Pulsed-wave Doppler ultrasonographic evaluation of hepatic veins during variable hemodynamic states in healthy anesthetized dogs

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Objectives—To quantify direction and velocity of blood flow in hepatic veins in dogs under different hemodynamic conditions by use of pulsed-wave Doppler ultrasonography.

Animals—10 healthy dogs.

Procedure—Dogs were anesthetized, and venous flow velocities in the quadrate lobe were measured. Arterial blood pressure, right atrial pressure, pulmonary artery pressure, and cardiac output were measured simultaneously. The timing of each waveform during the cardiac cycle was used to identify velocity profiles. Peak waveform velocities were measured during conditions of light anesthesia with isoflurane (baseline; period 1), cardiovascular depression following administration of high-dose isoflurane and esmolol IV (period 2), cardiovascular depression with crystalloid volume expansion (period 3), and high cardiac output induced with dobutamine (period 4). Hemodynamic measurements and maximum waveform velocities were compared among the 4 periods by use of an ANOVA and univariate and multivariate linear regression.

Results—During each study period, 4 distinct, low-velocity waves were identified. Mean velocities recorded during period 1 were as follows: retrograde atrial contraction a-wave, 7.3 cm/s; antegrade systolic S-wave, 15.0 cm/s; retrograde venous return v-wave, 2.7 cm/s; and antegrade diastolic D-wave, 11.4 cm/s. Mean S:D ratio was 1.27. During periods 3 and 4, S-wave velocity increased; D-wave velocity was highest during period 4.

Conclusions and Clinical Relevance—Consistent hepatic venous velocity profiles were observed in healthy dogs under different hemodynamic conditions. These findings provide baseline values that may be useful in evaluating clinical cases, but further study involving healthy, awake dogs and dogs with cardiac and hepatic diseases is required. (*Am J Vet Res* 2004;65:734–740)

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The direction and velocity of blood flow in abdominal vessels can be characterized by Doppler ultrasonographic evaluation,[1-4] and the patterns are generally particular to specific vessels.[5,6] Spectral pulsed-wave Doppler imaging in humans has revealed that normal hepatic veins have a multiphasic waveform, corresponding to the cardiac cycle and **right atrial pressures (RAPs)**. The multiphasic waveform is largely the result of pressure changes in the right atrium that are transmitted to the hepatic veins via the caudal vena cava. Fluctuations in RAP, minus the venous pressure in the hepatic venous system, create the instantaneous pressure gradients that move blood across the hepatic veins. The shape and component velocities of these waveforms have been characterized by use of Doppler ultrasonography.[1-3] In humans, large antegrade and small retrograde waves correspond to the specific phases of the cardiac cycle.

An ECG recording can be used as a timing reference for the hepatic venous waveforms (**Fig 1**). The prominent S-wave begins immediately after the QRS complex of the ECG and develops from both right atrial relaxation and apical displacement of the tricuspid valve annulus during ventricular contraction. Each of these events creates negative atrial pressure and promotes venous return from the liver. The S-wave is followed by a less negative or small retrograde v-wave, which occurs near the end of the T wave of the ECG. This v-wave is associated with right atrial overfilling against a closed tricuspid valve. Diastole is characterized by a prominent, antegrade D-wave. This diastolic wave follows the T wave and is caused by the negative atrial pressure

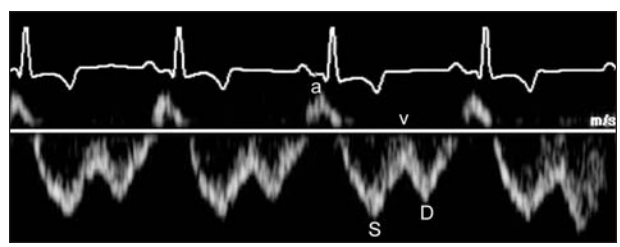

Figure 1—Waveform components of a pulsed-wave, spectral Doppler quadrate lobe hepatic vein tracing (with simultaneous ECG recording). The retrograde a-wave is a result of right atrial contraction and coincides with the P wave on the ECG tracing. The S-wave occurs immediately after the QRS complex and results from the negative pressure in the right atrium. The v-wave occurs toward the end of the T wave. The D-wave is caused by negative pressure in the right atrium as blood flows across the right atrium to the right ventricle.

