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REVIEWS

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Brachycephalic obstructive airway syndrome (BOAS): far beyond stenotic nares and elongated soft palate

Síndrome Obstrutiva Aérea Braquicefálica (SOAB): muito além das narinas estenóticas e do palato alongado

Paola Castro Moraes[1]*, Andreia Coutinho Facin[1], Ariadne Rein[1], Isabella de Almeida Fabris[1], Julia Banhareli Tasso[1], Mareliza Possa de Menezes[1]

ABSTRACT: Brachycephalic dogs have gained popularity worldwide in recent years; this preference is associated with the physiognomy of these animals, which resembles childlike features and has an important influence them being chosen as pets. However, selective breeding for extreme brachycephaly, as in the English bulldog, French bulldog and pug breeds, has given rise to a frequently occurring conformational respiratory disorder known as brachycephalic obstructive airway syndrome (BOAS). This is currently one of the most common anatomical disorders in small animals and has received increasing attention for its impact on animal welfare. It is still neglected, as some people consider it normal for brachycephalic breeds to snore, choke and manifest exercise intolerance. Although the most obvious clinical signs are related to breathing, BOAS can cause serious systemic consequences. Continuous respiratory effort in these dogs often results in increased intrathoracic pressure, leading to cardiovascular alterations such as pulmonary hypertension and cardiac overload. In addition, hypoxia can affect multiple organs, contributing to kidney, liver and gastrointestinal dysfunction. Early clinical and surgical management is essential to improve these animal's quality of life and prevent the progression of respiratory and systemic signs. Raising awareness about the care of brachycephalic dogs is essential, both for owners and veterinarians, in order to minimize the impact of this syndrome. This literature review aims to provide a current overview of BOAS and its systemic repercussions in brachycephalic dogs.

Keywords: brachycephaly; systemic inflammation; respiratory obstruction.

RESUMO: Cães braquicefálicos ganharam popularidade mundialmente nos últimos anos, e esta preferência está associada à fisionomia desses animais, que se assemelha a características infantis, o que exerce importante influência na sua escolha como animais de companhia. No entanto, a criação seletiva para braquicefalia extrema, como nas raças buldogue inglês, buldogue francês e pug, deu origem a um distúrbio respiratório conformacional, de ocorrência frequente, conhecido como síndrome obstrutiva aérea braquicefálica (SOAB). Essa é atualmente uma das desordens anatômicas mais frequentes em pequenos animais, e tem recebido crescente atenção por seus impactos no bem-estar animal. Ainda é negligenciada, uma vez que há quem considera normal das raças braquicefálicas sinais como ronco, engasgos e intolerância ao exercício. Embora os sinais clínicos mais evidentes estejam relacionados à respiração, a SOAB pode provocar consequências sistêmicas graves. O esforço respiratório contínuo nesses cães frequentemente resulta em aumento da pressão intratorácica, levando a alterações cardiovasculares, como hipertensão pulmonar e sobrecarga cardíaca. Além disso, a hipóxia pode afetar múltiplos órgãos, contribuindo para disfunções renais, hepáticas e gastrintestinais. O manejo clínico e cirúrgico precoce é fundamental para melhorar a qualidade de vida desses animais e evitar a progressão dos sinais respiratórios e sistêmicos. A conscientização sobre os cuidados com cães braquicefálicos é essencial, tanto para proprietários quanto para veterinários, a fim de minimizar o impacto dessa síndrome. A presente revisão de literatura objetiva trazer um panorama atual sobre a SOAB e sua repercussão sistêmica em cães braquicefálicos.

Palavras-chave: braquicefalia; inflamação sistêmica; obstrução respiratória.

INTRODUCTION

Brachycephalic obstructive airway syndrome (BOAS) is a major challenge in contemporary veterinary medicine, especially given the growing population of brachycephalic breeds and in particular those considered extreme, such as the French bulldog, English bulldog, and pug. Characterized by anatomopathological alterations that result in the partial obstruction of cranial airways, BOAS significantly compromises the well-being and quality of life of affected animals in systems other than just the respiratory. The intermittent hypoxia resulting from these alterations is recognized as a trigger for systemic inflammation and oxidative stress, in parallel to that observed in humans with obstructive sleep apnea. This review presents an up-to-date analysis of the main aspects related to the syndrome, with the aim of gathering and discussing the most relevant evidence available in the literature, in order to contribute to the understanding of the syndrome and improve decision-making by veterinarians.

[1] Department of Veterinary Clinics and Surgery, School of Agricultural and Veterinary Sciences, São Paulo State University (UNESP), Jaboticabal, Brazil

*Corresponding author: paola.moraes@unesp.br.
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HISTORY AND PRESENT CONTEXTUALIZATION

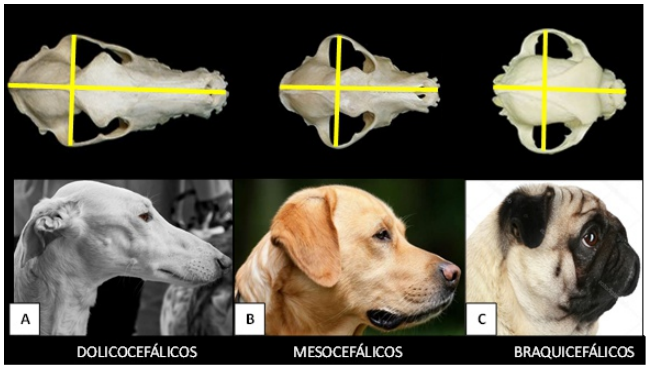
Domestic dogs (Canis lupus familiaris) are extremely diverse morphologically. This diversity is largely attributable to the breeding practices imposed by man over 2,000 years ago. Dogs can be classified into three groups based on their cranial proportions: brachycephalic (short and broad), dolichocephalic (long and narrow), and mesocephalic (with intermediate proportions) (Selba *et al*., 2020).

