Liver Size, Bodyweight, and Tolerance to Acute Complete Occlusion of Congenital Extrahepatic Portosystemic Shunts in Dogs

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Objective—To investigate the relationship between preoperative liver size, bodyweight, and tolerance to shunt occlusion in dogs with congenital extrahepatic portosystemic shunt(s) (CPSS).

Study Design—Longitudinal cohort study.

Animals—Dogs with CPSS (n = 35).

Methods—Ultrasonography was used to measure preoperative maximum transverse dimension of the liver (TS) of each dog. Intraoperative portal pressures were measured, before and after CPSS occlusion, via a jejunal vein catheter. Tolerance to shunt occlusion was judged on gross visceral observations, and on changes in portal pressure, central venous and mean arterial pressures.

Results—TS was significantly related to bodyweight (P < .05). Mean ratios for TS/bodyweight were calculated for dogs tolerant and intolerant of acute complete shunt occlusion. Dogs tolerant to occlusion had significantly higher TS/bodyweight ratios than dogs intolerant to occlusion (P = .025). Dogs with a TS/bodyweight ratio of > 7 were more likely to tolerate CPSS occlusion than dogs with a TS/bodyweight ratio of < 5 (P = .036). A model was generated to predict portal pressure rise after shunt occlusion, based on liver dimensions and bodyweight (R = 0.668). Intestinal oxygenation did not correlate significantly with tolerance to CPSS occlusion (P = .29).

Conclusion—In dogs with CPSS, liver size (relative to bodyweight) is significantly greater (P = .025) in dogs that are tolerant of full ligation than intolerant of occlusion.

Clinical Relevance—Preoperative measurement of bodyweight and liver size help indicate the likelihood of tolerance to acute complete occlusion of CPSS in dogs.

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INTRODUCTION

Congenital portosystemic shunt(s) (CPSS) are anomalous vessels that provide a low resistance conduit for blood to flow from the portal vein, or its tributaries, to a systemic vein such as the caudal vena cava orazygous vein. The consequent reduction in portal supply to the hepatic parenchyma acts to impair the liver’s function in detoxifying metabolites, which normally reach the liver via the portal venous circulation. This can lead to the development of hepatic encephalopathy. A reduction in portal venous blood flow also deprives the liver of hepatotrophic factors released from the intestines and pancreas, which may result in liver atrophy.1,2

Treatment of CPSS usually involves medical therapy to stabilize the dog, followed by surgical attenuation of the anomalous vessel. Many surgeons choose to perform complete ligation of a CPSS if occlusion of the vessel with a Rummel tourniquet appears to produce no adverse effects; however, 48–68% of dogs with congenital extrahepatic portosystemic shunts have signs of marked portal...
hypertension after complete CPSS occlusion. This potentially fatal sequela has led to development of methods of gradual complete CPSS occlusion, such as the ameroid ring constrictor or cellophane banding.

Objective assessment of tolerance to CPSS ligation is based on direct measurement of changes in portal venous pressure, central venous pressure (CVP), and systemic arterial pressure after vessel attenuation. Observation of gross visceral changes are equally important after CPSS attenuation. Intestinal and pancreatic pallor, congestion or cyanosis, uncoordinated, vigorous small intestinal peristalsis, and increased pulsation of mesenteric arteries may all reflect the onset of portal hypertension.

Acute complete CPSS ligation, when tolerated by a dog, has been reported to offer an improved long-term prognosis, compared with partial CPSS ligation. More recently, techniques of gradual progressive CPSS attenuation have gained favor. There is currently no reliable technique for preoperatively predicting the likely tolerance of a patient to complete ligation of a CPSS. Ultrasonography has been shown to be a reliable and accurate method for measuring hepatic volume in a wide variety of dog breeds and sizes when measurements were made immediately after euthanasia.

