Long-term survival and quality of life in dogs with clinical signs associated with a congenital portosystemic shunt after surgical or medical treatment

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Objective—To compare long-term survival and quality of life data in dogs with clinical signs associated with a congenital portosystemic shunt (CPSS) that underwent medical or surgical treatment.

Design—Prospective cohort study.

Animals—124 client-owned dogs with CPSS.

Procedures—Dogs received medical or surgical treatment without regard to signalment, clinical signs, or clinicopathologic results. Survival data were analyzed with a Cox regression model. Quality of life information, obtained from owner questionnaires, included frequency of CPSS-associated clinical signs (from which a clinical score was derived), whether owners considered their dog normal, and (for surgically treated dogs) any ongoing medical treatment for CPSS. A Mann-Whitney *U* test was used to compare mean clinical score data between surgically and medically managed dogs during predetermined follow-up intervals.

Results—97 dogs underwent surgical treatment; 27 were managed medically. Median follow-up time for all dogs was 1,936 days. Forty-five dogs (24 medically managed and 21 surgically managed) died or were euthanized during the follow-up period. Survival rate was significantly improved in dogs that underwent surgical treatment (hazard ratio, 8.11; 95% CI, 4.20 to 15.66) than in those treated medically for CPSS. Neither age at diagnosis nor shunt type affected survival rate. Frequency of clinical signs was lower in surgically versus medically managed dogs for all follow-up intervals, with a significant difference between groups at 4 to 7 years after study entry.

Conclusions and Clinical Relevance—Surgical treatment of CPSS in dogs resulted in significantly improved survival rate and lower frequency of ongoing clinical signs, compared with medical management. Age at diagnosis did not affect survival rate and should not influence treatment choice. (*J Am Vet Med Assoc* 2014;245:527–533)

Congenital portosystemic shunts in dogs result from persistent embryonic or aberrant vasculature that permits blood from the gastrointestinal tract to bypass the liver and enter the systemic circulation. Such vessels may lie within or outside of the liver parenchyma and are referred to as intrahepatic or extrahepatic, respectively. Large-breed dogs tend to have intrahepatic CPSS, whereas extrahepatic CPSS are more prevalent in small-breed dogs.[1,2] Purebred dogs are more likely to have CPSS than are mixed-breed dogs.[3,4] Congenital portosystemic shunts are distinct from acquired portosystemic shunts, which are generally multiple and arise secondary to increased portal pressure. Congenital portosystemic shunts can result in a variety of clinical signs, predominantly affecting the neurologic, gastrointestinal, and urinary systems.[5,6]

Abbreviations

CPSS	Congenital portosystemic shunt
HR	Hazard ratio

Congenital portosystemic shunts can be managed surgically, and various techniques are available to achieve full or partial occlusion of the shunting vessel.[7–15] The condition can also be treated medically with a combination of antimicrobial delivery, synthetic disaccharide administration, and dietary management.[7,16,17] Convincing evidence for the optimal management modality is lacking.[18] Furthermore, published long-term

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survival and quality of life data are limited, particularly for medically managed veterinary patients. It has been assumed that surgical correction is the treatment of choice because occlusion of the shunting vessel has the theoretical potential to restore normal physiology, and even partial occlusion can resolve clinical signs.[19,20] The proposed benefits of surgery must be offset against the risks of perioperative death and shunt persistence leading to ongoing clinical signs, as well as the possibility that multiple acquired shunts may develop as a consequence of increased portal pressure.[6,13,14,18] Potential disadvantages of medical management include the persistence of abnormal physiology, failure to resolve or control clinical signs adequately, and the need for lifelong medication, dietary manipulation, or both.

We hypothesized that survival rate and quality of life (as assessed by persistence of clinical signs) of dogs with clinical signs associated with CPSS would be affected by the choice of medical versus surgical management. In 2010, we reported the initial results of a multicenter, prospective cohort study[21] comparing survival time in dogs with CPSS managed surgically or medically. Findings suggested that, although dogs with CPSS can survive long term with surgical or medical management, surgical intervention was associated with a significantly improved probability of survival to the end of the study period. The purpose of the study reported here was to determine long-term survival data for the same cohort of dogs with CPSS[21] and to evaluate short-, medium-, and long-term quality of life as assessed by their owners.

