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Dogs ≥ five years of age at the time of congenital extrahepatic portosystemic shunt diagnosis have better long-term outcomes with surgical attenuation than with medical management alone

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OBJECTIVE
To determine the outcome in dogs diagnosed with congenital extrahepatic portosystemic shunts (EHPSS) at ≥ 5 years of age treated with medical management only (M) or with surgical attenuation (S). The hypothesis was that dogs undergoing surgical attenuation would have a longer survival time than dogs undergoing medical management only.

ANIMALS
351 dogs definitively diagnosed with EHPSS at ≥ 5 years of age.

PROCEDURES
Medical records from 2009 to 2019 at 16 veterinary teaching hospitals were evaluated. Data collected included signalment, clinical signs at diagnosis, clinicopathologic data, surgical and medical treatments, shunt morphology, clinical signs and medical treatments at 6 to 12 months after diagnosis, and survival time.

RESULTS
351 dogs (M, 119 [33.9%]; S, 232 [66.1%]) were included in the study. Survival time was longer with surgery than medical management (hazard ratio, 4.2; M, 3.4 years; S, 10.9 years). Continued clinical signs at 6 to 12 months after diagnosis were more common with medical management (M, 40% [33/88]; S, 14% [21/155]). Continued medical treatments at 6 to 12 months after diagnosis were more common in the medical management group (M, 78% [69/88]; S, 34% [53/155]). Perioperative mortality rate was 7.3%.

CLINICAL RELEVANCE
Dogs diagnosed at ≥ 5 years of age with EHPSS have significantly better survival times and fewer clinical signs with surgical attenuation, compared with medical management. Older dogs have similar surgical mortality rates to dogs of all ages after surgical EHPSS attenuation.

Congenital extrahepatic portosystemic shunts (EHPSS) are vascular anomalies, resulting from developmental errors in utero creating functional connections between the cardinal and vitelline systems.[1] These anomalous vessels connect the portal system to the systemic circulation, leading to toxin buildup within the body and resulting in a variety of clinical signs primarily affecting the neurologic, uri-

nary, and gastrointestinal systems. Although most dogs with EHPSS are diagnosed within the first 12 months of life,[2] there remains a population of dogs that are diagnosed later in life, either incidentally or due to the delayed development of clinical signs. Specifically, Miniature Schnauzers have been shown to be diagnosed with EHPSS after 7 years of age more often than other breeds.[3] Additionally, dogs with a portoazygous shunt morphology may be older than dogs with a portocaval shunt morphology at the time of diagnosis, which may be due to delayed development of clinical signs secondary to intermittent decreases in shunt fraction.[4] In dogs diagnosed later in life with evidence of portosystemic shunting, it is important to differentiate between a single congenital EHPSS and multiple acquired portosystemic shunts. Multiple acquired portosystemic shunts result from chronic portal hypertension and typically occur secondary to congenital noncirrhotic portal hypertension, hepatic fibrosis, or hepatic arteriovenous malformations.[1] Multiple acquired portosystemic shunts are easily differentiated from congenital EHPSS via imaging or direct visualization in surgery, based on their location in the abdomen, appearance, and the number of anomalous vessels present, as congenital EHPSS tend to be single vessels as compared to the multiple tortuous vessels seen with acquired portosystemic shunts.[1]

Treatment of EHPSS is focused on resolution of clinical signs via medical management or surgical attenuation of the anomalous vessel, resulting in increased blood flow to the liver via the portal system. The goal of medical management of EHPSS is to decrease production or increase elimination of ammonia from the body and to decrease the workload on the liver, resulting in a decrease in the frequency and severity of clinical signs in these patients. This is achieved through administration of lactulose, administration of antimicrobials such as metronidazole that decrease colonic bacterial loads, and diet change to a hepatic support diet. Surgical attenuation of the shunt is typically achieved by either partial or full ligation of the vessel or placement of a gradual occlusion device, such as an ameroid constrictor or thin film band. Gradual occlusion devices allow the portal system more time to adjust to the increased blood flow resulting from closure of the shunt vessel when compared to acute complete vessel ligation, which may result in fewer complications and better overall postoperative outcomes.[1]

