or were euthanised. Of the five dogs that developed moderate complications, 2 developed regurgitation and all 5 developed dyspnoea. All of the 5 dogs that developed severe complications had respiratory complications, none were reported to show regurgitation. Twenty seven dogs (33.3%) presented with regurgitation as part of the clinical signs, 8 of these dogs had mild regurgitation as a post-operative complication. An additional 11 dogs that had no history of regurgitation beforehand experienced mild regurgitation after surgery.

Seventy-eight of 81 dogs (96.3%) survived until discharge; 43 dogs in S^0 (97.7%) and 35 dogs in S^1 (94.6%). In S^0 79.5% of the dogs recovered completely uneventfully and experienced no complications, 18% exhibited mild complications. Only one dog in this group required intensive care monitoring and intervention; this dog was a 3 year 1 month male neutered French Bulldog who recovered poorly from surgery and became increasingly dyspnoeic over the subsequent 24-hour, post-operative period. This particular dog was suspected to have developed aspiration pneumonia and subsequently died due to respiratory arrest. 51.4 % of all dogs in S^1 had an uneventful recovery. Of the 4 dogs that experienced severe complications, 2 were euthanised. These included a 2 year 10 month old female neutered British Bulldog that was suspected to have developed severe post-operative aspiration pneumonia and a 6 year 11 month old male entire Pug who developed severe respiratory distress in the intensive care post-operatively. The owners elected euthanasia in these two patients because of the poor prognosis and costs associated with assisted ventilation. The two

other severe complications occurred in a 2 year 8 month old male neutered British Bulldog who developed severe aspiration pneumonia and was re-anaesthetised and ventilated for 36 hours after which he made an uneventful recovery and a 1 year 1 month old male neutered British Bulldog who developed post-operative upper airway dyspnoea. This animal was re-anaesthetised, noted to have peri-laryngeal swelling and a temporary tracheostomy was placed which was removed after 2 days. Individuals in the S^1 group had significantly more moderate and severe post-operative complications than those in S^0. Ordinal logistic regression showed that dogs in the sacculectomy group had a higher risk of developing moderate and severe complications ($P < 0.05$, OR = 2.97, 95% CI 1.59 – 5.56, and $P < 0.05$; OR = 6.40, 95% CI 2.97 – 13.83 respectively). There was no significant difference in development of mild complications between S^0 and S^1 ($P > 0.05$). The distribution of complications between the two groups is shown in Fig.1. Table 5 shows the distribution of complications according to breed. Excluding dogs that died or were euthanised while hospitalised, the median duration of hospital stay was 2 days (range 1 – 10 days). Dogs in S^1 had a longer median duration of hospital stay (3 days; range 1 – 10 days) compared to those in S^0 (2 days; range 1 – 6 days) ($P<0.05$).

225 **Discussion**

226 Within our study population, sacculectomy in dogs with BOAS was associated with an
227 increased peri-operative morbidity. Its widespread use in the treatment of dogs with
228 laryngeal saccule eversion, based on our results, remains controversial. This is in
229 agreement with previous studies that questioned the necessity of the procedure (Pink et
230 al., 2006, Poncet et al., 2006).

231 We included the three main breeds commonly presented with BOAS problems in our
232 study, Pugs, British Bulldogs and French Bulldogs (Poncet et al., 2005, Poncet et al.,
233 2006, Torrez and Hunt, 2006, Riecks et al., 2007, Fasanella et al., 2010). Males were
234 overrepresented in this study and a median age at presentation of 25 months was also
235 in agreement with previous studies (Poncet et al., 2005, Poncet et al., 2006, Riecks et
236 al., 2007, Fasanella et al., 2010, Lodato and Hedlund, 2012). Breeds were not evenly
237 distributed between our two study groups though. British bulldogs were
238 overrepresented in S^1 compared to S^0 and French Bulldogs were overrepresented in S^0
239 compared to S^1 ($P<0.05$). This could indicate that the saccule eversion in British
240 Bulldogs may have caused more subjective obstruction to the laryngeal lumen, as
241 assessed by the surgeon, than in French Bulldogs. Though there are no objective scoring
242 systems for degree of saccular eversion, British Bulldogs are generally found to have
243 the highest incidence of being affected by all currently known components of BOAS
244 (Riecks et al., 2007). The differences in complication rates found in British Bulldogs
245 and French Bulldogs could therefore be related to a difference in degree of severity of
246 disease rather than sacculectomy per se. Interestingly though, looking at Pugs
247 specifically, that were equally distributed between the groups with 19 Pugs in S^0 and
248 20 Pugs in S^1, the same overall conclusions appear to hold true. Of the 19 Pugs in S^0,
249 14 experienced no complications at all and 5 had only mild complications. Of the 20

