Evaluation of interoperator variance in shunt fraction calculation after transcolonic scintigraphy for diagnosis of portosystemic shunts in dogs and cats

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Objective—To determine interoperator variance in shunt fraction calculation.

Design—Case series.

Sample Population—101 transrectal portoscintigraphic studies.

Procedure—Results of dynamic portoscintigraphic studies were reviewed by 4 radiologists without knowledge of signalment, history, or medical profile. Results were judged to be negative or positive on the basis of the dynamic scan. Composite images were formulated, and hand-drawn regions of interest were determined for the heart and liver. Time-activity curves were generated, time-zero points were selected, curves were integrated during a 10-second interval, and shunt fractions were calculated.

Results—Radiologists were in agreement regarding positive versus negative results for 99 of 101 studies. Interoperator variance in shunt fraction calculation ranged from 0.4 to 59.6%. For 51 studies with positive results, variance ranged from 2.5 to 59.6% (mean ± SD, 22.8 ± 14.5%); differences among reviewers were significant. For 48 studies with negative results, variance in shunt fraction ranged from 0.4 to 25.9% (mean, 5.3 ± 5.8%); significant differences among reviewers were not detected. Shunt fraction calculations were not exactly reproducible among radiologists in 94 and 100% of studies with negative or positive results, respectively.

Conclusions and Clinical Relevance—Results suggest that shunt fraction values are not reproducible among operators. Range in variability was greater in studies with positive results. This factor may be of particular clinical importance in reassessment of patients after incomplete shunt ligation. (J Am Vet Med Assoc 2001;218:1116–1119)

Portoscintigraphy is recognized as an excellent diagnostic screening tool for detection of portosystemic shunting. Several radiopharmaceuticals and methods of administration have been investigated. The current imaging agent of choice for portoscintigraphy is sodium pertechnetate Tc 99m (Na99mTcO4). When administered rectally, approximately 14% of the administered dose is rapidly absorbed through the colonic mucosa and into the portal vasculature. Because Na99mTcO4 is neither extracted nor bound to the tissues it perfuses, a nuclear portogram results. Shunting is diagnosed if radiopharmaceutical activity is identified in the heart prior to the liver or if simultaneous activity in both organs is detected. When radiopharmaceutical activity is detected in the liver a minimum of 2 seconds before it is detected in the heart, shunting is ruled out.

Shunt fractions are calculated in an empirical attempt to quantify the percentage of total portal blood flow that is diverted through 1 or more shunt vessels. Regions of interest (ROI) for the heart and liver are typically hand-drawn from a composite image that comprises multiple still frames acquired during the initial pass of radiopharmaceutical through the portal vein to the heart. From these ROI, time-activity curves are generated, and time zero is selected (time at which activity in either liver or heart is twice that of background activity). The sum of counts during the period of time representing first-pass activity through the heart and liver is used to calculate a value for percentage shunting. Daniel et al found good correlation between scintigraphy fraction values obtained via rectal administration of Na99mTcO4 and values obtained via injection of radiolabeled microspheres into mesenteric veins. In comparing scintigraphy via rectal administration of Na99mTcO4 versus rectal administration of iodoamphetamine I 123 (IMP), Koblik et al determined that Na99mTcO4 overestimated shunt fraction values, particularly in large shunts. Iodoamphetamine I 123 is efficiently extracted and bound to amine receptors in the liver and lung and, therefore, is theoretically dispersed in the same manner as radiolabeled microspheres injected into the mesenteric vein. It has been postulated that the disparity in shunt fraction values between Na99mTcO4 and IMP is a reflection of the inherent inability to appropriately model the complex kinetics of Na99mTcO4 tracer uptake and distribution, and that differences in determination of organ ROI and time-zero selection among individuals are not substantial.

Approximately 100 portoscintigraphic studies are performed at our institution yearly. Many of these stud-
ies are reevaluations performed after surgical intervention or shunt occlusion. Thus, there is special interest in quantifying and comparing the degree of shunting that is evident before and after surgery. It was our hypothesis that portoscintigraphy performed via rectal administration of Na\textsuperscript{99m}TcO\textsubscript{4} is an excellent diagnostic test in determining the presence or absence of portosystemic shunting but that there is significant interoperator variability in shunt fraction calculation. The purpose of the study reported here was to determine interoperator variance in shunt fraction calculation.

