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Clinical assessment of brachycephalic airway obstructive syndrome using questionnaire and 6-minute walk test in French Bulldogs

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Abstract

Brachycephalic airway obstructive syndrome (BAOS) is an anatomical abnormality of the upper airway commonly found in brachycephalic breeds leading to clinical signs and physical capacity impairment. The purposes of this study were to objectively assess the severity of the clinical signs and physical capacity in French Bulldogs with BAOS using questionnaire and 6-minute walk test (6-MWT), respectively. A total of 26 French Bulldogs were enrolled in this study and divided into a normal group (n = 7), a moderate BAOS group (n = 8) and a severe BAOS group (n = 11). After history taking and physical examination, the questionnaire was answered by the owners and 6-MWT was performed in all dogs. The severity of the clinical signs from the total questionnaire scores in the moderate and severe BAOS groups were significantly higher than the normal group ($P < 0.05$ and $P < 0.001$, respectively). The 6-MWT distance of the normal group (521 ± 35 m) was significantly longer than the moderate BAOS group (422 ± 37 m) and the severe BAOS group (392 ± 50 m) ($P < 0.001$). Serious adverse clinical signs were not found during and after 6-MWT. Moreover, negative correlations were found between 6-MWT distance and questionnaire scores with the strongest negative correlation with the breathing sound scores ($r = -0.757$, $P < 0.001$). In conclusion, dogs with moderate to severe BAOS had a higher severity of clinical signs with lower physical capacity compared with normal dogs, both of which could be objectively assessed and presented as numerical data by questionnaire and 6-MWT. Thus, questionnaire and 6-MWT can provide clinical severity in detail for BAOS management.

Keywords: brachycephalic airway obstructive syndrome, French Bulldog, questionnaire, 6-minute walk test

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Introduction

At present, brachycephalic breeds such as the French Bulldog, the Pug and the English Bulldog, are increasingly popular (The Kennel Club, 2020). However, these breeds tend to have an anatomical abnormality of the upper respiratory tract commonly known as brachycephalic airway obstructive syndrome (BAOS) (MacPhail, 2013; Meola, 2013). The primary obstructive disorders are an elongated soft palate, stenotic nares, hypoplastic trachea and nasal conchae aberrance. This anatomical malformation induces negative pressure in the upper respiratory tract leading to secondary changes (i.e. everted laryngeal sacculae, everted tonsils, laryngeal collapse and bronchial collapse). BAOS dogs commonly present loud and abnormal breathing sounds (i.e. stertor, stridor and snoring), dyspnea, open mouth breathing, exercise and heat intolerance, sleep apnea, cyanosis and syncope in severe cases. Moreover, BAOS can cause gastrointestinal complications such as aerophagia, hypersalivation, regurgitation and vomiting (Poncet *et al.*, 2005; MacPhail, 2013). The severity of these signs can be increased at an environmental temperature over 19°C (Roedler *et al.*, 2013). Therefore, living in a hot and humid environment such as Thailand that has an average temperature of 28°C (The Thai Meteorological Department, 2020), can significantly impact clinical outcomes in many brachycephalic dogs.

BAOS can be diagnosed from history taking, physical examination, radiography and laryngoscopy. The clinical signs are routinely assessed by history taking and physical examination. Also, a functional grading system of BOAS severity was introduced into clinical practice and research settings recently (Liu *et al.*, 2015). However, general history taking may not be able to retrieve clinical sign information in detail. Also, physical examination can be interfered with by excitement of the dog in a hospital environment. Moreover, the functional grading system categorizes dogs with BAOS as grad 0 to III using only respiratory signs in pre- and post-exercise tolerance tests but it cannot provide variation or improvement within the same grade. Therefore, recent studies have used specific questionnaires that can provide ordinal data in all related clinical signs to objectively assess the frequency and severity of clinical signs in many situations of normal daily activities (Roedler *et al.*, 2013; Pohl *et al.*, 2016).