It is unknown whether medical or surgical treatment is the best option for the population of dogs diagnosed with EHPSS later in life. Anecdotally, many surgeons are hesitant to perform surgical attenuation of EHPSS in older dogs due to concern for a poor outcome secondary to postoperative complications or decreased capacity to return to normal liver function after attenuation. Dogs over 1 year of age at the time of surgery have been overrepresented for development of postattenuation neurologic dysfunction or seizures or have been found to have a poor postoperative clinical recovery in some studies.[5–9] Additionally, age was found to be a risk factor for development of postattenuation neurologic complications and seizures in a recent study,[10] with odds of developing this complication increasing approximately 1.5 times per year of age. However, in another study evaluating risk factors for postattenuation seizures, age was not found to be a factor.[11] A study focused on clinical outcome after surgical attenuation of EHPSS in dogs over 5 years of age found that surgery resolved clinical signs of liver dysfunction.[12] However, liver function, as determined by serum bile acid concentrations and fasting ammonia levels, did not return to normal in 4 of 9 dogs in which postoperative liver function tests were performed.[12] In another study[13] evaluating dogs of all ages diagnosed with EHPSS, surgical attenuation and medical management were compared, with a focus on long-term survival and quality of life. That study found the survival rate was significantly greater and frequency of clinical signs was lower overall in dogs undergoing surgical treatment, compared with medical management, and that age at the time of diagnosis had no effect on survival; however, the mean age of dogs in that study was only 14 months at the time of diagnosis.[13]

The objective of this study was to determine the outcome in dogs diagnosed with EHPSS at 5 years of age or older treated with medical management only (M) or with surgical attenuation (S). The hypothesis was that dogs undergoing surgical attenuation would have longer survival times after EHPSS diagnosis than dogs undergoing medical management only. A secondary hypothesis was that fewer dogs undergoing surgical attenuation of EHPSS would require medical treatments or have continued clinical signs at 6 to 12 months after diagnosis than dogs undergoing medical management only.

Materials and Methods

Medical records of client-owned dogs definitively diagnosed with EHPSS at ≥ 5 years of age presented to 16 veterinary teaching hospitals between January 2009 and June 2019 were evaluated. Definitive diagnosis of EHPSS was made via imaging by a board-certified radiologist (abdominal ultrasonography, CT angiography [CTA], MRI, or nuclear scintigraphy) or at the time of surgery by a board-certified surgeon. Dogs were included in the surgical attenuation group if they underwent surgical attenuation via gradual occlusion device (ameroid constrictor or thin film banding), ductal occlusion device, partial ligation, or complete ligation. Dogs were included in the medical management group if no surgical attenuation occurred, and they were administered at least 1 medical treatment (lactulose, antimicrobial, antiseizure medication, hepatic support diet) to ameliorate clinical signs related to EHPSS. Data collected included signalment (breed, sex, date of birth, reproductive status), weight at diagnosis, date of EHPSS diagnosis, clinical signs at diagnosis, clinicopathologic data, medical and surgical treatments employed, shunt morphology, clinical signs and medical treatments at 6 to 12 months after diagnosis, clinical signs and medical treatments at time of last follow-up, date of

last follow-up, and date and cause of death (if applicable). Clinical signs at diagnosis were grouped as consistent with hepatic encephalopathy, urinary tract signs, or gastrointestinal signs. Hepatic encephalopathy was defined as historical or current signs of head pressing, seizures, blindness, circling, postprandial lethargy, or abnormal mentation. Historical or current seizure activity was also separately evaluated. Urinary tract signs were defined as historical or current urolithiasis, stranguria, hematuria, or pollakiuria. Gastrointestinal signs were defined as historical or current failure to achieve or maintain appropriate body condition, anorexia, vomiting, or diarrhea.

