Ultrasonographic liver nodules are more often benign lesions in dogs with hemoperitoneum secondary to splenic tumor rupture

Alba R. Ramirez, DVM*; Samuel D. Stewart, DVM, DACVECC; Chand Khanna, DVM, PhD, DACVIM, DACVP

Emergency and Critical Care, Ethos Veterinary Health, Woburn, MA
*Corresponding author: Dr. Ramirez (alrocio@yahoo.com)

OBJECTIVE
To evaluate the reliability of preoperative abdominal ultrasonography as a staging tool for dogs with hemoperitoneum due to presumed splenic tumor rupture, focusing on the detection of metastatic lesions in the liver.

ANIMALS
99 dogs from 20 emergency and specialty hospitals across the US.

METHODS
Dogs with nontraumatic hemoperitoneum secondary to splenic tumor rupture were included. A post hoc analysis was conducted on data from a nationwide prospective trial investigating novel treatments for canine hemangiosarcoma. The accuracy of preoperative staging was assessed by comparing ultrasonographic findings with intraoperative observations and histologic findings.

RESULTS
On preoperative ultrasonography, there was a 20% incidence of liver lesions identified, with no association to liver lesions seen during operation. Notably, 22% of liver lesions observed during operation were missed on preoperative ultrasonography. The presence of liver lesions on preoperative ultrasonography was associated with a higher likelihood of a benign splenic tumor diagnosis. There was no association between the identification of liver lesions on preoperative ultrasonography and the presence of metastatic disease on liver biopsy, with a sensitivity and specificity of 19% and 82%, respectively. Additionally, ultrasound had low sensitivity in detecting intra-abdominal lesions beyond the liver and spleen, with 82% of these lesions missed preoperatively.

CLINICAL RELEVANCE
This study challenges conventional perceptions around the approach to staging in dogs with hemoperitoneum. These findings advocate for a reevaluation of the staging approach, with more comprehensive modalities like whole-body CT or MRI potentially being more warranted.

Keywords: hemoperitoneum, liver nodules, splenic mass, hemangiosarcoma, benign nodules

Received April 17, 2024
Accepted June 24, 2024
Published online August 7, 2024
doi.org/10.2460/javma.24.04.0254
©The authors
The use of abdominal ultrasonography is often included in the care of these patients. The purpose of this ultrasonography is both to determine the origin of the bleeding tumor and, more importantly, to look for the presence of possible metastasis within the abdomen. Specifically, the presence of liver or other intra-abdominal nodules on a preoperative abdominal ultrasonography may reasonably raise concerns for possible metastatic disease and may dissuade some owners from electing to go forward with treatment. Previous research investigating the prevalence of hepatic metastasis secondary to splenic hemangiosarcoma at the time of diagnosis is limited. Clendaniel et al. observed an overall 37% prevalence of hepatic metastasis from splenic hemangiosarcoma, consistent with findings by Hammond and Pesillo-Crosby. Another study reported that the presence of nodules on both the spleen and liver indicated a 48% likelihood of a splenic hemangiosarcoma diagnosis. A retrospective study of 14 dogs with retroperitoneal sarcoma reported an overall prevalence of metastasis to be 29%. Nine of the dogs in that study had a diagnosis of retroperitoneal hemangiosarcoma, with 3 of those dogs having concurrent metastasis, resulting in a hemangiosarcoma-specific prevalence of 33%. Recently we reported on a small cohort of dogs with splenic tumor rupture and found that only 33% of liver nodules found on preoperative ultrasonography were subsequently histologically confirmed to be metastatic hemangiosarcoma lesions. Accordingly, these preliminary data raise questions about the value of ultrasonography as a preoperative staging diagnostic for identifying potential metastatic disease in the liver. Furthermore, ultrasound failed to identify most omental metastases that were subsequently identified intraoperatively in this same cohort.

Based on these collective data, we were prompted to inquire whether relying solely on conventional abdominal ultrasonography as a method to detect the bleeding source and potential visceral metastasis is satisfactory for deciding to proceed with surgery. To address this query, we examined data obtained from a comprehensive prospective study (Ethos Precision Medicine Umbrella Study for Hemangiosarcoma [Ethos-PUSH]) involving dogs experiencing hemoperitoneum attributed to suspected splenic tumor rupture.

### Methods

#### Case selection criteria

This study included dogs with nontraumatic hemoperitoneum secondary to splenic tumor rupture that were being enrolled in a nationwide, prospective, multicenter randomized trial evaluating novel treatments for hemangiosarcoma (Ethos-PUSH). Dogs were enrolled through 20 emergency and specialty hospitals across the US from October 2020 to May 2022. The inclusion criteria required dogs to have a diagnosis of nontraumatic hemoperitoneum secondary to a ruptured splenic tumor, have no evidence of pulmonary metastasis on preoperative thoracic radiographs, and be scheduled to undergo splenectomy surgery with a board-certified surgeon or emergency department doctor.

