Dynamic computed tomographic quantitation of hepatic perfusion in dogs with and without portal vascular anomalies

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Objective—To compare hepatic, pancreatic, and gastric perfusion on dynamic computed tomography (CT) scans of clinically normal dogs with those of dogs with portal vascular anomalies.

Sample Population—Dynamic computed tomography (CT) scans of 10 clinically normal dogs and 21 dogs with portal vascular anomalies.

Procedures—Retrospective analysis of dynamic CT scans. Hepatic arterial perfusion, hepatic portal perfusion, total hepatic perfusion, hepatic perfusion index, gastric perfusion, and pancreatic perfusion were calculated from time attenuation curves.

Results—Mean ± 1 technology hepatic arterial perfusion was significantly higher in affected dogs (0.57 ± 0.27 mL/min•mL⁻¹) than in clinically normal dogs (0.23 ± 0.11 mL/min•mL⁻¹), and hepatic portal perfusion was significantly lower in affected dogs (0.52 ± 0.47 mL/min•mL⁻¹) than in clinically normal dogs (1.08 ± 0.45 mL/min•mL⁻¹). This was reflected in the hepatic perfusion index, which was significantly higher in affected dogs (0.59 ± 0.34), compared with clinically normal dogs (0.19 ± 0.07). Gastric perfusion was significantly higher in dogs with portal vascular anomalies (0.72 ± 0.44 mL/min•mL⁻¹) than in clinically normal dogs (0.41 ± 0.21 mL/min•mL⁻¹), but total hepatic perfusion and pancreatic perfusion were not significantly different. Among subgroups, dogs with congenital intrahepatic portosystemic shunts and dogs with arterioportal fistulae had higher hepatic arterial perfusion than those with normal dogs. Dogs with congenital intrahepatic portosystemic shunts also had an increase in gastric perfusion and hepatic perfusion index.


Hepatic vascular anomalies are rare in dogs and cats, but result in substantial morbidity and death. Congenital and acquired portosystemic shunts as well as arterioporal fistulae alter hepatic hemodynamics by routing portal blood flow away from the liver. The reduced portal blood flow causes microhepatia as well as neurologic and gastrointestinal clinical signs.

Hepatic perfusion has been studied in clinically normal dogs,1,6 naturally occurring portosystemic shunts,7 and surgically created shunts8 by use of a variety of invasive and noninvasive methods. To compensate for reduced portal blood flow, hepatic arterial, pancreatic, and small intestinal perfusion increases in dogs with portosystemic shunts and in people with portal hypertension.9,10 The hepatic arterial vascular resistance decreases with decreased portal flow, providing a 0.0025 mL/min•g⁻¹ increase in arterial flow for every 0.01 mL/min•g⁻¹ decrease in portal flow.11 The techniques generally used to measure hepatic perfusion include nuclear scintigraphy and Doppler ultrasonography.

The increase in arterial contribution to hepatic blood flow can be measured by use of the hepatic perfusion index. Dogs have been evaluated with nuclear scintigraphy, where the hepatic perfusion index is defined as the ratio of the slopes of arterial and portal portions of the hepatic time-activity curve.5,7 Computed tomography has been used in people to measure the hepatic perfusion index, which is defined as the ratio of absolute arterial to total hepatic flow.11,12 Iodinated contrast medium can be used as a perfusion tracer because of the linear relationship between density and concentration in CT. Both of these methods have shown an increase in the hepatic perfusion index in conditions where reduced portal blood flow exists, whether congenital or acquired.6,7,10,13

To calculate a separate arterial and portal flow in the liver, the TAC generated from dynamic CT must be divided into arterial and portal portions. In people, the peak attenuation of the spleen is used to signal the end of hepatic arterial enhancement. In dogs, dynamic CT

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performed at the level of the porta hepatis rarely contains the spleen as a reference organ. The pancreas and stomach are usually included in the dynamic CT and are also supplied by the celiac artery. We hypothesized that these organs could be used in place of the spleen to separate the hepatic TAC into arterial and portal components.

The purpose of the study reported here was to compare hepatic perfusion index, hepatic arterial perfusion, hepatic portal perfusion, total hepatic perfusion, gastric perfusion, and pancreatic perfusion on CT scans of clinically normal dogs with those of dogs with portosystemic shunts.