Materials and Methods

Dogs and study design—Details of the study design have been reported previously.[21,22] Briefly, dogs with clinical signs attributable to CPSS were prospectively recruited between June 1, 2002, and October 24, 2007, at 3 participating referral centers (School of Veterinary Sciences, University of Bristol; Queen's Veterinary School Hospital, University of Cambridge; and University Veterinary Hospital, University College Dublin). Inclusion criteria included a diagnosis of CPSS made on the basis of ≥ 1 routine diagnostic method (ultrasonography, portovenography, or exploratory laparotomy). Enrollment of dogs in the study was subject to informed owner consent. Formal institutional approval was not required because both management options were in routine use, in the absence of data to indicate superiority of one over the other.

Both surgical and medical management of CPSS were discussed with each owner, who was also informed of the prevailing uncertainty as to which was the treatment of choice. The decision as to which management modality was chosen for each dog was made by the owner after discussion with the attending clinician and therefore was not randomized. Treatment decision may have been influenced by the inherent bias of the attending clinician, financial considerations, perceived risks associated with surgery, or owner expectation of surgical management following referral to a specialist center. However, choice of management was not made on the basis of signalment, any clinical variable, or expected survival time.

All dogs underwent medical stabilization, consisting of a dietary, antimicrobial, and synthetic disaccharide regimen, for an initial (3-week) period. Diets consisted of commercially available products for dogs with hepatic or gastrointestinal disease or homemade diets that contained controlled amounts of high-quality, easily digestible protein and were fed as small portions at frequent intervals. Thereafter, medically managed dogs continued to receive a combination of dietary management, antimicrobials, and synthetic disaccharides, individually tailored to maintain control of the neurologic, gastrointestinal, and urinary signs associated with the CPSS. For dogs that underwent surgery, the specific intervention was chosen on the basis of location of the shunting vessel and surgeon preference; methods included use of an ameroid constrictor, cellophane band, or ligature. Complete ligation was attempted in all surgically managed dogs, with partial attenuation or a method designed to provide gradual attenuation used when the surgeon considered complete ligation impossible.

Information on the clinical condition of each dog was obtained through completion of a questionnaire[a] by owners at the time of study entry and during periodic follow-up telephone conversations. The presence and frequency of ongoing clinical signs attributable to portosystemic shunting was ascertained, along with the nature of any ongoing medical management and whether owners considered their dog to be normal with regard to the clinical signs that had initially prompted them to seek veterinary treatment. Information regarding the date of death was obtained from owners and referring veterinarians.

To assess owner perceptions of each dog's quality of life, a cumulative score was generated on the basis of the frequency with which owners observed clinical signs associated with neurologic (seizures, hyperactivity, restlessness, apparent blindness, head pressing, abnormal behavior, circling, or signs of severe depression), gastrointestinal (vomiting or diarrhea), or urinary (excessive drinking, urinating more frequently than usual, straining to urinate, or evidence of blood in urine) system abnormalities. Frequency of signs associated with each system was recorded as ≥ 1 episode in 24 hours (score, 3), less than once daily but more than once in the last month (2), ≤ 1 episode/month (1), or no signs in the previous 6 months (0). Thus, dogs with no clinical signs were assigned a cumulative clinical score of 0, whereas dogs with daily neurologic, gastrointestinal, and urinary signs were assigned the maximum cumulative clinical score of 9. The percentage of dogs with neurologic signs reported by owners was calculated for each management group, as was the percentage of dogs considered normal with regard to the clinical signs that initially prompted the owner to seek treatment. The proportion of surgically managed dogs that continued to receive medical management was also recorded. Prior to analysis, completed follow-up questionnaires were collated and grouped according to the following intervals after entry to the study: 3 to 12 months (91 to 365 days), 1 to 4 years (366 to 1,460 days), 4 to 7 years (1,461 to 2,555 days), and 7 to 10 years (2,556 to 3,650 days). If > 1 questionnaire was completed for the same dog within a defined follow-up interval, the clini-

cal scores were calculated for each questionnaire and the mean derived. If, on any of multiple questionnaires completed for the same interval, owners reported neurologic signs, ongoing medication (in surgical cases), or the opinion that their dog was not clinically normal, this finding was reflected in the analysis. Incomplete questionnaires were excluded from analysis.

