

## **Incidence rate of breast cancer, clinical and ultrasound approaches to diagnosing the same in dogs**

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### **Abstract**

Mammary gland tumors in dogs rank second among all newly diagnosed tumors in this species. Research goal was to study clinical/morphological characteristics of breast cancer in dogs with the use of ultrasound investigation. 34 dogs of different breeds and age groups with spontaneously emerging neoplasms of mammary glands were chosen for the study. To classify malignant tumors, the histological classification was applied. Complete examination of breast tumors was carried out with the help of clinical observation, ultrasound, radiologic, hematological and ultrasonographic methods applied. The largest percentage (23.5%) of animals with mammary gland neoplasms are mongrel female dogs. The breed predisposition was detected in dogs of the following breeds: Miniature Schnauzer - 11.9%, Standard Dachshund - 11.9%, American Bulldog, American Cocker Spaniel and Miniature Poodle - 8% each. Breast cancer was diagnosed in 29 animals (85.3%), 100% of those cases in the nodular form with microcalcifications in the tumor parenchyma. The horizontal orientation of growth is more often typical of breast cancer in the mammary gland pairs I and II at the initial stage of carcinogenesis, and is characterized by an inhomogeneous hypoechoic structure with sufficiently pronounced boundaries detected during the ultrasound investigation. The vertical orientation of growth is mainly typical of breast cancer in the mammary gland pairs III, IV and V from the very beginning of the disease. The ultrasonography usually shows: inhomogeneous hypoechoic structure containing inclusions in the form of cords or foci of a higher acoustic solidity; also clearly defined lateral acoustic shadows and dorsal echo enhancement; as well as unevenness and indistinctness of borders. The performed histological study within the current research revealed a multifocal, infiltrating epithelial neoplasm with distinct edges, surrounded by a large amount of fibrous tissue. The tumor consisted of a number of acini with a tendency of forming a network structure. The shape of cells was detected from round to irregular, the cytoplasm was found scarce, often with uneven borders, with the large central core, with chromophilic substance and 1-2 nucleoli. The cells were characterized by the pronounced anisocytosis and anisocariosis, and a great number of mitotic figures. Lymphatic invasion was observed. Ultrasound investigation of the mammary gland allows for performing percutaneous minimally invasive interventions and differential diagnostics of cystic and solid lesions of the mammary gland (96-100% accuracy), mastopathy and carcinoma conditions.

**Keywords:** Prevalence, Dogs, Cancerts, Diagnosis

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**معدل الإصابة بسرطان الثدي، والتشخيص بالطرق السريرية والامواج فوق الصوتية في الكلاب**

**في سالوتين، في كونسكي، اي مولكانوف، دي ديمكين، ان بادوكفين، اس سالوتينه**

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**الخلاصة**

تحتل أورام الغدة الثديية المرتبة الثانية بين جميع الأورام التي تم تشخيصها حديثاً في الكلاب. كان الهدف من البحث هو دراسة الخصائص السريرية/المورفولوجية لسرطان الثدي في الكلاب باستخدام فحص الموجات فوق الصوتية. تم اختيار 34 كلب من مختلف