In terms of exercise intolerance, a 6-minute walk test (6-MWT) is a submaximal exercise test that can reflect physical capacity related with low intensity activities. This test can assess the health status and therapy responsiveness of cardiovascular, pulmonary and neuromuscular diseases in dogs (Swimmer and Rozanski, 2011; Manens *et al.*, 2014; Cerda-Gonzalez *et al.*, 2016). The advantages of this test are simply, reasonable price and reproducibility with minimal technology requirements (Swimmer and Rozanski, 2011). Recently, 6-MWT was applied to quantify the effect of BAOS on physical capacity (Lilja-Maula *et al.*, 2017; Aromaa *et al.*, 2019). However, correlation between clinical signs and 6-MWT distances has not been fully elucidated. Therefore, the aim of this study

was to evaluate the clinical signs retrieved from the questionnaire, physical capacity using 6-MWT and their correlation in French Bulldogs with BAOS in Thailand.

Materials and Methods

This study was approved by the Chulalongkorn University Animal Care and Use Committee (Animal Use Protocol No.: 1931009) and performed at the Small Animal Teaching Hospital, Faculty of Veterinary Science, Chulalongkorn University, Bangkok, from February 2019 to February 2020. Twenty-six client owned French Bulldogs were included. Inclusion criteria were age of between 6 months to 6 years, normal body condition score (BCS) and no previous medical history of surgical correction for BAOS. Dogs with lower respiratory, cardiovascular and neuromuscular diseases were excluded from this study. After history taking, all the dogs were subjected to a complete physical examination, blood collection for hematology and blood chemistry, electrocardiography and cervicothoracic radiography. Laryngoscopic examination was performed only in dogs that presented BAOS clinical signs.

The dogs were divided into 3 groups: normal group (n = 7), moderate BAOS group (n = 8) and severe BAOS group (n = 11). The severity of BAOS was assessed from clinical signs using the functional grading system of BAOS (Liu *et al.*, 2015) and BAOS lesions. From this grading system, the normal group had no BAOS lesions or clinical signs. The moderate BAOS group had mild to moderate BAOS lesions and respiratory noise, inspiration effort or mild dyspnea without cyanosis or syncope both at rest and at exercise. The severe BAOS group had moderate to severe BAOS lesions and respiratory noise, inspiration effort or severe dyspnea with or without cyanosis and syncope both at rest and at exercise.

The questionnaire: the BAOS questionnaire in this study was modified from questionnaires in the previous studies by Roedler and colleagues (2013) and Liu and colleagues (2015). The questions were adjusted to be more suitable for climate and dog management in Thailand. The questionnaire was then translated into Thai by Thai veterinarians who graduated from an English-speaking country and were bilingual English and Thai veterinarians. The questionnaire consisted of a series of general questions (i.e. owner information and dog signalment) and specific questions regarding BAOS clinical signs that were grouped into four parts (Table 1). The BAOS clinical sign questions were scored according to the frequency of each clinical sign as follows: zero for never, one for 1-2 times per week, two for more than 2 times per week and three for always. The face-to-face questionnaire was performed after the owners received client education including short video clips containing abnormal breathing sounds and sleep apnea patterns. Then, the scores were combined for each part and the total score. Additional open-ended questions regarding to frequency and duration of outdoor activity, as well as recovery time, were also included at the end of this questionnaire.

Table 1 Questions used in each part of the questionnaire.

