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ARTICOLO

CONTRAST-ENHANCED ULTRASOUND IN CYSTIC ENDOMETRIAL HYPERPLASIA-PYOMETRA COMPLEX IN THE BITCH

A PRELIMINARY STUDY

IL PRODOTTO

ECOGRAFO VETUS 7

IL SISTEMA DI IMAGING AD
ULTRASUONI VETERINARIO
PREMIUM

I PRODOTTI

PANION SUPREME E PANION PRO

SISTEMI DI RISONANZA
MAGNETICA APERTA
DEDICATI ALLA VETERINARIA

HOUSE ORGAN BIMESTRALE AGOSTO-SETTEMBRE 2022

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CONTRAST-ENHANCED ULTRASOUND IN CYSTIC ENDOMETRIAL HYPERPLASIA- PYOMETRA COMPLEX IN THE BITCH

L'articolo di Marco Quartuccio, Luigi Liotta, Santo Cristarella, Giovanni Lanteri, Antonio Ieni, Tiziana D'Arrigo e Massimo De Majo



ECOGRAFO VETUS 7

Il sistema di imaging ad ultrasuoni veterinario premium



PANION SUPREME E PANION PRO

Sistemi di risonanza magnetica aperta dedicati alla veterinaria

ARTICOLO

**CYSTIC
ENDOMETRIAL
HYPERPLASIA
PYOMETRIA
COMPLEX
BITCH**

**CONTRAST ENHANCED
ULTRASOUND**



ETRIAL LASIA- TRA X IN THE

HANCED

ABOUT THE

ACEH SYNDROME

TO ASSESS, THROUGH CONTRAST ENHANCED ULTRASOUND (CEUS) EXAM, THE VASCULARIZATION IN ENDOMETRIAL MICROVESSELS IN CEH-PYOMETRA

SIMPLE SUMMARY

CONTRAST ENHANCED ULTRASOUND

In canine cystic endometrial hyperplasia-pyometra (CEH) syndrome, toxic factors and endometrial inflammatory reactions are responsible of increased blood flow and lower vascular resistance in uterine arteries.

Color Doppler ultrasound is regarded as an adjunctive tool for quantitative assessment of endometrial vascularization during uterine disorders.

The aim of this study was to assess, through contrast-enhanced ultrasound (CEUS) exam, the vascularization in endometrial microvessels in CEH-pyometra in order to evaluate the possibility of application in this syndrome.

In twelve female dogs with clinical symptoms related to pyometra, echographic, Color Doppler and CEUS exams were performed.

Histopathological examination revealed severe CEH and pyometra, immunohistochemical stain with CD 34 confirmed the presence of angiogenesis.

CEUS exam revealed a widespread, intense and rapidly developing homogeneous enhancement of the hyperplastic endometrium with absence of signal only in cystic areas.

All parameters of the quantitative analysis were not significantly influenced by region of interest dimension and position. CEUS may improve not invasive evaluations in the CEH-pyometra syndrome and virtually in CEH-mucometra.

ABSTRACT

In cystic endometrial hyperplasia (CEH)–pyometra syndrome, toxic factors and endometrial remodeling culminate in changes characterized by exudative and degenerative inflammatory reaction.

Recent studies on hemodynamic found an increased blood flow and lower vascular resistance in uterine arteries, suggesting color Doppler ultrasound as an adjunctive tool for quantitative assessment of endometrial vascularization during pyometra.

The aim of this study was to assess, through contrast-enhanced ultrasound (CEUS) exam, the vascularization in endometrial microvessels in CEH-pyometra in order to evaluate the possibility of application in this syndrome.

In twelve female dogs with clinical symptoms related to pyometra, B-mode, color Doppler and CEUS exams were performed.

In CEH-pyometra uteri, histopathological examination revealed severe CEH and pyometra, immunohistochemical stain with CD 34 confirmed the presence of angiogenesis.

CEUS exams revealed a widespread, intense and rapidly developing homogeneous enhancement of the hyperplastic endometrium, with absence of signal only in cystic areas.

All parameters of the quantitative analysis were not significantly influenced by region of interest dimension and position.