created when blood flows into the relaxing right ventricle. During this period, the tricuspid valve is open and the right atrium serves as a passive conduit for venous return. In late diastole, a small retrograde a-wave (caused by right atrial contraction) occurs after the P wave of the ECG tracing. As the right atrium relaxes, blood flow becomes antegrade once again until interrupted briefly by closure of the tricuspid valve.

In humans, analysis of hepatic venous waveforms has been useful in the diagnosis of unrecognized right-sided heart disease as the cause of vague abdominal symptoms, hepatomegaly, high liver enzyme activities, and ascites. Recognition of altered quantitative and morphologic hepatic vein waveform variables is a sensitive diagnostic tool to alert the ultrasonographer to underlying right-sided heart disease (such as tricuspid regurgitation,[2,7,8] dilated cardiomyopathy,[9] or constrictive pericarditis[10]) instead of a primary hepatic disease process. Characteristic alterations in hepatic vein waveforms also have been described in humans with primary liver diseases[11-14]; these alterations are thought to be secondary to changes in hepatic venous compliance, which has been altered by the surrounding disease-affected tissue.

Ultrasonographic examination of the liver is one of the most commonly performed procedures in dogs with hepatomegaly, ascites, or high serum liver enzyme activities. There are situations in which abdominal ultrasonographic examinations are performed and the hepatic veins are assessed as dilated[15,16]; however, this assessment is subjective. Although pulsed-wave Doppler waveforms of hepatic veins in dogs are described and appear to be similar to those of hepatic veins of humans,[17,18] to our knowledge, quantitative assessment of the waveforms in either healthy dogs or dogs with disease has not been reported. Measurement of hepatic vein waveforms by pulsed-wave Doppler ultrasonography might be useful for identification of dogs with cardiovascular disease and differentiation of those cases from dogs with primary liver disorders. The purpose of the study reported here was to quantify direction and velocity of blood flow in hepatic veins in dogs under different hemodynamic conditions by use of pulsed-wave Doppler ultrasonography. By doing so, we intended to investigate the consistency of these flow patterns and provide initial reference values for hepatic venous flow in healthy dogs.

Materials and Methods

Animals—Ten healthy, mixed-breed dogs were used. The 5 female and 5 male dogs were approximately 18 months of age and weighed between 18 and 25 kg. All dogs were individually housed in approved facilities within The Ohio State University Veterinary Teaching Hospital, and the study protocol was approved by the Institutional Laboratory Animal Care and Use Committee. Cardiac auscultation and echocardiography were performed to confirm the absence of cardiac disease in all dogs. Two 3-mL blood samples were collected from each dog for PCV assessment and serum biochemical analyses to assess that the dogs did not have systemic illness or high serum liver enzyme activities. Results of tests for the presence of heartworm antigen were negative in all dogs.

Sedation, analgesia, and anesthesia—Each dog was anesthetized to facilitate measurement of central hemodynamic variables during Doppler ultrasound examination of the hepatic veins. Food was withheld from the dogs (water provided) for a 12-hour period prior to anesthesia. Sedation was achieved via administration of acepromazine (0.025 mg/kg, IM) and butorphanol (0.2 mg/kg, IM). A 20-gauge, 1.25-inch catheter was placed in a cephalic vein. Anesthetic induction was achieved via administration of diazepam (0.2 mg/kg, IV) followed by thiopental (5 mg/kg, IV). The dogs were intubated, and anesthesia was maintained with 0.5% to 3% isoflurane in 100% oxygen, as required to create different hemodynamic conditions. Lactated Ringer's solution was infused at 10 mL/kg/h during the procedure. Dogs were permitted to ventilate spontaneously throughout the study. Direct arterial blood pressure, heart rate, respiratory rate, tidal volume, and inspired and expired anesthetic agent concentration were measured and used in conjunction with subjective variables (eg, jaw tone) to monitor the level of anesthesia. Continuous ECG monitoring was performed throughout the procedure in all dogs. Lidocaine was infiltrated into the skin and subcutaneous tissues surrounding the sheaths used for percutaneous catheterization of the jugular vein and metatarsal artery. After completion of the procedure, butorphanol (0.5 mg/kg, IM) was administered to each dog to promote a smooth recovery from anesthesia.

