Comparison of survival after surgical or medical treatment in dogs with a congenital portosystemic shunt

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Objective—To compare survival of dogs with a congenital portosystemic shunt (CPSS) that received medical or surgical treatment.

Design—Prospective cohort study.

Animals—126 client-owned dogs with a single CPSS.

Procedures—Dogs were examined at 1 of 3 referral clinics, and a single CPSS was diagnosed in each. Dogs received medical or surgical treatment without regard to signalment, clinical signs, or results of hematologic or biochemical analysis. Survival data were analyzed via a Cox regression model.

Results—During a median follow-up period of 579 days, 18 of 126 dogs died as a result of CPSS. Dogs treated via surgical intervention survived significantly longer than did those treated medically. Hazard ratio for medical versus surgical treatment of CPSS (for the treatment-only model) was 2.9 (95% confidence interval, 1.1 to 7.2). Age at CPSS diagnosis did not affect survival.

Conclusions and Clinical Relevance—Both medical and surgical treatment can be used to achieve long-term survival of dogs with CPSS, although results of statistical analysis supported the widely held belief that surgery is preferable to medical treatment. However, the study population consisted of dogs at referral clinics, which suggested that efficacy of medical treatment may have been underestimated. Although surgical intervention was associated with a better chance of long-term survival, medical management provided an acceptable first-line option. Age at examination did not affect survival, which implied that early surgical intervention was not essential. Dogs with CPSS that do not achieve acceptable resolution with medical treatment can subsequently be treated surgically. (*J Am Vet Med Assoc* 2010;236:1215–1220)

Congenital portosystemic shunts have been recognized in dogs since 1949.[1] They are anomalous intrahepatic or extrahepatic vessels that allow blood from the hepatic portal circulation to drain directly into the systemic circulation, thereby bypassing the liver. Although drainage from the caudal trunk of a fetus bypasses the liver through the ductus venosus, extrahepatic shunts in an adult animal are abnormal vessels that connect the portal vein or one of its tributaries (splenic, cranial mesenteric, caudal mesenteric, or gastroduodenal vein) to the caudal vena cava.[2] Early reports[3–6] regarding CPSS focused on clinical signs and pathological findings, whereas more recent studies[7–10] confirmed that affected dogs often grow poorly or have clinical signs related to the nervous, gastrointestinal, or urinary systems.

Abbreviations

CPSS	Congenital portosystemic shunt
DM	Dry matter

In dogs with CPSS, the shunting vessel diverts blood that has drained from the digestive tract away from the liver. Although the pathogenesis of the observed clinical signs has not been entirely elucidated, the prominent inciting cause is thought to be an increase in the concentration of gastrointestinal-derived factors (primarily ammonia) within the systemic circulation.[11,12]

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This suggests 2 possible methods of treatment: surgical redirection of blood through the parenchyma of the liver (usually by attenuation of the shunting vessel) or minimizing the load of gastrointestinal-derived factors entering the systemic circulation via medical management. Since the discovery of the condition, CPSS has been treated by use of either method or a combination of the 2 methods. It has been suggested that surgical treatment is preferable to medical treatment on the basis of the hypothesis that continued hypoperfusion of the liver will lead to continued atrophy and degeneration.[7,10,13,14] In addition, in contrast to medical treatment, successful surgical attenuation of shunts can (at least theoretically) effect a complete clinical recovery without the need for continuing medical or dietary treatments.[15] A disadvantage of surgical treatment is the inherent risk of perioperative death, with reported mortality rates between 2% and 27%.[10,15–19]

Although there is a long history for medical and surgical treatment of CPSS, results have almost exclusively been reported as case series, rather than as comparisons between alternative treatments. There are 2 outcome measures that require comparison: duration of survival and quality of life. In addition, the intriguing possibility that 1 treatment method may be superior for either outcome measure for a specific type of shunt (eg, extrahepatic vs intrahepatic) has not been addressed.