For dogs undergoing surgical attenuation, anesthesia time was defined as the time from intubation to the time inhalant or IV anesthetic agents were discontinued, and surgical time was defined as the time from the start of the skin incision to the time the skin closure was completed. Hypotension was defined as a mean arterial pressure of < 60 mm Hg or systolic pressure of < 90 mm Hg, measured by means of oscillometric, doppler, or direct arterial methods. Hypothermia was defined as a body temperature < 36.7°C. Postoperative complications were defined as seizures, clinical signs consistent with portal hypertension (combination of signs including but not limited to ascites, diarrhea, abdominal pain, and vomiting), ascites, aspiration pneumonia, hypotension, regurgitation, vomiting, or anorexia occurring in the period from the end of surgery to discharge from the hospital.

Primary care veterinarians and owners were contacted for follow-up via email or telephone. Dogs were considered lost to long-term follow-up if the last available update was greater than 18 months prior to study data analysis and the dog was alive at the time of that follow-up. At the time of follow-up, the following data were obtained: current patient status (alive or dead), current clinical signs, current medical treatments, and date of death (if applicable). Date of last follow-up was defined as the date of death (if applicable) or last contact if alive. Survival time was defined as the number of days from the date of EHPSS diagnosis to the date of death. If the exact date of death was not available, the first day of the month in which death occurred was used as the date of death. Follow-up time was defined as the number of days from the date of EHPSS diagnosis to the date of last follow-up.

Statistical analysis

All analyses were performed by use of commercially available statistical software (SAS version 9.4; SAS Institute). A significance threshold of 0.05 was used. Descriptive data were presented as mean ± SD for normally distributed data and median and interquartile (25th to 75th percentile) range (IQR) for nonnormally distributed data.

Histograms and Q-Q plots were examined to evaluate the assumption of normality. Mann-Whitney U-tests were used for comparisons of numeric variables between groups. Zero-truncated negative binomial regression was used to compare follow-up times between groups. The χ^2 test or Fisher exact tests were used to compare categorical variables between groups, as appropriate.

Kaplan-Meier curves were constructed to estimate survival times. Log-rank tests were utilized to test for effects on survival time. Cox proportional hazards analysis was used to estimate hazard ratios (HRs) and test for effects on survival time. A 2-factor Cox proportional hazards model was performed for each variable with $P < 0.05$ upon univariable analysis. Six possible confounders and variables of interest were identified for an initial multivariable model along with treatment group. The variable with the highest p-value was removed and this process iterated until there were no variables with $P > 0.05$ remaining in the final multivariable model. Logistic regression was used to test for effects on odds of presence of persistent clinical signs and continued need for medical treatments at 6 to 12 months between treatment groups and survival to discharge in the surgical attenuation group. No adjustments for multiple testing were performed as all variables besides treatment group were being evaluated as potential nuisance variables (ie, confounders); therefore, the more cautious strategy was to use unadjusted *P* values.

Results

Three hundred fifty-one dogs (M, 119 [33.9%]; S, 232 [66.1%]) were included in the study. Dogs in the medical management group (8 ± 2 years) were significantly ($P < 0.001$) older than dogs in the surgical attenuation group (7 ± 1 years). Eight (2.3%) sexually intact females, 167 (47.6%) spayed females, 9 (2.6%) sexually intact males, and 167 (47.6%) castrated males were included in the study. There was no significant ($P = 0.770$) difference in sex distribution between the groups. No significant ($P = 0.238$) difference in weight at the time of diagnosis was present between the groups. Thirty-seven breeds were represented, with the Yorkshire Terrier (78/351 [22.2%]), Shih Tzu (59/351 [16.8%]), and Miniature Schnauzer (33/351 [9.4%]) being the most common breeds. Mixed-breed dogs comprised 12% (43/351) of the study population.