Hemodynamic measurements—A 7-F thermodilution catheter[a] was placed percutaneously in the left jugular vein by use of a modified Seldinger technique; with fluoroscopic guidance, the tip of the catheter was positioned in the pulmonary artery. The catheter was interfaced to a physiologic recorder with a thermodilution cardiac output module[b] to measure RAP; **systolic**, **diastolic**, and **mean pulmonary artery pressure** (**SPA**, **DPA**, and **MPA**, respectively); and cardiac output. An arterial catheter (20 to 22 gauge) was placed in a metatarsal artery to measure **systolic**, **diastolic**, and **mean arterial blood pressure** (**SAP**, **DAP**, and **MAP**, respectively). In 1 dog, a metatarsal artery could not be accessed, and a 4-F catheter with an introducer sheath[c] was placed percutaneously in the right femoral artery. After dogs were positioned for ultrasonographic examination, pressure lines were balanced and calibrated. The level of the catheter entering the right atrium was considered to be the phlebostatic reference (designated zero). Pulsatile pressure tracings (main pulmonary and metatarsal arteries) were recorded on graph paper with a simultaneous ECG tracing. Mean pressures (right atrium and main pulmonary and metatarsal arteries) were measured by the physiologic recorder and verified by visual inspection of waveforms. Cardiac output was measured by thermodilution and a mean value calculated from 3 results that were within 20% of one another. Hemodynamic measurements were recorded during stable hemodynamic conditions (ie, < 10% change in heart rate and MAP during 5 minutes) and simultaneously with the ultrasound acquisition during 4 hemodynamic periods.

Ultrasonographic evaluation—Anesthetized dogs were placed in dorsal recumbency for abdominal ultrasonographic examination. Hair on the ventrum of each dog was clipped to allow good transducer-skin contact when coupled with an acoustic gel. The ECG leads were attached to record cardiac rhythm. A wideband transducer (7.5 or 8.5 MHz centered frequency[d]) was used for B-mode imaging. The B-mode images were obtained from the ventral aspect of the right side of the dog with the transducer positioned to obtain a longitudinal axis of the right medial and quadrate hepatic veins in the 9th to 11th intercostal space. These 2 hepatic vein branches were easily identified in all dogs because of their

close association to the gallbladder. The quadrate hepatic vein was chosen for evaluation because of its nearly parallel orientation to the Doppler ultrasound signal. Pulsed-wave Doppler was operated at 6.5 MHz. The 2-mm-wide pulsed-wave Doppler gate was placed within the central aspect of the quadrate hepatic vein approximately 2 cm from its bifurcation with the right medial hepatic vein. Doppler angle correction was applied when, on the basis of findings of simultaneous B-mode imaging, the angle of insonation was not parallel to the blood flow within the hepatic vein. The angle of insonation was always $< 60^{\circ}$. Duplex Doppler imaging allowed simultaneous (duplex) B-mode and pulsed-wave Doppler imaging.

Waveforms of the quadrate hepatic vein were recorded with simultaneous ECG tracings and hemodynamic measurements. Doppler waveform recordings were obtained at the end of expiration to avoid variations of the waveform resulting from respiratory and translational influences. Images were stored digitally and in print form. Waveform analysis was conducted by use of commercial software in the ultrasonographic equipment. Waveform features (a-, S-, v-, and D-segments) were characterized on the basis of the corresponding ECG recording. Measurements were obtained by use of electronic calipers and included direction and maximal velocity of the a-, S-, v-, and D-waves. Three complete waveforms were measured and the mean value of the maximum segmental velocities was calculated for each velocity peak.