السلالات والفئات العمرية تعاني من الإصابة بسرطان الغدة الثديية للدراسة. لتصنيف الأورام الخبيثة، حيث تم تطبيق التصنيف النسيجي لتلك الأورام. تم إجراء فحص كامل لأورام الثدي بمساعدة المراقبة الإكلينيكية، والموجات فوق الصوتية، والطرق الإشعاعية، وأمراض الدم. حيث سجلت أكبر نسبة (٢٣,٥ %) من الأورام الغدة الثديية في الكلاب الإناث الهجينة. اختلفت نسبة الإصابة في الكلاب حسب السلالة إذ كانت ١١,٩% في كل من سلالة Miniature Schnauzer و Standard Dachshund في حين كانت النسبة ٨% في كل من سلالة American Bulldo و American Cocker Spaniel و Miniature Poodle. شخيص سرطان الثدي في ٢٩ كلب من الكلاب قيد الدراسة وبنسبة (٨٥,٣ %)، كانت جميع الإصابات لتلك الحالات بشكل عقدي مع وجود تكلس ورمي في النسيج. غالباً ما يكون الاتجاه الأفقي للنمو نموذجياً لسرطان الثدي في أزواج الغدة اللبنية الأولى والثانية في المرحلة الأولية من التسرطن، ويتميز ببنية ناقصة الصيغ غير متجانسة مع حدود واضحة بشكل كافٍ تم الكشف عنها أثناء الفحص بالموجات فوق الصوتية. الاتجاه الرأسي للنمو هو النمط الرئيسي لسرطان الثدي في أزواج الغدد اللبنية الثالث والرابع والخامس منذ بداية المرض. عادة ما يظهر التصوير بالموجات فوق الصوتية: بنية ناقصة الصمغ غير متجانسة تحتوي على شوائب في شكل حبال أو بؤر صلابة صوتية أعلى؛ كما تحدد بوضوح الظلال الصوتية الجانبية وتعزيز الصدى الظهراني؛ فضلاً عن التفاوت وعدم وضوح الحدود. وكشفت الدراسة النسيجية التي أجريت في إطار البحث الحالي عن وجود ورم ظهاري متعدد البؤر يتسلل إلى حواف متميزة تحيط به كمية كبيرة من الأنسجة الليفية. يتألف الورم من عدد من الحويصلات مع ميل لتشكيل شبكة. كان شكل الخلايا دائري إلى غير منتظم ندرية في وجود السائتوبلازم، وغالباً مع حدود غير متساوية، مع جوهر مركزي كبير، مع مادة كروموفيلية ١-٢ نواة. تميزت الخلايا السرطانية بوضوح الـ anisocytosis و الـ anisocariosis والعدد الكبير من أشكال الانقسام. كما لوحظ الغزو للمفاوي. فحص الضرع بالأمواج فوق الصوتية يتيح الية تشخيص عبر الجلد مما يقلل من الحاجة للتدخلات بعمل فتح كما ان هذه التقنية تساعد في التمييز بين الإفات الصلدة والتكيسات في الضرع (بدقة ٩٦-١٠٠%)، وكذلك امراض وسرطانات الضرع.

## Introduction

Mammary gland tumors (MGT) in dogs have a rather high incidence rate and rank second among all newly diagnosed tumors in this species. Based on published literature, the risk of developing breast cancer (BC) in dogs is at least 50% of all cases of mammary gland (MG) neoplasms (1). The risk group is performed mainly by unneutered female dogs at the age from 5 to 16 years, and the peak incidence comes on animals from their middle age up to 10 years (2,3).

Epithelial malignant tumors in dogs (up to 90%) are characterized by the structure heterogeneity (4,5). BC prognosis depends on many factors, including the age of the animal, the localization and features of tumor growth, its histological type, the presence of metastases, etc.

Research goal was to study clinical and morphological characteristics of breast cancer in dogs with the use of ultrasound investigation.

## Materials and methods

Clinical observations and studies were conducted from 2014 to 2017 at the premises of the pet clinic at the Pet Center Zoostil (Volgograd, Russia) and the Department of Morphology, Animal Pathology and Biology of the Saratov State Agrarian University.

Dogs of different breeds, sex and age groups with spontaneously emerging neoplasms of mammary glands were chosen for the study. Upon admission to the clinic, animals with any visual signs of breast neoplasms were

selected for further studies and observations. No animals died during the research period.

To confirm the diagnosis, cytological studies using the method of fine needle aspiration biopsy (FNAB) were performed at primary admission. When using surgery as a treatment method, a morphological examination in the form of a histological study of tissue samples was performed in 100% of cases.