CEUS has the potential to improve clinical not invasive evaluations in the CEH-pyometra syndrome and virtually in CEH-mucometra.

KEYWORDS DOG; CYSTIC ENDOMETRIAL HYPERPLASIA; PYOMETRA; CONTRAST-ENHANCED ULTRASONOGRAPHY

AUTORI MARCO QUARTUCCIO, LUIGI LIOTTA, SANTO CRISTARELLA, GIOVANNI LANTERI, ANTONIO IENI, TIZIANA D'ARRIGO AND MASSIMO DE MAJO

INTRODUCTION

Cystic endometrial hyperplasia (CEH)–pyometra syndrome is a severe and frequent diestral disorder of intact bitches [1,2], its pathogenesis and differential diagnosis are a challenge to studies aimed at reproductive disorders.

There are numerous responsible factors of the CEH–pyometra syndrome, such as the joint action of steroid hormones (progesterone and estrogen) during the different stages of estrus cycle; the insulin-like growth factor 1 (IGF-1) as responsible of endometrial proliferation; the bacteriological toxic factors, mainly due to *Escherichia coli*; the endometrial remodeling by matrix metalloproteinases until the endometrial changes characterized by exudative and degenerative inflammatory reaction [3].

Some authors hypothesize that differential diagnosis element between pyometra and diestrus or CEH–mucometra in bitches is marked by the simultaneous expression of inflammatory mediators and endometrium proliferative pattern [4–7].

In inflammatory disorders, angiogenesis is activated by VEGF (vascular endothelial growth factor), an angiogenic mediator in many cell types mainly related to cytokines such as interleukin-1- α and interleukin-6 [8,9].

VEGF acts through its FLT-1 and KDR receptors, which directly participate in the regulation of angiogenesis and induce cell differentiation and transport in the uterine lumen and glandular epithelium [10].

The activation of FLT-1 and KDR receptors by VEGF culminates in cell migration to the target tissue [11].

The evaluation of the inflammatory and endometrial responses with changes in uterine hemodynamic as an effect to pathologic changes could contribute to a better understanding of the mechanisms involved in the pathogenesis of this syndrome in dogs and, therefore, for a more precise diagnosis of the disease.

In dogs, ultrasonographic evaluation of the uterus permits determining the thickness of the uterine walls and the presence of luminal contents differentiating pregnancy from pathologic conditions [12,13].

In women and cows, the increase in blood flow due to uterine pathologic conditions can be detected by Doppler ultrasound, but in dogs, this technique has been used to evaluate the blood flow of the uterine arteries during estrus, normal and abnormal pregnancies and the puerperium [14–17].

CYSTIC ENDOME TRIAL HYPERPLASIA

Recently, a study on hemodynamic, inflammatory and proliferative mechanisms in the uterine tissue of bitches with CEH and Pyometra found an increased blood flow and lower vascular resistance, suggesting color Doppler ultrasound as an adjunctive tool for quantitative assessment of endometrial vascularization during pyometra [2].

In the last few years, contrast-enhanced ultrasound has been introduced to clinical practice in human and veterinary medicine.

The research and advance in contrast-enhanced US (CEUS) imaging technology have been successfully applied in dogs in the evaluation of lesions of the liver, kidneys, spleen, urinary bladder, testes as well as prostate gland [18–27].

Studies conducted on rats in different stages of pregnancy and on macaques and humans have shown promising results in the dynamic evaluation of placental and intervillous perfusion [28–31], reducing worries concerning the use of contrast agents during pregnancy.

Several authors have recently validated the CEUS method in mares and in bitches to evaluate the microperfusion of the uterus during pregnancy and vascularization of the mammary gland during the estrous cycle of dogs without any apparent side effects [32–34].

Literature data on CEUS applications in endometrial pathology are relatively few and concerning only human species [35,36].

The aim of this study was to assess, through CEUS exam, the vascularization in the microvessels due to endometrial angiogenic stimulus in CEH-pyometra in order to evaluate the possibility of application as a diagnostic and prognostic tool in this syndrome.