We investigated the relationship between liver dimensions, bodyweight, and portal pressure changes after complete attenuation of extrahepatic CPSS in 35 dogs. Our hypothesis was that dogs with a smaller liver volume, relative to their bodyweight, would be less likely to tolerate acute complete occlusion of an extrahepatic CPSS.

**MATERIALS AND METHODS**

Dogs (n = 35) with congenital extrahepatic portosystemic shunts treated surgically (November 2005 to January 2007) were included. Dogs that had concurrent vascular anomalies including multiple extrahepatic shunts were excluded. Vascular anomalies were diagnosed by a combination of mesenteric portography, intraoperative findings, and histopathologic examination of liver biopsies. Primary hypoplasia of the portal vein was diagnosed by criteria described in the World Small Animal Veterinary Association classification scheme for circulatory disorders of the canine and feline liver.

**Presurgical Management**

Before surgery dogs were medically stabilized. Typically this consisted of 4 weeks administration of lactulose (Lactulose, TEVA, Leeds, Yorkshire, UK) and ampicillin (20 mg/kg every 8 hours), while feeding a low protein prescription diet (Hepatic, Royal Canin UK, Yeovil, Somerset, UK).

**Hepatic Ultrasonography**

Each dog's liver was examined ultrasonographically on the morning of surgery before administration of premedication. The liver was imaged in transverse section using a 7.5 MHz microconvex transducer (Technos MPX, Imotek International Ltd., Huntingdon, Cambridgeshire, UK), and the maximum mid-line depth of the liver was measured on each of 3 separate images following a standard protocol. The mean of these 3 measurements (TS) was recorded and used for statistical analysis. Dogs were examined in right lateral recumbency. All measurements were taken at end-expiration to minimize respiratory motion as a source of inaccuracy. The surgeon was unaware of the ultrasonographic measurements. Dogs were weighed immediately after the ultrasonographic examination.

**Surgical Procedure**

Dogs were premedicated with pethidine hydrochloride (3–5 mg/kg intramuscularly) and anesthesia induced with propofol (intravenously [IV] to effect) and maintained on isoflurane in a mixture of oxygen and nitrous oxide gases (typically, 2:1). Mean arterial pressure was recorded from a catheter placed in a dorsal metatarsal artery. CVP measurements were obtained from a catheter inserted into the external jugular vein and advanced toward the cranial vena cava. After ventral median celiotomy, a 22 g IV catheter was inserted into a jejunal vein. An extension line was attached to the jejunal vein catheter and flushed with heparinized saline (0.9% NaCl solution). Portal venous pressure was measured via a calibrated pressure transducer (DTX Plus, Becton Dickinson, Franklin Lakes, NJ) connected to an extension line. A pulse oximetry probe (Pulse oximeter 8500V, Nonin Medical Inc., Plymouth, MN) was applied to the small intestine at a distance of 2 mesenteric vascular arcades proximal or distal to the catheter site. Four baseline pressure readings were taken, spaced at 30-second intervals, beginning 30 seconds after flushing of the extension tubing. A mean value for baseline pressure was calculated. Small intestinal oxygen saturation readings were taken concurrently and a mean baseline value calculated. Mesenteric portography was performed by injecting Iohexol 300 mgI/mL (Omnipaque, Amersham Health, Little Chalfont, Buckinghamshire, UK) at a volume of 1 mL/kg via the jejunal vein catheter under fluoroscopic guidance, both to confirm and locate the portosystemic shunt.

Examination of the abdomen was conducted to identify the portosystemic shunt and, after dissection of the vessel, 2 metric polypropylene suture material was passed around the vessel and incorporated into a Rummel tourniquet. After complete occlusion of the portosystemic shunt with the tourniquet, jejunal vein pressure measurements were recorded at 30, 60, 90, and 120 seconds postocclusion. Small intestinal oxygen saturation readings were taken concurrently. A 2nd injection of Iohexol was administered under fluoroscopic guidance, to verify complete and correct occlusion of the shunting vessel.

