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# Effect of two sedative protocols and hepatosplenic disease on Doppler indices of splenic arteries in dogs: A preliminary study

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ABSTRACT

Doppler flow indices (DFIs), such as the resistive index (RI) and the pulsatility index (PI), are commonly used to characterize blood flow. Parenchymal infiltration of an organ and administration of sedative and anaesthetic drugs can affect DFIs by altering resistance to blood flow. In this prospective study, the effect on DFIs of two sedative protocols (acepromazine or dexmedetomidine, each combined with butorphanol) and the presence or absence of hepatic and/or splenic disease, was investigated in the splenic arteries of 75 dogs.

The RI and PI in splenic arteries of dogs sedated with dexmedetomidine and butorphanol were lower than those of dogs sedated with acepromazine and butorphanol. PI in splenic arteries was higher in animals with hepatosplenic disease than in healthy animals. Receiver Operating Characteristic (ROC) curves suggested that PI measured in canine splenic arteries could be useful in predicting the presence of hepatosplenic disease in the absence of other abdominal disease.



## Introduction

Doppler flow indices (DFIs) characterize resistance to flow in the vascular system (Kremkau, 1995). Commonly calculated indices are resistive index (RI), pulsatility index (PI) and systolic-to-diastolic peak velocity ratio (*S*/*D*). DFIs have the potential to be a relatively inexpensive, non-invasive, diagnostic and prognostic tool. They also present the advantage, compared to measurement of flow velocity, of being independent of insonation angle (Nelson and Pretorius, 1988).

Increased hepatic artery RI has been correlated with higher histologic fibrosis scores in humans (Piscaglia et al., 2001). Combined evaluation of splenic artery RI and portal blood flow has been proposed to distinguish portal hypertensive from haematological splenomegaly in cirrhotic patients (Piscaglia et al., 2002). Intra- and peri-tumoural arterial RI has been used to differentiate benign and malignant hepatic tumours (Wang et al., 2004a). Although B-mode ultrasonography has been used to differentiate benign from malignant splenic lesions in humans (Wang et al., 2000), splenic artery DFIs has not yet been investigated to our knowledge.

Flow obstruction and vasoconstriction cause greater reduction of diastolic compared to systolic blood flow, affecting vascular resistance in parenchymal organs and increasing RI and PI (Rifkin et al., 1987). Both intra- and extra-parenchymal factors, such as anaemia (Koma et al., 2005a,b), sedation (Novellas et al., 2007) and disease in other organs (Sato et al., 1987; Novellas et al., 2008), may affect RI and/or PI.

The cardiovascular effect of sedation and anaesthesia should be considered when interpreting the results of haemodynamic and vascular investigations for diagnostic or prognostic purposes. The effect of some sedative protocols on Doppler variables of different canine arteries has already been characterized (Rivers et al., 1997; Novellas et al., 2007; Miño et al., 2008). Medetomidine decreases the mean blood velocity in large abdominal arteries (Miño et al., 2008). Intramuscular (IM) administration of midazolam and butorphanol increases intrarenal and ocular blood flow resistance (Novellas et al., 2007). Administration of atropine and acepromazine, followed by diazepam and ketamine, decreases the RI in arcuate arteries compared to non-sedated dogs (Rivers et al., 1997). The effect of acepromazine, thiopental, and propofol on splenic size and echogenicity has been reported, but DFIs were not investigated (ÓBrien et al., 2004).

The purpose of this study was to characterize the effect of two sedative combinations and hepatosplenic disease on splenic artery RI and PI in dogs. We hypothesised that administration of sedation and presence of pathology would affect these DFIs.

### Materials and methods

#### *Animals*

Seventy-five client-owned dogs referred to Dick White Referrals (DWR) requiring abdominal ultrasound were included in this prospective clinical study. Informed consent for sedation and relevant investigations was obtained from all owners.

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Ethical approval to perform the study was granted by the local ethical committee at DWR. The age, sex and body mass of the dogs were recorded. All animals underwent physical examination and complete blood cell count and serum biochemistry profiles were obtained as part of the normal diagnostic process. Other laboratory investigations were performed only if deemed necessary to reach a diagnosis.

*Sedation protocol*

The sedative was chosen according to clinical judgment between the following two protocols: Group A: acepromazine 0.01 mg/kg (ACP 2 mg/mL, Novartis Animal Health) and butorphanol 0.2 mg/kg (Torbugesic 1%, Pfizer); group D: dexmedetomidine 0.001 mg/kg (Dexdomitor 0.5 mg/mL, Pfizer) and butorphanol 0.2 mg/kg. Sedation was administered slowly in the cephalic vein via a pre-placed intravenous (IV) catheter.

*Disease status*

Animals were considered 'healthy' in the absence of haematological and biochemical abnormalities or abdominal pathology. The other animals were considered to have hepatosplenic disease in the event of (1) presence of hepatic and/or splenic parenchymal abnormalities on ultrasonography, and/or (2) a twofold increase in one hepatic enzyme or increase of the activity of more than one hepatic enzyme. Animals with abdominal pathology not related to the spleen or liver were considered separately. Therefore, within each group of sedation, three subgroups were identified, namely, healthy dogs, dogs with hepatosplenic disease, and those with non-hepatosplenic abdominal disease. Ultrasound-guided, fine-needle aspirates or biopsies were obtained from the liver and/or spleen if clinically indicated.

*Splenic Doppler ultrasonography*

Examinations were performed by a single operator (IF) using a Philips HDI5000CV ultrasound machine and a 5–8 MHz electronic curvilinear array transducer. Each examination was performed 10 min after administration of sedation with the animal in right lateral recumbency. Splenic and hepatic size, echogenicity, echotexture, margination and distribution of lesions, if present, were assessed. The operator was unaware of the sedation administered.