Pugs in S[1], only 11 had no complications, 7 had mild, 1 had moderate and 1 had severe complications. Though this suggests, that at least in the Pug, sacculectomy indeed increases peri-operative morbidity, further studies would be needed to assess the effect of breed predisposition on the development of specific complications.

Complications encountered in this study were similar to previously reported post-operative complications of BOAS surgery including regurgitation, coughing, dyspnoea, cyanosis, and respiratory tract obstruction and aspiration pneumonia (Poncet et al., 2006, Fasanella et al., 2010, Senn et al., 2011, Torrez and Hunt, 2006). The respiratory complication rate i.e. dogs that had moderate and severe complications was 12.3% and mortality rate was 3.7%. Respiratory complication rate was similar to that reported in previous studies (11.1 – 26.2%(Torrez and Hunt, 2006, Fasanella et al., 2010, Poncet et al., 2006)). The mortality rate of 3.7% was similar as well with previous studies reporting 0 – 3.3% (Riecks et al., 2007, Oechtering, 2016, Torrez and Hunt, 2006, Poncet et al., 2006). The number of dogs needing a temporary tracheostomy tube in this study (n=1) appears low compared with previously reported studies (4.9-6.8%)(Torrez and Hunt, 2006, Poncet et al., 2006).

Regurgitation, defined as a passive reflux of previously swallowed material from the oesophagus, or stomach (Kahn, 2005) is often recognised as a complication following surgery (Torrez and Hunt, 2006) and was the most commonly found complication in our study as well. This likely reflects the high incidence of upper gastrointestinal pathology in brachycephalic breeds (Koch et al., 2003, Poncet et al., 2005). Anaesthesia, stress of hospitalisation, opioid medication and co-existent gastrointestinal disorders are possible contributing factors to peri-operative regurgitation. The number of dogs experiencing mild complications, i.e. <48 hours regurgitation, was not significantly different between surgical groups ($P<0.05$),

therefore no link between sacculectomy and post-operative regurgitation could be made.

Degree of laryngeal airway compromise and chondromalacia could be a factor affecting the incidence of complications after sacculectomy in the different breeds. Severity of laryngeal abnormalities, rima glottis size and chondromalacia vary between breeds, for instance Pugs have narrower, oval-shaped larynges compared to French bulldogs (Caccamo et al., 2014). It could be hypothesised that the narrower the rima glottis is, the more detrimental any further swelling would be. Degree of actual rima glottis obstruction was not scored in this study. Respiratory complications associated with upper airway swelling were generally only mild in this study however and not related to any specific breed.

The degree of rima glottis obstruction by laryngeal collapse specifically also likely influences the degree of swelling tolerated and therefore could affect the risk of postoperative complications as well. Evaluation of saccule eversion is currently subjective as there is no standardised grading of luminal obstruction created by the saccule eversion. Prospective studies could look into a ratio between the rima glottis and surface area obstructed by the everted saccules. The decision on whether or not to perform sacculectomy is currently decided by the surgeon on a case by case basis. It could be hypothesised that dogs with more significant eversion of the saccules or a higher grade of laryngeal collapse are more likely to experience post-operative complications following the sacculectomy procedure. The degree of laryngeal collapse was comparable in our two study groups ($P>0.05$), and therefore did not appear to be directly associated with risk of complication. Dogs in S^1 had a longer duration of hospital stay overall in our study ($P<0.05$), likely reflecting the longer recovery time needed before the surgeon was comfortable discharging the patient.