The study reported here was designed to address some of the unanswered questions regarding treatment of CPSS. We hypothesized that survival might be affected by type of treatment (surgical vs medical), anatomic location of the shunt (intrahepatic vs extrahepatic), or a combination effect between type of treatment and age of the affected dog at diagnosis.

Materials and Methods

Animals—Dogs examined at any of the 3 participating veterinary medical referral centers (Department of Clinical Veterinary Science, University of Bristol; Queen's Veterinary School Hospital, University of Cambridge; and University Veterinary Hospital, University College Dublin) were eligible for inclusion in the study. Dogs were prospectively recruited into the study from June 2002 through October 2007. Inclusion criteria required a diagnosis of CPSS made by use of 1 or more accepted diagnostic methods (ultrasonography, portovenography, or exploratory laparotomy) in accordance with standard clinical criteria.[20] Routine clinical data, including breed, sex, age at diagnosis, shunt type (intrahepatic or extrahepatic), and treatment group, were collected for each dog with CPSS. Enrollment of dogs in the study was subject to informed owner consent; formal institutional approval was not required because the 2 treatment options were both in routine use for the study population, with no prior data to prove one superior to the other.

Decision regarding treatment of CPSS—During the initial consultation at a referral center, each owner was informed of the prevailing uncertainty as to whether surgical or medical treatment of CPSS was associated with lower rates for complications or recurrence of clinical signs or with superior survival or quality of life. Ultimately, the decision regarding treatment method for each dog was made by each owner after discussion with the attending clinician; thus, the treatment decision may have been influenced by the inherent bias of the attending clinician, financial considerations, or the perceived risks associated with surgery. Therefore, treatment allocation was not randomized. However, there was no reason to believe that treatment choices made by the owners would systematically allocate specific categories of dogs to 1 of the 2 treatment options. However, many owners chose surgical intervention simply because it had been recommended by their referring veterinarian at the time of diagnosis. For the purposes of this study, each of the 2 treatment options was considered in its entirety and consisted of current best practices, rather than a specific surgical procedure or medical treatment.

Medical treatment—Medical treatment in the study consisted of dietary, antimicrobial, and synthetic disaccharide regimens developed for each dog in accordance with treatment principles reported elsewhere.[11] Dietary management consisted of a commercially available diet manufactured for dogs with liver disease (16% protein [DM basis][a] or 18% protein [DM basis][b]) or intestinal tract disease (24% protein [DM basis],[c] 26% protein [DM basis],[d] or 23% protein [DM basis; canned or dry products][e]) or a homemade diet based on high-quality digestible protein (eg, chicken and cottage cheese) plus rice or pasta. Both proprietary and homemade diets were offered in small portions at frequent intervals. Ampicillin was orally administered to most dogs, but other antimicrobials (eg, metronidazole) were also used at the discretion of each clinician. Lactulose was used in all dogs, with the dosage designed to result in soft feces. All dogs, regardless of whether they would ultimately receive long-term medical treatment or surgical intervention, received dietary, antimicrobial, and lactulose treatments concurrently during a 3-week stabilization period. Thereafter, each treatment was specifically designed for each dog to maintain control of the neurologic, gastrointestinal, and urinary signs associated with CPSS. Adequacy of control of clinical signs was determined by responses of owners to a series of predetermined questions asked at each monitoring session.

Surgical treatment—Several types of surgical interventions were used; choice was based on location of the shunting vessel and the preference of each surgeon, but surgical interventions included use of an ameroid constrictor, cellophane bands, and ligatures.[21–24] Complete ligation was attempted for all shunting vessels in all dogs, but when a surgeon considered this to be impossible (because of an unacceptably high portal venous pressure or visibly unacceptable alterations in intestinal perfusion), partial ligation or a method designed to provide gradual, delayed attenuation (ie, an ameroid constrictor or cellophane bands) was used. Dogs in which no degree of surgical attenuation of the patency of shunting vessels could be attained because of unacceptable portal hypertension were excluded from the study (n = 7 dogs), as was 1 dog that died prior to entry into a treatment group. After surgery, dogs were maintained for 4 weeks on the dietary and drug management regimen described for the medical treatment, which was followed by an additional 4 weeks of dietary management alone.