CONTRAST
ENHANCED
ULTRASOUND
HAS BEEN
INTRODUCED
TO CLINICAL
PRACTICE
IN HUMAN
AND
VETERINARY
MEDICINE.

RESU

ULTRASONOGRAPHIC EXAMINATIONS

Ultrasonographic examinations required about 30 min, CEUS procedure was well tolerated and no side effects were noted.

B-mode ultrasonographic exam of the uteri revealed an expansion of the uterine horns, presence of anechoic material with interspersed hyperechoic spots, irregular thickening, sometimes remarkable, with presence of polypoid exuberances of the endometrium that protruded into the uterine lumen.

Anechoic cysts of different volumes (0.3 to 0.5 cm in diameter) were interspersed in the thickness of the mucosa (Figure 2, left).

Ovaries showed the presence of small hypoechoic areas (attributable to corpora lutea) in both ovaries in all bitches, and no pathologic changes were suspected.

The evaluation with color power Doppler allowed to highlight vascular signals mainly at the endometrial level (Figure 2, right).

Power-Doppler investigation, when signals were detected, showed from

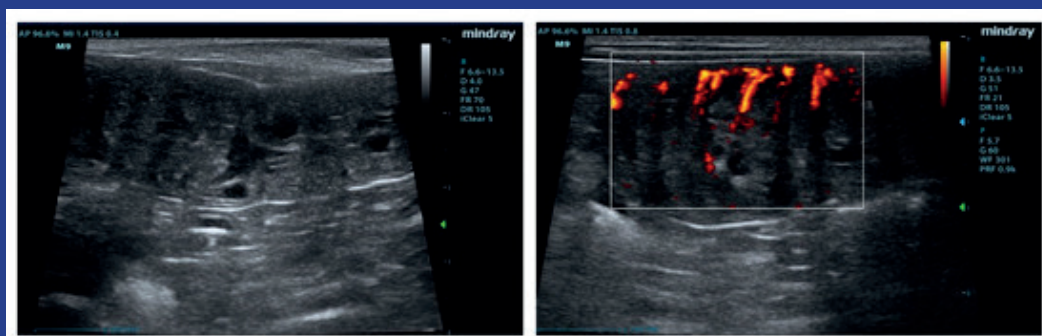


FIGURE 2. B-MODE AND COLOR DOPPLER IMAGES OF THE UTERUS. NOTE THE (LEFT) CAVITIES OF CYSTS AND (RIGHT) ENDOMETRIAL PROLIFERATION AND VASCULAR SIGNALS FROM THE SEROSA TOWARD THE LUMEN.

ULTS

mild to moderate endometrial vascularization. Blood flow signals were not seen in all images acquired in the same subject.

CEUS exams revealed a widespread and rapidly developing homogeneous enhancement of the hyperplastic endometrium at 6–8 s from inoculation of the contrast medium (wash-in); the wash-out showed a slow decrease of enhancement, with a persistence of echoes up to 2 min.

The enhancement was particularly intense in the hyperplastic endometrium, with absence of signal only in cystic formation, but evidence of enhancement in very thin peripheral vessels or necrotic areas; in the thin muscle layer, only small perpendicular vessels were evident (Figure 3).

Table 1 shows the results from ANOVA for the quantitative CEUS parameters recorded during the study.

All parameters of the quantitative analysis were not significantly influenced by ROI areas.