Blood urea nitrogen was significantly ($P < 0.012$) higher at the time of diagnosis in the medical management group (median, 8 mg/dL; IQR, 5 to 12 mg/dL) than in the surgical attenuation group (median, 7 mg/dL; IQR, 5 to 9 mg/dL). No significant difference was present between the groups in any other CBC or biochemical panel parameters (Hct, WBC count, neutrophil count, alanine aminotransferase and alkaline phosphatase activities, and concentrations of total bilirubin, total protein, albumin, cholesterol, or glucose levels). No significant difference was present between the groups when preoperative serum bile acid or ammonia levels were compared. More dogs ($P = 0.003$) in the surgical attenuation group (219/232 [94.4%]) exhibited clinical signs related to EHPSS at the time of diagnosis than dogs in the medical management group (101/119 [84.9%]). Dogs in the surgical attenuation group (138/232

[59.5%]) were also more likely (P = 0.002) to have clinical signs related to the urinary tract at the time of EHPSS diagnosis than dogs in the medical management group (50/119 [42.0%]). No significant difference was present between groups regarding the number of dogs exhibiting signs consistent with hepatic encephalopathy (P = 0.664), having seizures (P = 0.529), or signs related to the gastrointestinal tract (P = 0.720) at the time of EHPSS diagnosis.

Abdominal ultrasonography was the most commonly performed imaging modality (290/351 [82.6%]), followed by CTA (126/351 [35.8%]) and nuclear scintigraphy (74/351 [21.1%]). One hundred thirty-six dogs had more than 1 imaging modality performed (38.7%; 79 dogs underwent abdominal ultrasonography and CTA, 54 dogs underwent abdominal ultrasonography and nuclear scintigraphy, and 3 dogs underwent all 3 modalities). EHPSS was confirmed on 148 of 290 (51.0%) abdominal ultrasounds, 126 of 126 (100.0%) CTA studies, and 74 of 74 (100.0%) nuclear scintigraphy studies. EHPSS was diagnosed on abdominal magnetic resonance imaging in 1 dog. Three of 351 (0.85%) diagnoses were confirmed by means of cranial mesenteric arteriography. Twenty-six of 351 (7.4%) diagnoses were confirmed with surgical visualization of the EHPSS only.

At the time of EHPSS diagnosis, levetiracetam was more commonly prescribed (P < 0.001) in dogs in the surgical attenuation group (113/232 [48.7%]) than in the medical management group (21/119 [17.6%]). Administration of lactulose (P = 0.470; M, 92/119 [77.3%]; S, 187/232 [80.6%]), antimicrobials (P = 0.989; M, 83/119 [69.7%]; S, 162/232 [69.8%]), or a hepatic support diet (P = 0.421; M, 91/119 [76.5%]; S, 186/232 [80.2%]) was not different between the groups.

Shunt morphology was available from the imaging report or operative report for 318 of 351 (90.6%) dogs. Portoazygous shunts were present in 115 of 318 (36.2% overall; M, 43/110 [39.1%]; S, 72/208 [34.6%]). Portocaval shunts were present in 203 of 318 (63.8% overall; M, 67/110 [60.1%]; S, 136/208 [65.4%]).