A dog's tolerance to occlusion of its portosystemic shunt was based on it experiencing a portal venous pressure rise.
of <10 mmHg (13.6 cmH₂O) and a total portal venous pressure postocclusion of <16 mmHg (21.7 cmH₂O). The change in intestinal oxygenation during CPSS occlusion was recorded. Gross signs of intestinal and pancreatic congestion and cyanosis, intestinal hypermotility and hyperdynamic mesenteric arterial pulsation were assessed. These observations, along with any reduction in CVP and reduction in mean arterial pressure, were taken into consideration in judging tolerance to shunt occlusion. Dogs judged intolerant of complete occlusion were treated by placement of an ameroid ring constrictor or a cellophane band around their shunting vessel. A liver biopsy was taken and the celiotomy closed in layers.

Dogs subsequently found to have histopathologic evidence of concurrent hepatic disease were excluded from the trial. Surgery was performed by the same surgeon (I.P.D.) for all dogs. Dogs were monitored postoperatively for signs of hemorrhage, portal hypertension, and neurologic derangement.

Data Analysis

As an initial evaluation, mean TS/bodyweight ratio was calculated for all dogs that tolerated acute complete CPSS occlusion and for those that did not. A 2-tailed t-test was used to compare these 2 means. In similar fashion, a mean decrease in intestinal oxygenation was calculated for all tolerant dogs and all intolerant dogs. A 2-tailed t-test was used to compare these means. After inspection of a scatter-plot of portal pressure rise during CPSS occlusion versus TS/bodyweight ratio, the number of tolerant and intolerant dogs with a TS/bodyweight ratio of <5 mm/kg was compared with the number of tolerant and intolerant dogs with a TS/bodyweight ratio of >7 mm/kg. A Fisher’s exact test was used to determine if the number of tolerant dogs in these 2 TS/bodyweight ratio groups was significantly different at the 5% level.

Finally, multiple linear regression was used to investigate any potentially significant relationship between the magnitude of portal pressure rise during CPSS occlusion and each of the following variables: bodyweight, TS, TS/bodyweight ratio, (TS)², (TS)³, log bodyweight, log (TS)², and log (TS)³. The simplest model was chosen of those that best accounted for the variation seen in portal pressure rise, as judged by the adjusted R² value. Statistical software (SPSS14.0 for Windows, SPSS Inc., Chicago, IL) was used for calculations. Data were normally distributed and results are expressed as mean ± SD.

Table 1. Comparison of Dogs Tolerant and Intolerant of Complete Congenital Extrahepatic Portosystemic Shunts (CPSS) Occlusion

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>Tolerant Mean ± SD</th>
<th>Intolerant Mean ± SD</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean TS/bodyweight (mm/kg)</td>
<td>35</td>
<td>6.72 ± 2.18</td>
<td>5.09 ± 1.64</td>
<td>.025</td>
</tr>
<tr>
<td>Mean PO₂ decrease (%)</td>
<td>34</td>
<td>0.39 ± 2.91</td>
<td>2.10 ± 5.20</td>
<td>.29</td>
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</tbody>
</table>

*In 6 dogs, mean PO₂ decrease was calculated from an incomplete number of readings.

RESULTS

Thirty-five dogs (Table 1) met the inclusion criteria. Breeds included West Highland White Terrier (n = 13), Yorkshire Terrier (5), other terriers (9), Bichon frise (2), Shih Tzu (1), Chihuahua (1), other breeds (4). Mean body weight was 6.09 ± 3.21 kg (range, 1.07–18.95 kg). Mean transverse liver measurement was 33.62 ± 12.04 mm (range, 14.83–71.40 mm).

Twenty-seven dogs had shunts connecting the portal vein, or its tributaries, with the caudal vena cava. Eight dogs had portoazygous shunts. Mean increase in portal pressure during occlusion was 13.74 ± 9.95 mmHg (range, 0–38 mmHg [0–51.7 cmH₂O]).