The increase in the population of brachycephalic breeds, such as pugs, English bulldogs and French bulldogs, has been observed in recent years and, in this scenario, the care of dogs of these breeds is becoming more and more frequent in the routine of small animal surgery.

The word "brachycephaly" comes from the Greek "brachus" and "cephalus", which mean "short" and "head", respectively. The main breeds of brachycephalic dogs are: Shih Tzu, Pekingese, Lhasa apso, Yorkshire terrier, Maltese, Chihuahua, Cavalier King Charles spaniel, Boston terrier, Boxer, Pug, English bulldog, and French bulldog, with the last three breeds being considered extreme brachycephalic (Koch *et al*., 2003; Riecks; Birchard; Stephens, 2007; Meola, 2013). Extreme brachycephalic conformation is represented by the high cephalic index (CI), which is calculated by dividing the width of the skull by its length, expressed as a percentage (Mitze *et al*., 2022). The higher the CI, the shorter the dog's skull. On average, dolichocephalic dogs have a CI below 50, mesocephalic dogs have a CI between 50 and 60, and brachycephalic dogs have a CI above 60. The CI of some extreme brachycephalic breeds, such as the pug, can have a CI of 99 (Bognár *et al*., 2021).

Figure 1 illustrates the difference between brachycephalic, mesocephalic, and dolichocephalic dogs.

Figure 1 – Dorsal view of the anatomy of the skull and its respective representation in breeds of dolichocephalic (A), mesocephalic (B), and brachycephalic (C) dogs. The yellow lines indicate the width and length of the skull used to calculate the cephalic index (CI).



Source: public domain.

Brachycephalic dogs have gained popularity worldwide in recent times, with international data showing that the pug and French bulldog breeds were among the ten most popular breeds in England (Emmerson, 2014). Until 2021, for example, the average number of registrations of pug breed dogs remained at around 8,000 animals per year (The Kennel Club, 2024 and, in Brazil, the pug was the fifth most popular breed (CBKC, 2024). The French bulldog breed has seen a significant number of registrations, rising from 2,771 in 2011 to around 54,000 in 2021 (Shahbandeh, 2024) and, in Brazil, it is in second place as the breed preferred by Brazilians (CBKC, 2024). In the United States, the American Kennel Club (AKC, 2024) reported a 1000% increase in registrations of the breed, and it is in first place in the ranking of the most popular breeds.

However, data updated by The Kennel Club UK shows that there was a sharp drop (50% on average) in the registration of these breeds between 2022 and 2023, possibly due to the relentless concern and publicizing of all the health issues surrounding these breeds and, in addition, the presence of inspection and legislation regarding the purchase, sale and breeding in the countries that make up the United Kingdom (The Kennel Club, 2024).

A report published by the Eurogroup for Animalsin November 2023 entitled "Extreme Breeding in Europe – Mapping Legislation" provides a guide to current legislation on extreme dog breeding in all European countries. This manual received the support of important associations, such as the Federation of Veterinarians of Europe (FVE) and the Federation of European Companion Animal Veterinary Associations (FECAVA). The current legislation is based on the worldwide-recognized concept of the "five freedoms for animal welfare", established by the Brambell Committee (1965): freedom from hunger and thirst, freedom from fear and anxiety, freedom from discomfort, freedom from injury, pain and disease, and freedom to express their natural behaviour. Over the years, the model has been adapted, and animal welfare has been understood as the physical and mental state of an animal in relation to the conditions in which it finds itself, consisting of nutrition, environment, health, behavior, and mental state (Mellor; Reid, 1994).

The Netherlands has banned the ownership of some brachycephalic dogs and, in Norway, there is a ban on the trade and ownership of cavalier king charles spaniels. In Spain, article 27 of the animal welfare law prohibits "carrying out actions or practices of genetic selection that lead to serious problems or alterations in the animal's health" (Eurogroup for Animals, Extreme Breeding in Europe – Mapping of Legislation, 2023).

In Brazil, there is still no legislation on this issue. The Brazilian Confederation of Cynophilia (CBKC) regulates that referees cannot award animals that have any breathing difficulties, but it does not specifically mention brachycephalic obstructive airway syndrome. Only the CBKC is recognized by the FCI (International Cynological Federation), and there is only one studbookper country and a few technical articles on breed standards (CBKC, 2024).

Among domestic cats, the Persian, exotic shorthair, Himalayan, and Burmese breeds also have this skull conformation and, like dogs, have alterations related to brachycephaly (Plitman *et al.*, 2019). According to the Pet IPB Census in 2022, the cat population in Brazil has shown an average annual growth of 2.5%. Studies refer to the preference for acquiring brachycephalic cats due to the appearance

and behavior of these breeds, with guardians often being unaware or even ignoring the numerous health problems that these animals present on account of their anatomical conformation, similar to those found in dogs (Plitman *et al*., 2019; Berteselli *et al.*, 2023).

Such popularity has been linked to the physiognomy of brachycephalic dogs, which has an important influence on why they are chosen as pets, due to their resemblance to children's features (Packer; Murphy; Farnworth, 2017). A theory developed in 1949 by the Austrian ethologist Konrad Lorenz, known as the Kindchenschema ("fluffy effect"), proposes that we are attracted to characteristics such as large eyes, large head in proportion to the body, broad forehead, small nose and mouth, chubby cheeks, and small and soft bodies. Golle *et al*. (2013)'s pioneering research confirmed this theory in a study that used a questionnaire and photos of dogs and babies with different facial features (cuteness) on the babies' faces, and demonstrated that the presence of such attributes is important for the survival of the species, as it supposedly triggers care behavior, which involves feeding and protecting the puppies. Figure 2 shows one of the illustrations where this theory can be observed.