Two hundred thirty-two dogs underwent surgical attenuation. Gradual occlusion devices were used in 225 of 232 (97.0%) dogs, including 164 of 225 (72.9%) ameroid constrictors and 61 of 225 (27.1%) thin film bands. Complete ligation was performed in 4 of 232 (1.7%). Ductal occlusion devices were placed in the remaining 3 of 232 (1.3%). The method of shunt attenuation did not have any impact on survival time or survival to discharge. Postoperative complications occurred in 87 of 232 (37.5%) dogs, including anorexia (62/232 [19.2%]), regurgitation (15/232 [6.5%]), hypotension (14/232 [6.0%]), seizures (9/232 [3.9%]), portal hypertension (7/232 [3.0%]), vomiting (4/232 [1.7%]), aspiration pneumonia (3/232 [1.3%]), and ascites (2/232 [0.9%]). Postoperative seizures occurred in 6 of 119 (5.0%) dogs not receiving levetiracetam preoperatively and 3 of 113 (2.7%) dogs receiving levetiracetam preoperatively. Of the dogs undergoing surgical attenuation, 17 of 232 (7.3%) did not survive to discharge from the hospital. Cause of death or reason for euthanasia in these dogs included postattenuation seizures (n = 5), postattenuation neurologic signs without seizures (3), cardiac arrest with no obvious underlying etiology (3), portal hypertension (2), presence of acquired portosystemic shunts found intraoperatively (1), intravascular hemolysis and severe anemia (1), aspiration pneumonia requiring mechanical ventilation (1), and unresponsive hypotension (1). Factors impacting survival to discharge in dogs undergoing surgical attenuation included increased anesthesia time (P = 0.005; OR, 0.5; 95% CI, 0.3 to 0.8), increased surgical time (P = 0.006; OR, 0.4; 95% CI, 0.2 to 0.7), longer duration of hypotension (P = 0.001; OR, 0.2; 95% CI, 0.1 to 0.5), longer duration of hypothermia (P = 0.012; OR, 0.5; 95% CI, 0.3 to 0.9), occurrence of any postoperative complication (P < 0.001; OR, 0.1; 95% CI, 0.0 to 0.2), postoperative seizures (P < 0.001; OR, 0.03; 95% CI, 0.0 to 0.11), postoperative portal hypertension (P < 0.001; OR, 0.02; 95% CI, 0.0 to 0.12), postoperative ascites (P = 0.001; OR, 0.01; 95% CI, 0.0 to 0.19), postoperative aspiration pneumonia (P < 0.001; OR, 0.01; 95% CI, 0.0 to 0.11), and postoperative hypotension (P < 0.001; OR, 0.05; 95% CI, 0.01 to 0.16). For animals that survived to discharge, the mean time to discharge was 2.4 ± 1 days postoperatively.

Follow-up at 6 to 12 months after diagnosis was available for 243 of 351 (69.2%) dogs (M, 88/119 [73.9%]; S, 155/232 [66.8%]). Persistent clinical signs related to EHPSS at 6 to 12 months after diagnosis were more common (P < 0.001; OR, 4.2; 95% CI, 2.2 to 8.1) in the medical management group (33/88 [40%]) when compared to the surgical attenuation group (21/155 [14%]). Continued medical treatments at 6 to 12 months after diagnosis were required more frequently (P < 0.001; OR, 9.5; 95% CI, 5.0 to 19.0) in the medical management group (69/88 [78%]) than in the surgical attenuation group (53/155 [34%]). Regarding only dogs undergoing surgical management, persistent clinical signs at 6 to 12 months after diagnosis were present in 7 of 101 (6.9%) dogs undergoing surgical attenuation with an ameroid constrictor, 13 of 46 (28.3%) dogs undergoing thin film banding, 1 of 3 (33.3%) dogs undergoing complete ligation, and 0 of 2 dogs undergoing other occlusion methods. Continued medical management at 6 to 12 months was required in 27 of 101 (26.7%) dogs undergoing surgical attenuation with an ameroid constrictor, 25 of 46 (54.3%) dogs undergoing thin film banding, 1 of 3 (33.3%) dogs undergoing complete ligation, and 0 of 2 dogs undergoing other occlusion methods.