Materials and Methods

Study design—A retrospective case control study was performed on all dogs by use of CT scans of portosystemic shunts at the Matthew J. Ryan Veterinary Hospital of the University of Pennsylvania. As a retrospective review of images, approval by the animal care and use committee was not required. The inclusion criterion for all dogs was a dynamic CT scan, and affected dogs had a congenital or acquired portal vascular anomaly. Exclusion criteria were factors that would adversely affect perfusion calculation, such as severe motion artifact, streak artifact, and late hepatic enhancement. Records of 28 dogs with portosystemic shunts and a dynamic CT scan were identified. Seven of these were excluded because of motion artifact (1 record), high-density artifact (2), no reference organ included (3), and late hepatic enhancement (1). Records of a group of 12 clinically normal control dogs with dynamic CT scans meeting the above criteria were identified. Two of these dogs were excluded because of motion artifact (1) and late hepatic enhancement (1). Records of 21 dogs with portosystemic shunts and 10 clinically normal dogs were included in the study.

Signalment—The age range of the 21 affected dogs whose records were included in the study was 1 month to 4.3 years, with a mean age of 12.1 ± 11.4 months. The 10 clinically normal dogs ranged from 6 to 12 months in age, with a mean of 7.6 ± 2.2 months. Types of hepatic vascular anomalies included single extrahepatic portosystemic shunts (2 dogs), single intrahepatic portosystemic shunts (9), multiple acquired extrahepatic portosystemic shunts (4), and intrahepatic arterioportal fistulae with multiple acquired portosystemic shunts (6).

Image analysis—Dynamic CT images were made by use of a single detector row helical CT scanner. Acquisition parameters were 2- to 7-mm collimation, 80 to 120 kV, and 100 to 200 mA. A low dose of an iodinated contrast medium (0.5 mL/kg) was injected into a cephalic or jugular vein at a rate of 5 mL/s. Images were acquired with either a 5-second delay after injection with 2-second intervals for a total of 20 to 60 images or with no delay and a 1-second interval for 60 to 70 images.

Dynamic CT images were analyzed by use of freely available perfusion software and a spreadsheet program. Regions of interest were placed within the aorta, portal vein, liver, pancreas, and gastric wall (Figure 1).

Software analysis parameters were HU filter of 0 to 400, smoothing kernel of 1, 2 and 1 pixel, and logarithmic model. Time attenuation curves were generated from these regions of interest by use of the perfusion software, subtracted from baseline values for clinical normalization, and saved as spreadsheets.

Time attenuation curves for hepatic arterial perfusion, gastric perfusion, and pancreatic perfusion were analyzed with an equation as follows (equation 1):

\[
\text{Perfusion} \left( \text{mL/min}\cdot\text{mL}^{-1} \right) = \text{maximum gradient of } \text{TAC} \text{/peak arterial enhancement (HU)} \times 60
\]

Calculation of hepatic portal perfusion required an additional step. Because the liver has a dual blood supply, the portion of the hepatic TAC supplied by portal enhancement must also be determined. The direct method of calculating hepatic portal perfusion was developed to increase accuracy of the calculation by subtracting the arterial portion of the hepatic curve to leave a pure portal TAC and by use of the portal vein enhancement to normalize the portal perfusion rather than the aorta. To remove the arterial portion of the hepatic curve, a reference organ TAC was scaled to the slope of the arterial portion of the hepatic curve and then subtracted from it. The direct method was shown to be superior to the use of equation 1 (indirect method). The following equation describes the calculation of the direct method (equation 2):

\[
\text{Portal perfusion} \left( \text{mL/min}\cdot\text{mL}^{-1} \right) = \text{maximum gradient of corrected hepatic TAC/peak portal enhancement (HU)} \times 60
\]

For total hepatic perfusion, the arterial and portal perfusions were summed. Slopes were calculated with a minimum of 3 datum points.

Pancreatic and gastric perfusion was calculated for clinically normal and affected dogs, and the most con-
sistent organ was used as a reference organ. The celiac artery supplies both organs, and the time of plateau of arterial enhancement approximates the end of arterial enhancement in the hepatic TAC. All calculations were recorded in mL/min•mL\(^{-1}\) of tissue. The hepatic perfusion index was defined as the ratio of hepatic arterial perfusion to total hepatic perfusion (sum of arterial and portal perfusion).

**Statistical analysis**—Perfusion of the reference organs on CT scans was compared between clinically normal and affected dogs by use of the Student t test. Once the more uniform reference organ was identified, it was used to calculate the hepatic portal perfusion values. To determine differences between clinically normal and affected dogs with regard to hepatic arterial perfusion, hepatic portal perfusion, total perfusion, and hepatic perfusion index, the Student t test was used. Portal perfusion and related measurements were not calculated for dogs with arterioportal fistula because of the high incidence of hepatofugal flow.

