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Evaluation of the uterine wall echotexture changes following an induced abortion in mid–term pregnant bitches: preliminary study

Evaluación de los cambios de ecotextura de la pared uterina tras un aborto inducido en perras gestantes a medio plazo: un estudio preliminar

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ABSTRACT

The objective of this study was to evaluate structural echotexture changes in the uterine wall following abortion induction in bitches during the late embryonic/mid–gestation stage and to develop an evaluation method for the abortion process. A total of 10 healthy pregnant bitches of different breeds, ranging from 25 to 40 days (d) of gestation, were included in this study. In Group 1 (n=5), Aglepristone (10 mg·kg^{-1} bw, sc) was administered once daily for two consecutive d. In Group 2 (n=5), a combination of Aglepristone, Cabergoline, and Misoprostol was used for induction of abortion (IA). Prior to the induction of abortion, and at 24–hour intervals until completion of abortion (CA), the uterus and placenta were sonographically examined. Additional examinations were conducted on d 1 (CA+1), d 7 (CA+7), and d 14 (CA+14) after the abortion process was completed. Blood samples were taken on the same days to detect serum progesterone (P_4) levels. Selected echotexture parameters (homogeneity, contrast, gradient, and entropy) were assessed on sonographical images using image analysis software (Bs200Pro®). Contrast and gradient values significantly decreased on d CA, CA+1 and CA+7 compared to the IA state ($P<0.05$ and $P<0.01$). Contrast values were lower in G1 than G2 two days before abortion (CA–2) ($P<0.01$). Gradient levels were higher in G2 than in G1 on CA–2 ($P<0.01$). Homogeneity values of G2 were higher than in G1 on d CA–1 and CA+7 ($P<0.05$). Progesterone values showed a non–significant decrease after IA during the study period in both groups. In G2, a negative correlation between P_4 and homogeneity (r=-0.797) and a positive correlation between P_4 and contrast values (r=0.719) were found. In conclusion, echotexture analysis allows quantitative and objective evaluation of the uterine structure during abortion, but specific standard values need to be established for both medication protocols, taking into account individual factors.

Key words: Abortion; bitch; echotexture; uterus; placenta

RESUMEN

El objetivo de este estudio fue evaluar los cambios estructurales de ecotextura en la pared uterina tras la inducción de un aborto en perras durante la fase embrionaria tardía/media gestación y desarrollar un método de evaluación del proceso abortivo. Se incluyeron en este estudio un total de 10 perras gestantes sanas de diferentes razas, con edades comprendidas entre los 25 y los 40 días (d) de gestación. En el Grupo 1 (n=5), se administró Aglepristona (10 mg·kg^{-1} de peso vivo, vía oral) una vez al día durante dos días consecutivos. En el Grupo 2 (n=5), se utilizó una combinación de Aglepristona, Cabergolina y Misoprostol para la inducción del aborto (IA). Antes de la inducción del aborto, y a intervalos de 24 horas hasta la finalización del aborto (AC), se examinaron ecográficamente el útero y la placenta. Se realizaron exámenes adicionales el d 1 (AC+1), el d 7 (AC+7) y el d 14 (AC+14) tras la finalización del proceso de aborto. Los mismos días se tomaron muestras de sangre para detectar los niveles séricos de progesterona (P_4). Se evaluaron determinados parámetros de ecotextura (homogeneidad, contraste, gradiente y entropía) en las imágenes ecográficas utilizando un software de análisis de imágenes (Bs200Pro®). Los valores de contraste y gradiente disminuyeron significativamente en los d CA, CA+1 y CA+7 en comparación con el estado IA ($P<0,05$ y $P<0,01$). Los valores de contraste fueron inferiores en G1 que en G2 dos días antes del aborto (CA–2) ($P<0,01$). Los niveles de gradiente fueron mayores en G2 que en G1 en CA–2 ($P<0,01$). Los valores de homogeneidad de G2 fueron superiores a los de G1 en los días CA–1 y CA+7 ($P<0,05$). Los valores de P_4 mostraron un descenso no significativo tras la IA durante el periodo de estudio en ambos grupos. En G2, se encontró una correlación negativa entre P_4 y homogeneidad (r=-0,797) y una correlación positiva entre P_4 y valores de contraste (r=0,719). En conclusión, el análisis de ecotextura permite una evaluación cuantitativa y objetiva de la estructura uterina durante el aborto, pero es necesario establecer valores estándar específicos para ambos protocolos de medicación, teniendo en cuenta los factores individuales.