Hemodynamic manipulations—Hepatic venous velocity waveforms were recorded under different hemodynamic conditions that were induced via the administration of cardiovascular-active drugs or a crystalloid solution. These treatments were administered to alter cardiac function, vascular reactivity, and hemodynamic variables. Specific effects of these drugs on hepatic venous velocity were not addressed in this study. Hepatic venous velocity spectra were recorded during 4 discrete hemodynamic periods; these were a baseline period (period 1) and periods of cardiovascular depression (period 2), cardiovascular depression with volume expansion (period 3), and hyperdynamic circulation (period 4). For each period, the hemodynamic variables and hepatic venous velocities were recorded simultaneously after at least 5 minutes of stable heart rate and MAP measurements. Because of the levels of cardiac depression created during periods 2 and 3, the order of drug administration was not randomized because the last period effectively restored hemodynamic variables prior to anesthetic recovery.

Period 1 represented a baseline state achieved by a light plane of isoflurane anesthesia sufficient to maintain unconsciousness. Period 2 represented a state of depressed myocardial contractility, reduced systemic arterial blood pressure, and a small increase in cardiac filling pressures. These conditions were achieved with a concentration of inhaled isoflurane of approximately 3% to 4% and administration of the ultrashort-acting β-adrenoceptor blocker (esmolol[e]; bolus injection [100 μg/kg, IV] followed by a constant rate of infusion [25 μg/kg/min]). The treatments were continued until the MAP value had decreased by approximately 30% from the baseline value. During period 3, administration of esmolol and a high concentration of isoflurane were continued; however, cardiac filling pressures were increased significantly by rapid IV infusion of lactated Ringer's solution (rate, 150 to 180 mL/kg/h). This infusion was administered until the DPA value reached 16 to 20 mm Hg, at which point the infusion was slowed and hemodynamic variables stabilized prior to data acquisition. During period 4, conditions of hyperdynamic circulation with increased myocardial contractility, heart rate, cardiac output, and systemic arterial blood pressure were created. The esmolol infusion was terminated, isoflurane concentration was reduced to approximately 0.5%, and dobutamine[f] (a positive inotropic drug) was infused IV at a rate of 2.5 μg/kg/min; cardiovascular depression was effectively reversed in each dog during this treatment period.

After data collection, the catheters were removed and vascular entry sites were bandaged; dogs were allowed to recover from anesthesia. The dogs were continuously monitored until they were standing.

Data analyses—Hepatic venous velocity waveforms recorded by Doppler techniques were inspected in conjunction with the ECG tracings to identify representative waves.

Table 1—Mean ± SD and median (range) values of hemodynamic variables assessed in 10 healthy anesthetized dogs during a baseline period (period 1) and periods of cardiovascular depression (period 2), cardiovascular depression with volume expansion (period 3), and hyperdynamic circulation (period 4)

