

Insertion site of congenital extrahepatic portosystemic shunts influences clinicopathological findings in dogs

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Objective

Determine the influence of insertion site of extrahepatic portosystemic shunts (EHPSS) on clinicopathological findings in dogs.

Methods

A retrospective study was performed in dogs diagnosed with an EHPSS. Cases were eligible if EHPSS morphology was categorized as portoazygos (PA) shunts, portocaval (PC) shunts entering the prehepatic caudal vena cava at the level of the omental foramen, or portophrenic (PP) shunts. Furthermore, completed standardized questionnaires on clinical signs at diagnosis had to be available. Signalment, clinical scores, and findings on blood analyses and medical imaging were determined and statistically analyzed.

Results

Data of 104 dogs (15 PA, 70 PC, and 19 PP shunts) were included. Dogs with PC shunts were significantly younger than dogs with PA and PP shunts. Furthermore, dogs with PC shunts had a significantly lower body condition score and a significantly worse clinical score compared to dogs with PP shunts. Microcytosis and monocytosis were more pronounced in dogs with PC shunts compared to those with PP shunts. Finally, urea and creatinine concentrations were significantly lower and preprandial serum bile acids and fasted ammonia concentrations were significantly higher in dogs with PC shunts than in those with PP shunts.

Conclusions

Dogs with PC shunts are more likely to be presented at an earlier age, with more severe clinical signs and more distinct abnormalities in blood parameters compared to dogs with PP shunts.

Clinical Relevance

In older dogs with less distinct clinical signs suspected of having an EHPSS, screening for a PP shunt, which is more difficult to diagnose with ultrasonography, is recommended.

Keywords: EHPSS, hepatology, insertion site, canine, congenital

An extrahepatic portosystemic shunt (EHPSS) is an abnormal congenital vessel that typically consists of a single blood vessel that connects a tributary of the extrahepatic portal vein (PV) to the systemic circulation.¹ Consequently, blood coming from the gastrointestinal tract bypasses the liver, which cannot fulfill its function, leading to the release of various toxic metabolic compounds in the systemic circulation.² Dogs with an EHPSS can therefore show a large variety of clinical signs such

as neurological signs, urinary tract signs, gastrointestinal signs, and growth retardation.³

Different anatomical types of EHPSS have been described, and nomenclature of different types has often been focused on the originating vein.⁴⁻⁷ As proposed nomenclature is often cumbersome, the use of an anatomical-based nomenclature was recently proposed in a large retrospective study⁸ including 1,082 CT angiography (CTA) scans of dogs with EHPSSs. It has been stated that blood draining from the stomach typically contains less ammonia because it is mainly produced in the colon and small intestines and, hence, causes fewer clinical signs.⁹ Nevertheless, it has been hypothesized that all dogs with an EHPSS have hepatofugal flow in the extrahepatic PV, causing the majority of the portal blood to flow to the systemic circulation, irrespective of the portal tributaries involved

Received August 31, 2024

Accepted January 19, 2025

Published online February 21, 2025

doi.org/10.2460/javma.24.08.0541

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in the EHPSS.¹⁰ Recent studies^{8,11-18} suggest that the insertion of EHPSSs in the systemic circulation rather than the EHPSS origin influences the severity of clinical signs. The most common insertion sites of EHPSSs are the prehepatic caudal vena cava at the level of the omental foramen (portocaval [PC] shunts) occurring in 47.0% of dogs, the left phrenic vein (portophrenic [PP] shunts) in 31.4% of dogs, and the azygos vein (portoazygos [PA] shunts) in 21.1% of dogs.⁸ In the majority of PA shunts, the blood vessel runs through the esophageal hiatus, after which it enters in the thoracic part of the azygos vein,¹⁹ whereas PP shunts run within the diaphragm prior to draining into the posthepatic caudal vena cava.²⁰ By running through or within the diaphragm, the respiration cycle might influence the diameter of the EHPSS, which might on its turn have an impact on the amount of blood that flows through the EHPSS.^{8,11-18} Alongside the respiratory cycle, food boluses passing the gastroesophageal junction and dilatation of the stomach might influence the diameter of these types of EHPSS.¹⁴ Results of previous studies^{8,11-18} suggest a correlation between the morphological type of EHPSS and clinicopathological findings. In a case series, 3 out of 4 dogs that presented with hepatic encephalopathy at an older age had a PA shunt,¹¹ which was confirmed in larger retrospective studies, in which dogs with PA shunts were significantly older than those with PC shunts.^{12,14,17} Contrarily, in another retrospective study¹⁸ including 351 dogs diagnosed with EHPSSs at ≥ 5 years of age, only 36.2% of cases were diagnosed with a PA shunt, whereas the remainder were diagnosed with a PC shunt. As PP shunts enter the posthepatic caudal vena cava via the phrenic vein, PP shunts were likely classified as PC shunts, making it difficult to interpret these findings. In a large retrospective study⁸ assessing CTA images, it was found that both dogs with PA shunts and those with PP shunts were older at time of the CTA scan compared to dogs with PC shunts and that the latter dogs had also lower subjective portal perfusion scores, suggesting that more portal blood directly enters the systemic circulation. In addition, a retrospective study¹³ found that clinical signs were present in a significantly larger proportion of dogs with PC shunts (29 of 32 dogs), compared to those with PA and PP shunts (14 of 21 dogs, of which 12 had PA and 9 had PP shunts). Furthermore, that study demonstrated that dogs with PC shunts had significantly lower albumin concentrations compared to dogs with PA shunts.