A full abdominal ultrasonography was required for all dogs, which was performed by a board-certified radiologist or a board-certified internist; however, abnormal findings did not define eligibility of patients for the study. Abnormal splenic and liver lesions were defined as any discrete and measurable mass or nodule.

#### Post hoc analysis of Ethos-PUSH data

From the prospectively enrolled Ethos-PUSH cohort, dogs were eligible for inclusion in our study if they had preoperative abdominal ultrasonographic findings and intraoperative findings reported in a case report form or within the electronic medical record. Furthermore, each dog was required to have any abnormal lesions sampled for histopathology during operation (including those identified on preoperative ultrasonography). The ultrasonographic, surgical, and histopathologic results were recorded in a central database.

#### Statistical analysis

Statistical analysis was performed with a statistical software program (Prism, version 10.1.2; GraphPad Software Inc). Normality was assessed with Shapiro-Wilk tests, and descriptive data were reported with medians and ranges. Fisher exact tests were used to compare the presence of preoperative liver lesions to splenic tumor diagnosis and liver lesion diagnosis. A significance level of α = .05 was used.

### Results

#### Patient demographics

Ninety-nine dogs (36 female dogs [35 spayed and 1 intact] and 63 male dogs [62 neutered and 1 intact]) met the eligibility criteria for this study (Table 1). The median age of the dogs included was 10 years (range, 3 to 13 years; Table 2). The study group consisted of 29 mixed-breed dogs, 14 German Shepherd Dogs, 9 Golden Retrievers, 9 Labrador Retrievers, 5 Australian

<table>
<thead>
<tr>
<th>Table 1—Sex demographics of study population.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Entire population (n = 99)</strong></td>
</tr>
<tr>
<td>-------------------------------</td>
</tr>
<tr>
<td>Intact female</td>
</tr>
<tr>
<td>Spayed female</td>
</tr>
<tr>
<td>Intact male</td>
</tr>
<tr>
<td>Neutered male</td>
</tr>
</tbody>
</table>

HSA = Hemangiosarcoma.
Shepherds, 4 Boxers, 3 French Bulldogs, 3 Goldendoodles, 3 Labradoodles, 3 Pembrokes, 2 Great Pyrenees, 2 Siberian Huskies, and 1 each of Belgian Malinois, Bernese Mountain Dog, Boerboel, Border Collie, Chesapeake Bay Retriever, Chinese Crested, Cocker Spaniel, Dachshund, Doberman Pinscher, Greater Swiss Mountain Dog, Italian Greyhound, Newfoundland, and Portuguese Water Dog. There were similar breed demographics between dogs with splenic hemangiosarcoma and those with benign disease. The dogs had a median body weight of 30 kg (range, 7.1 to 58 kg).

**Concordance of liver lesion identification**

Twenty of 99 (20%) dogs had liver lesions identified on their preoperative ultrasonography. An additional 22 dogs had liver lesions identified intraoperatively that were not seen on preoperative ultrasonography. There was no correlation between nodule identification on preoperative ultrasonographic images and intraoperative findings (Table 3). There was a sensitivity of 40%, specificity of 72%, positive predictive value of 27%, and negative predictive value of 83%. When extrapolated to the whole cohort, 22 of 99 (22%) dogs did not have their liver lesions identified on preoperative ultrasonography.

**Association of liver lesion identification to splenic diagnosis**

In this cohort, 58 of 99 (59%) dogs were diagnosed with splenic hemangiosarcoma, 33 (33%) dogs were diagnosed with a benign splenic lesion, and 8 (8%) were diagnosed with other splenic malignancies (4 with stromal sarcoma, 2 with histiocytic sarcoma, 1 with carcinoma, and 1 with leiomyosarcoma). Seventeen of the 20 (85%) dogs with liver lesions identified on preoperative ultrasonography were diagnosed with benign splenic lesions (including 9 with nodular hyperplasia, 4 with hepatocellular glycogen-type vacuolation, and 4 with hematopoietic hyperplastic nodules). The 3 (15%) remaining dogs received malignant diagnoses (2 with hemangiosarcoma and 1 with carcinoma). There was a significant association between the presence of liver lesions on preoperative ultrasonography and splenic tumor diagnosis, with the presence of liver lesions being associated with a higher likelihood of a benign splenic tumor diagnosis ($P < .0001$).