Long-term follow-up was available for 201 of 351 dogs (57.3%; M, 92/119 [77.3%]; S, 109/232 [47.0%]). Follow-up time was not significantly different (P = 0.490) between groups (571 ± 952 days [range, 1 to 2,643 days; M] vs 537 ± 1,573 days [range, 1 to 3,962 days; S]). At study end, 149 of 201 (74.1%) dogs were deceased (M, 82/92 [89.1%]; S, 67/109 [61.5%]). Of the deceased dogs, 64 of 149 (43.0%; M, 41/82 [50.0%]; S, 23/67 [34.3%]) died of EHPSS-related causes, 55 (36.9%; M, 23/82 [28.0%]; S, 32/67 [47.8%]) died of non-EHPSS–related causes, and the cause of death was unknown for 30 (20.1%; M, 18/82 [22.0%]; S, 12/67 [17.9%]). Of the alive dogs, 20% (2/10; M) and 9.5% (4/42; S) had clinical

signs related to EHPSS, and 70% (7/10; M) and 33.3% (14/42; S) remained on medical management for EHPSS at the time of long-term follow-up.

Overall median survival time was 7.2 years. Cumulative probability of survival was higher ($P < 0.001$; HR, 4.2; 95% CI, 2.7 to 6.6) with surgical attenuation (10.9 years) than medical management (3.4 years; **Figure 1**). The probability of surviving to 1, 3, and 5

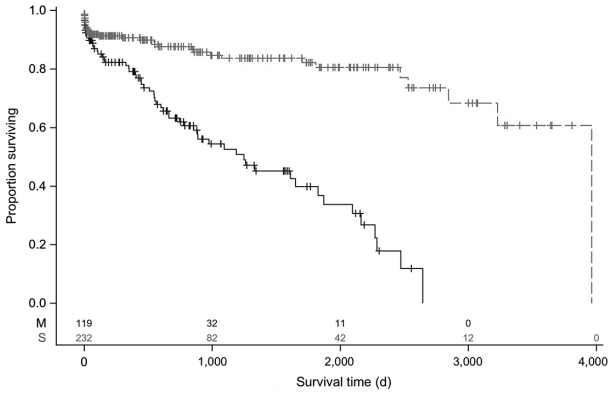

Figure 1—Kaplan-Meier curve of survival time from the date of diagnosis with congenital extrahepatic portosystemic shunt at ≥ 5 years of age to the date of death for 351 dogs treated with medical management (group M [solid line]; n = 119) versus surgical attenuation (group S [dashed line]; 232) at any of 16 participating veterinary teaching hospitals between January 2009 and June 2019. Tick marks indicate censored dogs; steps represent the death of ≥ 1 dog. Cumulative probability of survival was significantly ($P < 0.001$) higher for dogs in group S (median, 3,962 days; 95% CI, 3,228 to 3,962 days) than in group M (median, 1,248 days; 95% CI, 783 to 1,827 days).

years after diagnosis was 79 ± 4%, 53 ± 6%, and 40 ± 6% in the medical management group and 91 ± 2%, 84 ± 3%, and 81 ± 4% in the surgical attenuation group, respectively. Additional factors beyond treatment group negatively affecting survival time in a multivariable model were presence of hepatic encephalopathy at the time of EHPSS diagnosis ($P < 0.001$; HR, 2.3; 95% CI, 1.5 to 3.5) and a higher neutrophil count at the time of EHPSS diagnosis ($P < 0.001$; HR, 1.05 for each increase of 1,000 cells/µL; 95% CI, 1.02 to 1.07 for each increase of 1,000 cells/µL).

Discussion

The results of the present study indicated that surgical management of EHPSS in dogs diagnosed at ≥ 5 years of age led to longer survival times, decreased clinical signs, and reduced need for medical treatments at 6 to 12 months after diagnosis compared to dogs undergoing medical management only. The hypotheses were accepted on the basis of these results. Additionally, the presence of hepatic encephalopathy at the time of EHPSS diagnosis and higher neutrophil counts at diagnosis appeared to have a negative impact on survival time regardless of treatment group.