Ultrasound investigation was performed with the use of the ultrasonic medical diagnostic device 'Ultrasonic Diagnostic System SonoScape A-6 Vet.' and with the help of transducers 'micro-curvedarray C612' and 'lineararrayL745'. To examine superficial neoplasms, a high-frequency transducer 'lineararrayL745' (center frequency 7.5 MHz, frequency range 10-5 MHz, pitch 0.360 mm, angle/width 46mm) was used. To determine the nature of the blood flow, Doppler ultrasonography was performed with the use of 'ESAOTE MyLab40Vet' scanner and a 4-7.5 MHz multi-frequency phased transducer. Neoplasms were examined three-dimensionally, which made it possible to more accurately determine the size of neoplasms and their echostructure features.

Radiographic examination was carried out with the use of the mobile X-ray ward apparatus 'Arman 10J16-011' and 'ORANGE-1040HF EcoRay'. The X-ray examination produced images of two types: the right lateral view (with thoracic extremities positioned headward) and dorsoventral view. When analyzing X-ray images, the attention was drawn to the anatomical and topographical features of the contours of the heart, lungs, respiratory tracts and large blood vessels.

Hematologic studies were carried out with the use of the hematological analyzer 'Vet Auto Hematology Analyzer Mindray BC-2800', while biochemical blood tests were carried out with the use of the semi-automatic analyzer 'BioChem SA'.

### Research findings

During the research period 3240 dogs with diseases of various etiologies were clinically examined, among them 185 (5.7%) were diagnosed with oncology diseases. In 100% of cases (n=34), mammary gland tumors were recorded in female dogs, among them the number of sterilized animals was 5.9% (n=2).

Based on our research findings, female dogs of the following age groups were found prone to the development of MGT: up to 8 years - 14.7% (n=5), from 8 to 12 years - 73.6% (n=25), from 12 to 16 years - 8.8% (n=3), and over 16 years - 2.9% (n=1).

After studying the issue of breed predisposition to MG neoplasms in female dogs, we obtained the following results, presented in Table 1.

Table 1: Breed predisposition to mammary gland neoplasms (n=34)

Breed	Number of animals	Rate (%)
Miniature Schnauzers	4	11 (9)
Standard Dachshunds	4	11 (9)
American Bulldogs	3	8 (8)
American Cocker Spaniels	3	8 (8)
Miniature Poodles	3	8 (8)
Yorkshire Terriers	2	5 (9)
German Shepherd mixed breed dogs	2	5 (9)
Pugs	1	2 (9)
Russian Toy Terriers	1	2 (9)
Jagdterriers	1	2 (9)
Dobermanns	1	2 (9)
Airedale Terriers	1	2 (9)
Mongrel dogs	8	23 (5)
Total	34	100

Based on the data in Table 1, mongrel female dogs constitute the largest percentage (23.5%) of animals with MG neoplasms. Besides, the obtained results evidence the following breed predisposition to MG neoplasms in dogs: the Miniature Schnauzer makes 11.9%, the Standard Dachshund makes 11.9%, the American bulldog, the American Cocker Spaniel and the Miniature Poodle make 8% each.

Based on the results of morphological studies performed, benign tumors of mammary glands were

revealed in 14.7% (n=5) cases. At the same time, breast cancer was diagnosed in 85.3% (n=29) animals.

Based on the results of histological studies of tissue samples gathered during surgery (n=27), the following neoplasms were detected depending on their morphological type: adenocarcinoma in 74.1% of cases (n=20), solid carcinoma in 4.8% of cases (n=4), sarcoma in 7.4% of cases (n=2) and mammary carcinosarcoma in 3.7% of cases (n=1).

The performed histological study of the tissue samples showed that adenocarcinoma was the prevailing type of the detected neoplasms. As per microscope field of view, a multifocal infiltrating epithelial neoplasm with distinct edges, surrounded by a large amount of fibrous tissue was detected. The tumor consisted of a number of acini with a tendency of forming a network structure. The acini were lined with 1-3 layers of cells and had a thin vascular fibrous stroma. The shape of cells was detected from round to irregular, the cytoplasm was scarce, often with uneven borders, with the large central core, with chromophilic substance and 1-2 nucleoli. The cells were characterized by the pronounced anisocytosis and anisocariosis, and a great number of mitotic figures (up to 3-5 per high power field). Lymphatic invasion was observed.