1. Abnormal breathing sound
- Loud breathing while awake at rest
- Loud breathing while sleeping (snoring)
- Loud breathing while at exercise or excited
2. Exercise and heat intolerance
- Difficult breathing during exercise or excited in an air-conditioned room
- Difficult breathing during exercise or excited in hot weather
- Developing bluish gums or tongue during exercise or when excited
- Collapse after difficult breathing during exercise or when excited
3. Eating problems
- Eating fast or swallowing food without chewing
- Regurgitation or vomiting during or after eating
4. Sleeping problems
- Waking up several times or having difficulty falling asleep
- Inability to sleep without raising the chin or holding something in the mouth
- Having difficulty falling asleep in recumbent positions

Physical capacity test: 6-MWT was performed after a dog was acclimatized in a quiet air-conditioned room without other animals for at least 30 minutes. Before the test, heart rate (HR), respiratory rate (RR), oxygen saturation (SpO₂) and body temperature (T) were measured. The dog was fitted with a chest harness and walked along with the same veterinarian to avoid handling factor. The dogs walked on their own pace on a 5x5 m unobstructed walk path for 6 minutes. Immediately after the walk, HR, RR, SpO₂ and T were re-evaluated. Distances of the total walk were recorded in meters.

Statistical analysis: statistical analysis was performed using GraphPad Prism version 8.0.0. The parameters such as age, body weight, HR, RR, T, SpO₂ and walking distance were presented as mean \pm standard deviation (SD) for parametric data. The ordinal data from BCS and questionnaire scores were presented as median with range. The normal distribution of parametric data was confirmed by the Shapiro-Wilk test. The parametric data with normal distribution were compared among groups using one-way ANOVA with Tukey's multiple comparison test. Non-normal distributed parametric data and ordinal data were compared among groups using the Kruskal-Wallis test with Dunn's multiple comparison test. The correlations between 6-MWT distances and questionnaire scores were examined using Spearman's correlation test. *P* values less than 0.05 was considered statistically significant.

Results

Twenty-six French Bulldogs were enrolled in this study. The characteristics and BAOS lesions of all dogs are shown in Table 2. From physical examination, all dogs had normal heart and lung sound. All BAOS dogs had stertor sound, while mixed stertor and stridor sounds was found in one moderate BAOS dog and seven severe BAOS dogs. Blood profiles of all dogs were within normal limits. There was no statistical significance in blood parameters among groups.

Questionnaire: the results of the questionnaire scores in each question part of all dogs are presented in Table 3. The questionnaire scores in each part and total score of the normal group were significantly lower than the moderate and severe BAOS groups, except for the

eating part. There was no difference in questionnaire scores between the moderate and severe BAOS groups.

For breathing sound, none of the normal dogs presented loud breathing sounds when awake, exercising and excited, while snoring was noticed less than one time per week in five normal dogs. Most of the owners in both BAOS groups reported that their dogs had loud breathing sound in all activities. All BAOS dogs had loud breathing sounds during exercise and excitement with a higher frequency in dogs with severe BAOS. Almost half of the normal dogs developed mild dyspnea only when exercising in a hot environment, while all BAOS dogs presented a higher degree of dyspnea in both clinical presentation and frequency during exercise regardless of room temperature. Cyanosis and collapse during exercise were reported in four severe BAOS dogs. As for eating problems, all dogs exhibited the behavior of fast eating or not chewing food with more frequency in the severe BAOS group. Regurgitation and vomiting were reported by most of the owners in both BAOS groups. However, these eating problems showed a higher frequency in severe BAOS dogs. None of the normal dogs presented abnormal sleeping patterns, while three moderate BAOS dogs and seven severe BAOS dogs had sleep apnea. Half of the BAOS dogs were unable to sleep without raising the chin or holding something in the mouth. Difficulty falling asleep in recumbent positions was reported in only one severe BAOS dog.

From additional open-ended questions, the frequency of outdoor activities tended to be higher in the normal group. Moreover, four owners in the BAOS groups mentioned that they rarely took the dogs to exercise outdoors because of the breathing problems. The exercise duration per session and recovery times of all dogs are shown in Figure 1. Normal dogs were able to exercise longer and recover faster than BAOS dogs.