Figure 2 – A human baby and a pug exhibiting classic Kindchenschema features, including large eyes and a small nose.

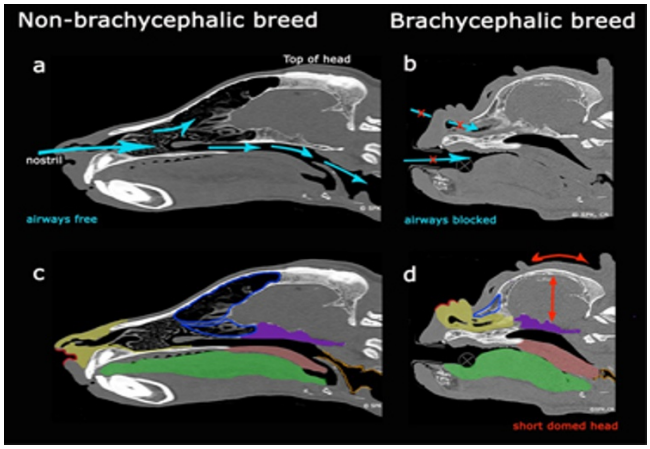
Source: Packer (2022).

Folha de São Paulo, in a report dated February 2, 2024, provides information on the life expectancy of brachycephalic dogs, citing an article recently published in the journal Scientific Reports(Mcmillan *et al.*, 2024), which reinforces the importance of information on these breeds in Brazil, even though most of the research published on the subject provides data from other countries.

Brachycephalic dogs, due their phenotypic characteristics such as prominent eyes and a wrinkled and round face, despite captivating guardians, have notable variations. These alterations, which come with the aim of improving breeds, result in anatomo-physiological modifications such as changes in cranial bone conformation, musculature, and eye arrangement, leading to negative consequences for the health of these animals (Costa; Steinmetz; Delgado, 2021). This unique combination of ocular and periocular anatomical and physiological characteristics, which are linked to the development of ocular surface diseases, is known as brachycephalic ocular syndrome (BOS). Other evidence supporting the link between ocular surface diseases and brachycephaly have increased, and specific problems such as keratoconjunctivitis sicca (dry eyes), corneal ulceration, pigmentary keratitis, medial entropion of the lower eyelid, and prolapse of the gland of the third eyelid are known to occur more frequently in the eyes of brachycephalic dogs when compared to non-brachycephalic dogs (Sebbag; Sanchez, 2022).

Still on the deleterious effects on the health of these animals, selective breeding for extreme brachycephaly (English bulldog, French bulldog, and pug breeds) has given rise to a frequently occurring conformation-related respiratory disorder known as brachycephalic obstructive airway syndrome (Dupré; Heidenreich, 2016; Ladlow *et al*., 2018). These breeds are affected by chondrodysplasia of the cranial longitudinal axis, generating the morphological conformation inherent to brachycephaly in dogs (Koch *et al*., 2003). Associated with the reduction in the cranial longitudinal axis, other anatomical changes contribute to the narrowing of the cranial respiratory tract (Koch *et al*., 2003; Meola, 2013), causing an increase in cranial air resistance which, in turn, prompts local soft tissue edema and, consequently, the worsening of air resistance and perpetuation of a vicious cycle (Koch *et al*., 2003; Meola, 2013; Ekenstedt; Crosse; Risselada, 2020). Figure 3 shows the difference in the proportion between bone space and soft tissue among a non-brachycephalic and a brachycephalic dog.

Figure 3 – Comparative CT images of a non-brachycephalic dog (a and c) and a brachycephalic dog (b and d). The soft tissues, in equal quantities in both dogs (gray areas), do not accompany the bone structure. In brachycephalic dogs, these soft tissues fill and obstruct the airways (blue arrows). In images c and d, the colors indicate: yellow – nasal passage; blue – frontal sinus; purple – skull base; pink – soft palate; green – tongue; red arrows – cranial box. "Airways free": free air passage; "airways blocked": blocked air passage; "non-brachycephalic breed": non-brachycephalicbreed; "brachycephalic breed": brachycephalic breed.



Source: Rusbridge; Knowler, 2018.

BRACHYCEPHALIC OBSTRUCTIVE AIRWAY SYNDROME (BOAS)

Brachycephalic obstructive airway syndrome is undoubtedly the most well-known alteration related to the conformation of these breeds; however, other frequent problems in these patients include skin fold pyoderma, shallow orbits with protruding eyeballsleading to an increased risk of corneal ulceration and eyeball prolapse, hemivertebrae which can be accompanied by spinal cord compression, Chiari

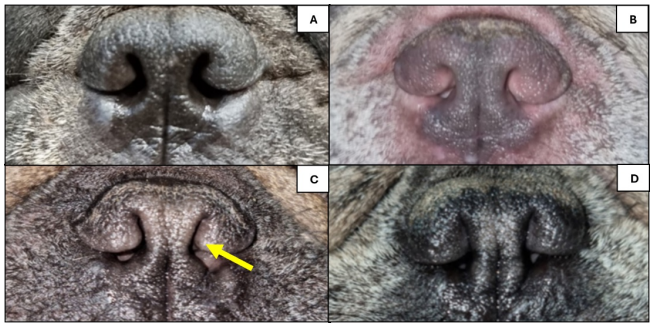
type malformation, dystocia, and dental malocclusion (Ladlow *et al.*, 2018).

