Evaluation of gradual occlusion of the caudal vena cava in clinically normal dogs

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**Objectives**—To devise a technique for gradual occlusion of the caudal vena cava in dogs and determine effects of complete occlusion of the caudal vena cava.

**Animals**—8 mixed-breed hounds that weighed between 25 and 30 kg.

**Procedure**—Baseline evaluation of dogs included serum biochemical analyses and determination of glomerular filtration rate (GFR) with dynamic renal scintigraphy and plasma clearance analysis. An occluder was placed around the vena cava in the region cranial to the renal veins. The occluder was attached to a vascular access port. The vena cava was gradually occluded over 2 weeks. The GFR was measured every 2 weeks after surgery, and venograms were performed every 3 weeks after surgery. Blood samples were collected every 48 hours for the first week and then weekly thereafter to measure BUN and creatinine concentrations and activities of alanine transaminase, alkaline phosphatase, and creatinine kinase. Dogs were euthanatized 6 weeks after surgery, and tissues were submitted for histologic examination. The GFR and biochemical data were compared with baseline values.

**Results**—Gradual occlusion of the caudal vena cava was easily and consistently performed with this method, and adverse clinical signs were not detected. Formation of collateral vessels allowed overall GFR to remain constant despite a decrease in function of the left kidney. Measured biochemical values did not deviate from reference ranges.

**Conclusions and Clinical Relevance**—Gradual occlusion of the caudal vena cava may allow removal of adrenal gland tumors with vascular invasion that would otherwise be difficult or impossible to resect. (Am J Vet Res 2003;64:1347–1353)

The adrenal glands are located in close proximity to the great vessels of the abdomen. This is especially true of the right adrenal gland, where the adrenal capsule is often continuous with the tunica externa of the vena cava. Vascular invasion may result from adrenal gland tumors and has been described most commonly in association with adrenocortical adenocarcinomas and pheochromocytomas. Tumor extension may involve the phrenicoabdominal vein, renal artery, renal vein, or vena cava and can result in hemorrhage. Additionally, tumor growth into the vena cava is problematic, often making surgical excision difficult, if not impossible, because of the risk of hemorrhage. Increased risk is encountered when a venotomy is performed to remove intravascular tumors or thrombi. Thus, a technique is needed that would allow removal of involved vascular structures while minimizing hemorrhage by eliminating the need for a venotomy. Additional benefits would include a more thorough excision of tumor cells through removal of the invaded caval wall and avoidance of potential complications associated with acute vascular occlusion and healing of the vessel wall after an incision.

Temporary occlusion of the cava reportedly is tolerated well by dogs, and occlusion of the cava with a balloon catheter has been performed. Other studies have described the effects of acute ligation of the vena cava proximal and distal to the renal veins. These studies all reported morbidity of the dogs attributable to the ligation technique, and some even reported fatalities of the dogs used in the studies. In these studies, effects of caval ligation on the kidneys were monitored by assessment of serum biochemical analyses (ie, BUN and creatinine concentrations), which has subsequently been determined to be an indicator of late-stage renal dysfunction.

In the study reported here, we investigated a potential surgical option for resection of adrenal gland tumors that have local vascular invasion that would make it difficult to excise the affected tissues by use of traditional methods. We hypothesized that gradual occlusion of the vena cava in dogs would allow sufficient collateral circulation to develop caudal to the invaded cava such that subsequent ligation and removal of the affected portion of the vena cava would be simplified, yet at the same time avoiding the negative adverse effects of acute ligation of the vena cava on renal function. After development of collateral vessels, the vena cava could be ligated cranial and caudal to the tumor, and the tumor and affected section of the vena cava could be excised en bloc without a venotomy; thus, the risk for hemorrhage would be minimized. We also hypothesized that gradual occlusion would not...
cause permanent adverse effects on renal function. The objectives of the study reported here were to evaluate whether gradual occlusion of the vena cava could be easily and reliably accomplished in dogs. Furthermore, we intended to quantify any adverse effects of this type of caval ligation on renal function.