The aim of the present retrospective study was to investigate the influence of the insertion of EHPSSs on the clinicopathological findings at time of diagnosis in a large cohort of dogs. It was hypothesized that dogs with PC shunts would be younger and would have more severe clinical signs and more severe abnormalities in blood parameters compared to dogs with PA or PP shunts.

Methods

Study population

Data of all dogs that were diagnosed with EHPSSs at the Veterinary Teaching Hospital of Ghent

University, Belgium, between January 2011 and June 2023 were retrospectively collected. During this period, several prospective studies were performed in dogs with EHPSSs, for which owners were asked to complete a standardized questionnaire on clinical signs at different moments in time. All dogs for which such a questionnaire was completed at the time of diagnosis were included. Furthermore, EHPSS morphology had to be accurate, based on diagnostic imaging and/or description in the surgical report, and had to fit in 1 of the 3 following categories: PA shunt, with the blood vessel entering the thoracic cavity before connecting to the azygos vein; PC shunt, with the blood vessel entering the caudal vena cava at the level of the omental foramen; or PP shunt. Dogs that underwent a previous EHPSS surgery were excluded. Only data available at time of diagnosis were included in this study.

Signalment

From all dogs, breed, age, sex, body weight, and body condition score (BCS) were noted. Since 2014, BCS has been scored on a scale from 1 to 9 and no longer on a scale from 1 to 5.²¹ The BCS was only included for dogs in which it was scored on a scale of 9, with a score of 4 and 5 corresponding to an ideal body weight.

Clinical signs

To quantify the severity of clinical signs, a clinical score, based on a previously published scoring system, was calculated for each dog.²² Briefly, clinical signs that occurred often were assigned 2 points, and those that occurred occasionally were assigned 1 point. Furthermore, depending on the type of complaints, some were multiplied. Gastrointestinal signs (hypersalivation, hyporexia, weight loss, vomiting, diarrhea, melena, and hematochezia) and urinary signs (hematuria, stranguria, dysuria, and pain while urinating) were not multiplied. Neurological signs (lethargy, unresponsiveness, disorientation, circling, head pressing, ataxia, and blindness) were multiplied by 2, and seizure activity and coma were multiplied by 3 (maximum possible score of 62).

The presence of muscle tremors, although noted, was not included in the clinical score, as this parameter had only been added to the standardized questionnaire in 2020. Yet it was recorded separately.

Blood analyses

Blood analyses were performed in different laboratories, and some of the reference ranges changed over time. To be able to compare all obtained data, a ratio was calculated for all blood values, as previously published.²³ A ratio of the value over the lower limit was used for blood parameters that are typically decreased in dogs with EHPSSs (Hct, MCV, albumin, glucose, total protein, and urea), whereas a ratio of the value over the upper limit was used for blood parameters that are typically increased in dogs with EHPSSs or those only having an upper reference limit (inflammatory cells, fasted ammonia, creatinine, liver enzymes, and serum bile acids).

Diagnostic imaging

The medical imaging techniques used to diagnose EHPSSs were noted if these were performed at the Veterinary Teaching Hospital of Ghent University. In dogs in which trans-splenic portal scintigraphy (TSPS) was performed, the shunt fraction (ie, a quantitative representation of the amount of portal blood flow bypassing the liver) was noted. Commonly reported secondary findings of EHPSSs that could be objectively measured were assessed. The presence of renomegaly was assessed by collecting sagittal measurements of the kidneys based on ultrasonography. In dogs that underwent CTA, the images were reviewed to measure the length of the L2 vertebral body (L2) and the renal length (RL), following which an RL:L2 ratio was calculated, as previously published.²⁴ The PV-to-aorta (Ao) ratio was measured; however, only data obtained from CTA images were retained for analysis, as it was not consistently determined on ultrasonography.