A previous study found that 92.2% of dogs undergoing sacculectomy achieved a good or excellent long term outcome (Riecks et al., 2007). Long term outcome of our patients was not assessed in this study. Although one report suggests that everted saccules do not regress after nares resection and staphylectomy only (Cantatore et al 2012), and are therefore an irreversible change, the benefit of sacculectomy still has to be demonstrated. It is currently unknown whether or not additional sacculectomy leads to a better long-term outcome than nares resection and staphylectomy alone. For prospective evaluation of longer term outcome of surgery for BOAS, and especially the effect of sacculectomy, comprehensive objective evaluation of outcome would be needed.

Limitations of this study reflect the fact that it is a retrospective study. There is a possibility that some of the clinical records may have been incomplete and some complications may have been underreported. Objective assessment of the degree of obstruction created by the saccules initially was not performed and there is no current standardised grading scheme. This is likely to be further confounded by the incorporation of several brachycephalic breeds in this study. The varying breeds are known to have different anatomical variations, as discussed above, and varying components and severity of BOAS that would have introduced bias to the results. A number of different board certified surgeons would have had primary responsibility over each case. This would have likely caused variation in the grading of the clinical signs and grade of laryngeal collapse despite there being a standardised grading scheme. Similarly, the pharyngolaryngoscopic examinations and imaging were not reviewed by a single clinician so there may have been variations in the anatomical abnormalities detected. It also biased the study population as surgical procedure performed depended on the preference of the surgeon; some surgeons never routinely performed

sacculectomy, some always, some only with a high subjective degree of obstruction. Surgical technique and experience may therefore have affected post-operative complications. Post-operative pain relief and medication may also have varied according to clinician preference marginally.

Though multiple factors (surgeon's preference, experience, patient factors, breed, severity of disease, peri-operative medication) in this study will have affected outcome, the findings suggest that sacculectomy itself may contribute to an increased risk for development of complications after BOAS surgery. Having considered the increased risk of this procedure and all possible confounding and contributing factors, sacculectomy may well be indicated in some individual patients on a case by case basis. Future prospective studies are needed to fully assess the main trigger factors for development of immediate post-operative complications and to help control variables and bias between groups.

In conclusion, this study showed that in the immediate post-operative period, dogs who were selected for and had a sacculectomy procedure performed, were more likely to develop moderate and severe complications. The role of sacculectomy in the treatment of BOAS remains controversial and the decision to carry out a sacculectomy should be carefully considered and the potential benefits must outweigh the risk of complications.

Conflicts of interest

The authors declare no conflict of interests related to this article

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Appendix

Table 1. Breed distribution across surgical groups

	Pug	British Bulldog	French Bulldog	Total
S^0	19	7	18	44
S^1	20	15	2	37
Total	39	22	20	81

($P<0.05$)

Table 2. Presenting clinical signs according to history distributed across surgical groups

	Total population (n=81)	S^0 (n=44)	S^1 (n=37)
Respiratory Noise	59	31	28
Dyspnoea (increased respiratory rate and effort)	47	27	20
Exercise Intolerance	35	18	17
Regurgitation	27	17	7
Cough	15	7	8
Collapse	14	6	8
Vomiting	12	6	6
Gagging \ Retching \ Dysphagia	9	5	4
Cyanosis	6	4	2
Sneezing \ Nasal Discharge	4	2	2
Inappetence	4	3	1

Table 3. Grade of laryngeal collapse distributed between surgical groups.