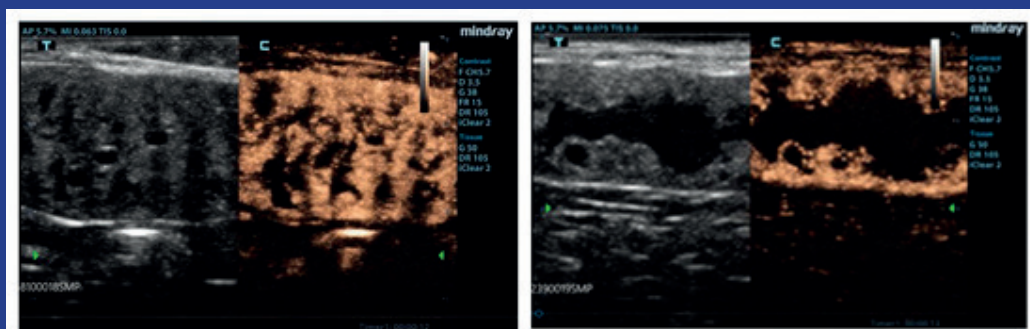


FIGURE 3. CONTRAST-ENHANCED IMAGES OF THE UTERUS. AFTER 10–12 S HYPERPLASTIC ENDOMETRIAL LAYER SHOWED (LEFT) AN AVID ENHANCEMENT WITH TORTUOUS PATTERN DUE TO PRESENCE OF CYSTS AND INTRALUMINAL MATERIAL. (RIGHT) WHEN UTERINE LUMEN IS FILLED WITH MATERIAL, VERY LARGE CYSTS ARE SURROUNDED BY VASCULARIZED TISSUE.



PRODOTTO

VE TUS 7

IL SISTEMA DI IMAGING AD
ULTRASUONI VETERINARIO PREMIUM

UNA NUOVA COLLABORAZIONE

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VETUS 7



VETUS 5EXP



VETUS 5



DC-N3 VET



M9VET



VETUS E7



TE5 VET



M6VET

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IMAGING
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DP-30 VET



DP-10 VET



IL SISTEMA DI IMAGING AD ULTRASUONI VETERINARIO PREMIUM

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VETUS 7

IMMAGINI CHIARE E PRECISE

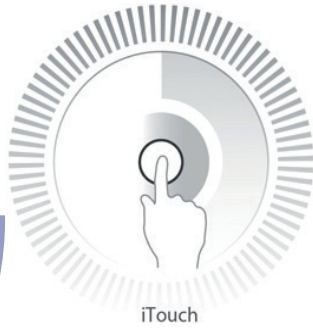
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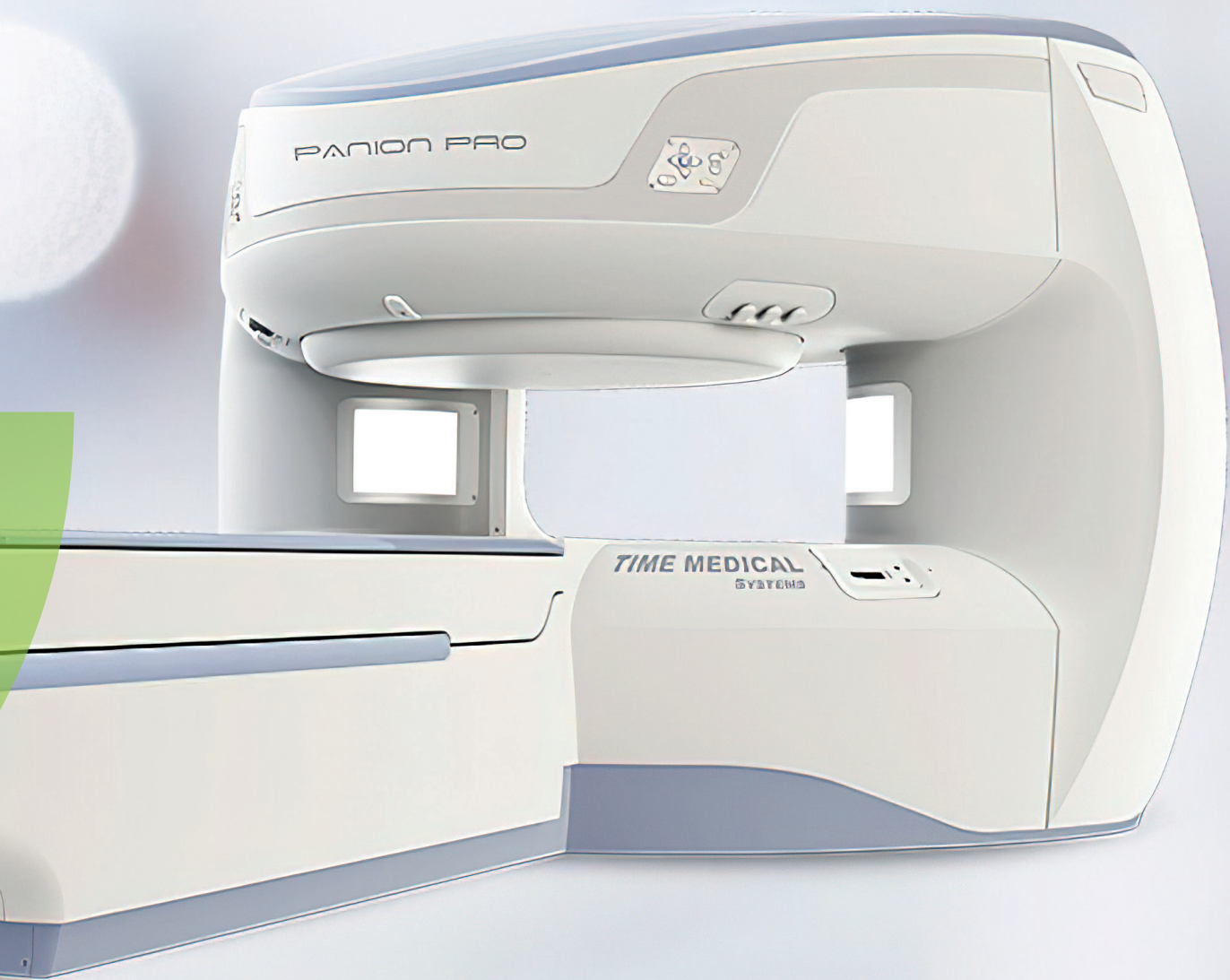
**Battery is optional configuration*