Outcome—Follow-up information on the clinical condition of each dog was obtained via telephone conversations with owners held at monthly intervals. During each conversation, owners were asked a series of predetermined questions designed to assist clinicians in determining the severity of the clinical signs in an objective manner.

Referring veterinarians reported whether death or euthanasia of dogs was associated with clinical signs related to the CPSS. For many reasons, including problems associated with transporting dead and dying dogs to a location for postmortem examination or further evaluation, categorization of the cause of death as shunt related or not shunt related was not intensively investigated. Follow-up data were collected continually on consecutive dogs, with the intent of achieving ≥ 100 dogs for the study. Data on serum biochemical variables were not used to assess outcome because these variables represent surrogate outcomes that are unreliable indicators of the success of the treatment in terms of survival or quality of life and the nature of the surgical and medical treatments meant that comparisons of these variables would not be informative (eg, medical treatments would not be expected to alter serum concentrations of bile acids).

Statistical analysis—Statistical analysis was conducted by use of statistical programs.[f,g] The response variable was survival time after entry into the study. Entry date was defined as the date of surgical intervention or 21 days after commencement of medical treatment for the surgical and medical treatments, respectively. A limited number of possible explanatory or confounding variables were examined, which included treatment type (surgical vs medical), age at diagnosis, and shunt type (intrahepatic vs extrahepatic). Log-rank tests were used as an initial quantitative exploratory analysis on each explanatory variable in turn, then stratified log-rank tests were used to detect possible interactions between treatment type and other factors. This analysis was used to aid in construction of a Cox regression model to better assess the effect of the variables and any associated interactions. Values of $P < 0.05$ were significant.

Results

Animals—A total of 126 dogs were enrolled in the study. All dogs had a single CPSS (110 dogs had an extrahepatic shunt, and 16 dogs had an intrahepatic shunt). An extrahepatic shunt was diagnosed in 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 crossbred dog, Cocker Spaniel, Italian Greyhound, Maltese Terrier, Miniature Wire-haired Terrier, Dachshund, Papillon, Schnauzer, Scottish Terrier, Siberian Husky, Smooth Fox Terrier, Terrier, and Weimeraner. An intrahepatic shunt was diagnosed in 3 Golden Retrievers, 3 Labrador Retrievers, and 1 each of Bernese Mountain Dog, Border Terrier, Deerhound, Doberman Pinscher, Estrala Mountain Dog, German Shepherd Dog, Italian Spinone, Miniature Schnauzer, Pomeranian, and West Highland White Terrier. West Highland White Terriers (28 [22.2%] dogs) and Yorkshire Terriers (18 [14.3%] dogs) together constituted more than a third of the study population (46 [36.5%] dogs).

Age at diagnosis for all dogs included in the study ranged from 60 to 2,190 days (mean, 429 days). Age at diagnosis for the 110 dogs with an extrahepatic shunt ranged from 60 to 2,190 days (mean, 450 days), whereas age at diagnosis for the 16 dogs with an intrahepatic shunt ranged from 60 to 420 days (mean, 174 days). Dogs with an intrahepatic shunt were significantly (P = 0.004 [Mann-Whitney U test]) younger than were dogs with an extrahepatic shunt at the time of diagnosis of the CPSS.

Of the 126 dogs recruited into the study, 99 (78.6%) were treated surgically (ameroid constrictor [n = 29], ligation [39], partial ligation [26], and cellophane bands [5]) and 27 (21.4%) were treated medically. The median follow-up period for all dogs in the study (including those that died or were euthanized for any reason after entry into the study) was 579 days. During the period of follow-up monitoring, 18 dogs died or were euthanized because of signs related to CPSS; data for the remaining dogs were censored in the survival analysis.