Statistical analysis—The outcome measure for survival analysis was defined as the time after entry into the study until death or euthanasia for any reason. Dogs lost to follow-up or still alive at the end of the study were censored from the analysis on the date of last contact. Entry date was defined as the date of surgical intervention for dogs in the surgical management group or 21 days after commencement of medical treatment for those in the medical management group. A limited number of prespecified possible explanatory variables were examined: management type (surgical vs medical), age at diagnosis, and shunt type (intrahepatic vs extrahepatic). Cox proportional hazards survival analysis was used to compare survival rates between the 2 management methods while controlling for interacting factors of shunt type and age at diagnosis.[b] The proportional hazards assumption was tested and supported by comparison of observed versus predicted values and by use of Schoenfeld residuals. The assumption of linearity of age was also tested and found to be valid. Values of $P < 0.05$ were considered significant. The Mann-Whitney *U* test was used to compare the mean age of dogs between management groups at the time of CPSS diagnosis and to compare clinical score data between groups at entry and at 3 to 12 months, 1 to 4 years, and 4 to 7 years after study entry.[c] Bonferroni correction was applied to address the multiple statistical comparisons; with 4 individual tests, values of $P < 0.0125$ (0.05/4) were considered to indicate a significant difference between groups for each follow-up interval analyzed.

Results

Of 134 dogs with CPSS, 8 were excluded from study entry (1 died prior to entry into a treatment group, and no surgical attenuation of the shunting vessels could be achieved owing to unacceptable portal hypertension in 7). Of 126 dogs initially enrolled in the study, 2 (both in the surgical management group) were subsequently removed after review of the clinical records revealed that no surgical attenuation had been achieved at the time of laparotomy, resulting in a final study population of 124 dogs.

Extrahepatic CPSS was diagnosed in 110 dogs, and intrahepatic CPSS was diagnosed in 14 dogs. Dogs with extrahepatic CPSS included 27 West Highland White Terriers, 18 Yorkshire Terriers, 7 Bichon Frises, 6 Jack Russell Terriers, 6 Miniature Schnauzers, 5 Border Terriers, 5 Cairn Terriers, 4 Shih Tzus, 3 Border Collies, 3 Norfolk Terriers, 3 Pugs, 3 Shetland Sheepdogs, 2 Labrador Retrievers, 2 Miniature Yorkshire Terriers, 2 mixed-breed dogs, and 1 each of Australian Terrier, Bassett Hound, Chihuahua cross, Cocker Spaniel, Italian Greyhound, Maltese Terrier, Miniature Wirehaired Dachshund, Papillon, Schnauzer, Scottish Terrier, Siberian Husky, Smooth Fox Terrier, Terrier, and Weimaraner. Dogs with intrahepatic CPSS included 3 Labrador Retrievers, 2 Golden Retrievers, and 1 each of Bernese Mountain Dog, Border Terrier, Deerhound, Doberman Pinscher, Estrela Mountain Dog, German Shepherd Dog, Italian Spinone, Miniature Schnauzer, and West Highland White Terrier.

Age at diagnosis for all 124 dogs included in the study ranged from 2 to 73 months (mean, 14 months). The 110 dogs with an extrahepatic shunt ranged in age from 2 to 73 months (mean, 15 months), whereas the 14 dogs with an intrahepatic shunt were 2 to 12 months (mean, 5 months) of age at diagnosis. Dogs with an intrahepatic shunt were significantly ($P = 0.001$) younger at the time of diagnosis than were dogs with an extrahepatic shunt.

Of the 124 dogs in the study, 97 (78%) were treated surgically (ligation [n = 39], ameroid constrictor [29], partial ligation [24], or cellophane band [5]) and 27 (22%) were treated medically. Surgically treated dogs included 44 males and 53 females, and 89 (92%) of these dogs had an extrahepatic shunt. Medically treated dogs included 11 males and 16 females; 21 (78%) had an extrahepatic shunt. Post hoc analysis revealed no significant difference between the 2 treatment groups with respect to age at diagnosis, the proportion of dogs with intrahepatic or extrahepatic CPSS, or the ratio of males to females.