Dogs were encountered with primary hypoplasia of the portal vein (3), arteriovenous fistula (1), and congenital interruption of the caudal vena cava (1); these 5 dogs were excluded from the study. Complete occlusion was performed in 17 dogs. Thirty-three dogs survived the peri- and postoperative period (dogs were typically discharged 4 days after surgery). One dog died postoperatively because of intra-abdominal hemorrhage. One dog was euthanatized, intraoperatively, at the owner’s request because complete ligation was not tolerated. One dog had seizures postoperatively but responded fully with supportive treatment. None of the dogs had marked postoperative clinical signs of portal hypertension and none had a 2nd surgery.

Neither bodyweight nor TS had a direct statistically significant relationship with portal pressure rise after CPSS occlusion. A significant relationship was found between bodyweight and TS (P<.05) and so this ratio (TS/bodyweight) was then used to compare tolerant and intolerant dogs. Dogs that tolerated full shunt occlusion had significantly higher TS/bodyweight ratios than dogs that did not tolerate occlusion (P<.05; Table 1).

There was no significant relationship between baseline portal pressure measurements (before shunt occlusion) and either bodyweight, TS, or TS/bodyweight ratio. Mean intestinal oxygenation change was calculated for these same groups and was not significantly different (P = .29). A data scatter-plot is shown for TS/bodyweight ratio versus portal pressure rise after shunt occlusion (Fig 1). Visual interpretation of these data suggests: after CPSS occlusion, dogs with a TS/bodyweight ratio <5 mm/kg are very likely to experience portal pressure rises >10 mmHg whereas dogs with a TS/bodyweight ratio >7 mm/kg are very likely to experience portal pressure rises <10 mmHg. Results of Fisher’s exact test showed that dogs with a TS/bodyweight ratio <5 mm/kg were more likely to be intolerant of CPSS occlusion whereas dogs with a TS/bodyweight ratio >7 mm/kg were more likely to be tolerant of CPSS occlusion (P<.05; Table 2).
Multiple linear regression analysis of the relationship between portal pressure rise after shunt occlusion (response variable), liver size, and bodyweight produced a best-fit model that included \( \log(\text{TS}^2) \) and \( \log(\text{bodyweight}) \) as factors and gave an \( R \) value of 0.668 and an adjusted \( R^2 \) value of 0.412. The model is

\[
\text{Portal pressure rise (mmHg)} = 65.81 + 32.71 \cdot \log(\text{wt}) - 25.25 \cdot \log(\text{TS}^2)
\]

Model: \( P < .0003 \) \( \log(\text{wt}) \):

\[ P < .001 \text{ SE} = 8.339 \]

Intercept: \( P < .001 \text{ SE} = 13.923 \cdot \log(\text{TS}^2) \):

\[ P < .001 \text{ SE} = 5.141. \]

Multiple linear regression was also used to investigate the best predictive model of change in intestinal wall oxygen saturation, as measured by pulse oximetry, after CPSS occlusion. In 7 of 35 dogs, not all pre- and postocclusion measurements for intestinal oxygenation were obtained because of technical difficulties with the pulse oximeter. No significant correlation between intestinal oxygenation changes and portal pressure changes were recorded during CPSS occlusion. Intestinal oxygenation changes did not have any significant relation to a dog’s tolerance to shunt occlusion (Table 1). Neither TS, bodyweight, or TS/bodyweight ratio were significantly related to change in intestinal oxygenation after CPSS occlusion.

**DISCUSSION**

We found that liver size, relative to bodyweight, is significantly greater (\( P < .05 \)) in dogs that are tolerant of complete CPSS ligation than those that are intolerant (Table 1). Two-thirds of dogs with TS/bodyweight ratios \(< 5 \text{ mm/kg}\) had portal pressure increase after shunt occlusion of \( > 10 \text{ mmHg} \) and therefore could be at substantial risk from portal hypertension, had their CPSS been ligated. Conversely, 9 of 11 dogs with TS/bodyweight ratios \( > 7 \text{ mm/kg}\) had portal pressure increases \(< 10 \text{ mmHg} \) and were considered tolerant of complete CPSS ligation (Fig 1).