Palabras clave: Aborto; perra, ecotextura; útero; placenta

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INTRODUCTION

The increasing surge in the population of stray animals presents a significant global concern with profound implications for both public health and the well-being of animals. The prevailing approach to tackle this issue revolves around reproductive control. Within the domain of veterinary medicine, procedures for reproductive control are not only legally endorsed but also routinely implemented, even during different stages of pregnancy [1].

In bitches (*Canis lupus familiaris*), unwanted mating is a common concern for pet owners due to the delicate care required for the pregnant bitch and the puppies after delivery [1, 2]. Several termination protocols have been introduced in the field of canine reproduction, some demonstrating hormonal changes, while others have investigated clinical findings after the induction of abortion. Anti-progestins, such as Aglepristone, are often used for pregnancy termination in bitches after mismating [3, 4]. Aglepristone, a progesterone (P_4) receptor blocker, exhibits greater affinity to progesterone receptors than natural progesterone and is the most frequently used anti-progestin for inducing abortion without a decrease in plasma P_4 concentrations. It is injected subcutaneously on two consecutive days for abortion induction [3, 5, 6].

The dopamine agonist Cabergoline has also been used for pregnancy termination in bitches [7, 8]. This agonist decreases prolactin secretion, leading to a decrease in P_4 levels, as Prolactin is a luteotropic agent in bitches [9, 10]. Misoprostol, a synthetic prostaglandin E_1 analogue which causes cervical dilatation, myometrial contractions, vomiting, diarrhea, among other effects, is used for the induction of abortion and labor, as well as the treatment of postpartum hemorrhage in women [11, 12] and induction of abortion in bitches [8, 13]. Combinations of these agents are often used to accelerate the abortion process [10, 13]. Agaoglu *et al.* [13] reported that the use of a combination of Aglepristone and Misoprostol resulted in faster cervical dilation, with all the animals in this group successfully completing the abortion procedure. However, in the other groups, abortion was not completed by the 6th day after treatment. In another study, pregnancies in bitches were terminated more quickly with a combination of Aglepristone and Cabergoline than with Aglepristone alone (6.8 versus 10.6 d) [10].

Examination of the reproductive tract in bitches is usually performed by ultrasonography. Different sonographical methods were proven useful for the evaluation of cyclic changes of the ovary, monitoring of pregnancy, embryonic death and the puerperium [14, 15]. Puerperium defines the period after the expulsion of the last fetus and placenta, and includes the involution and endometrial regeneration for normal return to cyclicity [16, 17]. In human medicine, high-frequency color Doppler ultrasonography allows the evaluation of uteroplacental circulation in early pregnancy. Pregnancy-related abnormalities have been associated with pregnancy complications such as hypertension, intrauterine growth restriction (IUGR), fetal distress, and early pregnancy failure [18, 19, 20]. The ability of Doppler sonography to analyze the circulation pattern even in the terminal branches of the uteroplacental circulation stimulates research for its potential application in examination of early and late gestational periods, in both human and veterinary medicine; the combination with echotexture analysis might be useful.