**Association of liver lesion identification to histologic diagnosis**

Of the 20 dogs with liver lesions identified on preoperative ultrasonography, 16 of these had a liver biopsy collected during operation. Liver biopsies were not collected in the remaining 4 dogs due to the absence of visual liver lesions intraoperatively. There were 49 dogs that did not have ultrasonographic liver lesions identified but still had a liver biopsy collected during operation due to the identification of lesions intraoperatively (29 focal-to-diffuse mottled hepatic parenchyma, 13 nodules, and 7 masses). Of the 16 dogs with liver nodules on preoperative ultrasonography, only 3 (19%) of these dogs were diagnosed as metastasis (2 with hemangiosarcoma and 1 with carcinoma), with the remaining 13 (81%) dogs receiving benign diagnoses (8 with nodular hyperplasia, 4 with hepatocellular glycogen-type vacuolation, and 1 with hematopoietic hyperplastic nodule). The lesions reported on the ultrasonography for the 3 dogs with malignant tumors were identified as 1 to a few small hypoechoic nodules measuring between 2 and 4 mm. The lesions reported on the ultrasonography as benign were identified as follows: 3 had diffuse mottled parenchyma with hyperechoic nodules measuring more than 5 mm, 4 had 1 to a few hyperechoic nodules measuring more than 10 mm, and 10 had hypoechoic nodules measuring more than 5 mm. Of the 49 dogs with no liver nodules seen on preoperative ultrasonography, 9 (18%) were diagnosed with metastatic disease and 40 (82%) were diagnosed with benign lesions. There was no association between the identification of liver lesions on preoperative abdominal ultrasonography and the presence of metastatic disease on liver biopsy (Table 4). There was a sensitivity of 19%, specificity of 82%, positive predictive value of 25%, and negative predictive value of 75%.

**Identification of lesions in other organs**

Eleven of the full cohort of 99 (11%) dogs had lesions identified in organs other than the spleen and liver.
liver on their preoperative ultrasonography. These included 2 lesions involving the mesentery and 1 each involving the omentum, cecum, adrenal gland, kidney, and mesenteric lymph node. There were also 4 lesions that weren’t noted to be associated with a specific organ. Only 3 (27%) of these lesions were identified intraoperatively (2 in the omentum and 1 in the cecum).

Seventeen of 99 (17%) dogs were identified with lesions in organs other than the spleen and liver during operation. The lesions noted intraoperatively included 13 in the omentum and 1 each in the stomach, cecum, pancreas, and diaphragm. Fourteen (82%) of these lesions were missed on the preoperative ultrasonography.

Fifteen of the 17 dogs with intraoperative lesions not associated with the spleen or liver had a biopsy collected from the organ during operation. This included 12 from the omentum and 1 each from the pancreas, cecum, and a splenic lymph node. Of the omental nodule biopsies, 6 of 12 (50%) were diagnosed as malignant hemangiosarcoma and the remaining 6 of 12 (50%) were classified as hematomas. The pancreatic nodule was identified as inflammation consistent with pancreatitis; the cecal lesion was identified as carcinoma, and the lymph node was identified as reactive. Of the 3 lesions reported on preoperative ultrasonography that were identified intraoperatively, 1 of them was found to be true metastatic carcinomatosis (33%).

**Discussion**

Preoperative ultrasonography is frequently utilized to assess for potential metastasis to inform surgical planning. However, to date, there remains a lack of evidence regarding the association between the identification of lesions on preoperative ultrasonography and the diagnosis of malignant or metastatic disease. For instance, in a study conducted by Millar and Zersen,10 the presence of cavitated splenic masses on abdominal ultrasonography did not support a diagnosis of malignancy. Furthermore, relying solely on lesion identification via ultrasonography may not offer a reliable means of determining the presence of metastatic disease. This concern is underscored by the findings of our study, wherein only 4 out of 31 (13%) dogs with preoperative ultrasound-detected lesions suggestive of possible metastasis (20 in the liver and 11 in other organs) were confirmed to have true metastatic disease.