Materials and Methods

Animals—Eight mixed-breed hound-type dogs (4 sexually intact males and 4 sexually intact females) weighing between 25 and 30 kg were acquired for use in the study. Prior to enrollment in the study, all dogs were deemed healthy on the basis of results of a physical examination, CBC, serum biochemical analyses, and heartworm antigen test. The protocol was approved by the Texas A&M University Laboratory Animal Care Committee.

Assessment of renal function—Dynamic renal scintigraphy by use of technetium 99m-diethylenetriaminepentaacetic acid (99mTc-DTPA) was performed to provide a baseline estimate of the global glomerular filtration rate (GFR) as well as the GFR for each kidney. In addition, global GFR was also estimated by use of plasma clearance analysis via 2 plasma samples obtained after administration of the same dose of 99mTc-DTPA. Food was withheld overnight from the dogs prior to the procedure, but access to water was not restricted. Dogs were not sedated for this procedure.

Data analysis was performed by 1 investigator (AMB). For dynamic renal scintigraphy, regions of interest were manually drawn around the kidneys, and the percentage of the radioactive dose that accumulated in each kidney between 1 and 3 minutes after the injection of radioisotope was obtained by use of a gamma camera. A spreadsheet was used to facilitate the calculations. The GFR estimation was corrected on the basis of background and depth and calculated by use of the following equation:

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GFR = \left(0.194 \times \frac{\text{percentage of the dose accumulated in the right kidney}}{\text{percentage of the dose accumulated in the left kidney}}\right) - 0.37
\]

For estimation of the global GFR by use of plasma clearance analysis, plasma samples were obtained from a peripheral vein 20 and 180 minutes after injection of 99mTc-DTPA. The number of radioactive counts per minute for each plasma sample was measured along with counts for a known standard, by use of a well counter. All counts were corrected on the basis of radioactive decay to the time of injection. The GFR was estimated by use of a simple monocompartment model, which was validated in another study. In accordance with university policy, the dogs were confined until their radiation counts had decreased to a safe value (2 mR/h, as measured on the surface of the dogs with a Geiger counter; this value was generally reached within 12 to 24 hours).

Surgical procedures—One week later, the dogs were medicated by IM injection of butorphanol tartrate (0.2 mg/kg) and glycopyrrolate (0.011 mg/kg), and anesthesia was induced by IV injection of propofol (4 to 6 mg/kg). Dogs were then intubated, and anesthesia was maintained by administration of 1.5 to 2.5% isoflurane in oxygen. Lactated Ringer’s solution was administered IV at a rate of 22 mL/kg/h for the first hour and then at a rate of 11 mL/kg/h for the remainder of the surgical procedure.

The entire abdomen and caudal aspect of the right thorax were clipped and prepared aseptically with chlorhexidine scrub. A ventral midline incision was made that extended from the xiphoid cartilage to 3 cm caudal to the umbilicus. The linea alba was incised, and the abdominal cavity was exposed by use of self-retaining retractors. A complete exploration of the abdominal cavity was performed to identify any preexisting abnormalities. The duodenum was retracted to expose the abdominal vena cava and right kidney. Malleable retractors were used to retract the right lobes of the liver in a cranial direction. Using blunt dissection, we exposed a 2-cm section of the vena cava immediately caudal to the right hepatic lobes and cranial to the renal and phrenicocostal veins. A piece of expanded polytetrafluoroethylene materiala measuring 2 X 6 cm was positioned around the vena cava. The ends of the material were sutured together by use of 3-0 polydioxyanoneb suture in a continuous pattern such that the material encircled the cava without compressing it. This material was used to prevent traumatic damage to the vessel wall during occlusion.

Silk suture (2-0) was passed through 1 end of an injectable occluder. The occluder was positioned to encircle the vena cava and expanded polytetrafluoroethylene material. The silk suture was then passed through the other end of the occluder and tied to make a complete ring around the vena cava (Fig 1). A 4-cm incision was made over the tenth intercostal space on the right side, and the subcutaneous tissues were bluntly dissected to form a small pocket. A curved hemostat was tunneled from the subcutaneous pocket caudally to the abdominal cavity, and an incision was made through the abdominal musculature to allow the hemostat to enter the peritoneal cavity. Silicone tubing of the occluder was grasped with the hemostat and pulled into the pocket. We used a 35-mL syringe to aspirate as much air as possible from the peritoneal cavity and injected 20 mL of normal saline to minimize the chance of air embolism. The silicone tubing was tied to the silk suture, completing the encirclement of the vena cava (Fig 1). The abdominal incision was closed in layers, and the dogs were monitored for 24 hours before discharge.