Computer-assisted echotexture analysis programs were introduced many years ago for purposes such as differentiation of breast tumors from healthy tissues in human medicine [21, 22] as well as recognizing and treating placental disturbances during pregnancy in a timely manner [23]. Echotexture analysis enables quantitative and objective assessment of the examined tissues [24, 25]. This technique is based on the mathematical relations of the pixels in ultrasonographic images, which are represented numerically (0-255), in the shades of gray, according to their brightness intensity [25, 26]. In veterinary reproduction, echotexture analysis programs are used for determining cyclic changes of the endometrium [27] and corpus luteum [26] and endometrial changes after treatment of endometritis [28] in cows. Computer-assisted image analysis was used for the assessment of postpartum endometrial echotexture changes in cows instead of the subjective evaluation of the real time ultrasound images [28, 29]. Furthermore, it was used for the evaluation of the endometrial changes in echotexture parameters in cyclic and early pregnant goats [30]. Mülazimoğlu *et al.* [31] reported significant differences between malignant and benign canine mammary tumors in terms of echotexture parameters, and the analysis system was used for assessment of ovarian echotexture changes in bitches [32].

According to literature knowledge, echotexture analysis has not yet been utilized for monitoring the abortion process previously. The hypothesis of this study suggests that echotexture analysis of the uterus during abortion in bitches might reveal characteristic changes in the endometrium throughout the abortion course. This could aid in recognizing abnormalities from the normal abortion process, potentially enabling early intervention.

The objective of this study was to assess the feasibility of utilizing echotexture analysis for monitoring both the abortion process and the subsequent involution period post-abortion. To achieve this objective, changes in certain echotexture parameters were examined following induction of abortion in mid-term pregnant dogs using two different treatment protocols. The hypothesis postulated that variations in uterine structure during the abortion process would exhibit disparities between the two medication protocols. The hypothesis was that the change in uterine structure during the abortion process would differ between the two medication protocols.

MATERIALS AND METHODS

Animals and treatments

A total of 10 healthy pregnant bitches from different breeds, aged 1 to 5 years, with a body weight ranging from 12 to 34 kg, and at 25 to 40 days (d) of gestation were included in this study with the written consent of their owners. All animals had a history of unwanted pregnancy. The animals were assigned randomly into two groups. Two bitches on the 40th d of pregnancy were randomly assigned to both groups to ensure homogeneity. The remaining bitches were less than 35 d of gestation. The pregnant bitches were adopted from an animal shelter by the owners, under the condition that the bitches would undergo ovariohysterectomy afterward.

Since post-abortion surgery is less risky for the bitch, abortion was induced in all animals. In Group 1 (G1, n=5) Aglepristone (Alizin®, Virbac Animal Health, New Zealand, 10 mg·kg^{-1}, SC) was administered once daily on two consecutive days. In Group 2 (G2, n=5) a combination of Aglepristone, Cabergoline (Galastop®, Ceva Sante Animale, Libourne, France, 5 µg·kg^{-1} PO) and, Misoprostol (Cytotec®, Ali Raif Ilaç Sanayi, Istanbul, Türkiye, 200 µg for bitches with less than 20 kg bw, 400 µg for bitches with greather than 20 kg bw, intravaginally), was used for induction of abortion (IA). Aglepristone was administrated as in G1, while Cabergoline and Misoprostol were administrated daily until completion of abortion. The animals were hospitalized until the abortion process was completed. Animal experiments were conducted under a protocol approved by the Animal Experiments Local Ethics Committee of Ankara University (No: 2009–50–247).

Examinations, sampling and hormonal analyses

Pregnancy was determined by trans–abdominal ultrasonography (USG) (Falco Vet 100, 6–8 MHz linear array transducer, (PieMedical, Imaging BV, Maastricht, The Netherlands). The image settings (brightness and contrast) of the ultrasonography apparature, the probe angle in image acquisition, the distance of the probe to the target tissue (tissue depth), and the positions of the dogs (supine position) were uniform. Determination of the gestational age was performed by the measurement of fetal and extrafetal structures reported by Luvoni and Grioni [33] and Yeager *et al.* [34] For this purpose, crown–rump length (CRL), extrafetal structures (ICC: inner chorionic cavity, OUD: outer uterine diameter) and biparietal diameter were measured during ultrasonographic examinations. Abortion process and the following period (d1, d7 and d14) were monitored by daily inspection of the vaginal discharge, vaginoscopy and ultrasound examinations. Determination of cervical dilatation and uterine discharge during vaginoscopic examination was considered as start of abortion (SA) and absence of any fetus/fetal structures during USG examination was also considered as the completion of abortion process (CA). After determination of the d of CA, two (CA–2) and one d (CA–1) before abortion were determined retrospectively. The period between start of treatment (pregnancy diagnosis, induction of abortion=IA) and CA was recorded. All bitches were hospitalized until CA, received commercial dry dog food twice a day and water *ad libitum*.

