



## Maternal brachycephaly only does not influence umbilical artery resistance in late canine pregnancy

[A braquicefalia materna, isoladamente, não influencia a resistência da artéria umbilical no final da gestação em cães]

### "Scientific Article/Artigo Científico"

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#### Abstract

The popularity of canine brachycephalic breeds is rising in many countries of the world. Brachycephalic dogs are predisposed to developing brachycephalic obstructive airway syndrome (BOAS), resulting in lower partial pressure of oxygen in the arterial blood which might influence foetal haemodynamic parameters. Therefore, this study aimed to evaluate the influence of the maternal morphological characteristic (brachycephaly) on the resistive index of the umbilical artery (RIUA) during late pregnancy. This was a non-randomized and cross-sectional study that included data of foetuses from 42 clinically healthy pregnant bitches. The RIUA was measured in 137 foetuses, from 68 and 69 brachycephalic and non-brachycephalic bitches, respectively, between the seventh to ninth weeks of pregnancy. Gestational age was determined by ultrasonography according to foetal biparietal diameter (BP) by measuring two to four foetuses/pregnant bitch. Female dogs with at least one foetus diagnosed with a consistent heart rate below 180 bpm were not included in the present study. There was a significant weekly decrease in the RIUA of foetuses from both brachycephalic and non-brachycephalic bitches, from the seventh until the last week of evaluation. No differences were detected in the RIUA at the same gestational week between foetuses from brachycephalic and non-brachycephalic bitches. In conclusion, maternal brachycephaly only is not able to induce RIUA changes in canine foetuses during late pregnancy.

**Keywords:** foetal Doppler; umbilical cord; resistive index; brachycephalic dogs

#### Resumo

A popularidade de raças braquicefálicas tem aumentado em vários países do mundo. Cães braquicefálicos são predispostos ao desenvolvimento da síndrome obstrutiva das vias aéreas (SOVA), causando a redução da pressão parcial de oxigênio no sangue arterial, o que pode influenciar parâmetros hemodinâmicos fetais. Dessa forma, objetivou-se com este estudo avaliar a influência da característica morfológica materna (braquicefalia) sobre o índice de resistividade da artéria umbilical (IRAU) no final da gestação. Trata-se de um estudo não randomizado, transversal, que incluiu os dados de fetos oriundos de 42 cadelas prenhas e clinicamente saudáveis. O IRAU foi mensurado em 137 fetos, entre a sétima e a nona semana de gestação, sendo 68 provenientes de cadelas braquicefálicas e 69 de cadelas não braquicefálicas. A idade gestacional foi estimada de acordo com o diâmetro biparietal (DBP) dos fetos, a partir da mensuração de dois a quatro fetos/cadela. Cadelas com pelo menos um feto diagnosticado com uma frequência cardíaca inferior a 180 bpm não foram incluídas no presente estudo. Foi observada uma redução semanal significativa nos valores do IRAU, tanto das cadelas braquicefálicas quanto das não-braquicefálicas, entre a sétima até a nona semana de gestação. Não foram detectadas diferenças no IRAU para a mesma semana de gestação entre fetos de cadelas braquicefálicas e não-braquicefálicas. Em conclusão, a braquicefalia, isoladamente, não é capaz de induzir alterações no IRAU dos fetos caninos no final da gestação.

**Palavras-chave:** Doppler fetal; cordão umbilical; índice de resistividade; cães braquicefálicos.

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## Introduction

The popularity of canine brachycephalic breeds is rising in many countries (Fawcett et al., 2019). However, brachycephalic dogs are predisposed to inherited conformational disorders, which can result in lower blood oxygen (Packer et al., 2015; Canola et al., 2018) and even systemically healthy brachycephalic dogs were prone to have lower blood oxygen levels (Hoareau et al., 2012). Another characteristic of brachycephalic breeds is a high susceptibility to dystocia, with reports of caesarean indices higher than 80% (Bergstrom et al., 2006; Evans and Adams, 2010). Since parturition is a critical event (Beccaglia et al., 2016), appropriate caesarean management is essential to avoid either premature birth or intrauterine foetal suffering (Giannico et al., 2016).

Therefore, foetal monitoring by ultrasound has become a routine procedure in canine reproduction (Mantiziara and Luvoni, 2020), allowing the evaluation of foetal development and the prediction of parturition (Blanco et al., 2008; Miranda and Domingues, 2010). The pulsed-wave Doppler is an ultrasonographic technique that permits real-time haemodynamic assessment of a single vessel (Giannico et al., 2015). The resistive index (RI) is a haemodynamic variable frequently assessed and measures the relationship between peak systolic velocity and end diastolic velocity (Pourcelot, 1974; Batista et al., 2018).