The median follow-up period for all dogs in the study (including those that died or were euthanized for any reason after entry) was 1,936 days. During the follow-up period, 45 dogs died or were euthanized; median survival from the time of study entry for these dogs was 759 days (range, 0 to 3,323 days). Although a number of dogs died or were euthanized during the follow-up period because of signs that could be directly related to portosystemic shunting (eg, persistent hepatic encephalopathy), many dogs died or were euthanized by the referring veterinarian because of clinical signs that may or may not have been attributable to CPSS. Postmortem examination was not performed in most cases, so no attempt was made to classify deaths as to whether they were related wholly or in part to portosystemic shunts.

Of the 27 dogs in the medical treatment group, 24 (89%) died or were euthanized during the follow-up period. Median survival time for dogs in this group was 836 days from study entry. Follow-up times for the 3 medically treated dogs still alive at last contact were 169, 2,811, and 2,948 days (the first of these was lost to longer-term follow-up). Of the 97 dogs in the surgical treatment group, 21 (22%) died or were euthanized during the follow-up period. Because of the large number of surgically managed dogs still alive at the time of last contact, it was not possible to estimate median survival time for this group. Follow-up time for the 76 surgically treated dogs still alive at last contact ranged from 38 to 3,415 days (median, 2,156 days). Seven surgically treated dogs were lost to follow-up during the study period. Mortality rate during the perioperative period (≤ 7 days after surgical intervention) was 4% (4/97 dogs); additionally, 1 dog died during the postoperative period of a second surgery performed (205 days after the initial surgical intervention) to complete

occlusion of the CPSS. No medically treated dogs died or were euthanized ≤ 7 days after study entry.

Survival analysis—Survival analysis (controlled for shunt type and age at diagnosis) revealed that the survival rate of surgically managed dogs was significantly ($P < 0.001$) greater than that of dogs that underwent medical treatment (HR, 8.11; 95% CI, 4.20 to 15.66). There was no significant effect of age at diagnosis (HR, 1.00; 95% CI, 0.97 to 1.02) or of shunt type (HR, 1.06; 95% CI, 0.43 to 2.63) on survival. Reanalysis incorporating an additional interaction factor between age at diagnosis and management type also revealed no significant ($P = 0.41$) effect of this interaction (HR, 0.98; 95% CI, 0.94 to 1.02), although this analysis did result in an increase in overall HR for survival rate associated with management type (HR, 10.86; 95% CI, 4.15 to 28.43; $P < 0.001$). The associated Kaplan-Meier plot (**Figure 1**) illustrates the difference in survival times between treatment groups during the long-term follow-up period.

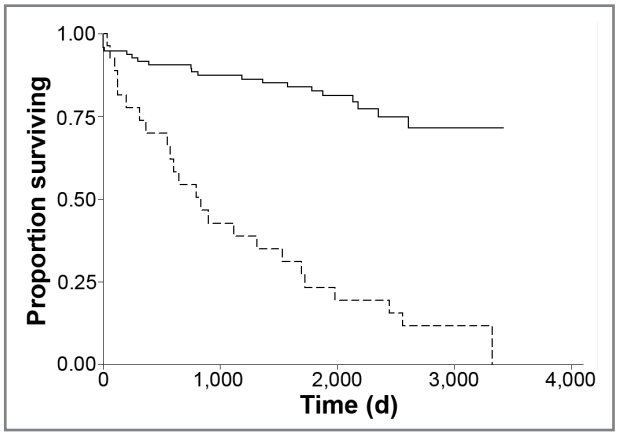

Figure 1—Kaplan-Meier survival curves of the relationship between time after study entry and the proportion of surviving animals for 124 dogs with both clinical signs and a diagnosis of CPSS at recruitment between June 2002 and October 2007. Dogs underwent surgical treatment (97 dogs [solid line]) or medical management (27 dogs [dashed line]). Study entry was defined as the date of surgical intervention or 21 days after commencement of medical treatment.