Some risk factors predispose animals to brachycephalic syndrome, such as the animal's breed, obesity, hyperactivity, sedation, humid and hot climates, allergic reactions, and some diseases such as pneumopathies and endocrinopathies, which can cause the patient's weight to increase and consequently worsen breathing (Koch *et al.*, 2003; Oechtering, 2010). The occurrence of clinical signs in puppies is less frequently reported, but, when present, they tend to be more serious cases. Furthermore, dogs can be asymptomatic up to two or three years of age and the predisposition between genders shows a 2:1 trend between males and females (Meola, 2013).

The anatomical components that cause BOAS are divided into primary and secondary. Primary components include congenital features such as stenotic nostrils, soft palate prolongation, macroglossia, tracheal hypoplasia, and nasal turbinate hyperplasia (Mitze *et al.*, 2022).

Among the primary components, stenotic nostrils, in which the nostril wing is deformed and the opening is narrow, sometimes reduced to just a vertical slit with almost complete obstruction depending on severity, force these dogs to breathe with their mouths open almost continuously (Ekenstedt; Crosse; Risselada, 2020). Nostril stenosis is the most cranial alteration of the syndrome and is therefore the first barrier to the passage of air, increasing inspiratory effort (Koch *et al.*, 2003). Figure 4 illustrates the stenotic nostrils according to severity.

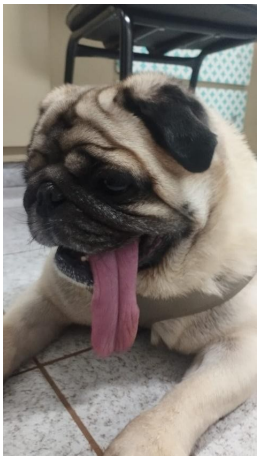
Figure 4 – Photographic images showing the degrees of nostril stenosis in French bulldog dogs. A) open nostrils; B) nostrils with slight narrowing; C) moderate stenosis – the wings of the nostrils are only open at the bottom (arrow); D) severe stenosis – the nostrils are almost closed.



Source: CIGEV (General Surgery and Veterinary Endoscopy-FCAV-Unesp Jaboticabal, 2024).

In addition to the nostrils, the prolongation of the soft palate, where the displacement extends beyond the tip of the epiglottis, allows the palate to vibrate and its redundant tissue to obstruct the glottal rhyme during inspiration (Ekenstedt; Crosse; Risselada, 2020). Macroglossia (long, thick tongue) contributes to the dorsal displacement of the soft palate, causing the narrowing of the nasopharynx and hindering the passage of air, increasing inspiratory effort (Siedenburg; Dupré, 2021). Figure 5 shows a pug patient with marked macroglossia.

Figure 5 – Photographic image of a 9-year-old pug patient with marked macroglossia.

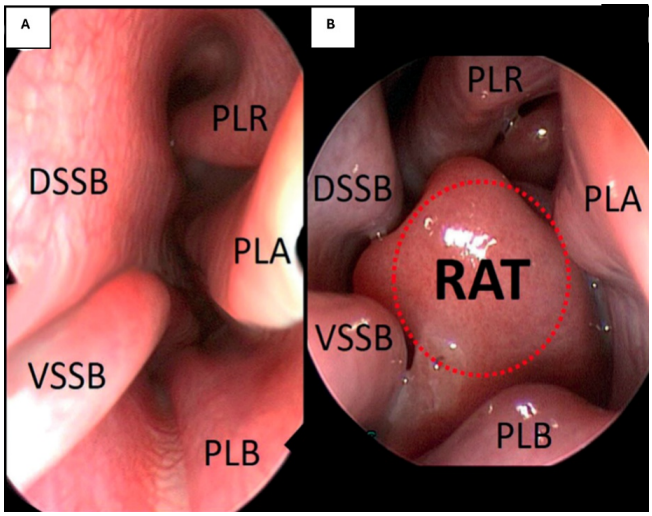


Source: CIGEV (General Surgery and Veterinary Endoscopy-FCAV-Unesp Jaboticabal, 2024).

The trachea of brachycephalic dogs is clearly hypoplastic, narrower than that of dolichocephalic or mesocephalic dogs. However, this primary alteration is due to the anomaly during embryogenesis, and not a sequel to the more cranial respiratory obstruction (Koch *et al.*, 2003).

The nasal conchae of brachycephalic dogs are compacted within an extremely short muzzle and have fewer branches compared to mesocephalic dogs, which leads to a decrease in the nasal mucosa's surface area. The decreased branching of the nasal concha and increased contact points interrupts laminar flow and compromises thermoregulation (Figure 6). Heat intolerance, despite the difficulty of measuring this symptom, is a frequent complaint from guardians of brachycephalic dogs (Ladlow; Liu, 2021).