6-MWT: all dogs were able to perform 6-MWT with good compliance. An increased breathing sound was found in half of the severe BAOS dogs. However, other serious complications (i.e. dyspnea, cyanosis, muscle weakness and syncope) were not found in this study. The 6-MWT parameters including HR, RR, T, SpO₂ and walk distance of dogs in normal, moderate and severe BAOS groups are shown in Table 4. At pre-walk,

severe BAOS dogs had significantly higher T than normal dogs ($P < 0.01$). However, the body temperatures of all dogs were within normal limit. The distance of 6-MWT was higher in the normal group than the moderate and severe BAOS groups ($P < 0.001$). At post-walk, HR was significantly lower in the normal group compared with both BAOS groups, while RR

and T were significantly lower in normal group compared with the severe BAOS group.

6-MWT distances showed negative correlations with total questionnaire scores and the scores in each part (Table 5). The strongest negative correlation was found between 6-MWT distances and breathing sound scores.

Table 2 Dog characteristics and BAOS lesions of the normal group (n = 7), the moderate BAOS group (n = 8) and the severe BAOS group (n = 11).

Parameters	Normal	Moderate BAOS	Severe BAOS
Age (months)	14.3 ± 5.2 ^a	21 ± 9.1 ^a	35.4 ± 16.4 ^b
Sex: Male and female (number)	M = 2, F = 5	M = 7, F = 1	M = 8, F = 3
Weight (kg)	10.8 ± 2.1	13.2 ± 2.6	12.9 ± 2.2
BCS (5 scale)	3 (3-3.5)	3 (2.5-3.5)	3 (3-3.5)
Elongated soft palate (number)	0	8	11
Stenotic nares (number)	0	7	11
Mild		0	1
Moderate		4	1
Severe		3	9
Hypoplastic trachea (number)	0	0	2
Laryngeal sacculles (number)	N/A	4	9
Laryngeal collapse (number)	N/A	4	9
Stage I		2	1
Stage II		2	8
Stage III		0	0
Everted tonsils (number)	N/A	6	10
Single site		2	3
Both sites		4	7

Data was presented as number of dogs, except age and weight were presented as mean and standard deviation and BCS was presented as median with range. ^{a,b} values with superscript within columns are significantly different at $P < 0.05$.

Abbreviation: BAOS: brachycephalic airway obstructive syndrome; M: male; F: female; BCS: body condition score.

Table 3 Scores of questionnaire in each question part of the normal group (n = 7), the moderate BAOS group (n = 8) and the severe BAOS group (n = 11).

Parameters	Normal	Moderate BAOS	Severe BAOS
Total questionnaire score	3 (2-4) ^a	15 (11-18) ^b	19 (10-23) ^b
Breathing sound	1 (0-1) ^a	6 (3-8) ^b	8 (4-9) ^b
Exercise and heat tolerance	0 (0-1) ^a	4.5 (3-6) ^b	6 (4-7) ^b
Eating	2 (1-3) ^a	3 (1-4) ^{a,b}	3 (1-5) ^b
Sleeping	0 (0) ^a	1.5 (0-3) ^b	1 (0-4) ^b

Data was presented as median with range. ^{a,b} values with superscript within columns are significantly different at $P < 0.05$.

Abbreviation: BAOS: brachycephalic airway obstructive syndrome.