Urolithiasis

The presence of urolithiasis was determined with a combination of different methods. Dogs with a history of urolithiasis were listed as dogs with urolithiasis, irrespective of the presence of uroliths at time of diagnosis of EHPSSs. Furthermore, dogs that had uroliths based on ultrasonography (defined as hyperechoic structures in the urinary tract causing acoustic shadowing) or CTA were also listed as dogs with urolithiasis.

Statistical analysis

Statistical analyses were performed with SPSS Statistics 28 (IBM). Normality of variables was assessed with Shapiro-Wilk tests. Parametric data are presented as mean $\pm$ SD, whereas nonparametric data are presented as median (range). Differences in parameters between different groups were assessed with 1-way ANOVA tests for parametric data, whereas Kruskal-Wallis tests were used for nonparametric data. Multiple comparison tests were always performed with Bonferroni correction in case statistical differences were present. To assess renal size, the mean size of the left and right kidneys based on ultrasonography and the mean RL:L2 ratio of the left and right kidneys based on CTA were used for statistical analyses. Results were considered statistically significant if *P* values were $< .05$.

Results

Study population

An initial screening of the database resulted in 170 cases of EHPSSs, from which 66 dogs were excluded for various reasons: 22 because of uncertain EHPSS type, 4 because of unsuitable EHPSS type, 2 because of previous EHPSS surgery, and 38 because of no questionnaire being available. The remaining group consisted of 15 dogs with a PA shunt, 70 dogs with a PC shunt, and 19 dogs with a PP shunt. In 98 dogs, EHPSS morphology was based on diagnostic imaging and confirmed during surgery. In 4 dogs, EHPSS morphology was solely based on ultrasonography with dynamic

images confirming the presence of a PC shunt in all dogs. Finally, in 2 dogs, only CTA was performed, revealing a PA shunt.

Signalment

Dogs of 25 different breeds were included (**Table 1**). At diagnosis, the median age for dogs

Table 1—Distribution of morphological extrahepatic portosystemic shunt types across the different dog breeds in this study.

Breed	Total	PA shunt	PC shunt	PP shunt
Basset fauve de Bretagne	1		1	
Bichon Frise	5		5	
Bolanka Zwetna	1		1	
Border Collie	2		2	
Chihuahua	5	2	2	1
Collie	1		1	
Crossbreed	6	1	4	1
Dachshund	10	2	8	
Englisch Bulldog	1		1	
Hannover Hound	1		1	
Havanese	3		3	
Italian Greyhound	1		1	
Jack Russell Terrier	3	1	2	
Maltese	17		17	
Miniature Dachshund	2		2	
Miniature Pinscher	4		4	
Miniature Schnauzer	7	1	1	5
Norwich Terrier	1	1		
Papillon	2		1	1
Pug	4	1	2	1
Shih Tzu	3	1	1	1
Small Munsterlander	1			1
Standard Schnauzer	1			1
West Highland White Terrier	2		2	
Yorkshire Terrier	20	5	8	7

PA = Portoazygos. PC = Portocaval. PP = Portophrenic.

with PA, PC, and PP shunts was respectively 850 days (range, 121 to 3,555 days), 215 days (range, 79 to 3,190 days), and 635 days (range, 240 to 2,645 days). Dogs with a PC shunt were significantly younger compared to dogs with a PA or PP shunt (*P* = .005 and .001, respectively). For each EHPSS morphologic type, the distribution of sex approximated a fifty-fifty partition, resulting in no significant relationship between sex and EHPSS morphology (*P* = .916; **Table 2**). The median body

Table 2—Distribution of sex per morphological extrahepatic portosystemic shunt (EHPSS) type.