**Materials and Methods**

Scans obtained during portoscintigraphic studies performed in 101 dogs and cats between September 1997 and September 1998 were used in this study. All scans were considered to be of diagnostic quality. All portoscintigraphic studies had been performed by use of a standard protocol.\textsuperscript{1} Most patients were admitted to the hospital on the day of the procedure. Enema administration and feeding prior to portoscintigraphy varied. Scans were performed with patients in right lateral recumbency on the gamma camera surface. One to 5 mCi of Na\textsuperscript{99m}TcO\textsubscript{4}, followed by 10 to 20 ml of room air, was administered into the distal portion of the colon by use of a 5-F infant feeding tube. Scanning was initiated just prior to deposition of the radiopharmaceutical into the colon to assure complete first-pass shunting of Na\textsuperscript{99m}TcO\textsubscript{4} from the portal vein to the heart. Each dynamic study consisted of a series of 2-second static images acquired during a 2.5-minute period. Scans were initially stored on computer and later archived to disk.

All scans were independently reviewed on a computer monitor by 4 radiologists (VF5, CDL, LMM, REP). Studies were chronologically randomized, and patient signalments and histories were not provided. Each radiologist first determined, on the basis of review of the dynamic scan, whether results were negative or positive with regard to evidence of a portosystemic shunt. Radiologists were then asked to create a composite image from the 75 images acquired every 2 seconds during the 2.5-minute dynamic series. Hand-drawn ROIs for the heart and liver were created from the composite image by each reviewer for every patient. These ROIs were copied onto each individual frame of the dynamic series, and the images were displayed in cinematic fashion. Reviewers were allowed to adjust image brightness to their personal level of preference for diagnostic interpretation and ROI selection. Time-activity curves were generated from the heart and liver ROIs. Time zero, defined as the point at which radioactivity in either the heart or liver was twice that of background activity, was determined by the individual who had created the curves from their hand-drawn ROI. Representative heart and liver time-activity curves were then integrated during a 10-second period, beginning at time zero. Shunt fraction percentage for the 10-second period was calculated as heart count divided by the sum of heart and liver counts, multiplied by 100. The composite image with heart and liver ROIs and time-activity curves with the selected time-zero point were saved to disk for each patient by each reviewer. Reviewers were not allowed to alter their work once an evaluation was complete. Scan assessments and measurements were performed by use of computer software.\textsuperscript{b}

**Statistical analyses**—Shunt fraction data were entered onto a spreadsheet. The 4 shunt fraction values determined for each patient were expressed as a mean ± SD. The interaction between shunt classification (positive or negative) and operator was evaluated by use of ANOVA with repeated measures. A value of \( P < 0.05 \) was considered significant.\textsuperscript{a}

**Results**

The reviewers were in subjective agreement as to which studies yielded negative or positive results for 99 of 101 patients. The 2 studies for which reviewers were not in agreement were not included in further statistical evaluation. Interoperator variance in calculation of shunt fractions ranged from 0.4 to 59.6% (ie, the shunt fraction calculated by 1 radiologist differed by 59.6% from the shunt fraction calculated by another radiologist) overall. Fifty-one studies yielded positive results, indicating portosystemic shunting; in this group, interoperator variance for each study ranged from 2.5 to 59.6% (mean ± SD, 22.8 ± 14.5%), and differences among radiologists were significant (\( P < 0.05 \)). This significance was almost entirely attributable to differences between reviewer No. 3 and the other reviewers (Table 1). Forty-eight studies yielded negative results for portosystemic shunting; in this group, interoperator variance for each study ranged from 0.4 to 25.9% (mean, 5.3 ± 5.6%), and differences among radiologists were not significant. Complete agreement between radiologists (to within 1%) was obtained for 3 studies, all of which yielded negative results for portosystemic shunting. In 10 of the studies with negative results, 1 or more of the radiologists had calculated shunt fractions > 15%. The signalments and clinical profile of these patients were reviewed. Eight small-breed dogs (Shih Tzu, Norwich Terrier, Miniature Schnauzer, Chihuahua, Miniature Pinscher, Yorkshire Terrier, Toy Poodle, and Pomeranian), 1 large-breed dog (Labrador Retriever), and 1 cat (domestic shorthair) were represented.

**Discussion**

Results of the study reported here support our hypothesis that shunt fraction values are generally nonreproducible among individuals. In general, ranges of variability were greater for studies with positive results for shunting. Several factors may have contributed to the interoperator variance observed in our study, including overall scan quality, ROI selection, and time-zero designation.