Blood sampling started just before the induction of abortion and was performed daily until CA and also on d 1 (CA+1), 7 (CA+7) and 14 (CA+14) after abortion in all animals. Samples were centrifuged at 1100 G force for 15 min (Heraeus Labofuge GL®, Germany) and stored at -20°C (Arçelik® 4253, Türkiye) until hormonal analysis. Serum P_4 concentrations were measured by using radioimmunoassay (RIA) kit (Immunotech, Prague, Czech Republic). An automatic open analyzer system (Stratec SR 300, Birkenfeld, Germany) was used to detect radioactivity following the manufacturer's protocol. Results are given in ng·mL^{-1}.

Acquisition and evaluation of ultrasonographic images

All groups of bitches underwent sonographic examinations on the same d as blood collection. Ultrasound examinations captured BMP–formatted images of the uterine wall and fetuses, which were then saved in PNG format and assigned to their respective groups. To minimize artifacts and identify images best representing the physiological and pathological conditions, 3 to 10 images were recorded during each ultrasonography examination. The image that most accurately represented the specific period was selected for subsequent analysis. Recorded ultrasonographic images were imported into the image processing software (Bs200Pro®, BAB Digital Imaging System, Ankara, Türkiye). Regions of interest (ROI) were defined according to established methods in the literature [1, 9, 35]. Four regions of interest (ROI) with 10 pixels per site (100 square pixel) were selected for both the uterine wall and placenta in each ultrasonographic image by the software (FIG. 1). Within these ROIs, echotexture parameters (homogeneity, contrast, gradient, and entropy) were assessed using a pixel–based color analysis system and were automatically calculated by the software. For a detailed description of the echotexture parameters, refer to Zabitler *et al.* [35] Utilizing the database transfer module of the software, the

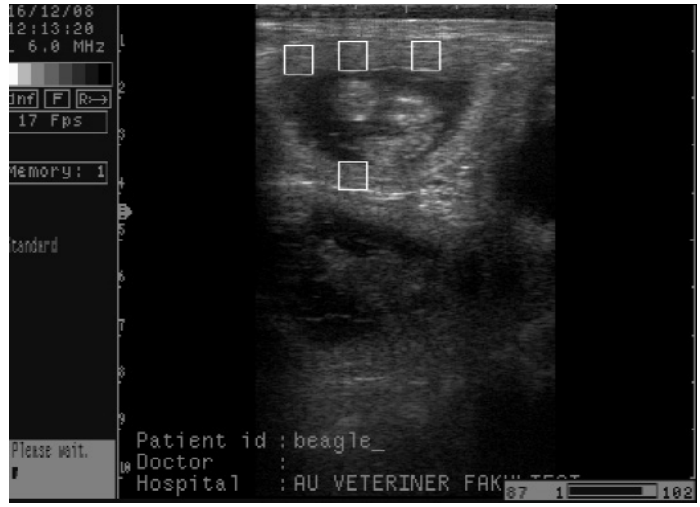

FIGURE 1. A representative ultrasound image with defined regions of interest (ROIs) for echotexture analysis. Figure captions: At day 35 of gestation, the ultrasound image depicts the uterus and fetus during abortion. Four regions of interest (ROIs) are positioned in the uterine wall and placenta, both in the upper and lower regions of the uterus

data was regularly transferred to MS Excel® software. Eight images were captured and saved for each parameter (5×8=40), and in each image, four ROIs were examined (40×4=160 ROIs).