Of the 27 dogs treated medically, 21 (77.8%) had an extrahepatic shunt and 11 (40.7%) were males. Of the 99 dogs treated surgically, 89 (89.9%) had an extrahepatic shunt and 45 (45.5%) were males. 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.

Of the 27 dogs receiving medical treatment, 14 (51.9%) were still alive at the completion of the study. Follow-up time for medically treated dogs ranged from 169 to 1,642 days (mean, 938; median 1,048 days). Of the 99 dogs receiving surgical treatment, 87 (87.9%) were still alive at the completion of the study. Follow-up time for surgically treated dogs ranged from 15 to 1,807 days (mean, 696 days; median, 597 days). Median survival time for all 18 dogs that died was 164 days; medically treated (n = 8) and surgically treated (10) dogs that died after treatment had similar survival times ($P = 0.99$; t = 0.007 [Student t test]). Mortality rate during the perioperative period (up to 7 days after surgical intervention) was 4.0% (4/99 dogs); 1 additional dog died during the postoperative period after a second surgery was performed to complete occlusion of the CPSS (surgery performed 205 days after the initial surgical intervention). No dogs treated medically died or were euthanized within 7 days after entry into the study.

Of the 126 dogs in the study, 7 (5.6%) died from other causes. Survival time from entry into the study until death of these 7 dogs ranged from 127 to 1,877 days (mean, 768 days; median, 572 days). Of the 27 dogs treated medically, overall mortality rate during the study was 48.1% (13/27 dogs); 8 of 27 (29.6%) dogs were deemed to have died of shunt-related causes (signs consistent with hepatic encephalopathy [6], abdominal varices [1], and dysuria [1]), and the other 5 (18.5%) were deemed to have died of causes unrelated to CPSS (external trauma [3], perforating intestinal foreign body [1], and pulmonary fibrosis [1]). Of the 99 dogs treated surgically, overall mortality rate was 12.1% (12/99 dogs); 10 of 99 (10.1%) dogs were deemed to have died of shunt-related causes (seizures or collapse [5] and surgical complications [5]), and the other 2 (2.0%) dogs were deemed to have died of causes unrelated to CPSS (accidental fall [1] and disturbance of lipid metabolism [1]).

Therefore, 101 of 126 (80.2%) dogs were still alive at the completion of the study; follow-up period for these 101 dogs ranged from 15 to 1,807 days (mean, 729 days; median, 613 days). Medically treated dogs continued to receive the same drug and dietary regimens as described previously; owners of surgically treated dogs were advised to resume feeding a typical diet at 2 months after surgery, but many owners preferred to continue to feed the special diets because they were concerned about the possibility of recurrence of clinical signs.

Survival analysis—A Kaplan-Meier survival plot was created to illustrate the relative rate of survival associated with each of the 2 treatment types (**Figure 1**). The probability of survival was lower in dogs receiving medical treatment than the probability of survival for dogs receiving surgical treatment. To evaluate this relationship in more detail, a Cox proportional hazards model was used. It was hypothesized that there may have been additional effects of shunt type and age at diagnosis. However, results of an analysis of deviance suggested that these effects (or their interactions) did not explain significant amounts of the deviance over and above the effect for treatment type. Importantly, age or its interaction with treatment type did not have a significant effect on survival time. The hazard ratio for medical versus surgical treatment of CPSS for the treatment-only model was 2.9 (95% confidence interval, 1.1 to 7.2).

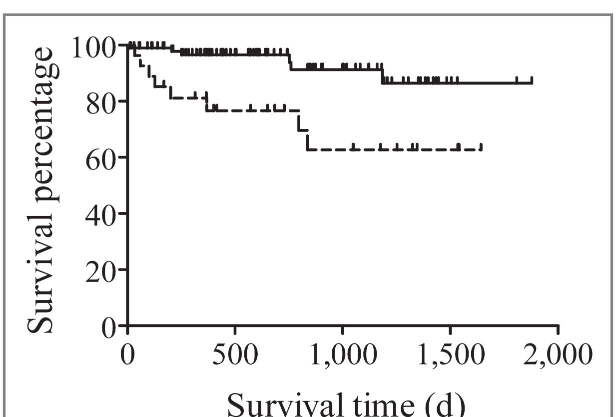

Figure 1—Kaplan-Meier survival curves of the relationship between time after entry into the study and the percentage of surviving animals for dogs with CPSS that received surgical treatment (99 dogs [solid line]) or medical treatment (27 dogs [dashed line]). Entry date was defined as the date of surgical intervention or 21 days after commencement of medical treatment for the surgical and medical treatments, respectively.