Dogs with portosystemic shunts are known to have relatively small liver volumes.\(^{14,15}\) When a portosystemic shunt is occluded, venous return from the splanchnic viscera is obliged to flow entirely through the hepatic portal vasculature. In dogs with a poorly developed hepatic vascular bed, this may result in a marked reduction in overall splanchnic venous return and a large increase in portal venous pressure, with possible splanchnic hypoxia, ischemia, and ultimately necrosis.\(^3\)

Gross changes affecting the splanchnic viscera, as previously described, and portal pressure values are used by surgeons to assess if a dog can safely tolerate shunt occlusion. It may seem intuitive that, in dogs with congenital extrahepatic portosystemic shunts, those with a particularly small liver volume with respect to their bodyweight, are likely to have a less developed total hepatic venous bed. These dogs may then be at particular risk of marked portal hypertension, if their shunts are completely ligated and are more suited to methods of gradual shunt occlusion (e.g. ameroid ring constrictor, cellophane banding).\(^{10,11}\)
Measurement of portal venous pressure during portosystemic shunt procedures has long been used to help judge tolerance of a dog to complete CPSS occlusion. Portal pressure values of 7–10 mmHg as an incremental change during occlusion or 14–18 mmHg as an absolute postocclusion value have been proposed as guidelines for tolerance of complete CPSS ligation. It is worth noting that these guidelines for tolerance are criteria that surgeons have adopted empirically, based on clinical experiences, relating measured portal pressures to gross observations during surgery and to postoperative complications. Perhaps unsurprisingly, there are no prospective studies, to our knowledge, where all dogs' CPSS have been fully ligated, the postligation portal pressure and gross observations noted and subsequent survival or death recorded.

The gold standard in evaluating any method of attenuating CPSS must be long-term clinical outcome. A variety of methods have been reported for assessing response to surgery and include measurement of serum bile acids or ammonia concentrations, calculation of scintigraphic shunt fractions, and the resolution of clinical signs with or without ongoing reliance on prescription diets or medication. The variety of techniques for assessing outcome confound attempts to compare different studies. Some studies have specifically investigated complete versus partial ligation of CPSS and found that complete ligation offers a better long-term prognosis. Hottinger et al reported that of 14 dogs having single-surgery partial ligation of a CPSS and that were followed long-term, 11 developed recurrence of clinical signs, whereas 18 dogs that had complete ligation were clinically normal. Hunt and Hughes reported that 9 of 31 dogs with partially ligated CPSS had clinical signs related to portosystemic shunting at long-term follow-up whereas only 1 of 16 dogs that had complete ligation had recurrent signs. Johnson et al reported the results of ligation of portosystemic shunts in 46 dogs; of cases with long-term follow-up, 9 of 9 dogs with complete ligation were clinically normal whereas only 4 of 7 dogs that had partial ligation were clinically normal. Reasons for failure of partial ligation to resolve clinical signs in many dogs may be related to ongoing impairment of the liver's ability to intercept toxic metabolites carried in the portal venous circulation and to an ongoing process of liver atrophy as the liver continues to be deprived of hepatotrophic factors released by the intestines and pancreas.

More recently, methods of gradual progressive CPSS attenuation have gained favor. These techniques aim to reduce the need for intraoperative monitoring of portal pressure, reduce the risk of development of life-threatening portal hypertension, and may also reduce the incidence of subclinical portal hypertension in the postoperative period, which may then decrease the development of secondary acquired shunts. However, a possible criticism of these techniques is that they may not always result in eventual complete occlusion of the CPSS, and so only partial occlusion is achieved. It is difficult to compare long-term clinical outcomes of gradual occlusion techniques with complete ligation because no large scale prospective randomized studies have been performed. Nonetheless, there is a strong case to say that complete ligation of a CPSS is a desirable goal, when it does not produce significant portal hypertension.