Quality of life analysis—The proportion of dogs for which quality of life questionnaires were completed varied among the 4 follow-up intervals (3 to 12 months, 1 to 4 years, 4 to 7 years, and 7 to 10 years). Information obtained from completed questionnaires for dogs in each management group at the time of study entry and during each follow-up interval was summarized (**Table 1**). This included the proportion of dogs that owners considered to be normal with respect to the clinical signs that initially prompted them to seek treatment; the proportion of dogs that had ongoing neurologic signs; mean clinical scores reflecting the absence or frequency of neurologic, gastrointestinal, or urinary tract signs; and the proportion of surgically managed dogs that continued to receive any form of medical treatment associated with the initial diagnosis (ie, antimicrobials, synthetic disaccharides, or a special diet [alone or in combination]).

At study entry, the mean cumulative clinical score (reflecting frequency of signs associated with neurolog-

Table 1—Summary data from completed owner questionnaires at the time of study entry and during various follow-up intervals for 124 dogs with both clinical signs and a diagnosis of CPSS at recruitment between June 2002 and October 2007.

Time and group	No. of dogs surviving*	No. of completed questionnaires	No. (%) of dogs considered clinically normal†	No. (%) of dogs with neurologic signs†	No. (%) of surgically treated dogs receiving medical treatment†‡		Clinical score	
					Any treatment	Diet only	Mean	Median (range)
At entry								
Surgical	97	12	3 (25)	7 (58)	—	—	3.1	2.5 (0–8)
Medical	27	10	7 (70)	3 (30)	—	—	2.4	2 (0–6)
Total	124	22	10 (45)	10 (45)	—	—	2.8	2 (0–8)
3–12 mo								
Surgical	90	12	8 (67)	4 (33)	5 (42)	2 (17)	1.5	0 (0–5)
Medical	25	10	7 (70)	7 (70)	—	—	3.3	3.75 (0–6)
Total	115	22	15 (68)	11 (50)	—	—	2.3	2.5 (0–6)
1–4 y								
Surgical	86	15	12 (80)	3 (20)	5 (33)	3 (20)	1.1	0 (0–6)
Medical	19	11	5 (45)	9 (82)	—	—	2.7	2.25 (0–7.3)
Total	105	26	17 (65)	12 (46)	—	—	1.8	1.25 (0–7.3)
4–7 y								
Surgical	75	46	41 (89)	5 (11)	11 (24)	10 (22)	1.1	0 (0–6)
Medical	9	6	3 (50)	5 (83)	—	—	3.2	3.5 (1–5)
Total	84	52	44 (85)	10 (19)	—	—	1.3	1 (0–6)
7–10 y								
Surgical	23	22	20 (91)	3 (14)	4 (18)	0 (0)	1.0	0 (0–3)
Medical	4	3	2 (67)	2 (67)	—	—	3.5	4 (0–6.5)
Total	27	25	22 (88)	5 (20)	—	—	1.3	0 (0–6.5)

Owners completed the first questionnaire at the time of study entry (defined as the date of surgical intervention or 21 days after commencement of medical treatment). Data for the 4 follow-up intervals (3 to 12 months [91 to 365 days], 1 to 4 years [366 to 1,460 days], 4 to 7 years [1,461 to 2,555 days] and 7 to 10 years [2,556 to 3,650 days]) were collected via telephone call with the owners. Frequency of clinical signs associated with neurologic, gastrointestinal, or urinary systems was recorded as ≥ 1 episode in 24 hours (score, 3), less than once daily but more than once in the last month (2), ≤ 1 episode/month (1), or no signs in the previous 6 months (0); the scores for each system were added together to create a cumulative clinical score (range, 0 to 9). *Includes all dogs for which survival time reached the start of the follow-up interval. †Percentage was determined on the basis of the number of dogs for which questionnaires were completed. ‡Ongoing medical treatments included antimicrobials, synthetic disaccharides, or a special diet (alone or in combination).

ic, gastrointestinal, and urinary system abnormalities [alone or in combination]) for the surgically managed group was slightly higher than that for the medically managed group, although the difference was nonsignificant ($P = 0.61$). For all 4 follow-up intervals, the mean clinical score for the surgically managed group was lower than that for the medically managed group; however, statistical analysis was only performed on clinical score data for the first 3 follow-up intervals because the number of medically managed dogs that had information reported during the 7- to 10-year interval was small. After Bonferroni correction, only the clinical scores for the 4- to 7-year interval were significantly ($P = 0.004$) different between management groups.