Colour flow Doppler was used to identify an intrasplenic branch of the splenic artery near the hilus of the splenic body. Duplex Doppler (pulsed wave and colour flow Doppler) was used to measure spectral parameters. Doppler settings (gain, angle of insonation, pulse repetition frequency, focus, gate size) were adjusted as necessary, maintaining the angle of insonation always below 60°.

The profile of blood flow velocity over time was recorded during three consecutive heart cycles (systole/diastole). For each cycle, RI and PI were automatically calculated from peak systolic velocity, end-diastolic velocity and time average mean velocity, and then the mean was used for statistical analysis:

$$\mathrm{RI} = \frac{S - D}{S}$$

$$\mathrm{PI} = \frac{S - D}{Mean}$$

where $S$ is the peak systolic velocity, $D$ the end-diastolic velocity, and *Mean* the mean Doppler velocity

*Arterial systolic blood pressure and pulse rate measurement*

Systolic blood pressure and pulse rate were determined in 22 animals, immediately after splenic Doppler ultrasonography. Systolic blood pressure was estimated using an occlusive cuff of appropriate size (width approximately 40% of the circumference of the limb) and a Doppler flow detector (VetBP Doppler, Sonomed) in one of the forelimbs. The measurements were performed in triplicate and the mean calculated for statistical analysis.

*Statistical analysis*

ÓAgostino and Pearson omnibus normality test and visual inspection of plotted data were used to determine whether the distribution of the examined variables was normal. Mann–Whitney *U* test was used to compare age and body mass of animals receiving different sedations. Kruskal–Wallis test followed by Dunńs multiple comparison test was used to compare the age, body mass, splenic artery PI and RI in dogs with the same disease status but receiving a different sedation (i.e. PI/RI of healthy dogs belonging to group A vs. healthy dogs belonging to group D), and in dogs receiving the same sedation but with different disease status (i.e. PI/RI of healthy dogs belonging to group A vs. dogs with hepatosplenic disease belonging to group A). An unpaired *t* test was used to compare the DFIs in dogs with different sedation, ignoring disease status. The prognostic value of DFIs was explored using Receiver Operating Characteristic (ROC) curve analysis after pooling the DFIs values of dogs receiving different sedation. Differences were considered significant if $P < 0.05$. Prism (GraphPad) was used to perform statistical analysis.

Sample size calculation, based on preliminary measurement of RI in the splenic artery, was performed prior to beginning the study and suggested that enrolling 30 dogs per group would have allowed to detect a difference of 20% with power 80% and $\alpha = 0.05$. The achieved power was calculated post hoc for each variable compared, given the current sample and the observed mean and standard deviation and assuming as null hypothesis absence of effect of sedation on DFIs.

## Results

Seventy-five dogs were enrolled in the study, of which 44 were allocated to group A and 31 to group D. Within group A, 9 dogs were considered healthy, 13 had abdominal pathology unrelated to the spleen or liver, and 22 had hepatosplenic disease. Within group D, 8 dogs were considered healthy, 8 had abdominal pathology unrelated to spleen and liver, and 15 had hepatosplenic disease (Table 1).

Heart rate and systolic blood pressure were measured in 11 dogs in group A (3 healthy, 4 with hepatosplenic disease, and 4 with non-hepatosplenic abdominal disease) and 11 dogs in group D (2 healthy, 5 with hepatosplenic disease, 4 with non-hepatosplenic abdominal disease). There was no significant difference between groups A and D regarding age, body mass and systolic blood pressure. Heart rate was significantly lower in dogs belonging to group D. The RI and PI in splenic arteries were significantly lower in dogs of group D (Table 2).

**Table 1**
Distribution and number of dogs in each group of sedation depending on disease status.

| Disease status | Number of dogs |
|---|---|
| *Group A (n = 44)* | |
| Healthy | 9 |
| Hepatosplenic disease | 22 |
| Splenic BNH or EMH | 5 |
| Hepatic BNH or vacuolar changes | 3 |
| Hepatitis | 4 |
| Hepatic and splenic lymphoma | 1 |
| Splenic sarcoma | 1 |
| Splenic lymphoma | 2 |
| Splenic nodule | 1 |
| Increased liver enzymes | 5 |
| Non-hepatosplenic abdominal disease | 13 |
| Lymphocytic–plasmacytic gastritis | 2 |
| Inflammatory bowel disease | 1 |
| Fungal urinary tract infection | 1 |
| Dietary hypersensitivity | 1 |
| Focal enteritis | 1 |
| Glomerulonephritis | 1 |
| Prostatic sarcoma | 1 |
| Intestinal foreign body | 1 |
| Recurrent bloating | 1 |
| Idiopathic renal haemorrhage | 1 |
| Rectal polyp | 2 |
| *Group D (n = 31)* | |
| Healthy | 8 |
| Hepatosplenic disease | 15 |
| Splenic BNH or EMH | 2 |
| Steroid-induced hepatopathy | 1 |
| Cholangiohepatitis | 1 |
| Cholangitis | 1 |
| Splenic/hepatic ultrasonographic changes | 6 |
| Increased liver enzymes | 4 |
| Non-hepatosplenic abdominal disease | 8 |
| Chronic renal failure | 1 |
| Rectal mass | 1 |
| Pyelonephritis | 1 |
| Metastatic lymphadenopathy | 2 |
| Carcinomatosis | 1 |
| Inflammatory bowel disease | 2 |

BNH, benign nodular hyperplasia; EMH, extramedullary haematopoiesis.