Spatial and temporal resolution is inherently poor in nuclear scintigraphy, compared with most other imaging modalities. Few photons can be collected during the short time intervals used for image acquisition; therefore, any additional causes of decreased resolution compound the difficulty in separating structures in close proximity to each other. Factors that contribute to the quality of the scintigraphic scan include adequate radiopharmaceutical dose, uptake as a bolus, absence of patient motion, and lack of excessive background radioactivity. Failure to administer an adequate dose of radiopharmaceutical may result in poor count...
Mean shunt fractions determined by radiologist No. 3 for studies with positive results were significantly different from those of the other 3 radiologists; this was not thought to be the result of error. All radiologists were similarly trained, and the protocol for scan evaluation was reviewed as a group prior to the initiation of the study. An adequate explanation for this difference cannot be offered.

Multiple references cite 10 to 15% shunting during an 8- to 12-second time interval as the cut-off point above which results are considered positive for portosystemic shunting. Van Vechten et al observed that shunt fraction values are higher in clinically normal dogs of small breeds, compared with values in dogs of large breeds. In our study, results were considered negative for shunting by all reviewers for 10 studies for which 1 or more reviewers calculated shunt fraction as > 15%. Review of signalment and clinical profile of these patients revealed that 8 were small-breed dogs, 1 was a large-breed dog, and 1 was a cat. Extreme patient motion was the cause of inaccurate calculations for 1 dog. Single extrahepatic shunts had been diagnosed in the cat and a Chihuahua previously, and recheck scans had been performed 6 to 8 weeks after application of a ring constrictor on the shunting vessel. It is possible that continued shunting attributable to incomplete closure of the ring constrictor was still occurring. The development of multiple extrahepatic shunts attributable to prolonged portal hypertension could not be ruled out. Neither animal had clinical signs of disease at the time of reevaluation. An intrahepatic shunt had been diagnosed in the large-breed dog, a Labrador Retriever. At surgery, the shunt vessel was identified in the left medial liver lobe. Because of abnormally high portal pressures measured during complete ligation of the shunting vessel, only partial ligation was performed. The portoscintigraphic reevaluation was performed 3 months after surgery, and shunt fraction value agreement was within 1% among reviewers. Continued shunting through the partially attenuated intrahepatic vessel was suspected, although the development of multiple extrahepatic shunts could not be ruled out. Clinically, the dog did not have signs of persistent shunting. Because of the improved clinical condition of these 3 patients after surgery, further invasive diagnostics were not pursued, so persistent shunting was not observed.

For 2 studies, radiologists disagreed regarding whether shunting was present. Simultaneous radioactivity was seen in the heart and liver in both studies. Although simultaneous activity is usually considered to indicate shunting, other features of the scans led reviewers to question this finding. In 1 dog, patient movement compromised interpretation, and shunt fraction values ranged from 7.2 to 43.1%. In the second dog, the liver appeared adequate in size although it was dorsally displaced by what was presumed to be fat in the falciform ligament; shunt fraction values ranged from 22.9 to 29.6%. One dog had surgery 6 months previously for an extrahepatic shunt, at which time a ring constrictor was placed on the shunting vessel. Bile acid concentrations were slightly greater than reference range value at the time of reevaluation, although the
owners reported that the dog seemed clinically normal. Because of the dog’s improved clinical condition, additional surgery was not performed, although persistent shunting was suspected on the basis of high bile acid concentrations and persistently high shunt fraction values. The second dog had surgery for correction of an intrahepatic shunt 3 years before reevaluation. Bile acid concentrations determined 1 month prior to reevaluation were high. The owners reported that the dog was less active than dogs of similar age. Overall, the dog was in good body condition (body condition score, 7/10). Surgical exploration revealed a patent intrahepatic shunt. We therefore recommend that when results of scintigraphy are inconclusive but other clinical data are consistent with portosystemic shunting, further diagnostic procedures such as mesenteric venography or surgical exploration should be considered.

There is some evidence that partially ligated shunts may become occluded. Determination of shunt fraction values after surgery may give an idea of long-term prognosis or need for additional surgery. Questions arise, however, regarding when the reevaluation should be performed and at what shunt fraction value additional surgery should be considered. Although persistent shunting may be revealed by nuclear scintigraphy in a clinically normal patient, the long-term manifestations of shunting are unknown. Because accurately quantifying shunting by use of available methods is difficult, the authors believe that basing further treatment solely on fraction values would be unwise. Although scintigraphy performed via rectal administration of radiopharmaceuticals is a highly reliable diagnostic test for diagnosis of portosystemic shunting, results should be interpreted in the context of additional medical and clinical information. High scan quality is a necessity for increasing the accuracy of calculated values, but even with high quality scans, interoperator variance in shunt fraction determination, particularly in studies with positive results, is substantial.

References