The results of this study were consistent with previously published findings, which reported that dogs of all ages diagnosed with EHPSS and undergoing surgical attenuation had a significantly higher survival rate compared to dogs undergoing only medical management with an HR of 8.1.[13] In the present study, surgical attenuation also resulted in a longer survival time; however, the HR in our study was lower at 4.2. The findings indicated that, in older dogs diagnosed with EHPSS, the difference in death rate between dogs receiving only medical management compared to dogs undergoing surgical attenuation may not be as pronounced as that in younger dogs diagnosed with EHPSS. Survival times for dogs undergoing medical management only were similar between the present study and the previous study (3.4 years vs 2.3 years).[13]

Although treatment group categorization (medical management or surgical attenuation) had the highest impact on overall survival time, both the presence of hepatic encephalopathy signs and higher neutrophil counts at the time of diagnosis were also found to decrease overall survival time in the multivariable model. Age at diagnosis had no impact on overall survival time in this population. Higher leukocyte counts have been found to decrease the likelihood of a successful overall outcome after EHPSS surgery[5]; however, higher leukocyte counts were also found to be associated with an increased probability of overall survival in dogs undergoing ameroid ring constrictor placement for EHPSS attenuation in another study.[14] In a study[15] specifically focused on leukocytosis, portal vein partial oxygen tension, and portal bacteremia in dogs with single congenital portosystemic shunts, leukocytosis was not found to be associated with morbidity or death. Prior studies have shown that increased WBC counts in dogs with EHPSS may be associated with poor clearance of bacteria or hepatic endotoxin from portal circulation or due to impaired reticuloendothelial function.[15,16] These conflicting results make it challenging to know the importance of higher leukocyte or neutrophil counts in EHPSS cases and how that may affect outcome or survival. A prospective study evaluating the impact of leukocyte and neutrophil counts may help to determine the true impact of these findings on outcome of dogs with EHPSS.

The presence of hepatic encephalopathy at diagnosis was associated with decreased overall survival time in this study. Preoperative hepatic encephalopathy has been previously associated with development of postattenuation neurologic signs and postoperative seizures.[10] In another study, preoperative neurologic signs were not found to be associated with decreased short-term survival or an unsatisfactory long-term outcome.[5] Interestingly, inflammation is noted to be an important potentiator of hepatic encephalopathy in human medicine.[17] It has been found that administration of nonsteroidal anti-inflammatory medications improved learning ability in rats with experimentally induced hepatic encephalopathy.[18] Additionally, dogs with congenital portosystemic shunts that are exhibiting signs of hepatic encephalopathy have increased C-reactive protein levels.[19] This link between inflammation and hepatic encephalopathy may explain the find-

ing that both neutrophilia and the presence of hepatic encephalopathy led to decreased survival times in this study population. Additionally, as the dogs in the study reported here were older at the time of EHPSS diagnosis, their central nervous system was potentially subjected to toxins causing signs of hepatic encephalopathy for a longer period of time than dogs diagnosed at a younger age. It was possible that chronic hepatic encephalopathy and exposure to toxins may have led to irreversible neurologic changes that decreased overall survival time. Although acute hepatic encephalopathy leads to severe astrocyte swelling resulting in increased intracranial pressure, chronic hepatic encephalopathy, as is seen with many dogs with EHPSS, results in development of Alzheimer type II astrocytes, which still develop swelling but with less acute sequelae.[20] Further research is necessary in this area.

In this study, 36.2% of dogs had a portoazygous shunt as compared to 23.6% to 36% in prior studies of dogs of all ages with EHPSS.[4,13,14,21,22] Interestingly, specifically regarding dogs 5 years of age or older diagnosed with EHPSS, 46.7% of dogs in another study[12] had a portoazygous shunt morphology. In 1 study,[4] a significant difference in age at first diagnosis was noted when dogs with portoazygous shunts were compared to dogs with portocaval shunts. Dogs with portocaval shunts were diagnosed at a mean age of 12.3 months whereas dogs with portoazygous shunts were first diagnosed at a mean age of 32.3 months in that study.[4] It has been previously proposed that dogs with portoazygous shunts have milder clinical signs due to intermittent shunt vessel occlusion during gastric distension after eating or compression of the shunt at the diaphragm during normal respiration.[23] These reported milder clinical signs could explain why dogs diagnosed later in life may be more likely to have portoazygous shunts than the general population of dogs with EHPSS.