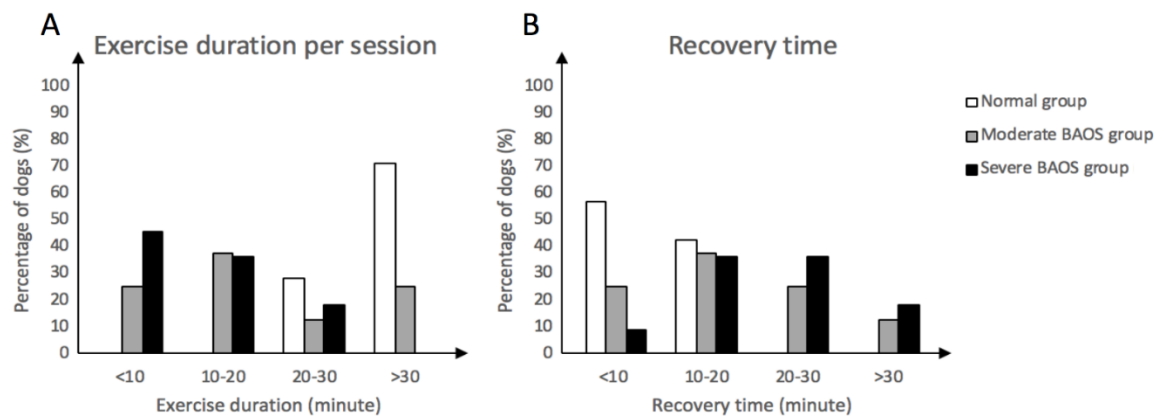


Figure 1 Approximate exercise duration per session (A) and recovery time (B) of the normal group (n = 7), the moderate BAOS group (n = 8) and the severe BAOS group (n = 11).

Table 4 6-MWT parameters of the normal group (n = 7), the moderate BAOS group (n = 8) and the severe BAOS group (n = 11).

Parameters	Normal	Moderate BAOS	Severe BAOS
HR (beat per minute)			
Pre-walk	119 ± 14	129 ± 8	128 ± 9
Post-walk	129 ± 14 ^a	149 ± 16 ^b	151 ± 12 ^b
RR (breath per minute)			
Pre-walk	33 ± 5	51 ± 17	55 ± 24
Post-walk	48 ± 5 ^a	75 ± 31 ^{a,b}	98 ± 45 ^b
T (F)			
Pre-walk	100.7 ± 0.5 ^a	101.3 ± 0.5 ^{a,b}	101.7 ± 0.6 ^b
Post-walk	101.0 ± 0.5 ^a	101.8 ± 0.9 ^{a,b}	102.2 ± 0.8 ^b
SpO₂ (%)			
Pre-walk	98 ± 1 ^a	96 ± 1 ^b	97 ± 1 ^{a,b}
Post-walk	98 ± 1	97 ± 2	96 ± 1
6-MWT Distance (meters)	521 ± 35 ^a	422 ± 37 ^b	392 ± 50 ^b

Data was presented as mean and standard deviation. ^{a,b} values with superscript within columns are significantly different at $P < 0.05$. Abbreviation: 6-MWT: 6-minute walk test BAOS: brachycephalic airway obstructive syndrome; HR: heart rate; RR: respiratory rate; T: body temperature; SpO₂: oxygen saturation.

Table 5 Spearman's correlation between 6-MWT distances and questionnaire scores in all dogs (n = 26).

Parameters	r	P value
Total questionnaire score	-0.621	0.0007
Breathing sound score	-0.757	<0.0001
Exercise and heat tolerance score	-0.547	0.0038
Eating score	-0.478	0.0135
Sleeping score	-0.333	0.0968

Discussion

Brachycephalic airway obstructive syndrome is a common anatomical problem found in brachycephalic breeds (Oechtering *et al.*, 2016). This problem causes upper airway obstruction leading to increased airway resistance which can induce soft tissue inflammation and malformation. The degree of respiratory obstruction can be graded from the severity of respiratory signs (Liu *et al.*, 2015). In moderate to severe cases, affected dogs usually present abnormal breathing sounds, heat and exercise intolerance, regurgitation and vomiting, sleep apnea, collapse and death (Poncet *et al.*, 2005; Roedler *et al.*, 2013). In this study, BAOS clinical signs could be retrieved from history taking, questionnaire and physical examination in all BAOS dogs. Moreover, BAOS could reduce physical capacity measured by 6-MWT in these French Bulldogs. Strong negative correlations were also found between 6-MWT distance and breathing sound scores and total questionnaire scores.