An important limitation of ultrasonography for preoperative staging is that the entire abdomen may not be able to be imaged due to the size/conformation of the dog, the presence of bowel gas, obesity, or anatomical barriers such as the rib cage. Hemangiosarcoma can also present as microscopic lesions or involve multiple sites, some of which may not be clearly discernible on ultrasonography. One study11 highlighted significant variability in the ultrasonographic appearance of hepatic parenchymal lesions across all diagnoses, with no statistically significant associations observed between ultrasonographic appearance and diagnosis. In the present study, hepatic lesions on abdominal ultrasonography for dogs with metastatic disease were described as hypoechoic nodules measuring between 2 and 4 mm. However, this same appearance of hepatic lesions was also observed in most of the benign lesion cases; therefore, there were no discernable differences in ultrasonographic appearance to differentiate between benign and malignant lesions. With the new and growing field of artificial-intelligence–guided diagnostic imaging interpretation, the ability to differentiate these lesions may become possible in the future. In the study by Millar and Zersen,10 the presence of cavitory masses or nodules did not support a diagnosis of malignancy; however, the study did suggest that abdominal ultrasonography may not be helpful in distinguishing malignant from benign lesions but could aid in surgical planning and confirming the presence of a bleeding mass. Therefore, if the trigger for deciding whether to pursue surgical intervention is based on lesions identified on preoperative ultrasonography, there are concerns that this could lead to dogs with benign disease that would be curable with surgery alone to instead be euthanized over the fear of possible metastatic disease.

In the context of liver lesions identified on preoperative ultrasonography in dogs with ruptured splenic tumors, it is essential to recognize that the presence of these lesions does not unequivocally imply liver metastasis. The prevalence of hepatic metastasis has been subject to examination across several studies. Pintar et al12 observed a notably high prevalence of 47.6%. Conversely, studies by Hammond and Pesilco-Crosby7 and Carloni at al13 reported lower prevalences ranging from 34.4% to 37%. Other studies14,15 have documented comparatively lower prevalence rates between 28% and 30%.

Our study contributes significantly to this discussion by reporting an overall prevalence of liver metastasis in dogs with hemoperitoneum secondary to a ruptured splenic tumor at a markedly lower rate of only 12%, indicating a notable departure from previously reported figures. An explanation for this difference could be the prospective nature of this study, compared to the retrospective nature of most of these previous studies, demonstrating the potential impact of underlying biases inherent within retrospective data.

Eleven of the 12 (92%) dogs diagnosed with hepatic metastasis had hemangiosarcoma and the remainder had carcinomatosis. Furthermore, we showed that only 15% of liver lesions identified on preoperative ultrasonography were histologically confirmed to be metastatic, whereas the remainder of the lesions were determined to be benign lesions. Similar findings have been noted in another study.9

Given the inherent limitations of ultrasonography as a staging diagnostic, CT scans or MRI could be more ideal approaches to patient staging. They can provide detailed visualization of affected organs and tissues, aid in surgical planning, and assist in assessing the overall prognosis. Furthermore, these modalities allow for the scanning of the whole dog and not just a single body cavity, allowing for the opportunity to detect metastatic lesions that otherwise likely would not be seen on ultrasound (ie, intramuscular metastases).10,14,16,17 The major disadvantages of CT and MRI are the cost to the owner, their limited availability outside of regular business hours, the need for trained personnel to perform the imaging, and the additional time required under anesthesia in a potentially unstable patient.
The incidence of hepatic nodular hyperplasia and other similar benign pathologies increases with age, with a previous study reporting up to 70% of older dogs showing the presence of benign liver lesions. It is important to recognize the prevalence of these age-related lesions when discussing the results of staging diagnostics with pet owners.

In the present study, 17% of patients had intraoperative lesions identified in organs other than the liver or spleen; 18% of those lesions were suspected on preoperative ultrasonography. This demonstrates a low sensitivity for metastasis identification with ultrasonography in other organs, similarly as in the liver.

A potential limitation of this study was that splenectomy procedures were performed by a combination of board-certified surgeons and emergency department doctors. All veterinarians performing the splenectomy procedures for these dogs had undergone specific training in biopsy collection for this study; however, the difference in experience level could still have introduced a bias due to missed lesions that weren’t sampled. Additionally, it cannot be definitively confirmed that the lesions identified in organs other than the liver and spleen on preoperative abdominal ultrasonography had biopsies collected from the same lesion site once in operation.

In summary, these data suggest favorable outcomes for dogs with hemoperitoneum, with a lower incidence of metastasis than historically believed. Abdominal ultrasonography, when used as a preoperative staging diagnostic, has been shown to have a low sensitivity for the detection of metastatic lesions. Therefore, a more comprehensive approach, such as whole-body CT or MRI, may be necessary and is an active area of investigation for the authors. Nonetheless, further advancements in diagnostic imaging may allow for improved detection of metastatic lesions, such as higher-resolution ultrasound machines and the use of artificial intelligence platforms.

Acknowledgments

None reported.

Disclosures

The authors have nothing to disclose. No AI-assisted technologies were used in the generation of this manuscript.

Funding

The authors have nothing to disclose.

ORCID

A. Ramirez https://orcid.org/0000-0002-4729-7927
S. Stewart https://orcid.org/0000-0003-1148-2589

References