According to histopathological differentiation, the diagnosed tumors were distributed as follows: 22.2% of cases (n=6) with a high degree of differentiation, 40.8% of cases (n=11) with an average degree of differentiation, and 37% of cases (n=10) with a low degree of differentiation.

According to histopathological differentiation, tumors with a moderate degree of differentiation were the most frequent ones. They were detected with lesions of extensive growth of abnormal tumor tissue, those lesions being separated from each other by thin connective tissue layers. Tumor tissue consisted of small cells with scanty cytoplasm, large nuclei, abundant chromatin condensation, mitotic figures. There were also found multinucleated cells, focal necrosis, focal hemorrhages in the tumor tissue. Stroma in most cases was moderately pronounced. Moderate blood vessel filling, stasis and erythrocyte sludge was registered. Single atrophied glands with a preserved histostructure were detected in tumor and perilesional tissue within a loose stroma.

Metastatic lesions of regional lymph nodes were detected in 17.2% of cases (n=5) at the primary admission. Remote metastases were not diagnosed either by X-ray or ultrasound investigation.

During the research period, 29 female dogs were diagnosed a nodular form of BC, constituting 85.3% cases of all MGT and 100% cases of all animals diagnosed with BC. Tumors burdened with hematoma formation were detected in 10.3% of cases (n=3), (Figures 1 and 2).

Figure 2 clearly displays the hypoechoic, heterogeneous structure of the tumor parenchyma with hyperechoic

microcalcinations providing an acoustic shadow. The neoplasm is surrounded with a cavity with anechoic contents (blood). Dorsal echo enhancement is also clearly displayed.



Figure 1: Adenocarcinoma of the mammary gland burdened with the hematoma formation. Jagdterrier female dog of 12 years old.

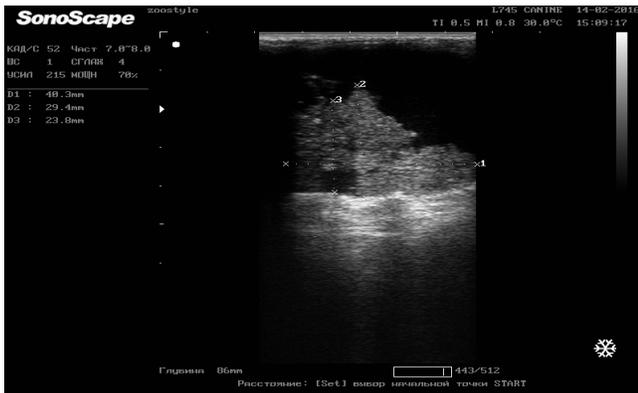


Figure 2: Ultrasound image of adenocarcinoma of the mammary gland burdened with the hematoma formation. Jagdterrier female dog of 12 years old.

In terms of number of tumor nodes in MG per one animal, the following pattern was revealed: one tumor node per animal in 58.6% of cases (n=17) and more than one node per animal in 41.4% of cases (n=12).

The prevalence rate of tumor nodes was also determined depending on their location in MG pairs: in pairs I, II - in 31% of cases (n=9) and in pairs III, IV, V - in 69% of cases (n=20).

The horizontal orientation of growth is more often typical of breast cancer in the mammary gland pairs I and II in the initial stage of carcinogenesis, and is characterized by an inhomogeneous hypoechoic structure with sufficiently

pronounced boundaries detected during the ultrasound investigation (Fig. 3).

The vertical orientation of growth is mainly typical of breast cancer in the mammary gland pairs III, IV and V from the very beginning of the disease. The ultrasonography shows inhomogeneous hypoechoic structure containing inclusions in the form of cords or foci of a higher acoustic solidity; also clearly defined lateral acoustic shadows and dorsal echo enhancement; as well as unevenness and indistinctness of borders (Fig. 4).

The presence of microcalcifications in the tumor parenchyma is rather characteristic of the nodular form of BC in dogs (Fig. 5).



Figure 3: Ultrasound image of adenocarcinoma localized in the mammary gland pair I. Miniature Schnauzer female dog of 9 years old.