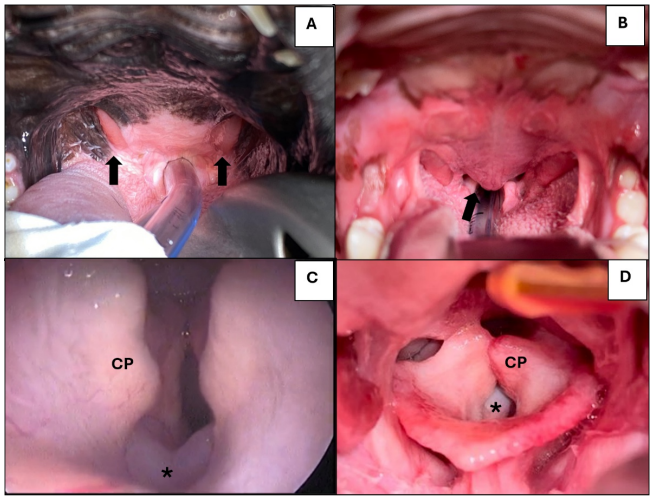
Figure 6 – Rhinoscopic images of a mesocephalic (A) and a brachycephalic (B) patient. A shows the structures without alterations. In B, there is swelling of the ventral septum (VSSB), dorsal septum (DSSB), plica recta (PLR), plica alaris (PLA), plica basalis (PLB) and the presence of a rostral aberrant turbinate (RAT), which causes the obstruction. Note the multiple points of mucosal contact (asterisk).



Source: Oechtering *et al.* (2016).

Secondary components, caused by increased turbulence and air resistance, include palate hypertrophy/thickening, hypertrophied tonsils, laryngeal edema, laryngeal sac eversion, and laryngeal collapse (Meola, 2013). These alterations are a consequence of the greater effort needed to maintain ventilation in the airways, which present increased resistance to the passage of air (Canola *et al.*, 2018; Krainer; Dupré, 2022). The chronicity and the impact of cranial airway alterations lead to a negative pressure required to perform inspiratory work. This induces mucosal edema, soft tissue thickening (Ekenstedt; Crosse; Risselada, 2020) and predisposes fatigue and degeneration of the laryngeal cartilages, causing laryngeal collapse (Macphail, 2020). Figure 7 illustrates some of the secondary components of the syndrome.

Figure 7 – Photographic (A and B) and laryngoscopic (C and D) images showing some secondary components of brachycephalic obstructive airway syndrome in different patients (dogs). A) hypertrophy of the tonsils (black arrows); B) prolongation and thickening of the soft palate (black arrow); C) eversion of the laryngeal sacs (*) (grade-I laryngeal collapse) and D) medialization of the cuneiform processes (CP) and eversion of the laryngeal sacs (*) (grade-III laryngeal collapse).



Source: CIGEV (General Surgery and Veterinary Endoscopy-FCAV-Unesp Jaboticabal, 2024; image D courtesy of Dr. Andreia Facin).

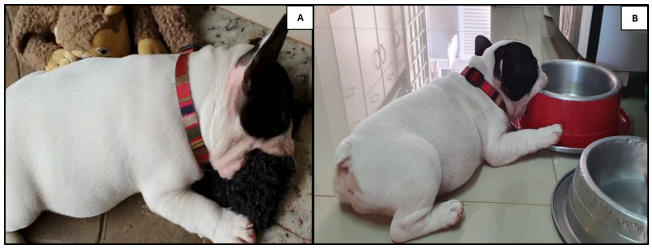
Affected dogs may show one or more components of the syndrome, so the extent and severity of the clinical signs, as well as the deterioration in quality of life, show that breeding patients with pronounced brachycephaly is an animal welfare concern.

Patients affected by the syndrome have progressive clinical signs. In the respiratory system, changes can cause inspiratory and expiratory dyspnea, rales, aerophagia, orthopneic position, cough, hyperactivity, hyperthermia, sleep disorders, choking, and reverse sneezing (Hinchliffe; Liu; Ladlow *et al.*, 2019; Doyle *et al.*, 2020; Lameu *et al.*, 2020), causing increased respiratory noise, increased respiratory effort, decreased exercise tolerance, and, in severe cases, syncope (Aiken, 2021).

BRACHYCEPHALIC OBSTRUCTIVE AIRWAY SYNDROME (BOAS) AND OBSTRUCTIVE SLEEP APNEA SYNDROME IN HUMANS (OSA)

BOAS is compared to obstructive sleep apnea (OSA) syndrome in humans, which is also characterized by anatomical factors causing upper airway obstruction, similar to those previously described in brachycephalic dogs (Hendricks *et al.*, 1987; Neelapu *et al.*, 2017). Sleep disturbance in dogs can encompass a wide range of abnormalities, such as sleeping with the mouth open (including with objects in the mouth), sitting in elevated positions, sleep fragmentation and apnea, which causes hypersomnolence during the day (Mitze *et al.*, 2022). Figure 8 shows a patient with a clear sleep disorder, using objects to keep his mouth open and allow air in.

Figure 8 – Photographic images of a two-month-old French bulldog patient using a plush toy (A) or feeder (B) in his mouth during sleep, in order to keep it open and allow air to pass through.



Source: CIGEV (General Surgery and Veterinary Endoscopy-FCAV-Unesp Jaboticabal, 2024).

Niinikoski *et al.* (2023) described a method for obtaining an index of obstructive events during sleep using a device (collar), which records such occurrences as snoring and the number of apneas or hypopneas (partial obstructions). Based on answers provided by the guardians of the dogs in that study, another publication by the team provided results on sleep disorders, demonstrating the relationship between the severity of the syndrome and obesity with sleep quality (Niinikoski *et al.*, 2024).

In human medicine, the assessment of severity in OSA is often carried out by polysomnography, a test which measures the apnea-hypopnea index (Neelapu *et al.*, 2017). In veterinary medicine, the severity of respiratory obstruction in dogs affected by BOAS has been previously investigated and reported using different methods. Liu *et al.* (2015) defined a functional grading system for the severity of BOAS based on data obtained by whole-body plethysmography and submaximal exercise tests. However, plethysmography is not widely available in veterinary medicine, so the classification of the syndrome, which is based on a four-grade functional scoring system, is carried out with the evaluation before and after a three-minute exercise tolerance test. The BOAS functional grading system is shown in Table 1.