EHPSS type	n	Male	Female
PA shunt	15	7 (2 neutered)	8 (3 neutered)
PC shunt	70	36 (7 neutered)	34 (8 neutered)
PP shunt	19	9 (4 neutered)	10 (9 neutered)

weight was 3.3 kg (range, 1.5 to 8.8 kg) for dogs with a PA shunt, 3.1 kg (range, 1.0 to 16.0 kg) for those with a PC shunt, and 6.3 kg (range, 1.2 to 29.3 kg) for dogs with a PP shunt, which was not significantly different between the EHPSS types

($P = .075$). A 9-point scale BCS was available for 97 dogs, of which 14 had a PA shunt, 66 a PC shunt, and 17 a PP shunt. The median BCS for dogs with PA, PC, and PP shunts was respectively 4 (range, 2 to 6), 3 (range, 1 to 5) and 4 (range, 3 to 7) out of 9. Pairwise comparisons showed a significant difference between PC and PP shunts ($P < .001$).

Clinical signs

Median clinical scores of dogs with PA, PC, and PP were 14 (range, 4 to 32), 17 (range, 0 to 46), and 7 (range, 0 to 22), respectively. A significant difference in clinical scores was found between dogs with PC and PP shunts ($P < .001$; **Table 3**), meaning that dogs with a PC shunt showed more severe clinical signs at presentation. No differences were found in clinical scores

for gastrointestinal and urinary signs between the different EHPSS types, but neurological scores were significantly higher in dogs with PC shunts compared to those with PP shunts ($P < .001$). Muscle tremors were noticed in 3 of 7 dogs with a PA shunt (in 1 dog often and in 2 dogs rarely), in 9 of 13 dogs with a PC shunt (often in 5 dogs, rarely in 4 dogs), and in 3 of 6 dogs with a PP shunt (often in 2 dogs and rarely in 1 dog). All but 2 dogs had clinical signs suggestive of the presence of an EHPSS at time of diagnosis. In 1 dog with a PC shunt that had a clinical score of 0 at time of diagnosis a full blood analysis was performed by the referring veterinarian, as the dog was often trembling, was eating less, and had weight loss. The dog was reported to be much more active, to have much better appetite, and to have less polyuria/polydipsia following

Table 3—Median (range) of clinical scores in dogs with different morphological EHPSS types.

Clinical signs	PA shunt	PC shunt	PP shunt	<i>P</i> value
Gastrointestinal signs	4 (0–8)	4 (0–12)	4 (0–7)	.182
Urinary signs	0 (0–8)	0 (0–8)	0 (0–6)	.237
Neurological signs	8 (0–28)	11 (0–40)	4 (0–16)	< .001
Total clinical score	14 (4–32)	17 (0–46)	7 (0–22)	< .001

Presented *P* values refer to differences between the 3 EHPSS types. Differences following multiple comparison testing are presented within the text.

Table 4—Differences in results of hematology between the morphological EHPSS types.

Hematology	<i>n</i>	Mean $\pm$ SD or median (range)	<i>n</i> above upper limit ref	<i>n</i> under lower limit ref	<i>P</i> value
Hct					.467
PA shunt	13	1.12 $\pm$ 0.21	0	4	
PC shunt	69	1.06 $\pm$ 0.25	1	29	
PP shunt	19	1.13 $\pm$ 0.21	0	4	
MCV					.011
PA shunt	13	0.99 (0.86–1.18)	0	7	
PC shunt	69	0.97 (0.78–1.18)	0	44	
PP shunt	19	1.05 (0.89–1.32)	1	5	
Leukocytes					.854
PA shunt	12	0.87 (0.42–2.18)	4	0	
PC shunt	69	0.85 (0.25–2.14)	23	1	
PP shunt	19	0.86 (0.44–2.69)	5	0	
Basophils					.620
PA shunt	12	0.50 (0.10–2.00)	1	0	
PC shunt	67	0.30 (0.00–3.21)	8	0	
PP shunt	17	0.32 (0.00–1.20)	2	0	
Eosinophils					.976
PA shunt	12	0.28 (0.01–0.99)	0	1	
PC shunt	67	0.32 (0.00–1.39)	3	6	
PP shunt	18	0.27 (0.02–0.99)	0	3	
Lymphocytes					.368
PA shunt	12	0.50 (0.26–1.08)	2	0	
PC shunt	69	0.63 (0.18–1.63)	9	1	
PP shunt	18	0.59 (0.25–1.11)	1	0	
Monocytes					.015
PA shunt	12	0.89 (0.26–3.90)	4	0	
PC shunt	68	1.03 (0.12–6.31)	37	0	
PP shunt	18	0.54 (0.15–1.82)	5	0	
Neutrophils					.785
PA shunt	12	0.82 (0.30–2.59)	4	0	
PC shunt	67	0.76 (0.11–2.28)	16	2	
PP shunt	18	0.82 (0.22–2.32)	5	1	

Presented values are ratios of actual value over the lower limit (Hct and MCV) or higher limit (inflammatory cells). Presented *P* values refer to differences between the 3 EHPSS types. Differences following multiple comparison testing are presented within the text.

ref = Reference interval.

treatment for EHPSSs. One dog with a PP shunt that had a clinical score of 0 at time of diagnosis was screened for the presence of an EHPSS, as one of its siblings was diagnosed with an EHPSS. No changes in clinical signs were noticed following treatment for EHPSSs.