Figure 1—Photograph obtained during surgical placement of the occluder to encircle the vena cava in a dog. Notice that a band of expanded polytetrafluoroethylene material has been placed around the vena cava to prevent damage to the vessel from the occluder.
from the silicone tubing and occluder. Following establishment of negative pressure in the system, 50% dextrose solution was used to fill the tubing and occluder. A hemostat fitted with rubber covers on the jaws of the hemostat was used to maintain the dextrose solution in the tubing without damaging the tubing. A subcutaneous injection port was filled with 50% dextrose solution and connected to the silicone tubing to create a closed system. The injection port was secured to the subcutaneous tissues overlying the tenth rib by use of 3 interrupted sutures of 3-0 polydioxanone. The remaining subcutaneous tissues were closed with 3-0 polydioxanone in a continuous pattern, and the skin was closed in a routine manner.

The occluder was observed while 1 mL of dextrose solution was simultaneously injected into the port through a Huber needle. This observation was to ensure complete inflation of the occluder and subsequent occlusion of the vena cava. The dextrose solution was then aspirated such that the occluder was again in a neutral position. The abdomen was closed in a routine manner.

While still anesthetized, the dogs were then moved to the radiology unit and positioned in dorsal recumbency. A fluoroscopy table for initial venograms. The right inguinal area was clipped and aseptically prepared. The femoral pulse was digitally palpated, and a 16-gauge, over-the-needle catheter was inserted in a femoral vein. A guide wire was passed cranially into the femoral vein, and the catheter was removed. A vascular dilator was passed over the wire and then removed. A 6-F introducer catheter was passed over the wire into the vessel, and the wire was then removed. The catheter was flushed with heparinized saline (0.9% NaCl) solution to ensure patency. During fluoroscopy, 20 mL of iohexol was injected into the vena cava via the right femoral artery. Fluoroscopy was used to assist in cannulation of the vena cava. The site of the occluder was established, and it was determined that the vena cava was patent. The injection was recorded on videotape, and spot radiographs were taken during the iohexol injection. The iohexol injection was repeated after the occluder was filled with 1 mL of dextrose solution to evaluate the caudal cava during occlusion. Immediately after this evaluation, the dextrose solution was aspirated via the injection port. The dogs were allowed to recover from anesthesia and administered doses of butorphanol (0.4 mg/kg, IM) as needed for postoperative pain.

Occlusion of the vena cava—The day after surgery, 0.15 mL of dextrose solution was injected into each occluder through a Huber needle to begin occlusion of the vena cava. The same amount was injected every 48 hours during a 2-week period (total of 7 injections) to fill the 1-mL volume of the occluder and subsequently occlude the vena cava. The dextrose solution was then aspirated such that the occluder was again in a neutral position. The abdomen was closed in a routine manner.

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The vena cava was successfully occluded during a 2-week period in all dogs, as determined by assessments of venograms obtained 3 weeks after surgery. At that time, extensive formation of collateral vessels was evident (Fig 2). Vessels formed between the renal capsule, renal veins, and vena cava to the lumbar veins and vertebral veins and sinuses. We did not detect flow through the vena cava cranial to the occluder.