Hemodynamic variable*	Period	Mean ± SD	Median (range)
Heart rate (beats/min)	1	71.3 ± 3.9	71.5 (63–76)
	2	97.2 ± 11.5	94 (85–115)
	3	106.1 ± 13.7	100 (94–136)
	4	120.7 ± 24.2	118 (83–167)
Systolic arterial pressure (mm Hg)	1	108.8 ± 16.8	106.5 (86–135)
	2	70.5 ± 13.7	66 (56–101)
	3	69.3 ± 16.3	67.5 (48–101)
	4	150.5 ± 32.6	142 (105–205)
Diastolic arterial pressure (mm Hg)	1	48.6 ± 4.6	48 (43–59)
	2	35.2 ± 6.6	34.5 (27–50)
	3	35.8 ± 5.3	35 (29–45)
	4	74.2 ± 19.6	67.5 (54–104)
Mean arterial pressure (mm Hg)	1	64.4 ± 6.4	63 (56–76)
	2	46.6 ± 7.1	46 (40–63)
	3	47.1 ± 7.8	47 (37–60)
	4	96.3 ± 21.5	85 (74–129)
Right atrial pressure (mm Hg)	1	3.3 ± 1.1	3.5 (2–5)
	2	4.5 ± 2.1	4 (2–9)
	3	13.3 ± 1.5	13 (11–16)
	4	5.2 ± 1.3	5 (3–7)
Systemic vascular resistance (dynes•sec•cm^{-5})	1	1,975 ± 339	1,963 (1,573–2,779)
	2	1,543 ± 549	1,397 (1,048–2,880)
	3	767 ± 235	671 (439–1,200)
	4	1,121 ± 512	1,138 (501–2,267)
Systolic pulmonary arterial pressure (mm Hg)	1	15.2 ± 2.2	15 (11–19)
	2	14.9 ± 3.0	15 (10–20)
	3	24.5 ± 1.3	24 (23–27)
	4	25.4 ± 3.1	26 (18–29)
Diastolic pulmonary arterial pressure (mm Hg)	1	5.9 ± 1.6	6 (3–8)
	2	7.9 ± 2.7	7.5 (4–13)
	3	17.8 ± 1.1	18 (16–20)
	4	13.3 ± 3.5	14 (8–18)
Mean pulmonary arterial pressure (mm Hg)	1	9.5 ± 1.2	10 (7–11)
	2	11.3 ± 2.7	11 (8–17)
	3	21.5 ± 1.0	21 (20–23)
	4	18.8 ± 3.2	19.5 (12–22)
Cardiac output (L/min)	1	2.5 ± 0.5	2.5 (1.9–3.3)
	2	2.3 ± 0.5	2.2 (1.5–3.0)
	3	3.7 ± 1.0	3.3 (2.8–6.2)
	4	7.5 ± 2.7	7.9 (2.4–12.3)
Stroke volume (mL)	1	34.2 ± 6.9	37.1 (26.8–44.0)
	2	24.3 ± 6.2	23.9 (14.3–32.9)
	3	32.4 ± 4.0	33.5 (28.0–45.6)
	4	58.4 ± 15.4	64.6 (24.0–73.6)

*For each variable, the *P* value from repeated measures ANOVA for overall effect (treatment period) was < 0.001.

Table 2—Pair-wise comparisons (*P* value indicated) of mean values of hemodynamic variables obtained from 10 healthy anesthetized dogs during a baseline period (period 1) and periods of cardiovascular depression (period 2), cardiovascular depression with volume expansion (period 3), and hyperdynamic circulation (period 4)

	P value					
	Periods compared					
Hemodynamic variable	**1 vs 2**	**1 vs 3**	**1 vs 4**	**2 vs 3**	**2 vs 4**	**3 vs 4**
Heart rate (beats/min)	< 0.001	< 0.001	< 0.001	0.379	0.004	0.145
Systolic arterial pressure (mm Hg)	< 0.001	< 0.001	< 0.001	0.961	< 0.001	< 0.001
Diastolic arterial pressure (mm Hg)	< 0.001	0.002	< 0.001	0.992	< 0.001	< 0.001
Mean arterial pressure (mm Hg)	< 0.001	< 0.001	< 0.001	1.000	< 0.001	< 0.001
Systolic pulmonary pressure (mm Hg)	0.983	< 0.001	< 0.001	< 0.001	< 0.001	0.689
Diastolic pulmonary pressure (mm Hg)	0.143	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Mean pulmonary pressure (mm Hg)	0.129	< 0.001	< 0.001	< 0.001	< 0.001	0.010
Right atrial pressure (mm Hg)	0.356	< 0.001	0.060	< 0.001	0.763	< 0.001
Cardiac output (L/min)	0.827	0.015	< 0.001	0.002	< 0.001	< 0.001
Stroke volume (mL)	0.011	0.989	< 0.001	0.023	< 0.001	< 0.001