Dogs with a TS/bodyweight ratio > 7 mm/kg often tolerate complete shunt occlusion and so attempts at complete ligation, after test occlusions are a worthwhile use of the surgeon's time. Conversely, dogs with a TS/bodyweight ratio < 5 mm/kg are much less likely to tolerate complete CPSS ligation and this information may lead the surgeon to dispense with intraoperative test occlusions and portal pressure measurements by selecting a gradual occlusion technique and so reduce both surgical and anesthetic time.

Measurement of Liver Volume

Various techniques have been described to assess liver volume in dogs. Ultrasonographic assessment of liver volume has been shown to be an accurate and reliable method. The technique is simple, non-invasive, and uses readily available equipment. An earlier study reported that ultrasonography was not useful in measuring liver volume in dogs. This study was limited to 16 dogs whereas the study by Barr et al assessed 100 dogs. Both studies had potentially confounding factors. In the study by Godshalk et al, these included general anesthesia and a delay of 24–48 hours between ultrasonography and liver weight measurement. In the study by Barr et al, these included euthanasia immediately before ultrasonography and no vessel ligation before liver removal for weighing. The reasons for better correlation in the study by Barr et al are unknown.

Most recently, use of helical computed tomography has been reported to estimate liver volume in dogs. Dogs with CPSS had livers that were, on average, 36.4% smaller than those of control dogs. A relationship between tolerance to shunt closure and liver size was not examined but the authors noted that the only dog with a portosystemic shunt in their population, which tolerated complete ligation of its shunt at the 1st surgery, had a liver volume in the normal range for dogs.

Blood Flow Measurement

We decided before the study not to attempt measurement of blood flow through the portal vein or CPSS. These variables are expected to influence portal pressure
changes after CPSS occlusion because dogs with a relatively high CPSS flow will experience a comparatively larger blood flow diversion into the hepatic venous bed. However, portal flow is known to vary significantly during the respiratory cycle. Furthermore, the longitudinal axis of the portal vein is frequently perpendicular to the ultrasound beam when measuring the maximum transverse distance across the liver, while quantitative measurement of flow is more accurately and reliably obtained when blood flow is nearly parallel to the sound beam. We acknowledge that had a reliable method of measuring venous flow through the portal vein and CPSS been practical and data gathered, an improved model to describe portal pressure changes after CPSS occlusion may have been possible.

Multiple linear regression analysis yielded a model of portal pressure rise after shunt occlusion:

\[
\text{Portal pressure rise (mmHg)} = 65.81 + 2.71 \cdot \log(\text{bodyweight}) - 25.25 \cdot \log(\text{TS}^2).
\]

This model was not tested as a predictive model. There was no significant correlation between intestinal oxygenation changes and any other measured variable. Furthermore, readings were not always generated at each time point by the pulse oximeter after CPSS occlusion. Pressure is exerted by the probe spring on the intestinal wall and this may have been sufficient to have affected blood flow through the tissue. Furthermore, application of the probe to the intestinal wall frequently resulted in a prolonged peristaltic response in the intestine adjacent to the probe, which is also likely to have affected tissue perfusion and thus oxygenation. Intestinal surface oximetry measurement has been identified as a potentially useful method for evaluating the effect of reduced splanchnic venous return on intestinal oxygenation. This technique used a probe that was applied gently to the serosal surface of the intestine but did not grip the tissue.

Summarily, we found that liver volume, relative to bodyweight, affects the tolerance to acute complete occlusion of CPSS in dogs. Ultrasonographic measurement of liver size and measurement of bodyweight may provide a useful preoperative indication of the feasibility of complete ligation of extrahepatic CPSS in dogs.

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