In terms of dog characteristics, the average age in the severe BAOS group was significantly higher than the other groups. However, all dogs in this study were still within young adult age for French Bulldogs. In this study, the average ages of both BAOS groups were similar to previous studies (Roedler *et al.*, 2013; Pohl *et al.*, 2016). Although, BAOS clinical signs were usually detected when the dogs were two to four years (MacPhail, 2013), some owners in this study reported that they had noticed the abnormal breathing sounds since their dogs were less than 1 year old. This early clinical presentation could result from higher BAOS severity, as well as the hot and humid environment in Thailand. Although, obesity can increase the severity of clinical presentation in dogs with BAOS (Liu *et al.*,

2015), all the dogs in this study had normal body condition scores (range 2.5-3.5/5). Approximately 80% of the BAOS cases in this study were male dogs, which was similar to other clinical studies that reported male dogs had higher incidence than female dogs (Poncet *et al.*, 2005; Poncet *et al.*, 2006). On the other hand, a welfare study in brachycephalic dogs found that female French Bulldogs had more incidences than males (25/44 dogs) (Aromaa *et al.*, 2019). However, there is no study that can confirm any correlation between gender and BAOS. Nevertheless, the gender of clinical cases may be influenced by owner preference and gender may affect the anatomical structures and dog activity. Male dogs had more muscle mass surrounding the nasopharynx than female dogs, therefore, this could cause more extraluminal compression of the airway (Roedler *et al.*, 2013).

The analysis of the questionnaire indicated that the scores for all parts including breathing sound, exercise and heat intolerance, eating and sleeping, were significantly higher in the moderate and severe BAOS groups than those of the normal group, especially the breathing sound and exercise and heat intolerance parts. The questionnaire results were similar to previous studies in dogs with BAOS, compared with mesocephalic breed dogs (Rolder *et al.*, 2013).

As for breathing problems, all of the BAOS dogs in this study had stertor, stridor and snoring sounds which were more frequent in the severe BAOS group, while only snoring was reported in the normal group. However, the functional grading system used in this study relied on the clinical evaluation of breathing sounds at rest or a pre-exercise tolerance test but not during sleeping. Exercise and heat intolerance are the serious clinical signs related to BAOS. Most of the BAOS cases in this study presented severe exercise and

heat intolerance and were unable to perform long durations of exercise in hot weather, especially in dogs with severe BAOS. This could be due to the combination of reduction in ventilation capacity and heat loss efficacy. According to the anatomical abnormality of nasopharynx found in BAOS, ventilation is impaired due to a narrowing of the upper respiratory tract leading to an increase in negative pressure in the airway. In severe cases, some part of upper respiratory tract may completely collapse (MacPhail, 2013). Nasal ventilation and surface area are the major factors of evaporative thermoregulation in dogs, thus BAOS can significantly reduce heat loss in affected dogs. Therefore, most of the dogs with BAOS were unable to increase ventilation and evaporation during exercise leading to exercise intolerance problems including cyanosis, early exhaustion, inability to perform strenuous exercise and collapse, especially in hot and humid weather where the efficiency of evaporation is reduced. In Thailand, the estimated annual temperature is 28°C with highest temperatures of 44°C, and the average annual humidity was 78% in 2019 (Weather-and-climate.com, 2019; The Thai Meteorological Department, 2020). These high ambient temperatures and humidity could cause mild exercise and heat intolerance (i.e. inspiratory effort) in some normal dogs, while exercise and heat intolerance were more severe (i.e. dyspnea, early exhaustion and inability to perform strenuous exercise) in both BAOS groups. Moreover, cyanosis and collapse were reported in some dogs in the severe BAOS group. These heat and exercise tolerance results were in-agreement with the open-ended answers regarding duration and frequency of exercise and recovery time, in which normal dogs had more ability to perform outdoor activities and had a faster recovery time, compared with BAOS dogs, especially the severe BAOS group.