Discussion

In this prospective cohort study, we evaluated long-term survival in a cohort of clinically affected dogs with CPSS that underwent surgical (n = 97) or medical (27) management and found a significantly improved survival rate for dogs in the surgical management group. The unadjusted HR for survival rate in these dogs was approximately 8 times that of dogs that had medical treatment alone, although the confidence interval did not exclude a difference as large as 16-fold or as low as 4-fold. Even this lower estimate of the difference is of appreciable clinical importance. Neither age at diagnosis nor shunt type appeared to affect survival. However, the small number of dogs with intrahepatic CPSS in the study cohort (14) reduced the power to detect a small effect of shunt type on this outcome.

The median length of follow-up in the present study (1,936 days) was > 3 times that of our previous study[21] evaluating these same dogs (579 days). In the present study, we considered all deaths or euthanasias in the survival analysis, irrespective of cause. Given the lack of clinicopathologic or postmortem data to support a definite cause of death in many cases, this approach prevented bias resulting from deaths being misclassified as related or unrelated to CPSS. Indeed, death of any cause is considered by many investigators to be a more appropriate and valid endpoint than disease-related deaths when assessing survival in clinical studies.[23–25]

The analysis of owners' perceptions of the presence or absence of clinical signs potentially associated with CPSS in their dogs (as a measure of quality of life) appeared to support the survival analysis results and found a significantly lower mean clinical score, indicative of fewer or less frequent clinical signs, in surgically managed dogs at the 4 to 7–year follow-up interval. Although some surgically managed dogs received ongoing medical management, the proportion of dogs for which this was reported decreased with time after intervention (although this was not analyzed statistically), and ongoing treatment of some dogs consisted of dietary management alone. The necessity of a therapeutic diet for those dogs with surgically managed CPSS that continued to receive it was not assessed, and it is possible that owners simply preferred to provide the same diet or did so because they were concerned about the possibility of recurrence of clinical signs. It should be borne in mind that the assessment of absence or presence and frequency of clinical signs was made on the basis of owners' opinions and recall, and the questionnaire was not designed to assess the severity of signs. This approach had certain strengths, including being simple, repeatable, and cost-free for the owners. It can also be argued that owners are perhaps most likely to detect subtle changes in behavior or clinical signs in their pets. The weaknesses of this approach were that no objective measures were assessed to support an owner's assertions. Each owner may have had a different frame of reference for what they considered to be normal or abnormal behavior and differing ability to detect the presence and frequency of clinical signs. Whether owners' perceptions of dogs' status in this regard may vary depending on the type of management their pet received is open to question. The composite clinical score weighted neurologic, gastrointestinal, and urinary clinical signs equally and was not a validated measure of quality of life. Also, completed follow-up questionnaires were only available for a subset of cases within each of the follow-up intervals assessed, so it is impossible to be certain that these results were representative of the surviving cohort of patients at each time period. For example, owners who completed follow-up questionnaires may have been those either most or least satisfied with their pet's progress, which may have polarized the results.

Results of the present study strongly suggested that surgical treatment of clinically affected dogs with CPSS can result in an improved survival rate, compared with that in dogs receiving medical management, and further supported the conclusions of our previous study[21] on the management of CPSS in dogs. In addition, evidence that the number and frequency of clinical signs were lower in surgically treated dogs during long-term follow-up, with a significant difference between groups 4 to 7 years after intervention, suggested that these dogs may also have a better quality of life. Surgery is associated with a small but important risk of perioperative death, which some owners may be unwilling to accept. In some situations, such as when an owner is unwilling or unable to consent to surgical treatment of the dog's condition, medical management remains an acceptable treatment option. Median survival time from study entry in medically managed dogs was > 2 years, and approximately one-fifth survived for > 6 years from the time of study entry. However, owners of dogs with CPSS, particularly those who elect medical management of the condition, should be counseled regarding the possibility of recurrent clinical signs that may require adjustment to their management, or even hospitalization with more intensive treatment, to support them through a crisis. If attending veterinarians or owners believed that medically managed dogs (or any dog with recurrence of clinical signs related to CPSS) had a poorer prognosis, this may have contributed to a decision for euthanasia and thus influenced survival rate in that group.