Measured variables included maximum velocities of the a-, S-, v-, and D-waves; cardiac output; SAP, DAP, and MAP; central venous pressure; and SPA, DPA, and MPA. Stroke volume was calculated as cardiac output divided by heart rate. Systemic vascular resistance was calculated into Wood units (dyne-s-cm^{-5}) as follows:

$$\text{Systemic vascular resistance} = ([\text{MAP} - \text{RAP}]/\text{cardiac output}) \times 80$$

An S:D ratio was calculated to account for possible differences in velocities that might be attributable to subtle differences in sample volume placements among dogs.

Variables were compared among the 4 periods by a repeated measures ANOVA or by a Friedman test when the data were not distributed normally. When significant differences between means (or medians) were identified, a multiple pair-wise comparison procedure was performed with a Tukey (or Dunn) test. Univariate correlation coefficients (Pearson or Spearman) relating hemodynamic variables to the maximum velocities of a-, S-, v-, and D-waves were calculated. Multivariate, stepwise linear regression was also calculated using the hemodynamic variables to predict any relationship to the S-wave and D-wave velocities. Statistical analyses were conducted by use of commercial software.[g] Significance level was set at $\alpha = 0.05$ (ie, values of $P < 0.05$ were considered significant).

Results

The experimental protocol yielded 4 hemodynamic periods characterized by different hemodynamic states (**Table 1 and 2**). Hepatic venous waveforms were recorded in all dogs for each treatment period (**Table 3 and 4**).

Table 3—Mean ± SD and median (range) values of velocities of hepatic vein waveform components (a-, S-, v-, and D-waves) and S:D ratio* assessed via pulsed-wave Doppler ultrasonography in 10 healthy anesthetized dogs during a baseline period (period 1) and periods of cardiovascular depression (period 2), cardiovascular depression with volume expansion (period 3), and hyperdynamic circulation (period 4)

Waveform	**Period**	**Mean ± SD**	**Median (range)**	***P* value†**
a-wave (cm/s)	1	7.3 ± 2.1	7.5 (4–11)	0.004
	2	6.5 ± 2.5	6 (3–10)	
	3	9.8 ± 3.2	9.5 (5–15)	
	4	10.6 ± 4.6	10 (4–20)	
S-wave (-cm/s)	1	15 ± 6.7	13.5 (8–28)	< 0.001
	2	14.4 ± 4.4	14.5 (8–20)	
	3	22.8 ± 8.5	22 (12–36)	
	4	20.1 ± 10.5	16 (11–43)	
v-wave (cm/s)	1	2.7 ± 4.0	2 (–2–12)	0.039
	2	2.1 ± 2.6	2 (–1.0–7)	
	3	5.7 ± 3.2	6 (1–10)	
	4	3.8 ± 2.3	4 (–1–7)	
D-wave (-cm/s)	1	11.4 ± 2.8	11.5 (7–17)	0.012
	2	8.5 ± 3.4	8 (4–16)	
	3	11.0 ± 3.8	10.5 (6–16)	
	4	14.3 ± 6.9	11 (7–26)	
S:D ratio	1	1.3 ± 0.3	1.2 (1.0–1.9)	0.012
	2	1.8 ± 0.7	1.5 (1.1–3.5)	
	3	2.3 ± 1.4	1.7 (1.4–6.0)	
	4	1.5 ± 0.6	1.3 (0.8–2.8)	

Negative symbol denotes antegrade blood flow directed away from the transducer and toward the heart. *S:D ratio = Ratio of S-wave velocity-to-D-wave velocity. †Value obtained via a repeated measures ANOVA for overall effect.