Figure 4: Ultrasound image of a nodular form of adenocarcinoma localized in the mammary gland pair IV. Standard Dachshund female dog of 10 years old.

There are four types of vascular pattern based on the nature of vascularization. In case of the third type, both peri- and intranodular (mixed) blood flow is detected; while the fourth type is characterized by intranodular blood flow

only. The presence of the 3<sup>rd</sup> and 4<sup>th</sup> types of the tumor vascularization is generally regarded as an indirect sign of a malignant process.

While examining 29 female dogs with a morphologically confirmed diagnosis of BC, the intra- and perinodular blood flow was recorded in 26 animals (89.7%), while perinodular blood flow was recorded in 3 dogs (10.3%). Thus, the intra- and perinodular (mixed) type of blood flow is evidenced as the most characteristic one of BC in female dogs (Fig. 6).



Figure 5: Ultrasound image of microcalcifications in the adenocarcinoma parenchyma of MG. German Shepherd mixed breed female dog of 9 years old.

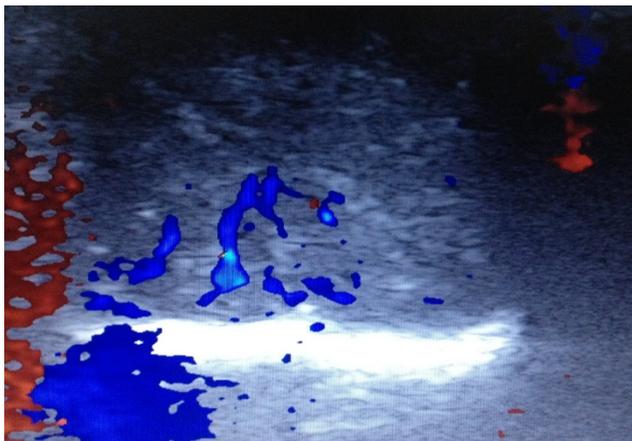


Figure 6: Doppler ultrasonography. III stage breast cancer. Example of the intra- and perinodular (mixed) type of blood flow (type 3).

#### American Bulldog female dog of the age 9 years 7 months

The results obtained through the hematological examination show an increase in the platelets number up to

$662.56 \pm 37.9 \times 10^9/L$  in dogs diagnosed with stage II and stage BC as compared to normal  $458.99 \pm 28.4 \times 10^9/L$  ( $p \leq 0.05$ ). No statistically significant differences in the number of erythrocytes and leukocytes were detected.

The results obtained through the biochemical blood test show an increase in the total protein by 12% ( $80.6 \pm 3.02$  g/l) as compared to normal  $71.87 \pm 4.89$  g/l, ( $p \leq 0.05$ ). Such blood values as glucose, SGOT (serum glutamic oxaloacetic transaminase), SGPT (serum glutamic pyruvic transaminase), total bilirubin, creatinine, urea, calcium and phosphorus did not show any statistically significant differences as compared to the normal values.

## Discussions

MG neoplasms are quite widespread and rank third after lymphomas and skin tumors (6).

Neoplastic diseases in dogs are quite widely spread within the examined territory. A high percentage of diagnosed neoplasms in animals is apparently caused by emissions from the metallurgical, chemical and fuel industry enterprises located within the urban territory, as well as by an increased content of nitrogen oxides, formaldehyde and phenol in the air.

Ultrasound investigation as a diagnostic method is constantly increasing its potential due to the improvement of existing techniques and the development of new ones. Ultrasonic mammography as one of the methods for diagnosing MG neoplasms has shown its high efficacy (6). The most essential signs of a nodular form of BC at the ultrasound investigation are as follows: an irregular shape, mainly anechoic structure, unclear boundaries, dorsal echoic enhancement, and lateral acoustic shadows. Currently an ultrasound investigation enables to diagnose cystic and solid lesions of MG (96-100% accuracy rate), mastopathy and carcinoma. This kind of investigation also makes it possible to perform minimally invasive percutaneous interventions under the visual control.

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