To determine whether perfusion measurements differed by shunt type, analysis of variance was performed. Single intrahepatic shunt, single extrahepatic shunt, multiple acquired extrahepatic shunt, and arterioportal fistula groups were compared with clinically normal dogs by use of the Dunnett 1-tailed t test. All analyses were performed by use of a statistical software program.
affected and clinically normal dogs (Table 1). Hepatic arterial perfusion was significantly higher and hepatic portal perfusion was significantly lower in affected dogs, compared with those in clinically normal dogs. Total hepatic perfusion did not differ between affected and clinically normal dogs (Figure 2). Dogs with portal vascular anomalies had a significantly higher hepatic perfusion index than did clinically normal dogs (P = 0.003).

The difference in mean perfusion variables between clinically normal dogs and subgroups of dogs with vascular anomalies was determined (Table 2). Hepatic arterial perfusion was significantly increased in dogs with intrahepatic shunts and arterioporal fistulae, compared with clinically normal dogs. Hepatic portal perfusion and total perfusion were not significantly different between clinically normal dogs and subgroups of dogs with vascular anomalies. The hepatic perfusion index was significantly higher in dogs with congenital intrahepatic shunts, compared with clinically normal dogs. Pancreatic perfusion was not significantly different between clinically normal dogs and subgroups of dogs with vascular anomalies. Gastric perfusion was increased in dogs with arterioporal fistula, compared with that in clinically normal dogs, but this difference was not significant (P = 0.093).

**Discussion**

The perfusion variables calculated in our study by use of dynamic CT agreed well with values reported in the literature, which lends credence to its use in determining perfusion noninvasively. Further studies are required to validate the repeatability of hepatic perfusion in a single dog, as portal perfusion can vary after feeding and with different composition of diets. All dogs undergoing CT had food withheld overnight, so this may not have affected the hemodynamics at the time of our study. Hepatic perfusion is inherently variable between dogs, with a mean value in the range of 1.0 to 1.3 mL/min•g⁻¹. This variability will be a natural limitation of hepatic perfusion measurement.

Because the CT method involves drawing regions of interest and calculating slopes, there may be interobserver and intraobserver variation in calculating the variables. Repeatability of calculation was not assessed in our study.

The pancreas was used as a reference in correcting the hepatic curve for arterial perfusion (direct method). Pancreatic values were not significantly different between clinically normal and affected dogs, which supports the use of the pancreas as a reference organ in the calculation. Gastric perfusion was significantly different in dogs with intrahepatic shunts, compared with clinically normal dogs, which may affect the direct method calculation. The stomach is also more prone to motion artifact from peristalsis. The use of the pancreas as a reference organ provided physiologic values of hepatic portal perfusion and revealed differences between clinically normal and affected dogs. With direct CT, the pancreas is an acceptable substitute for the spleen in calculating hepatic portal perfusion.

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Table 2—Comparison of mean hepatic perfusion variables of dogs grouped by shunt type to clinically normal dogs.