It is well known that foetal vascularisation is an indicator of nutrient and oxygen supply to the foetus (Nautrup, 1998; Di Salvo et al., 2006), consequently the RI of the umbilical artery (RIUA) is a good parameter to diagnosis foetal stress caused by disorders in placental blood flow and foetal hypoxia (Giannico et al., 2015). Currently, RIUA is assessed to determine the timing of parturition and foetal suffering (Beccaglia et al., 2016) and the evaluation of this parameter might be worthwhile in brachycephalic breeds, since brachycephalic bitches are more prone for dystocia and caesarean section (Bergstrom et al., 2006; Evans and Adams, 2010).

Considering the importance of RIUA for the evaluation of foetal haemodynamic, as well as the expected reduction in the RIUA in late pregnancy (Di Salvo et al., 2006), the aim of this study was to evaluate the influence of the brachycephaly on the RIUA reduction pattern during the late stages of pregnancy.

## Material and Methods

### *Animals*

This was a non-randomized and cross-sectional study that included data from 42 clinically healthy pregnant female dogs (primiparous or pluriparous) of different ages (1–6 years old) presented to a veterinary diagnostic centre for routine gestational ultrasound diagnosis. Twenty-one bitches were brachycephalic (Pug = 9, Shih Tzu = 9, Lhasa Apso = 2, French Bulldog = 1) and 21 non-brachycephalic (German Spitz = 6, Mongrel = 4, Yorkshire Terrier = 3, Teckel = 3, Dobermann Pinscher = 3, Beagle = 1, Brazilian Terrier = 1).

Ultrasound evaluations were performed once per bitch and all bitches included in the present study were in the late gestational period ( $\geq 45$  days), since reductions in the RIUA were previously detected from the sixth week of gestation (Nautrup, 1998; Di Salvo et al., 2006).

It was not possible to monitor the oestrous cycle of the bitches included in the present study. Therefore, gestational time was determined according to foetal biparietal diameter (BP) average, after measuring two to four fetuses/pregnant bitch, and the bitch size was also taken into account for calculation (Beccaglia et al., 2016). It is worth mentioning that the accuracy ( $\pm 2$  of prediction of parturition) of BP for determining gestational age decreases along the pregnancy, ranging from 88.4 to 69.8% at the sixth and ninth weeks of pregnancy, respectively (Beccaglia and Luvoni, 2012).

### *Umbilical Doppler evaluation*

The RIUA was measured in 137 fetuses, 68 from brachycephalic and 69 from non-brachycephalic bitches, during the late stages of pregnancy. All evaluations were performed by the same sonographer using the same equipment (MyLabFive, Esaote, Genova, Italy), with a 3.5 to 10 MHz linear multifrequency transducer (LA332 appleprobe, Esaote, Genova, Italy). The bitches were positioned in dorsal recumbency, without sedation (Freitas et al., 2017), abdominal hair was clipped to optimise image quality, and acoustic gel was applied to the transducer and abdominal wall. Bitches with at least one foetus diagnosed with a consistent heart rate below 180 bpm were not included in the present study, as this finding is indicative of foetal suffering (Smith, 2012) and might influence the RIUA (Beccaglia et al., 2016). Two to five fetuses were monitored on both sides

of the abdomen. Colour Doppler was used to localise the umbilical cord, followed by pulsed-wave Doppler to obtain three consecutive waveforms in the mid-cord site of the umbilical cord, as the location of Doppler sampling affects Doppler waveform (Giannico et al., 2015). The waveforms' averages were used to automatically calculate the RIUA using the ultrasound software.

#### Statistical analyses

All analyses were performed using Past software (Version 3.18). The normal distribution of the RIUA data was assessed and corroborated by the Shapiro–Wilk test. The RIUA data of foetuses from brachycephalic and non-brachycephalic bitches were grouped according to gestational week (7th, 8th and 9th week of pregnancy). Comparisons of the obtained means within group

(brachycephalic or non-brachycephalic) at different gestational weeks, or between groups within the same gestational week, were evaluated by a several-sample test ANOVA, followed by Tukey's pairwise comparison. For all analysis, a *P*-value of 5% was considered significant.

#### Results

Within the same gestational week, there was no difference ( $P > 0.05$ ) in the RIUA between foetuses from brachycephalic and non-brachycephalic bitches. The RIUA values decreased significantly in foetuses from both brachycephalic and non-brachycephalic bitches from the seventh week of gestation until the last week of evaluation (Table 1).

**Table 1.** Resistive index of the umbilical artery (RIUA, means  $\pm$  SEM) of different foetuses from brachycephalic and non-brachycephalic bitches in late gestation.

	RIUA		
	Gestational week		
	7	8	9
Brachycephalic ( $n=68$ )	0.82 $\pm$ 0.01 <sup>a</sup> ( $n=14$ )	0.74 $\pm$ 0.01 <sup>b</sup> ( $n=27$ )	0.69 $\pm$ 0.01 <sup>c</sup> ( $n=27$ )
Non-brachycephalic ( $n=69$ )	0.80 $\pm$ 0.01 <sup>a</sup> ( $n=16$ )	0.76 $\pm$ 0.01 <sup>b</sup> ( $n=24$ )	0.68 $\pm$ 0.01 <sup>c</sup> ( $n=29$ )

Within a row, values without a common letter differ ( $P < 0.01$ ).