Venograms obtained 6 weeks after surgery appeared identical to those obtained 3 weeks after surgery. Occlusion of the vena cava was maintained, and formation of collateral vessels appeared to be static angiographically. In the 6-week venogram, the left kidney of the dog in which a selective renal angiogram was performed (+ weeks after surgery; Fig 3) had multiple triangle-shaped perfusion defects within the cortex. However, normal clearance of the contrast material into the collecting system was identified.
Serum biochemical values (ie, BUN and creatinine concentrations and activities of ALT, ALP, and CK) for all dogs remained within reference ranges throughout the study period. Statistical analysis revealed that postoperative values did not differ significantly from mean preoperative values except for ALT activity on day 4 after surgery ($P = 0.04$). Mean GFR for all dogs before surgery was 3.07 mL/min/kg (range, 2.67 to 3.56 mL/min/kg; reference range, ≥ 2.5 mL/min/kg). Two weeks after surgery, (ie, at the time complete occlusion of the vena cava was accomplished), mean GFR was 2.69 mL/min/kg (range, 2.1 to 3.47 mL/min/kg). Four weeks after surgery, mean GFR increased to 2.89 mL/min/kg (range, 2.17 to 3.36 mL/min/kg), and by 6 weeks after surgery, mean GFR was 3.1 mL/kg/min (range, 2.07 to 4.14 mL/min/kg). Three of the remaining 7 dogs had GFR values of < 2.5 mL/min/kg at 2 weeks after surgery; however, at 4 and 6 weeks after surgery, only 1 dog had GFR values of < 2.5 mL/min/kg.

Renal scintigraphy also provided data for measuring the percentage of the GFR contributed by each kidney. Although there was an increase in the percentage contribution of GFR from the right kidney, mean global GFR was maintained above the established reference value of 2.5 mL/min/kg throughout the study.

Statistical analysis did not reveal significant ($P = 0.18$) differences at any time point between the mean GFR value determined by use of imaging methods and the corresponding mean GFR value determined by use of plasma clearance analysis. When the mean GFR value for either method was compared for all 4 time points (ie, baseline and 2, 4, and 6 weeks after surgery), there was not a significant ($P = 0.40$) difference between the baseline GFR and any subsequent GFR measurements. There was a significant ($P = 0.02$) difference for the contribution of each kidney to the global GFR between baseline values and values measured 4 weeks after surgery; the contribution of each kidney did not differ significantly 2 or 6 weeks after surgery (Fig 4).

Gross findings during necropsy were consistent with results of venograms. Extensive formation of collateral vessels was evident caudal to each occluder. Multiple tortuous vessels were found extending from the renal capsules, vena cava, and iliac veins to the lumbar veins, vertebral veins, and azygous vein. There was mild fibrosis around each occluder and the associated vena cava. The abdominal organs appeared grossly normal, except for the right kidney of 1 dog, which had a polar infarct.

Histologic changes were consistently mild. All dogs had a bursa of organized connective tissue around the injection port but without evidence of inflammation. There was a mild granulomatous reaction...
between the occluder and vena cava associated with the expanded polytetrafluoroethylene material. The vena cava at the site of each occluder had changes, including intimal fibrosis, subintimal fibrosis, intimal thickening, and villous elastosis. The vena cava caudal to each occluder had endothelial hypertrophy and mild scalloping of the intima; however, the vena cava cranial to each occluder appeared normal. Intravascular thrombi were found caudal to the occluder in 4 of 7 dogs, ranging in size from 0.5 to 1 cm². Pathologic changes in the kidneys were consistently mild. Minimal interstitial edema and interstitial nephritis were evident in 6 dogs, and mild mesangial glomerulonephropathy was found in 4 dogs. We did not detect gross or histologic changes associated with the liver, adrenal glands, intestines, or other abdominal organs.

Discussion

Analysis of results of the study reported here indicates that gradual occlusion of the vena cava can be easily performed in clinically normal dogs by use of an injectable occluder device without associated morbidity or fatalities. All dogs in the study attained complete constriction of the abdominal vena cava cranial to the adrenal glands, and clinical abnormalities were not evident. Formation of collateral vessels was seen on venograms within 3 weeks after occlusion, which allowed for normal venous return from the caudal portion of the body. None of the dogs had evidence of pain or weakness in the hind limbs, edema, or other adverse effects associated with impairment of venous return. Additionally, diarrhea or other signs of intestinal lymphangiectasia that may be associated with abnormal venous flow were not seen.

Surgical placement of the occluder was technically simple and easy to perform. Mean surgical time required for placement was 40 minutes. A surgical assistant was invaluable for retraction of the liver during placement of the occluder. The use of expanded polytetrafluoroethylene material around the vessel may not be necessary. It was included in this study because of results of another study in pigs with induced hypertension in which occlusion of the aorta without use of a protective fabric around the aorta occasionally resulted in vessel rupture. With caval occlusion, the lower pressure attained and the difference in the structure of the vascular wall may make inclusion of such material unnecessary.