As highlighted in our previous report,[21] the dogs in this study were not randomly assigned to receive one of the management options, and despite the prospective collection of data and preplanned analysis, the results are subject to the same limitations that apply

to many observational studies. In view of the nature of this study and notwithstanding the fact that post hoc analysis revealed no significant difference between the 2 treatment groups with respect to age at diagnosis, the proportion of dogs with an intrahepatic or extrahepatic CPSS, or the ratio of males to females, it is impossible to exclude the possibility of bias in case allocation. No further equivalency testing of clinical or clinicopathologic variables at the time of recruitment was performed, so it is possible that some differences in these variables may have existed between the 2 management groups at the start of the study, and an independent effect on outcome of ≥ 1 unexamined variables cannot be ruled out. At the time of study enrollment, there was no reason to suspect that clinicians were allocating cases into management groups on the basis of expected prognosis. It was also impossible to control the type of medical and surgical management undertaken, which varied among institutions. These potential sources of bias could be addressed in future studies. In the present study, only a single CPSS was identified in each dog. However, because advanced imaging was not performed in every patient, it is possible that some dogs had > 1 shunting vessel. Furthermore, it must be emphasized that this study population included only dogs with clinical signs attributable to CPSS; results are not applicable to survival, quality of life, or optimal management modality in dogs in which CPSS is diagnosed fortuitously.

Definitive diagnosis and surgical management of CPSS are generally perceived to require referral to a specialist institution. However, medical management of a suspected CPSS can be undertaken in first opinion practice. We did not assess survival or owner perceptions of ongoing clinical signs for that population of dogs; therefore, the true efficacy of medical management of CPSS may have been underestimated. The fact that most cases in this study were managed surgically may be explained if owners had the expectation that their pet's condition would be managed through surgical intervention at a referral institution. Nevertheless, the results of this study suggested that surgical management is superior to medical management for the population of dogs with clinical signs of CPSS referred to a specialist center for definitive diagnosis and treatment.

Two further results have important implications for the treatment of CPSS. First, this analysis supported the finding of our initial study[21] that age at diagnosis does not appear to affect survival and, critically, the analysis revealed no evidence that age at diagnosis influences the success of the chosen management method. This supports our previously stated conclusion[21] that there is no indication that surgical treatment must be performed in early life to be beneficial. The second important conclusion is that we found no evidence that surgically managed patients develop a disproportionate incidence of late complications. The difference in rates of death between the 2 management types remained stable throughout the duration of the study (the assumption of proportional hazards was confirmed by regression diagnostics). Further, the mean clinical score for surgically managed dogs decreased throughout the follow-up period and remained lower than that of medically managed dogs. This suggests that some of the postulated complications of surgery, such as the development of acquired shunts due to persistent low-grade portal hypertension, did not occur at high enough rates to affect these variables appreciably.

Very few reports on medical management of CPSS in dogs have been published, so the treatments given to the medically managed cohort in the present study may have been suboptimal. Recent studies[26] in humans suggest that protein-restricted diet and synthetic disaccharide regimens may not be efficacious in treating hepatic encephalopathy, despite widespread use in the past. To our knowledge, efficacy of these treatments has not been critically assessed in dogs. Furthermore, recent investigations[27,28] of CPSS in humans and dogs suggest that concurrent inflammatory disease may trigger and exacerbate the clinical signs of hepatic encephalopathy. Management aimed at identifying and treating inflammation, as an alternative or adjunct to the traditional focus on targeting gastrointestinal ammonia production through protein-controlled diets, synthetic disaccharides, and antimicrobial administration, may be more efficacious in controlling signs of hepatic encephalopathy.

An area not addressed by this study that merits further investigation is whether dogs with some subtypes of CPSS, such as those with a particularly low or high shunting fraction, respond better to a particular management modality. Furthermore, given the multicenter nature of this study and the fact that a variety of surgical techniques and medical managements were used, it remains to be determined whether subtypes of CPSS should be managed with different surgical or medical approaches. The increasing adoption of minimally invasive interventional radiologic techniques for CPSS occlusion, as recently reported by Weisse et al,[29] means that this management modality should also be considered when designing future prospective trials to assess long-term survival and quality of life data.

a. Questionnaire available from the corresponding author upon request.
b. Stata, version 11, StataCorp, College Station, Tex.
c. GraphPad Prism, version 5, GraphPad Software Inc, San Diego, Calif.

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