Discussion

To our knowledge, the study reported here provides the first direct comparison of survival between medical and surgical treatment in a prospective study of dogs with CPSS. Analysis of these data provides a reasonably strong indication that surgical treatment is associated with longer survival than is medical treatment. However, many caveats must be added to this statement.

Importantly, this study was not conducted on a randomized group of patients, which could have influenced the results obtained. Given that all of these dogs had been referred by another veterinarian (primary-care veterinarian) to a referral center for further treatment and a bias toward surgical referral was evident, it is certainly possible that the true efficacy of medical treatment for dogs with CPSS might have been underestimated in this study. Dogs in which CPSS was satisfactorily diagnosed and treated medically by a primary-care veterinarian would have been excluded from this study because they would not have subsequently been referred for surgery. Surgical treatment of CPSS is a procedure generally performed by board-certified veterinarians and is restricted to referral centers, whereas medical treatment can be provided at most primary-care facilities. Another unknown is whether dogs that died after medical treatment might also have died after surgical treatment and vice versa.

A second reservation is that survival simply represents 1 aspect of success of treatment. The quality of life for animals with CPSS also needs consideration because mere longevity is not always an appropriate outcome for pets. Quality of life is difficult to analyze because it typically is a subjective assessment that can be difficult to reduce to an unequivocal measure for comparative statistical analysis. However, a prejudice would be that once an animal has recovered from the intervention, the quality of life for surgically treated animals would be expected to be better because liver function (as assessed at a minimum by the use of serum biochemical variables) often returns to normal[25] and animals would be less susceptible to destabilizing events such as dietary indiscretion or hemorrhage in the gastrointestinal tract. Therefore, it might be expected that surgery would have benefits greater than those for medical treatment in this regard, but authoritative statements cannot be made without further investigation. A related reservation regarding interpretation of the results is that analysis of the specific details of the postsurgical medical management (such as feeding of reduced-protein diets) for each dog was cumbersome (because of the extensive variability) but may have influenced the longevity of those animals. The possible role of adjuvant medical treatment requires further investigations in future studies on quality of life.

Only 18 (14.3%) dogs enrolled in this study died of shunt-related disease within the time frame of the study (< 5 years), although the median survival time for dogs that died was < 164 days for both types of shunts and both types of treatments. These results are consistent with the highly variable prognosis for CPSS treatment, as discussed in another study.[26] Moreover, the manner in which results have been reported means that robust comparative conclusions cannot be drawn. The rela-

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tively small number of dogs that died also raises concerns about the power of the study to detect differences. There is clearly sufficient power to evaluate the effect of treatment type on survival, which was the fundamental issue the study was designed to address; however, the power to detect other differences, such as effects of age at diagnosis or shunt type, was substantially lower. According to statistical rule-of-thumb guidelines, multifactorial analysis is sufficiently powered when there are 7 to 10 events/analyzed factor[27]; clearly, the data reported here were only marginally sufficient to fulfill that criterion. However, inspection of the results obtained by use of the Cox regression model would suggest that other factors have little additional predictive value on prognosis and that detection of significant effects would require a much larger number of events and therefore inclusion of hundreds of dogs.

The categorization of causes of death as shunt related or not shunt related was not completely robust because it relied on the judgment of the referring veterinarian, without further investigations or postmortem examination. This possible source of error is almost impossible to eliminate from this type of study because owners will rarely travel long distances to referral centers with an animal that has died or that is seriously ill and will be euthanized at the time of arrival. In this study, analysis of the stated causes of death provided reasonable confidence in accuracy of the categorization.