VE
TUS

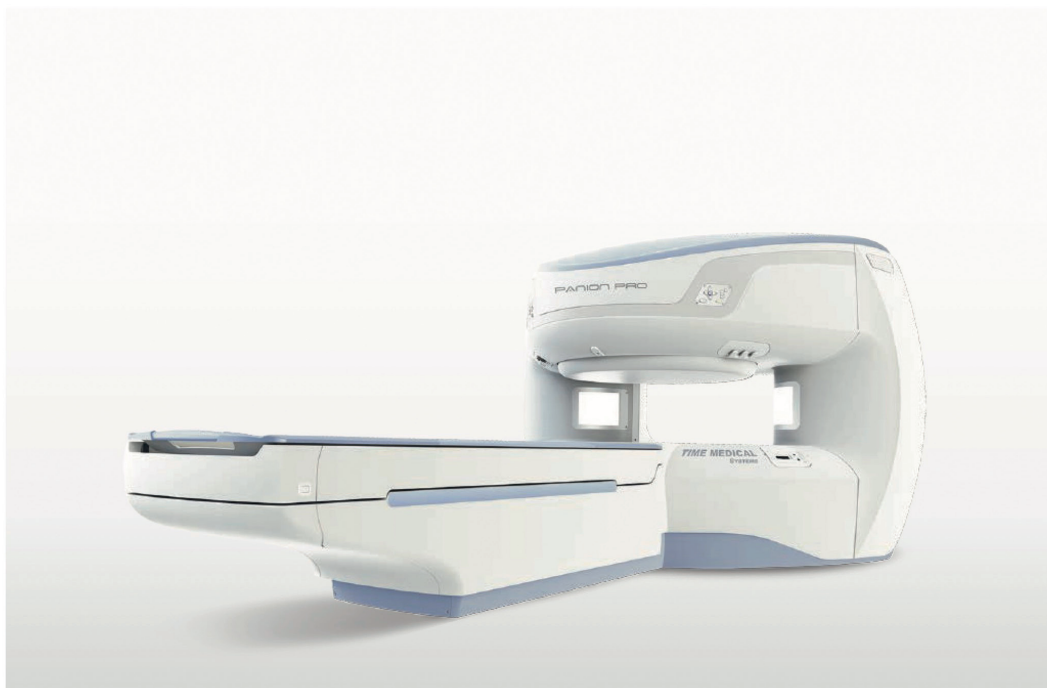
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