There was no difference between foetuses from brachycephalic and non-brachycephalic bitches within the same gestational week. Gestational time was determined according to foetal biparietal diameter.

#### Discussion

To our knowledge, this is the first study that compares the RIUA between foetuses from brachycephalic and non-brachycephalic bitches in late pregnancy. Although the accuracy of measurement of the biparietal diameter to predict gestational time decreases in late pregnancy (Beccaglia and Luvoni, 2012), the significant reduction of RIUA averages along late pregnancy in foetuses from both brachycephalic and non-brachycephalic bitches is in accordance with previous studies (Nautrup, 1998; Di Salvo et al., 2006; Miranda and Domingues, 2010). Moreover, this reduction was an expected result, due to the progressive development of foetal perfusion, with an increase in umbilical artery diastolic flow associated with placental maturation (Di Salvo et al., 2006; Miranda and Domingues, 2010; Feliciano et al., 2014).

The brachycephalic animals in the present study were not selected based on a diagnosis of brachycephalic obstructive airway syndrome

(BOAS) nor was blood oxygen measured. However, it is important to consider the high prevalence of BOAS in brachycephalic breeds (Packer et al., 2015) and the lower partial pressure of oxygen in the arterial blood compared to non-brachycephalic dogs even in systemically healthy brachycephalic dogs, attributable to hypoventilation due to morphological characteristics (Hoareau et al., 2012; Canola et al., 2018).

Therefore, we consider it a reasonable speculation that animals from the brachycephalic group might have lower blood oxygen, with a higher influence on the foetal haemodynamic particularly after the seventh week of pregnancy, considering the increasing foetal dimensions (Miranda and Domingues, 2010) and concurrently higher foetal oxygen demand (Murray, 2012). However, if this was the case, no differences in the RIUA were detected between foetuses from brachycephalic and non-brachycephalic bitches, at any gestational week evaluated in the present

study, which could be associated with structural and functional modification in the maternal canine cardiovascular haemodynamic during pregnancy (Souza et al., 2017; Ward et al., 2020).

In bitches, it has been reported that normal pregnancy results in increased cardiac output and hypertrophy and a time-dependent fall in vascular resistance of the uteroplacental artery (Di Salvo et al., 2006; Blanco et al., 2011a), and failures in maternal cardiovascular adaptation to gestation might result in obstetric complications and a reduction in the uterine artery RI (Blanco et al., 2011b; Blanco et al., 2012). It is noteworthy that foetal adaptation to transient hypoxia, characterised by a short-term adjustment through baro- and chemoreceptor reflexes, differs from chronic hypoxia. Homeostatic regulations during chronic hypoxia are not fully understood (Wood and Keller-Wood, 2019), but an enlarged capillary bed in placental vasculature in sheep (Krebs et al., 1997), as well as increased functional gaseous exchange in the human placenta (Reshetnikova et al., 1994), have been reported.

Furthermore, during normal pregnancy, women born and raised at a very high altitude (above 4100–4300 m) present higher uterine blood flow compared with women at low altitude (400 m), compensating for the effects of hypoxia (Browne et al., 2015). This adaptation to long-term hypoxemia at high altitudes, besides influencing uterine blood flow (Moore, 2003; Moore et al., 2011), raises foetal and maternal circulating haemoglobin (Murray, 2012). Also, reduces foetal vascular resistance, probably as a consequence of compensatory arteriolar dilatation induced by foetal hypoxia induced by reduced oxygen in the maternal circulation (Di Renzo et al., 1992). It is of note that in guinea pigs experimentally exposed to hypoxia from middle to term pregnancy, an increase in the resistance and pulsatility index of the uterine arteries were detected, with no change observed in the umbilical arteries (Turan et al., 2017). However, as hypoxia was not determined in the present study, it is not possible to infer about adaptations in the systemic and uteroplacental haemodynamic to prevent RIUA alteration in late pregnancy.

### Conclusion

The foetuses from both brachycephalic and non-brachycephalic bitches present a progressive and similar reduction in RIUA in late pregnancy. Further studies with pregnant bitches under proven

hypoxia would contribute to better comprehension of the adaptation of the uterine and foetoplacental haemodynamic during canine pregnancy.

### Conflict of interest

None of the authors have any conflict of interest to declare. The authors alone are responsible for the content and writing the paper.

### Ethical Committee

This work involved the use of non-experimental animals only (included owned animals data from retrospective ultrasonographic evaluation). Established internationally recognized high standards ('best practice') of individual veterinary clinical patient care were followed. Ethical approval from a committee was therefore not necessarily required, in compliance with normative N. 22/2015, from the National Council of the Control of Animal Experimentation.

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