	Grade I	Grade II	Grade III	Total
S^0	32	12	0	44
S^1	22	13	2	37
Total	54	25	2	81

($P>0.05$)

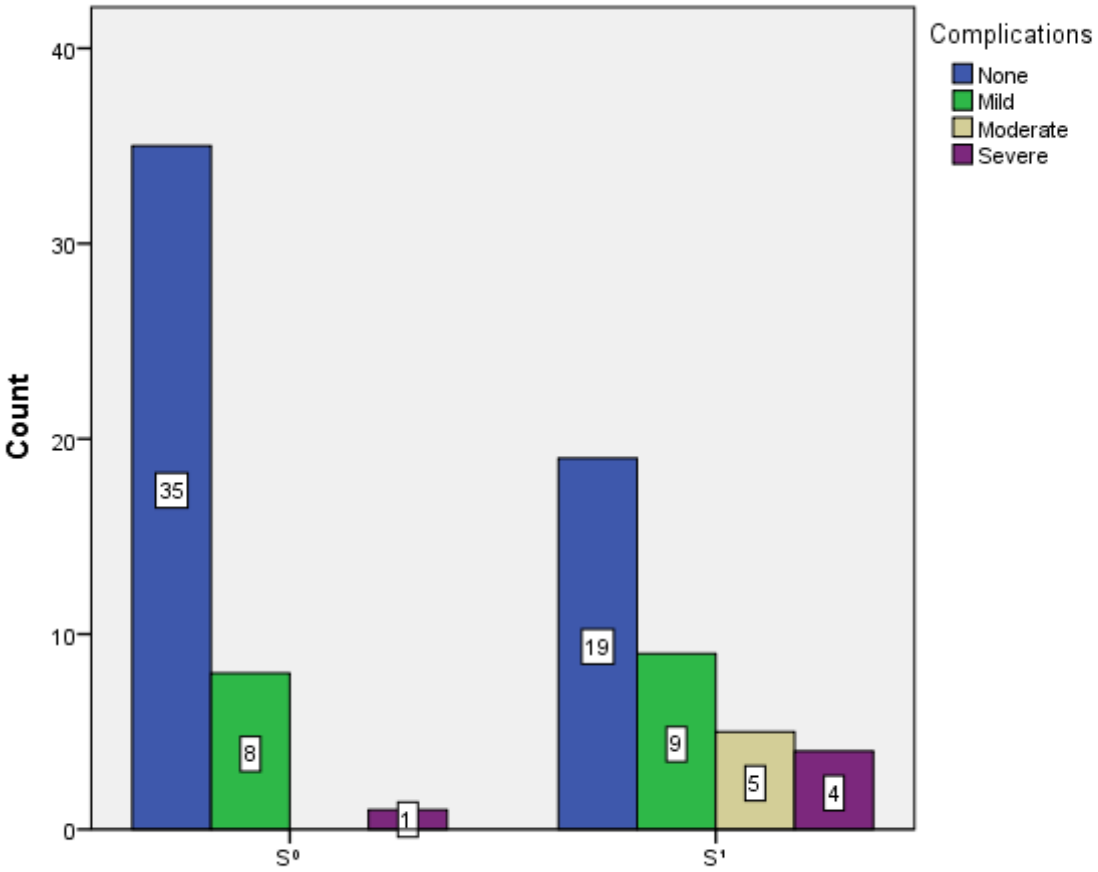
Table 4. Complications distributed between surgical groups

	None	Mild	Moderate	Severe	Total
S^0	35	8	0	1	44
S^1	19	9	5	4	37
Total	54	17	5	5	81

Table 5. Complications distributed between breeds

	Pug	British Bulldog	French Bulldog	Total
None	25	11	18	54
Mild	12	4	1	17
Moderate	1	4	0	5
Severe	1	3	1	5
Total	39	22	20	81

Figure 1. Distribution of complications by surgical group



The criteria for a mild complications were any dogs who had less than 48 hours of post-operative regurgitation.

Moderate complications were those who had greater than 48hrs of regurgitation, mild coughs post-operatively and any episode of spontaneously resolving dyspnoea.

Severe complications included any dyspnoea requiring intervention, including temporary tracheostomy tube placement, the need for mechanical ventilation or resulting in euthanasia or death.