Statistical analyses

Statistical calculations were conducted using SPSS® software (Version 14.0 for Windows, Chicago, IL, USA). The normality of distributions was assessed through Marginal Homogeneity and Kolmogorov–Smirnov Z Tests. To determine differences between values before and after treatment, the Wilcoxon Test was employed. Group comparisons were made using the Mann–Whitney U test. Results are expressed as mean ± standard deviation ($\bar{x}$ ± SD). A *P*–value of less than 0.05 was considered statistically significant

RESULTS AND DISCUSSION

Aglepristone is the most preferred medical agent for termination of pregnancy in the bitch [3, 4, 10, 36]. Combinations of Aglepristone with Cabergoline, misoprostol or PGF2α have been used to shorten the abortion period [1, 13, 37]. In this study, the aim was to evaluate the changes in echotexture parameters rather than the effects of the treatments on abortion process when Aglepristone was used alone or in combination with Cabergoline and Misoprostol. For this purpose, echotexture parameters; gradient, entropy, homogeneity and contrast were observed during and after the abortion process.

This study encountered a significant limitation due to the restricted number of animals included. The utilization of data from animals at various stages of pregnancy (d 25–40) has constrained the assessment of results based on specific pregnancy periods. While a substantial portion of the study focused on animals in the first half of pregnancy (less than 35th d), the small sample size prevented the evaluation of values from two 40–d pregnant dogs in a separate group. Therefore, there is a pressing need for more comprehensive prospective studies, involving a larger cohort of animals, to gain a deeper understanding of the biological significance inherent in these results.

There was no difference between the days of pregnancy in the groups (G1: 32.0 ± 6.2 and G2: 34.6 ± 3.6 d, $P>0.05$).

A brownish vaginal discharge was observed during vaginoscopy at the onset of abortion, while a hemorrhagic/pinky discharge was noted after the completion of abortion. The abortion process was completed in 4.2 ± 0.5 d in G1 and 5.8 ± 0.4 d in G2 ($P>0.05$). Inductions of abortion were successful in 100% of cases (n=10). In G1, all bitches completed abortion on d 6, while in G2, only 40% of bitches achieved abortion by the same d ($P<0.05$). The remaining bitches in G2 underwent abortion on d 7 (TABLE I).

TABLE I
Completed abortions during the time period after induction

Groups	Distribution of completion rates of abortions by days				
	Day 3	Day 4	Day 5	Day 6	Day 7
G1	20% (1/5)	60% (3/5)	60% (3/5)	100%[a] (5/5)	–
G2	0 %	0 %	40% (2/5)	40%[b] (2/5)	100% (5/5)

Values within a row with different superscripts differ significantly ([a,b] $P<0.05$). G1 (n=5): Aglepristone only. G2 (n=5): Aglepristone, Cabergoline and Misoprostol

In this study, abortion was completed in 4.2 d in G1 and 5.8 d in G2, with placental separation and fetus expulsion occurring slightly faster in G1 than in G2. Previous research has suggested that combining Aglepristone with Misoprostol or Cabergoline induces abortion earlier than Aglepristone alone [13]. Similarly, the study conducted in cats indicated that the combination with MIS (AGL+MIS) can achieve better results than the use of AGL alone [38]. This effect is likely due to additive effects, as observed in the bitch, where the acceleration of cervical dilatation after the combined use of AGL and MIS. This is supported by MIS causing long–term and intense uterine contractions [39, 40]. In this study, the combination with Misoprostol did not significantly accelerate abortion. The main finding is that abortion can be completed with Aglepristone alone in a relatively short time, and the additional use of Cabergoline and Misoprostol may not be necessary, at least not with the medication protocol used here.