Blood analyses

Results of hematology and biochemistry are presented in **Tables 4 and 5**. Hematology revealed that dogs with a PC shunt had more severe microcytosis ($P = .008$) as well as monocytosis ($P = .012$) compared to dogs with a PP shunt. Biochemistry indicated that ALP was significantly more increased in dogs with a PC shunt compared to those with a PA shunt ($P = .037$). Dogs with a PC shunt had higher fasted ammonia ($P = .002$) and preprandial bile acid concentrations ($P = .046$) compared to dogs with a PP shunt, but lower concentrations of urea ($P < .001$) and creatinine ($P = .002$). A significant difference in

albumin was found between groups ($P = .039$); however, following pairwise comparisons, there were no significant differences between the different groups.

Diagnostic imaging

Diagnostic imaging was performed in-house in 96 dogs. In 53 dogs, ultrasonography was the only diagnostic imaging technique used to diagnose the EHPSS. Ultrasonography was combined with TSPS in 16 dogs and with a CTA in another 15 dogs. In 5 dogs, all 3 diagnostic imaging techniques were performed. Six dogs only underwent TSPS and, in 1 dog, only CTA was performed.

Based on the TSPS, the median shunt fraction was 92% (range, 82% to 98%) for dogs with a PA shunt ($n = 5$), 92% (range, 71% to 99%) for dogs with a PC shunt (16), and 93% (range, 82% to 98%) for dogs with a PP shunt (6). No significant difference was found between the EHPSS types and shunt fraction ($P = .994$).

Table 5—Differences in results of biochemistry between the morphological EHPSS types.

Biochemistry	n	Mean $\pm$ SD or median (range)	n above upper limit ref	n under lower limit ref	P value
Albumin					.039
PA shunt	14	1.30 (0.97–1.57)	0	1	
PC shunt	62	1.14 (0.48–1.68)	1	11	
PP shunt	16	1.31 (0.28–1.91)	1	3	
ALP					.007
PA shunt	13	0.44 (0.06–2.04)	4	0	
PC shunt	64	1.14 (0.09–9.12)	34	0	
PP shunt	18	0.68 (0.19–1.68)	5	0	
ALT					.192
PA shunt	13	1.40 (0.15–4.57)	8	0	
PC shunt	64	1.74 (0.23–18.89)	49	0	
PP shunt	18	1.33 (0.27–4.49)	10	0	
Creatinine					.003
PA shunt	11	0.34 (0.21–0.67)	0	3	
PC shunt	66	0.32 (0.08–2.26)	2	25	
PP shunt	18	0.57 (0.22–2.89)	3	1	
Glucose					.440
PA shunt	10	1.43 (1.13–2.00)	1	0	
PC shunt	62	1.30 (0.68–3.54)	5	7	
PP shunt	16	1.45 (0.91–4.73)	1	1	
Total protein					.112
PA shunt	13	1.09 $\pm$ 0.18	0	4	
PC shunt	64	1.00 $\pm$ 0.18	0	27	
PP shunt	18	1.08 $\pm$ 0.21	0	5	
Urea					< .001
PA shunt	12	1.35 (0.88–5.72)	0	2	
PC shunt	66	1.20 (0.32–7.23)	1	20	
PP shunt	17	3.03 (1.08–8.63)	3	0	
Fasted ammonia					< .001
PA shunt	15	1.47 (0.47–5.47)	11	0	
PC shunt	67	3.13 (0.40–11.11)	62	0	
PP shunt	19	1.07 (0.05–11.11)	11	0	
Preprandial bile acids					.016
PA shunt	11	4.88 (0.74–26.40)	10	0	
PC shunt	58	9.47 (1.20–33.95)	58	0	
PP shunt	18	5.43 (0.28–25.82)	16	0	
Postprandial bile acids					.515
PA shunt	5	7.27 (4.23–17.37)	5	0	
PC shunt	24	6.03 (1.57–21.87)	24	0	
PP shunt	14	6.28 (1.54–12.11)	13	0	

Presented values are ratios of actual value over the lower limit (albumin, glucose, total protein, and urea) or higher limit (liver enzymes, creatinine, fasted ammonia, and serum bile acids). Presented P values refer to differences between the 3 EHPSS types. Differences following multiple comparison testing are presented within the text.