Table 4—Pair-wise comparisons (*P* value indicated) of mean values velocities of hepatic vein waveform components (a-, S-, v-, and D-waves) and S:D ratio assessed via pulsed-wave Doppler ultrasonography in 10 healthy anesthetized dogs during a baseline period (period 1) and periods of cardiovascular depression (period 2), cardiovascular depression with volume expansion (period 3), and hyperdynamic circulation (period 4)

	P value					
	Periods compared					
Waveform component	**1 vs 2**	**1 vs 3**	**1 vs 4**	**2 vs 3**	**2 vs 4**	**3 vs 4**
a-wave	0.705	0.186	0.104	0.019	0.009	0.990
S-wave (–)	1.000	< 0.001	0.038	< 0.001	0.031	0.309
v-wave	0.963	0.100	0.814	0.036	0.533	0.438
D-wave (–)	0.094	0.958	0.671	0.237	0.007	0.375
S:D ratio	0.162	0.013	0.879	0.651	0.503	0.070

See Table 3 for key.

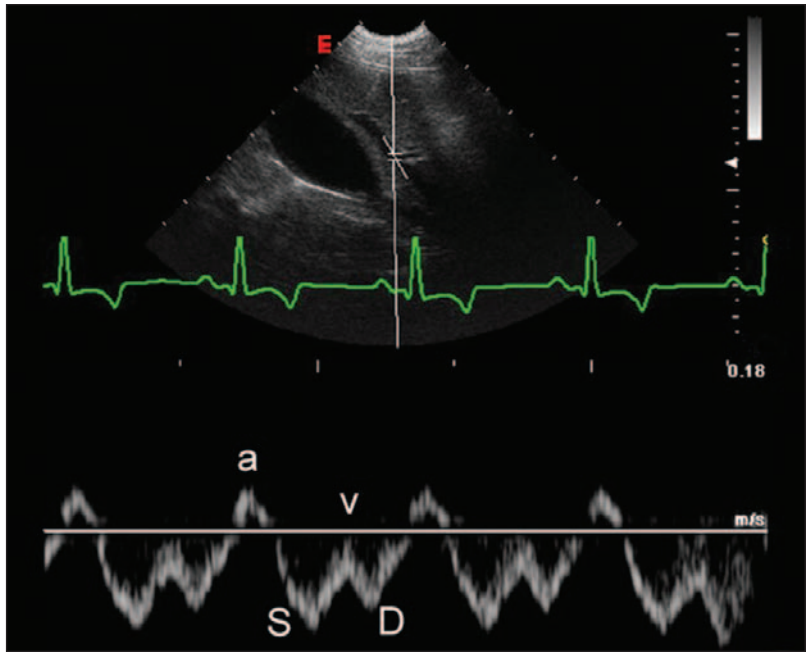

Figure 2—Duplex Doppler ultrasonographic image of the quadrate hepatic vein and its relationship to the gallbladder in a healthy anesthetized dog (with simultaneous ECG recording). The spectral pulsed-wave Doppler tracing is below the B-mode image. The Doppler line with sample volume (2 mm) is placed within the central portion of the vein. The right medial hepatic vein is just outside the plane of the ultrasound beam and not seen in this image. a = The a-wave component. S = The S-wave component. v = The v-wave component. D = The D-wave component.

The hepatic venous waveforms recorded during the baseline period 1 were multiphasic with 2 prominent antegrade (S and D) and 2 small retrograde (a and v) waves (**Fig 2**). These waves were identified consistently in all dogs by use of the simultaneously acquired ECG tracing. The a-wave was retrograde and correlated to the P wave of the ECG tracing. The S-wave was antegrade and occurred at the end of the QRS complex. The v-wave was retrograde and followed the S-wave; it corresponded to the end of the T wave of the ECG tracing. The D-wave was antegrade and followed the v-wave; it occurred between the T and P waves of the ECG tracing.