Due to the use of different treatment methods in the groups, a mild decrease in P_4 was observed in G1, while it was more pronounced but non–significant in G2. In G2, a decrease in P_4 levels was observed from 24.73 ng·mL^{-1} on d IA to 5.35 ng·mL^{-1} on d CA–2. In G1, the respective values were 13.48 ng·mL^{-1} and 13.42 on d IA and CA–2. No correlation was found between the echotexture parameters and P_4 values in G1, whereas a negative correlation between P_4 and homogeneity (r=-0.797, $P<0.05$) and a positive correlation between P_4 and contrast values (r=0.719, $P<0.05$) were observed in G2.

When the data of all dogs in both groups were evaluated from induction to the 14[th] d after completion of abortion, significant changes were observed only in gradient and contrast values. Both parameters exhibited a significant decrease ($P<0.05$ and $P<0.01$) on the d of abortion (CA) as well as on the 1[st] (CA+1) and 7[th] (CA+7) d after abortion, compared to the d of induction of abortion (IA) (TABLE II).

This study provides preliminary results of the changes in the echotexture of the uterus before, during and after the abortion in bitches; no comparable study was found in the literature. So far, these results can only be compared to those obtained with similar methods, materials and settings during normal canine pregnancy; a previous study provided first results Zabitler *et al* [35]. Unfortunately, comparisons between studies are only possible, when the settings are standardized; this includes the sonographic evaluation and the analysis of the image. This results therefore must be considered as preliminary data and await confirmation by further examinations and other groups.

There are studies showing that uterine echotexture parameters (gradient, homogeneity, contrast) change dependent on pregnancy stage and cycle stage, also dependent on steroid hormone concentrations; the P_4 level or the estrogen–progesterone ratio [27, 30, 35, 41]. In the presented study, no relation was found between the echotexture parameters and P_4 values in G1; however, a negative correlation between P_4 and homogeneity (r=–0.797) and a positive correlation between P_4 and contrast values (r=0.719) were calculated in G2 comparable to previous studies. The latter might be explainable by a quicker change in uterine structures during the ongoing abortion. Homogeneity was higher after completion of abortion than before the initiation of abortion, probably due to a quick maceration and ongoing resorption of tissues and fluids during and after the abortion. Together with the markedly decreased P_4 concentrations, the negative correlation can be explained. However, the course of progesterone is not believed to be causative for the differences in uterine structure.

In both G1 and G2, there was no significant difference in gradient values across the days based on the applications. However, in both groups, gradient values exhibited a significant decrease ($P<0.01$, $P<0.05$) at the d of abortion (CA) and on the seventh d after abortion (CA+7) compared to the d of abortion induction (TABLE III). The mean gradient levels were higher in G2 (14.7) than in G1 (11.3) two d before abortion (CA–2) ($P<0.01$); conversely, these levels were higher ($P<0.01$) in G1 on d 14 after abortion (CA+14). No significant difference was found on the d of abortion completion between the two groups

TABLE II
Echotexture parameters of the uterine wall before and after the abortion process in all animals

Echotexture Parameters	Induction of abortion	Days before abortion		Completion of abortion	Days after abortion		
	IA	CA – 2	CA – 1	CA	CA + 1	CA + 7	CA + 14
Gradient (n=40)	13.7 ± 0.6[a]	13.2 ± 0.5	12.4 ± 0.5	12.2 ± 0.7[b**]	12.0 ± 0.4[b**]	11.7 ± 0.5[b**]	15.4 ± 1.0
Homogeneity (n=40)	5.8 ± 0.3	5.4 ± 0.2	6.2 ± 0.3	6.5 ± 0.3	5,9 ± 0,3	6.1 ± 0.3	4.8 ± 0.3
Entropy (n=40)	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.04 ± 0.0	1.0 ± 0.0
Contrast (n=40)	44.9 ± 4.8[a]	37.9 ± 4.1	36.1 ± 3.9	38.6 ± 6.5[b*]	32.4 ± 2.6[b**]	31.5 ± 3.1[b**]	76.8 ± 16.4

IA: Induction of abortion, CA: End of abortion. CA1/CA2: One/two days before the abortion; CA+1, CA+7, CA+14: 1, 7 and 14 days after abortion; Values within a line with different superscripts differ significantly ([a,b*] $P<0.05$, [a,b**] $P<0.01$)