For dogs with PA ($n = 12$), PC (62), and PP (12) shunts, the median kidney lengths on ultrasonography were 4.3 cm (range, 3.3 to 5.3 cm), 4.4 cm (range, 3.1 to 7.7 cm), and 4.5 cm (range, 3.5 to 6.4 cm) respectively, which were not significantly different between groups ($P = .606$). Images of CTA were available for review in 20 dogs (5, 10, and 5 dogs with a PA, PC, and PP shunt, respectively). Median RL:L2 ratio was 2.8 (range, 2.4 to 3.9) for dogs with a PA shunt, 3.0 (range, 2.2 to 3.5) for dogs with a PC shunt, and 3.0 (range, 2.6 to 3.3) for dogs with a PP shunt. No significant difference was present between RL:L2 ratio and EHPSS types ($P = .999$). The median PV:Ao ratio was 0.7 (range, 0.5 to 1.0) for dogs with a PA shunt, 0.8 (range, 0.5 to 1.2) for dogs with a PC shunt, and 0.9 (range, 0.7 to 0.9) for dogs with a PP shunt, which was also not significantly different between groups ($P = .516$). In 2 of 5 dogs with a PA shunt and 3 of 10 dogs with a PC shunt, the PV:Ao ratio was ≤ 0.65 , whereas the PV:Ao ratio was ≥ 0.80 in 2 of 5 dogs with a PA shunt, 7 of 10 dogs with a PC shunt, and 4 of 5 dogs with a PP shunt.

Urolithiasis

Urolithiasis was present in 6 of 15 dogs with a PA shunt, in 29 of 70 dogs with a PC shunt, and in 9 of 19 dogs with a PP shunt. No statistical difference was found between the different groups ($P = .882$).

Discussion

This study revealed that the insertion site of EHPSSs has an impact on clinicopathological findings. Dogs with a PC shunt were presented at a significantly younger age than dogs with a PP or PA shunt. Furthermore, compared to dogs with PP shunts, dogs with PC shunts had a significantly lower BCS, significantly more severe clinical signs, and more distinct abnormalities on blood analyses.

Dogs with a congenital EHPSS are typically presented at a relatively young age, although some dogs will only show overt clinical signs at a later time in life.³ The results of the current study concurred with those of previous retrospective studies^{12,17} that revealed that dogs with PA shunts were older at diagnosis compared to those with PC shunts. In one of these studies,¹² 135 dogs were retrospectively included, and dogs were classified as having either a PC shunt (75%) or a PA shunt (25%). As no PP shunts were mentioned in that study, they might have been classified as PC shunts. In the other study,¹⁷ 7 dogs with PA shunts, 20 with PC shunts, and 7 with PP shunts were included. In the latter study,¹⁷ no significant difference in age at presentation was found between dogs with PC and PP shunts despite the reported lower mean age in dogs with a PC shunt compared to those with a PP shunt. This might be a type 2 error caused by their smaller study population (20 with PC shunts and 7 with PP shunts). Previous literature suggests that both dogs with a PA shunt and those with a PP shunt have fewer and less severe clinical signs than dogs with a PC shunt.¹³⁻¹⁵ The current study revealed that only dogs with PC shunts had a significantly higher clinical score than those with PP shunts. It appeared that dogs with PA shunts

take more time to develop clinical signs, but once clinical signs develop, they are as severe as in dogs with PC shunts, whereas clinical signs remain less severe, even at older age, in dogs with PP shunts. Differences in the course of the azygos and phrenic vein might explain this finding. Although the phrenic vein is often very dilated in dogs with PP shunts, the vessel has a rather flattened aspect, as it is located between the muscle and tendon of the diaphragm on one side and the fascia on the other side.²⁵ Tensioning of the diaphragm during respiration will likely have an impact on the diameter of the vessel, resulting in a changeable diameter and hence a fluctuating amount of blood flowing through PP shunts. Portoazygos shunts typically traverse the diaphragm through the esophageal hiatus.²⁰ The diameter of PA shunts could be decreased when food boluses pass the esophagus, but fewer changes in diameter are expected during the respiratory cycle compared to PP shunts. Finally, SDs of clinical signs, and more specifically from neurological signs, were rather wide, especially in dogs with PA and PC shunts. This might (in part) explain why no differences in clinical scores were found between these groups.