<table>
<thead>
<tr>
<th>Perfusion measurement</th>
<th>Status</th>
<th>No. of dogs</th>
<th>Difference of mean values (mL/min•mL⁻¹)</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic arterial perfusion</td>
<td>CI</td>
<td>9</td>
<td>0.39*</td>
<td>0.10–0.67</td>
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<td></td>
<td>CE</td>
<td>2</td>
<td>0.07</td>
<td>-0.40–0.54</td>
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<td></td>
<td>MA</td>
<td>4</td>
<td>0.04</td>
<td>0.05–0.70</td>
</tr>
<tr>
<td></td>
<td>APF</td>
<td>6</td>
<td>0.33*</td>
<td>0.01–0.64</td>
</tr>
<tr>
<td>Hepatic portal perfusion</td>
<td>CI</td>
<td>7</td>
<td>-0.45</td>
<td>-1.08–0.18</td>
</tr>
<tr>
<td></td>
<td>CE</td>
<td>2</td>
<td>-0.71</td>
<td>-1.68–0.27</td>
</tr>
<tr>
<td></td>
<td>MA</td>
<td>2</td>
<td>-0.82</td>
<td>-1.80–0.16</td>
</tr>
<tr>
<td></td>
<td>APF</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Total hepatic perfusion</td>
<td>CI</td>
<td>7</td>
<td>-0.04</td>
<td>-0.65–0.57</td>
</tr>
<tr>
<td></td>
<td>CE</td>
<td>2</td>
<td>-0.64</td>
<td>-1.59–0.31</td>
</tr>
<tr>
<td></td>
<td>MA</td>
<td>2</td>
<td>-0.35</td>
<td>-1.30–0.60</td>
</tr>
<tr>
<td></td>
<td>APF</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Pancreatic perfusion</td>
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<td>0.31</td>
<td>-0.28–0.90</td>
</tr>
<tr>
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<td>CE</td>
<td>2</td>
<td>-0.04</td>
<td>-0.96–0.87</td>
</tr>
<tr>
<td></td>
<td>MA</td>
<td>3</td>
<td>-0.04</td>
<td>-0.96–0.87</td>
</tr>
<tr>
<td></td>
<td>APF</td>
<td>5</td>
<td>-0.22</td>
<td>-0.92–0.49</td>
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<tr>
<td>Gastric perfusion</td>
<td>CI</td>
<td>7</td>
<td>0.57*</td>
<td>0.10–1.03</td>
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<tr>
<td></td>
<td>CE</td>
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<td>0.13</td>
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</tr>
<tr>
<td></td>
<td>MA</td>
<td>4</td>
<td>0.003</td>
<td>-0.55–0.56</td>
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<tr>
<td></td>
<td>APF</td>
<td>6</td>
<td>0.27</td>
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<tr>
<td>Hepatic perfusion index</td>
<td>CI</td>
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<td>0.38*</td>
<td>0.02–0.74</td>
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<tr>
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<tr>
<td></td>
<td>APF</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Significant (P < 0.05) difference between affected and clinically normal dogs. †Unitless measure. CI = Congenital intrahepatic shunt. CE = Congenital extrahepatic shunt. MA = Multiple acquired extrahepatic shunts. APF = Arterioporal fistula. NA = Not applicable.
Dogs with intrahepatic portosystemic shunts had significantly increased gastric perfusion, compared with clinically normal dogs. Increased duodenal and pancreatic perfusion has been observed in dogs with experimentally created portosystemic shunts; however, gastric perfusion remained within normal limits. Experimentally created shunts are extrahepatic and are performed in adult dogs with developed portal vasculature. The hemodynamics are likely different from a congenital intrahepatic shunt in which hepatic portal vessels are hypoplastic or aplastic. Possible explanations for the increased gastric perfusion in dogs with intrahepatic portosystemic shunts include increased flow through the gastric artery, unidentified varices, and gastric inflammation. Two of the dogs in the present study developed duodenal ulcers; however, the cause was undetermined.

The hepatic artery was able to maintain a normal total hepatic blood supply in dogs with portal vascular anomalies. Looking at the differences between mean arterial and portal perfusion in clinically normal and affected dogs, a 0.6 mL/min·mL⁻¹ ratio of increase in arterial perfusion occurs for every 1 mL/min·mL⁻¹ decrease in portal perfusion, which is higher than the 0.25:1 ratio reported in physiologic experiments. This may reflect the lifelong duration of altered response rather than the shorter periods experienced by dogs with experimentally created shunts. Such dogs have a decrease in total portal perfusion, whereas the congenitally affected dogs did not.

The hepatic perfusion index was significantly increased in the affected dogs as a group and in dogs with intrahepatic shunts as a subgroup. This index should be a reliable measurement of hepatic perfusion, as it eliminates variation caused by cardiac output and contrast bolus dynamics. The variant used in nuclear medicine has shown similar alterations in dogs with portosystemic shunts and a reduction in the index after corrective vascular surgery. One of the more common hemodynamic methods used to diagnose and monitor dogs with portosystemic shunts is the shunt fraction. This scintigraphic technique quantifies the fraction of blood that bypasses the liver through a portosystemic shunt and has been shown to be correlated with outcome of surgery to correct the shunt. Limitations to the shunt fraction exist such as inaccuracy and the shunt fraction does not measure perfusion of the liver directly. Many dogs undergoing partial ligation of a shunt have persistent flow after surgery, which may not correlate directly with the change in perfusion of the liver. Measurements of perfusion by use of CT could offer a direct measurement of the initial hepatic perfusion and the change in postsurgical hepatic perfusion.

Evaluation of hepatic, gastric, and pancreatic perfusion is feasible with dynamic CT. The absolute perfusion values obtained by this method are within the expected range when calculated for clinically normal dogs and reveal significant differences between clinically normal dogs and those with congenital portal vascular anomalies. This noninvasive technique can be applied to the organ as a whole or to selected segments by use of regions of interest and will be a useful tool in evaluating perfusion in dogs with hepatic vascular anomalies.

References