This grading system has been previously established and validated (Liu *et al.*, 2015; 2016). The clinical classification is based on respiratory signs before (pre TTE) and immediately after a three-minute exercise tolerance test (post TTE) with a trot speed of approximately 6 to 8 kilometers per hour performed by

Table 1 – Functional grading system for brachycephalic obstructive airway syndrome (BOAS) based on respiratory signs before and after the exercise tolerance test (ETT).

		Breathing sounds[a]	Inspiratory effort[b]	Dyspnea, cyanosis, syncope[c]
Grade 0	Pre TTE	Not audible	Absent	Absent
	Post TTE	Not audible	Absent	Absent
Grade I	Pre TTE	Not audible or discreet	Absent	Absent
	Post TTE	Discreet	Absent or discreet	Absent
Grade II	Pre TTE	Discreet to moderate	Discreet to moderate	Absent
	Post TTE	Moderate to severe	Moderate to severe	Mild dyspnea, cyanosis or syncope absent
Grade III	Pre TTE	Moderate to severe	Moderate to severe	Moderate to severe dyspnea, with or without cyanosis. Exercise intolerance
	Post TTE	Severe	Severe	Severe dyspnea, with or without cyanosis or syncope

the investigators. Presentation of at least one sign of the highest degree determines the final score.

[a]Breath sounds will be diagnosed by nasopharyngeal auscultation. Discrete: audible only under auscultation; moderate: audible intermittently, without the need for a stethoscope; severe: constantly audible, without the need for a stethoscope.

[b]Abnormal breathing cycle characterized by evidence of increased effort to inhale air, with use of the diaphragm and/or accessory muscles and/or nasal widening with increased panting. Mild: breathing with a regular pattern and minimal use of the diaphragm; moderate: evidence of use of the diaphragm and accessory breathing muscles; severe: marked use of the diaphragm and accessory breathing muscles.

[c]Dogs that present episodes of syncope and/or cyanosis as documented by the guardian through the questionnaire evaluation will be classified as grade III without TTE. Mild dyspnea: signs of discomfort; moderate: irregular breathing and signs of discomfort; severe: irregular breathing with signs of discomfort and difficulty breathing.

Diagnosis of the syndrome's components should be based on history, clinical signs at rest and after exercise, physical examination, and preferably radiographic and tomographic imaging tests, as well as rhinoscopy and laryngoscopy. The complete history often addresses exercise intolerance or reluctance, collapse or obvious cyanosis during exercise or excitement, eating disorders including choking or difficulty eating, regurgitation, any sleep disturbances including frequent "choking" awakenings and sleeping with the head raised or in abnormal positions (Packer, 2022).

The respiratory obstruction caused by BOAS, as with OSA, has systemic consequences in addition to the respiratory effects (Koch *et al*., 2003; Inancli; Enoz, 2010). Among these abnormalities, gastrointestinal changes (Lodato; Hedlund, 2012; Kaye *et al.*, 2018, Freich; German, 2021), cardiovascular changes (Hoareau *et al*., 2012), evidence of hypercoagulability (Hoareau; Mellema, 2015; Crane *et al.*, 2017), lower arterial oxygen pressures (Hoareau *et al*., 2012; Canola *et al*., 2018) and middle ear effusions (Mitze *et al*., 2022) have been previously reported.

Although the subclinical inflammation profile has already been proven in healthy brachycephalic patients affected only by respiratory syndrome (Facin *et al*., 2020), little is known about the role of acute and chronic inflammation markers in these patients. In human patients with obstructive sleep apnea, major consequences are also observed due to pro-inflammatory cytokines such as tumor necrosis factor α (TNF-α), interleukin 1β (IL-1β) and interleukin 6 (IL-6). These compounds also play a role in oxidative stress, causing damage to the body (Ciftci *et al.*, 2004; Nadeem *et al*., 2013). Furthermore, it is possible that OSA not only increases inflammatory factors, but also blocks the expression of anti-inflammatory cytokines, such as interleukin 10 (IL-10), which inhibits a range of pro-inflammatory responses, including those affecting the vessel wall (Chen *et al*., 2020).

A study carried out by Rancan *et al*. (2013) on dogs with BOAS observed that, even at early stages, it is possible to find increased values of TNF-α, which raise according to severity, proving the importance of the role of this compound in the syndrome. The same result was found in a series of studies on humans (Ciftci *et al*., 2004; Bravo *et al*., 2007; Nadeem *et al*., 2013).

Chronic inflammation and reactive oxygen species (ROS) or free radicals comprise a large area of research (Nadeem *et al*., 2013; Al-Mughales *et al*., 2022). These molecules originate from situations of hypoxia followed by oxygenation, and react with other molecules against which they collide, causing loss of electrons and modifying their molecular structures (Yu, 1994). There are two main groups of ROS: the radical ones, which include hydroxyl (HO), superoxide (O2-), peroxyl (ROO-), and alkoxyl (RO); and the non-radical ones, which are made up of oxygen, hydrogen peroxide and hypochlorous acid (Andrade Junior *et al*., 2005; Barreiros; David; David, 2006).

Recent studies have shown the potential effect of oxidative stress, with the release of ROS and pro-inflammatory cytokines for neurodegeneration, as well as other organic disorders such as hypertension,

respiratory failure and cardiac alterations, which are normally present in more advanced stages of obstructive sleep disease in humans, possibly due to the chronic inflammation that causes alterations in the lung parenchyma (Merelli *et al*., 2021).