Similar to the findings of Murakami et al,¹⁷ dogs with PA, PC, and PP shunts did not significantly differ in body weight, which is not unexpected, as a large variety of breeds were included. Dogs with PP shunts, however, had a significantly higher BCS compared to dogs with PC shunts. Most likely, this can be explained by the less severe clinical signs observed in dogs with PP shunts.

Analysis of hematological parameters resulted in significantly more pronounced microcytosis and monocytosis in dogs with PC shunts compared to dogs with PP shunts. Microcytosis is frequently seen in dogs with EHPSSs, but the underlying cause is not yet fully understood.²⁶ It has been previously reported that hepatic encephalopathy leads to a significantly higher risk of monocytosis,²⁷ which is consistent with the observations in the current study.

Biochemical analysis resulted in significantly lower concentrations of creatinine and urea in dogs with PC shunts compared to dogs with PP shunts. Since dogs with PC shunts are overall younger and in a worse clinical condition, they have less muscle mass, leading to lower values of creatinine.²⁸ Although dogs with PC shunts were also significantly younger than dogs with PA shunts, the BCS and clinical score of dogs with PA shunts did not significantly differ from those with PC shunts. Urea is lower due to a decreased liver perfusion, reducing the amount of ammonia that is converted in urea. Furthermore, dogs with PC shunts had significantly higher concentrations of fasted ammonia and preprandial bile acids compared to dogs with PP shunts. Both blood ammonia and bile acid concentrations are liver function tests, which are often used for the diagnosis of PSS.²⁹ It is important to realize that, when diagnosis is only based on these commonly used tests, PP shunts might have been missed in several dogs included in the current study: 8 of 19 dogs and 2 of 18 dogs did not exceed the upper limit of fasted ammonia and preprandial bile acid concentrations,

respectively. In the dog with a PP shunt that did not have clinical signs and was screened for the presence of an EHPSS, both fasting ammonia and preprandial bile acids were within normal limits, whereas postprandial bile acids were very high. Also, in the retrospective study of Fukushima et al,¹⁴ significantly higher fasting ammonia concentrations were found in dogs with splenocaval shunts (a subtype of PC shunts; $n = 21$) compared to those with a splenophrenic shunt (a subtype of PP shunts; 64). This finding supports the hypothesis that for EHPSSs, the point of insertion has an influence on the parameters in blood analysis. The latter study¹³ also found that dogs with splenophrenic shunts had significantly lower serum ALP activities than dogs with splenocaval and gastrocaval ($n = 29$) shunts. In the current study, dogs with PC shunts had significantly higher serum ALP activity compared to dogs with PA shunts; a similar tendency was also seen in dogs with PP shunts, but significance was not reached. Clinical laboratories routinely determine total ALP concentrations in blood, which encompasses a variety of isoenzymes.³⁰ These isoenzymes can be found in multiple tissues, such as liver, kidneys, and bone. During bone growth, ALP concentrations are typically increased, with the highest concentrations seen during the first 16 weeks of life, after which a gradual decrease is found until 1 year of age.³⁰ The older age of dogs with PA (and PP) at diagnosis could thus affect this result; however, as most laboratories adapt the reference values to the age of the dog,³¹ as is the case in the laboratory used in the current study, it is unlikely to explain the difference. Another possible explanation is an increase in kidney-specific ALP.³⁰ In a previous study,¹⁷ renal size was significantly larger in dogs with PC shunts compared to those with PA and PP shunts; however, this was not confirmed in the current study. Several hypotheses have been proposed to explain the underlying pathophysiology. Deppe et al³² suggested that renomegaly might be caused by an increased renal metabolic function, such as ammoniogenesis or gluconeogenesis, to compensate for the decreased hepatic function. Although no significant difference was found in renal sizes between dogs with different EHPSS morphologies in the current study, it is possible that dogs with PC shunts had a higher renal metabolism causing an increase in total ALP activity. More studies are needed to confirm this hypothesis.