(*P*>0.05). However, it was observed that in both groups on the day of CA, the mean gradient value decreased, and the mean contrast value increased compared to the d of IA (TABLE III). In pregnant bitches, depending on pregnancy stage and reproductive hormones, many structural changes occur due to a change in uterine blood flow, proliferation and secretion of endometrial glands, and an increase in tissue thickness, tissue edema and placenta formation [35]. After parturition or during abortion, the situation changes which is mirrored in the changings of contrast and gradient in the present study; however, to a highly differing degree and this is believed to be due to the different medication protocols.

Gradient is a measure of the differences in grey structures [42] and when there is no difference in grey value between pixels, the average gradient value is zero, indicating a perfectly homogeneous image. Contrast, on the other hand, is employed to determine the intensity variations of different grey values within the selected region of interest (ROI) [43]. In this study, significant decreases were observed in gradient and contrast values on days CA, CA+1, and CA+7 (*P*<0.01), which could be associated with the reduction in the diameters of the endometrial glands and the removal of abortion material during the involution procedure of the uterus, particularly in the first 14 d of the puerperal period. The increasing values on day CA+14 might reflect the regeneration of the endometrium. These results suggest that uterine changes during abortion could be identified by alterations in gradient and contrast, providing valuable insights for monitoring abortion; however, variations exist based on the medication scheme, with the disparity likely attributable to the use of Misoprostol.

Contrast values of G1 significantly decreased between the day of IA, CA+1 and CA+7 (*P*<0.05). In G2, a significant decrease was observed only between the day of IA and CA (*P*<0.05). Gradient and contrast values were significantly lower in G1 compared to G2 on the day of CA–2 (*P*<0.01) and on the day of CA + 14 (*P*<0.05) (TABLE III)

Treatment with PGE1 not only significantly increased myometrial contractions but also decreased total collagen content and connective tissue amount, possibly linked to increased collagenase activity. Consequently, mean gradient and contrast levels were higher in G2 than in G1 two days before abortion (CA–2) (*P*<0.01). Similarly, observed homogeneity differences between the two groups may also be attributed to uterine contractions and endometrial bleeding induced by Misoprostol. Homogeneity and gradient levels exhibit contrasting behaviors [27] and higher homogeneity values indicate more uniform gradient combinations [24], as also observed in this study.

In both the first and second groups, there was no significant change in entropy values in the post-application period and the post-abortion period (*P*>0.05). However, a significant difference (*P*<0.05) between the two groups was observed only on the d of CA+7 (TABLE III).

In the first group, homogeneity values significantly decreased between the d of IA and d CA+14 (*P*<0.05). In contrast, in G2, significantly higher values were obtained on d CA and CA + 7 compared to the d of IA (*P*<0.05). Furthermore, homogeneity values of G2 were higher than G1 on d CA–1 and CA+7 (*P*<0.05; TABLE III).

Misoprostol, a Prostaglandin E1 analog, induces cervical dilatation and uterine contractions. Cervical dilation involves complex molecular factors [44] and collagen molecule rearrangement, reduced collagen fibers, and increased elasticity contribute to the opening process [45, 46]. Misoprostol administration may alter endometrial tissue thickness [47], induce severe uterine contractions, and cause endometrial bleeding [48]. In the presented study, G2, where Misoprostol was administered, experienced more vigorous uterine contractions, likely contributing to differences compared to G1 during uterine involution after abortion. The observed differences in uterine echotexture between the two groups are likely primarily due to these effects of Misoprostol.