In this study, the scores in the eating part showed some variation in regurgitation, vomiting, eating fast and swallowing food without chewing, however, the eating scores were significantly higher only in the severe BAOS group compared with the normal group. Although, BAOS can induce eating problems, other factors such as feeding regimen (e.g. types and palatability of food and numbers of meals per day) and social facilitation can impact eating behavior in dogs (Case, 1999). For sleeping problems, both BAOS groups had higher scores than the normal group. Relaxation of upper airway muscles during sleep can reduce the distension of the upper airway leading to sleep apnea in dogs with BAOS and some dogs may develop abnormal sleeping positions that can increase upper airway ventilation. These BAOS problems could be improved after surgical correction of the primary lesions in clinical studies (Pohl *et al.*, 2016; Thunyodom *et al.*, 2019).

From 6-MWT, T at pre-walk was higher in the severe BAOS group compared with the normal group. The dogs in the BAOS groups with higher T had higher RR than normal limits indicating that BAOS could reduce evaporative heat loss even in an air-conditioned room (24°C with 65% humidity). Moreover, the 6-MWT distances in both BAOS groups were lower than the normal group, which was similar to previous

studies (Lilja-Maula *et al.*, 2017; Aromaa *et al.*, 2019). Besides the severity of BAOS, walk distances could be altered by familiarity with short-leashed walking and test setting especially in terms of ambient temperature and humidity, length of walk path and number of turns (Sutayatram *et al.*, 2018). However, the effects of anatomical factors including leg length and gait patterns on walking distance were controlled in this study, as all included dogs were young adult French Bulldogs with body weights and BCS-matching among groups. At post-walk, all 6-MWT parameters were within normal limits in all normal dogs, while those BAOS dogs with higher T at the beginning developed tachycardia, tachypnea and hyperthermia. Thus, BAOS had a negative effect on physical capacity related with several systems such as the cardiovascular, respiratory and thermoregulatory systems. However, this physiological exertion recovered within five to ten minutes. According to the low risk of adverse events, 6-MWT may be more clinically feasible compared with the exercise tolerance test used in the functional grading system, where the dogs had to trot on a treadmill at a speed of 4-5 mile/h (approximately 6-8 km/h). From clinical observation, dogs with moderate to severe BAOS and dogs that were not familiar with the treadmill could not run on treadmill at this high speed. Also, this exercise tolerance test should be concerned when using dogs with BAOS that had a history of cyanosis and/or syncope (Liu *et al.*, 2015). Moreover, strong negative correlations were found between 6-MWT distance and questionnaire scores with the strongest negative correlations with breathing sound scores, the most common clinical sign in BAOS. Nevertheless, the exercise and heat tolerance scores exhibited only moderate negative correlation with 6-MWT distance. The lower the intensity and the cooler the environment of 6-MWT compared with routine exercise activity might cause the weaker correlation in this study.

These findings indicated that both questionnaire and 6-MWT were clinically feasible in French Bulldogs with BAOS in terms of quantitative clinical information, animal safety, ease and inexpensiveness of the tests. Although a questionnaire is less time consuming and does not require controlled test setting and trained personal, 6-MWT may be more appropriate in cases where information regardless of the severity and frequency of clinical signs cannot be provided by the owners as many owners are too busy to supervise dogs during exercise and the weather in Thailand is not suitable for outdoor activity.

A major limitation of this study was the small number of dogs in each group. However, only French Bulldogs were included in this study to minimize variation among breeds. Questionnaire scores depended on the owners' knowledge, honesty, observation and recalled memory which could lead to less accuracy information. Moreover, a dog's temperament such as timidity and energetic nature can affect the level of normal physical activity and compliance in the physical capacity test.

In conclusion, dogs with moderate to severe BAOS had a higher degree of clinical signs with lower physical capacity, both of which could be assessed by questionnaire and 6-MWT. Thus, medical management

and/or surgical correction of BAOS lesions is recommended for all BAOS dogs, and questionnaire and 6-MWT should be incorporated in the treatment response evaluation.

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