The association between sleep disorders, such as OSA, in humans with inflammatory bowel disease (IBD) is already well evidenced, mainly due to changes in intestinal permeability and motility (Ghiasi *et al*., 2017; Gombert *et al*., 2019; Orr, 2020). Activation of the immune system due to the migration of immune cells and release of pro-inflammatory cytokines is observed in patients suffering from significant sleep disturbances (Nácher *et al*., 2007; Tang *et al*., 2009). The intermittent hypoxia of OSA is a trigger for the induction of systemic inflammation and the production of free radicals, leading to changes in the gut microbiota (Neroni *et al.*, 2021).

The gut microbiota plays an important role in the production of serotonin precursors and essential signaling molecules for the central nervous system and the neuroendocrine system (Kennedy *et al.*, 2014). It is estimated that approximately 90% of the serotonin in humans is produced by bacteria present in the gut (Yano *et al.*, 2015). Serotonin is the precursor of melatonin, which regulates the sleep-wake cycle through daily hormonal fluctuations. Recent studies indicate a direct relationship between melatonin levels in the host and some intestinal bacteria (Neroni *et al*., 2021). Regarding BOAS, several authors confirm the association of gastrointestinal signs with respiratory syndrome, with a direct correlation between the signs presented and the degrees of brachycephalic syndrome (Poncet *et al*., 2005; Poncet *et al*., 2006; Kaye *et al*., 2018).

The correlation between these signs and the intestinal microbiota is still poorly reported. In addition, these alterations affect various organ systems and impact the composition of the commensal microbiota by various mechanisms. Research suggests that anatomical, racial, age and bodily variations, and geographical location can influence bacterial composition in dogs (Vangrinsven *et al*., 2022).

Dysbiosis not only indicates a significant imbalance in the composition of the gastrointestinal microbiota (Gombert *et al*., 2019), but also the loss of mutualistic relationships in this microbial ecosystem (Ghiasi *et al.*, 2017). It is associated with oxidative stress, deficits in uric acid and amino acid metabolism, and changes in the oxidation-reduction balance, which worsens inflammation and tissue healing, and is capable of significantly impacting the health status of the host and leading to disease (Gombert *et al*., 2019). In addition, bacterial imbalance is related to the suppression of the immune system, metabolic and cognitive disorders, and increased permeability of the intestinal barrier, which can cause the migration of intestinal bacteria and toxins to surrounding tissues and the systemic circulation, giving rise to local and generalized inflammation (Kanaly; Shaheen; Vaughn, 2009).

Obstructive sleep apnea syndrome can lead to the disruption of the intestinal barrier and changes in the composition of the microbiota (Poncet *et al*., 2005). Snoring can also affect the gut microbiota and have long-term consequences (Honda; Littman, 2012). A study in mice showed that administering probiotics through the diet can improve sleep quality, control brain function, and stress responses (Wostmann *et al*., 1983). Other research has also shown how gut dysbiosis can act as a mediator between OSA and systemic hypertension (Carding *et al*., 2015; Omori *et al*., 2017).

Human studies report the importance of the microbiota in maintaining respiratory and gastrointestinal health, affecting resistance to pathogens and immune responses (De Steenhuijsen Piters *et al*., 2015) and being influenced by intrinsic and extrinsic factors. It has been shown that changes in the nasal microbiota in humans with OSA are related to the local inflammation generated by the syndrome (Wu *et al*., 2019). In dogs, the literature is scarce on studies that associate the microbiota with the anatomical conformation or breed of these animals, especially brachycephalic dogs.

Unlike OSA in humans, the systemic repercussions that airway obstruction can cause in dogs, depending on its severity, are not yet fully understood. Furthermore, it is important to know whether the correct treatment of the components of the syndrome in these patients could reduce these consequences.

Treatment

Due to the potential risks associated with the surgical treatment of BOAS, conservative treatments should be considered before any surgical intervention, particularly in less severe cases. Some patients may improve with exercise restriction and weight loss, since many dogs with the syndrome are overweight, a condition which may increase the severity of clinical signs (Packer; Tivers, 2015; Liu *et al*., 2017).

Lifestyle changes can reduce the worsening of signs, for example, guardians should be advised to avoid exposing dogs to activities and environments that markedly increase oxygen demand, in particular excessive exercise, hot weather, and stressful situations. Instead, walks should be short, only at cool times of the day, and chest collars should be used so as not to put pressure on the cranial airways (Packer *et al*., 2015).

The surgical treatment of the anatomical abnormalities of brachycephalic syndrome is 94.2% successful in improving the clinical signs of patients (Meola, 2013). It is recommended that surgical procedures be carried out when the patient is still young, thus avoiding alterations in the soft tissues that generate secondary components. However, some studies have also reported good results in adult patients (Dupré; Heidenreich, 2016).

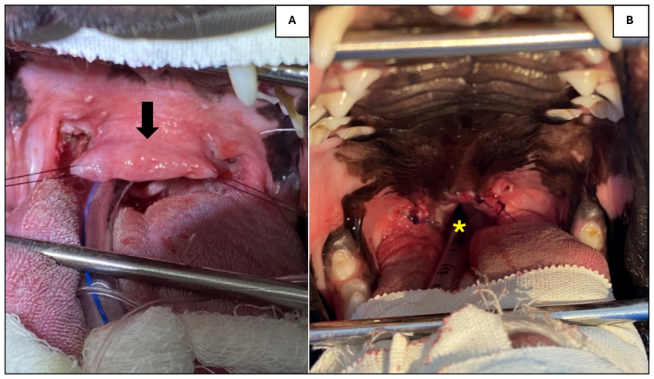
The most commonly performed surgical techniques include wedge resection of the nasal cartilage (Bowlt; Moore, 2009), staphylectomy (Hobson, 1995), partial tonsillectomy (Dulisch, 2003), and ventriculectomy (Hobson, 1995). More recently, modified and advanced techniques such as folded flap palatoplasty (Haimel; Dupré, 2015), nasal vestibuloplasty (Oechtering; Schuenemann, 2010), and laser turbinectomy (Oechtering *et al*., 2016, Liu *et al.*,

2019) have been reported. The treatment of laryngeal collapse is based on severity and can range from the removal of the everted laryngeal sacs (grade-I collapse) to the removal of the cuneiform process of the arytenoid cartilage to enlarge the rima glotidis, which is the opening between the vocal cords and the arytenoid cartilages of the larynx (grade-III collapse) (Meola, 2013).