After abortion and during uterine involution, the diameter of the uterine horns and blood flow to the uterus decrease, influenced by the type of delivery in the bitch [49] and the course of abortion, as demonstrated in this study. Significant differences between groups,

TABLE III
Changes in the echotexture parameters between two treatment groups

Parameter A (n=20)		Induction of abortion	Days before abortion		Completion of abortion	Days after abortion			*P*
		CA – 2 (n=20)	CA – 1 (n=20)	CA (n=20)	CA	CA+1 (n=20)	CA+7 (n=20)	CA+14 (n=20)	
Gradient	G1	14.4±1.0^{a*}	$^{\#}$11.3±0.4 (n=16)	13.2±0.6	12.6±1.1^{b*}	12.4±0.6	12.2±0.6^{b*}	$^{\#}$17.1±1.6	^{a,b*}<0.05
	G2	13.1±0.8^{a}	$^{¥}$14.7± 0.8	11.6±0.8	11.8±0.9^{b*}	11.6±0.5	11.2±0.7^{b**}	$^{¥}$12.8±0.7 (n=12)	^{a,b*}<0.05 ^{a,b**}<0.01
P		>0.05	<0.01	>0.05	>0.05	>0.05	>0.05	<0.05	
Entropy	G 1	1.0±0.0^{a}	1.0±0.0^{a} (n=16)	1.0±0.0^{a}	1.0±0.0^{a}	1.0±0.0^{a}	$^{\#}$1.0±0.0^{a}	1.0±0.0^{a}	^{a}>0.05
	G 2	1.0±0.0^{a}	1.0±0.0^{a}	1.0±0.0^{a}	1.0±0.0^{a}	1.0±0.0^{a}	$^{¥}$1.0±0.0^{a}	1.0±0.0^{a} (n=12)	^{a}>0.05
P		>0.05	>0.05	>0.05	>0.05	>0.05	<0.05	>0.05	
Homogeneity	G 1	6.2±0.6^{a}	5.9±0.3 (n=16)	$^{\#}$5.5±0.4	6.4±0.4	5.4±0.4	#5.3±0.4	4.7±0.5^{b*}	^{a,b*}<0.05
	G 2	5.4±0.4^{a}	4.9±0.4	$^{¥}$6.8±0.5	6.5±0.6^{b*}	6.5±0.5	$^{¥}$6.8±0.5^{b*}	5.0±0.4 (n=12)	^{a,b*}<0.05
P		>0.05	>0.05	<0.05	>0.05	>0.05	<0.05	>0.05	
Contrast	G 1	49.6±7.4^{a}	$^{\#}$24.9±1.6 (n=16)	38.9±3.6	44.2±10.5	36.4± 4.2^{b*}	32.2±3.6^{b*}	$^{\#}$32.4±5.4	^{a,b*}<0.05
	G2	40.3±6.2^{a}	$^{¥}$48.3±6.7	33.4± 7.1	33.1±7.8^{b*}	28.4± 2.9	30.7±5.1	$^{¥}$42.7±10.4 (n=12)	^{a,b*}<0.05
P		>0.05	<0.01	>0.05	>0.05	>0.05	>0.05	<0.05	

IA: Induction of abortion, CA: End of abortion. CA1/CA2: One/two days before abortion; CA+1, CA+7, CA+14: 1, 7 and 14 days after abortion. G1 (n=5): Aglepristone only. G2 (n=5): Aglepristone, Cabergoline and Misoprostol. Statistical difference between rows is shown by letters (^{a,b}), statistical difference between columns by asterisks ($^{\#,¥}$). Values shown with different letters / asterisks are significantly different from each other (*P*<0.01; *P*<0.05) especially in contrast and gradient values on day CA-2 and CA+14 compared with IA, indicate distinct effects of the two treatments on endometrial and uterine changes before abortion and during involution. Changes in echotexture parameters during involution are, among other factors, a result of regeneration in the endometrium, as observed in the regeneration after the treatment of endometritis in cows [28].

CONCLUSIONS

Echotexture analysis allows quantitative and objective evaluation of the examined tissues. Abortion performed after implantation and mid-pregnancy causes characteristic tissue echotexture, and different drugs used to induce abortion can lead to different changes in tissue echotexture. Monitoring the change in the uterine structure during abortion is promising, but specific standard values need to be established for both medication protocols, taking into account individual factors.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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