In this study, 7.3% of dogs that underwent surgical attenuation did not survive to discharge. This was consistent with the perioperative mortality rate of 2% to 7.9% reported after EHPSS attenuation in recent studies[5,14,21,24–26] focused on outcome with gradual attenuation devices. Additionally, the rate of postattenuation seizures of 3.9% in the surgical attenuation group in this study was comparable to postattenuation seizure rates in recent studies of dogs of all ages, ranging from 3.3% to 8.0%.[5,10,27–29] The similarity between these results in dogs of all ages with EHPSS and the population of dogs in the present study indicated that dogs that are older at the time of EHPSS diagnosis are not at an increased risk of death or postattenuation seizures in the immediate postoperative period after surgical EHPSS attenuation. This information was in direct contrast to studies indicating that age at the time of surgical attenuation leads to poor clinical outcomes or increased risk of postattenuation neurologic complications.[6,10] Based on the results presented here representing data from a large number of dogs, it is indicated to consider surgical attenuation of EHPSS in dogs of all ages to provide the best possible survival time and long-term outcome for these patients.

Factors associated with perioperative death in the present study included anesthesia and surgery time, duration of hypotension and hypothermia, and occurrence of postoperative complications. Postoperative complications, specifically seizures and abdominal distension, were also found to be associated with perioperative death in a previous study.[5] In that study, higher leukocyte counts were also associated with perioperative mortality[5]; however, although higher neutrophil counts were associated with decreased long-term survival overall in this study, there was not a specific association with perioperative death. As there were not enough perioperative deaths in the present study to allow for multivariable analysis, it is possible that some of the factors found to be significantly associated with survival to discharge may be related to one another and are not a significant factor on their own. For example, it may be that increased anesthesia or surgical time led to increased durations of hypothermia or hypotension. In any case, efforts should be made to safely minimize anesthesia and surgical time when possible and to prevent hypotension and hypothermia intraoperatively to limit potential negative outcomes.

The type of gradual occlusion device used for EHPSS attenuation and the use of preoperative levetiracetam were not associated with survival to discharge or with overall survival time. This outcome with different gradual occlusion devices was consistent with recent studies finding no difference in long-term outcome when comparing ameroid ring constrictor or thin film band placement.[21,24,26] Additionally, recent studies have also shown no effect of preoperative levetiracetam administration on development of postoperative seizures in dogs undergoing surgical attenuation.[10,27,29] Although we evaluated the effect of levetiracetam administration on survival to discharge after surgery and on long-term survival time, we did not directly evaluate the implication of levetiracetam administration on seizure risk in this population.

The main limitation of this study was its retrospective nature, which highlighted the possibility that not all medical records were complete. Due to this, it was not possible to determine the reason some dogs underwent medical management only rather than surgical attenuation. These management outcomes are impacted by owners' decisions whether to pursue medical management or surgery and are likely based on financial considerations as well as perceived quality of life. These dogs were also treated at 16 different veterinary medical hospitals with different procedures and protocols, which may have affected the results. Additionally, long-term follow-up was not available for every dog that met the inclusion criteria, which also may have biased the results to include patients with persistent clinical signs or less-than-ideal outcomes.

In conclusion, dogs diagnosed with EHPSS at ≥ 5 years of age have significantly longer survival times, decreased clinical signs, and decreased need for medical treatments with surgical attenuation compared to medical management alone. The results of this study refuted findings of prior studies that indicate older dogs have poor clinical outcomes or increased risk of neurologic complications with surgical attenuation.[6,10] For this reason, surgical attenuation should be considered as an option in all cases

in which general anesthesia and surgery are considered safe and appropriate for the dog. The presence of hepatic encephalopathy signs or higher neutrophil counts at diagnosis may decrease the chances of long-term survival. Further research is needed to understand the reason behind the impact of these factors on survival time in these cases.

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