The surgical treatment of BOAS is individualized, depending on the severity of the air obstruction and the abnormalities found in each patient (Cantatore *et al*., 2012). Poncet *et al*. (2005) reported that 92% of the dogs operated on had a significant improvement in their signs within six weeks of the surgical procedure.

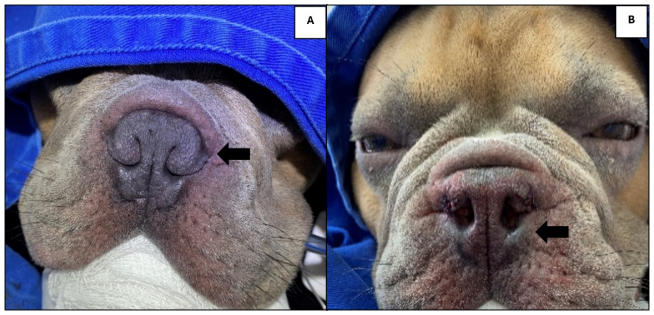
Figures 9 and 10 illustrate the before and after of surgical treatment for some components of the syndrome.

Figure 9 – Photographic images of a French bulldog patient undergoing folded flap palatoplasty. In A, note the lengthening and thickness of the palate. In B, at the end of the procedure, the unobstructed larynx can be seen (yellow asterisk).



Source: CIGEV (General Surgery and Veterinary Endoscopy-FCAV-Unesp Jaboticabal, 2024).

Figure 10 – Photographic images of a French bulldog patient undergoing rhinoplasty for stenotic nostrils. In A, severe stenosis of the nostrils (arrow). In B, at the end of the procedure, the nostrils are open (arrow).



Source: CIGEV (General Surgery and Veterinary Endoscopy-FCAV-Unesp Jaboticabal, 2024).

A study carried out by researchers at the University of Cambridge in the UK (Ladlow *et al.*, 2018) shows the risk factors for the syndrome and predictors of response to treatment. Treatment success is directly proportional to the time of onset of clinical signs, the presence of laryngeal collapse and the body conformation of each breed.

Cranial airway surgery, as well as the hospital environment, can also cause anxiety in these patients, which may have a profound impact on possible post-operative complications. Treatment with maropitant, omeprazole and trazodone has been described, starting 24 hours before surgery. The patient should be treated with an anti-inflammatory dose of intravenous dexamethasone sodium phosphate at the time of induction of anesthesia (Aiken, 2021).

Post-operative surgical complications of BOAS include respiratory distress, which may require a new induction of anesthesia, pharyngeal edema, hemorrhage, regurgitation, pneumonia and death (Ree *et al*., 2016; Lindsay *et al*., 2020). Fenner, Quinn and Demetriou (2020), in a retrospective study, correlated the presence of regurgitation in younger dogs with a more severe history of respiratory disorders, with the French bulldog breed being the most affected. Lindsay *et al*. (2020) correlated the occurrence of post-operative complications with the presence of previous respiratory diseases and a history of emergency care. They also described the importance of monitoring the patient for at least 24 hours after the surgical procedure in order to minimize these complications. The presence of a guardian at the patient's side, according to a study conducted by Camarasa *et al.* (2023), greatly reduces stress and minimizes the occurrence of complications in the immediate postoperative period.

Recent research has evaluated the effectiveness of different protocols, both medicinal and surgical, in the perioperative period, with the aim of reducing common complications such as local edema, postoperative regurgitation, aspiration pneumonia, and respiratory distress (Filipas; Owen; Adami, 2024; Wallace, 2024; Grimes *et al*., 2025; Hill *et al.*, 2025). However, there are still differences in the literature, since the clinical evolution of these patients is directly related to factors such as the severity of the syndrome, the experience of the multidisciplinary team (surgical, anesthetic and postoperative monitoring) and the hospital structure available.

Prognosis

The prognosis for patients affected by BOAS varies according to age, the severity of the disease at the time of diagnosis and the response to individualized surgical correction of the syndrome's components. In general, patients who undergo early surgical treatment have a significantly improved quality of life and a lower risk of secondary complications, such as laryngeal collapse. Factors such as postoperative management and the presence of comorbidities also directly influence prognosis (Liu *et al*., 2017; Fenner; Quinn; Demetriou, 2020). Therefore, individualized assessments and continuous monitoring of brachycephalic dogs are essential to optimize long-term results.

The concern and search for an improvement in these animals' quality of life is intense, given the number of articles published periodically in an attempt to understand what are the repercussions of the syndrome and how to minimize its effects, whether through management, surgery or even attempts to

standardize the breeding of these breeds. In Brazil, there is no specific legislation on the subject, although there are proposals for draft laws, which have yet to be adequately substantiated. It is the duty of veterinarians to be aware of all the problems surrounding the syndrome, which is not the case in this country.

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