Although no statistical differences were found in the PV:Ao ratio based on CTA, none of the dogs with a PP shunt had a PV:Ao ratio ≤ 0.65 , which is suggestive for the presence of an EHPSS based on ultrasonography.³³ Besides, a large number of dogs in all EHPSS morphology groups had a PV:Ao ratio ≥ 0.80 based on CTA, which is a cutoff value based on ultrasonography to exclude the presence of an EHPSS.³³ The PV:Ao ratio on CTA has been reported in 100 dogs without evidence of hepatic, cardiac, or vascular anomalies to be 0.91 with a 95% CI of 0.88 to 0.94.³⁴ Although no cutoff values of the PV:Ao ratio on CTA have been reported for different hepatic vascular anomalies, a retrospective study showed that dogs with splenophrenic shunts had significantly higher PV:Ao ratios based on CTA (median, 0.83; range, 0.37 to 1.31; $n = 64$) than dogs with splenoazygos shunts (median, 0.62;

range, 0.00 to 1.30; 38), right gastrocaval shunts (median, 0.55; range, 0.00 to 0.75; 29), and splenocaval shunts (median, 0.55; range, 0.00 to 1.03; 21).¹⁴ The PV:Ao ratios in the latter study are also higher than the reported PV:Ao ratio in dogs without vascular anomalies in all EHPSS morphology groups, with only a subgroup of dogs with PC shunts (right gastrocaval shunts) having lower PV:Ao ratios.¹⁴ More research is needed to determine PV:Ao ratios in dogs with different hepatic vascular anomalies and identify whether cutoff values can be used.

Findings of this study might aid in the diagnosis of EHPSSs in dogs. When an older dog is presented with subtle clinical signs and subtle anomalies on blood analyses that might be caused by a PSS, one must consider the presence of a PP shunt. As PP shunts typically run alongside the minor curvature of the stomach before entering the phrenic vein, they might be difficult to diagnose during ultrasonography.³⁵ Both a distended stomach and air-filled lungs might complicate the visualization of this EHPSS type. Hence, performing a CTA scan as an initial diagnostic imaging technique could be justified.

Although the current study was retrospectively conducted, it was largely based on data that were collected in a prospective way in the light of larger research projects concerning EHPSSs in dogs. Nevertheless, the current study had some limitations. No power analysis was performed, as insufficient data for clinical scores were present in the literature and the lack of results of bloods tests and medical imaging were not an exclusion criteria. Furthermore, all information regarding clinical signs was originally provided by the owners of the dogs. Every owner has their own interpretation of *often* or *seldom*, which could affect the scores attributed to the clinical signs. In addition, clinical signs such as "abnormal behavior" are not always easy to assess, since there is no reference to compare to. As EHPSSs are congenital, these dogs might have been "abnormal" since birth, and therefore, no apparent changes in behavior might have been noted by the owners. Only after successful surgery might owners realize which clinical signs their dogs initially had and how severe they were. In addition, the majority of dogs with EHPSSs are presented at a young age, leaving the owners little time to get to know the behavior and clinical signs of their dogs. Another limitation is that clinicopathological findings are not only determined by the location of insertion of the EHPSS. Other factors, such as the origin, diameter, length, and tortuosity, will have an impact on the resistance of the EHPSS, resulting in a lesser or greater proportion of blood bypassing the liver. Furthermore, as blood analyses were not all performed in the same laboratory and some of the reference ranges changed over time, ratios were calculated. Although ratios give a good indication of differences between the studied groups, these might be more difficult to interpret by clinicians. Furthermore, calculating ratios over the lower limit for certain parameters and over the upper limit for other parameters might introduce a bias. Nevertheless, from all parameters in which both

lower and upper limits were available, the abnormalities identified in the dogs of this study were all expected and well-known abnormalities in dogs with EHPSSs (such as presence of microcytic anemia, hypoalbuminemia, hypoproteinemia, hypoglycemia, low urea, and presence of leukocytosis).³ Although our inclusion criteria were stringent and it is unlikely that EHPSS types were misclassified, findings of our study might be difficult to compare to those in the literature, especially with studies^{12,18} in which only dogs with PA and PC shunts are mentioned. It is likely that in the latter studies, dogs with PP shunts were classified as dogs with PC shunts. Finally, despite the fact that most included dogs participated in previous prospective studies, neither blood analyses nor medical imaging techniques were standardized in any of these studies, causing missing data. In particular, the large number of abdominal ultrasounds to diagnose EHPSSs, which were performed by a large number of different operators in an inconsistent way, contributed to incomplete information. As ultrasonography is a dynamic study and only limited videos and still images were available, additional data could not be collected by reviewing images.

In conclusion, the point of insertion of the EHPSS is associated with the age and the amount/severity of clinical signs at diagnosis. The relationship of the EHPSS to the diaphragm seems to have an impact on clinicopathological findings.

Acknowledgments

None reported.

Disclosures

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

Funding

The authors have nothing to disclose.

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