We initially planned to conduct a randomized study to compare the treatment options, but there was resistance among both clinicians and clients at the participating centers. Concerns were raised that it would be unacceptable to withhold surgery because it was believed to be associated with a superior prognosis. Also, there was a conviction that it was unacceptable to compel owners to expose their dog to the risk of death during the perioperative period associated with surgical intervention. Results of this study suggest there is sufficient evidence of good long-term survival with each treatment and their comparative efficacy such that randomized studies to compare these treatment options could be reconsidered. On the other hand, in light of the reasonably strong evidence for a superior overall outcome for surgical treatment, perhaps future studies would be better aimed at addressing more specific issues, such as comparisons of medical and surgical treatment for defined subtypes of CPSS. For instance, it would be pertinent to determine whether animals that respond poorly to surgical intervention would also have short survival periods after medical treatment.

An issue that was not addressed by our analysis is whether any particular method of surgery or incomplete occlusion of a shunting vessel was associated with a poorer outcome than would have been achieved by use of another surgical method or complete occlusion. This omission was inevitable because the involvement of several centers meant that different surgical techniques were preferred by various surgeons, and the choice of surgical intervention for each dog was considered optimal for each individual patient. Similarly, there was no attempt to compare one type of medical treatment with another because medical treatment was determined for each dog by the attending clinician, which resulted in large variation in the medical treatments among patients.

It traditionally has been suggested that the liver of medically managed dogs undergoes progressive fibrosis, and this progressive fibrosis is prevented by surgery.[7,27] However, the evidence is equivocal. In the only case series[28] of which the authors are aware, it was reported that all 5 dogs with CPSS that were treated medically developed progressive portal fibrosis, compared with 1 of 2 dogs treated surgically that developed progressive portal fibrosis. However, these results are difficult to interpret because detailed description of the histopathologic findings was omitted in that case series.[28] Progressive deterioration of the liver has not been detected histologically in medically treated dogs, and attenuation of the shunt vessel is not always associated with resolution of hepatic damage.[29] Furthermore, because results for histologic examination of liver biopsy specimens obtained during surgery cannot be used to predict outcome after surgery,[30] histologic examination of liver biopsy specimens may not provide a suitable endpoint for comparison of treatment efficacy.

The prolonged survival of many dogs and the small numbers of dogs that died by the end of the study have prompted the authors to continue follow-up monitoring of the dogs that remained alive, with the intent of defining life expectancy in affected dogs. In addition, owners will also be asked to allow postmortem collection of liver samples for histologic examination.

Analysis of the data in the study reported here suggests that in terms of overall survival time, surgical treatment is preferable to medical treatment for dogs with a CPSS. However, this conclusion must be tempered because of the nonrandomized nature of the study. Age at diagnosis does not have a significant effect on survival time after either type of treatment; thus, there is no evidence to suggest that surgery needs to be performed early during treatment. Instead, there is support for a scheme of management consisting of initial medical treatment, which can be followed by surgical intervention for those dogs that do not respond adequately.

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a. Royal-Canin hepatic support, Crown Pet Food Ltd, Castle Cary, Somerset, England.
b. Hills l/d, Hill's Pet Nutrition Ltd, Watford, Hertfordshire, England.
c. Royal-Canin sensitivity control, Crown Pet Food Ltd, Castle Cary, Somerset, England.
d. Hills i/d, Hill's Pet Nutrition Ltd, Watford, Hertfordshire, England.
e. Eukanuba intestinal, Proctor and Gamble Petcare Europe, Geneva, Switzerland.
f. GraphPad Prism, version 5.00 for Windows, GraphPad Software, San Diego, Calif.
g. R, version 2.8.1, R Foundation for Statistical Computing, Vienna, Austria. Available at: www.R-project.org. Accessed Mar 15, 2010.

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