We chose to fill the occluder with 50% dextrose solution to induce occlusion, because use of a hypertonic solution would likely reduce osmotic leakage and loss of occlusion over time. We did not detect evidence of osmotic leakage from the occluder during the study.

When injecting solution into the occluder, it is important to use a Huber point needle, which does not cause holes in the injection port during placement. Use of hypodermic needles will result in holes in the injection port that can lead to leakage of fluid and loss of occlusion. Placement of the injection port in a location over the expanded polytetrafluoroethylene material around the vessel was invaluable for retraction of the liver during placement. A surgical assistant was invaluable for retraction of the liver during assessment of venograms. Perhaps the proximity of the occluder to the more cranial right renal vein increased intravascular pressure to the right side to a greater extent than for the more caudally located left renal vein, thus providing a greater stimulus for formation of collateral vessels. Alternatively, dogs may simply have a higher propensity for developing collateral vessels on the right side. An increase in formation of collateral vessels extending from the right
kidney would result in less resistance to blood flow, leading to a larger percentage of the blood volume passing through the right kidney. This could account for the increased contribution of the right kidney to the global GRF, compared with the contribution of the left kidney. By the end of the study, a return of renal function was evident in most of the dogs.

The decrease in renal function was not perceived clinically in the dogs. However, all dogs had normal renal function prior to occlusion. The effects of caval occlusion on dogs with preexisting renal dysfunction have not been evaluated, and the procedure cannot be recommended for those animals at this time.

This technique was designed with the goal of providing gradual occlusion of the vena cava by use of the occluder, which could then be followed by ligation of the vena cava at the site of occlusion and cranial to the diseased section of the cava with subsequent surgical excision of the diseased section of the vena cava. Long-term effects of ligation and removal of a section of the vena cava are unknown at this time and should be evaluated in future studies. However, adverse consequences of permanent occlusion are not anticipated, because collateral circulation developed caudal to the ligation.

Our study had other limitations or areas that may be addressed by investigators conducting similar studies in the future. The changes in GFR values between the 2 kidneys were not anticipated when designing this project and are difficult to explain objectively. Measurement of local arterial and venous pressures during occlusion may help explain these findings. Alternatively, Doppler ultrasonographic evaluation may be helpful in evaluating renal perfusion during occlusion.

The measurement of GFR by use of the imaging technique does involve some subjectivity, because the regions of the kidneys to be measured are determined by the operator. The effect of this subjectivity was minimized in several ways in our study. One investigator (AMB) analyzed all GFR data and had access to images obtained prior to occlusion to ensure that areas of measurement were consistent. There was no significant difference seen between GFR measurements obtained by use of the imaging technique and plasma clearance analysis in which it is not necessary for the operator to outline the area of the kidney. In addition, monitoring serial urine samples for changes in sediment, urine specific gravity, and proteinuria may have been useful in detecting renal disease, such as increased glomerular pressure.

Measurements were not made to evaluate adrenal gland function in these dogs. There was no clinical evidence of altered adrenal gland function, and gross or histologic changes were not seen in the adrenal glands during postmortem examination. Adrenal gland function should be evaluated in future clinical studies of dogs with adrenal gland tumors to check for changes attributable to occlusion of the vena cava.

On the basis of the study reported here, gradual occlusion of the vena cava appears to be a simple and effective procedure that is tolerated well by dogs and results in consistent formation of collateral vessels caudal to the occluder with a transient decrease in renal function. Additional studies are needed to evaluate the use of gradual occlusion in the treatment of adrenal gland tumors that have invaded the vena cava. Additional areas of study include a shorter period to induce occlusion and the effect of occlusion on a diseased vessel. Surgical removal of adrenal gland tumors is technically demanding and will continue to have the risk of hemorrhage, especially during dissection of the adrenal mass. However, the use of gradual occlusion of the vena cava as part of the treatment of adrenal gland tumors that have invaded the vena cava may make it easier to completely remove intravascular tumors or thrombi.

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