A state of cardiovascular depression was achieved during period 2 (Table 1 and 2), as judged by marked decreases in values of SAP, DAP, MAP ($P < 0.001$), and ventricular stroke volume ($P = 0.01$). During period 2, heart rate was increased, compared with that recorded during period 1, and was likely a reflex response to reduced arterial blood pressure. Hepatic venous waveforms were similar to those recorded during period 1. Compared with the baseline period, no significant differences in maximum velocities or in S:D ratio were evident (**Fig 3**; Table 4).

Period 3 was characterized by persistent depression of systemic arterial pressure; compared with baseline data, values of MAP were significantly ($P < 0.001$) decreased, largely as a result of reduced systemic vascular resistance (Table 1). Compared with baseline values, cardiac output increased ($P < 0.001$) during period 3. Presumably this was associated with increases in heart rate ($P < 0.001$) and reestablishment of ventricular stroke volume caused by marked increases in cardiac filling pressures. After volume infusion, both DPA and RAP were more than 3 times as great as baseline values ($P < 0.001$). The hepatic venous waveforms were similar to those recorded during periods 1 and 2, except for the S-wave, which increased in velocity ($P < 0.001$). Except for this finding and a higher S:D ratio ($P = 0.013$), there were no significant differences in variables during period 3, compared with baseline period 1 measures (Table 4; Fig 3).

During period 4, a hyperdynamic state was achieved with marked increases ($P \leq 0.001$) in stroke volume, cardiac output, and arterial blood pressure, compared with data recorded during the other 3 periods (Table 1). Hepatic venous waveforms obtained during period 4 were similar to those recorded during the preceding 3 periods (Fig 3). There was a significant ($P = 0.038$) increase in S-wave maximum velocity during period 4, compared with those recorded during period 1 (Table 4; Fig 3).

Pearson or Spearman correlation coefficients were generated to test the strength of association between each hemodynamic variable and hepatic venous velocity. Although significant correlations were identified between several variables, including cardiac filling pressures and S-wave velocity, the coefficients of determination (r^2) were low with none exceeding 0.20; these were not considered clinically important. Multivariate modeling involving a combination of independent hemodynamic variables did not improve the prediction of S- or D-wave velocities.

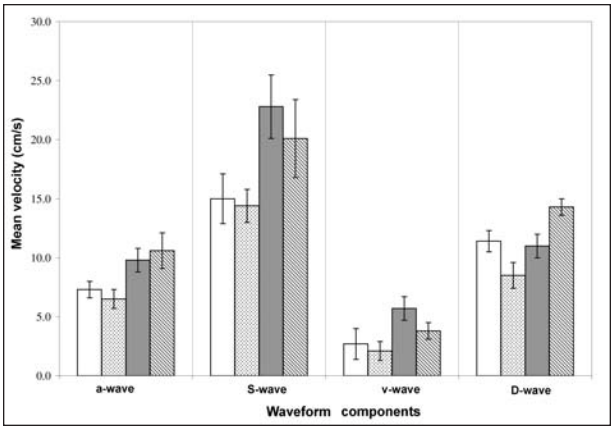

Figure 3—Mean maximum hepatic venous velocities of waveform components (a-, S-, v-, and D-waves) assessed via pulsed -wave Doppler ultrasonography in 10 healthy anesthetized dogs during a baseline period (period 1; white bars) and periods of cardiovascular depression (period 2; dotted bars), cardiovascular depression with volume expansion (period 3; gray bars), and hyperdynamic circulation (period 4; striped bars). Error bars represent SDs of the means.

Discussion

In the study of this report, qualitative and quantitative aspects of hepatic venous flow were assessed via pulsed-wave Doppler ultrasonography in healthy, anesthetized dogs. Multiphasic waveforms were recorded consistently during different hemodynamic states. These were characterized by 2 antegrade (S and D) waves that represent blood flowing towards the heart, 1 retrograde a-wave that represents blood flowing away from the heart, and a very small, generally retrograde v-wave. Our qualitative findings are similar to hepatic vein waveforms described in reports of abdominal vascular ultrasonographic examinations in dogs[17,18] and humans.[2] As in humans, the waveforms obtained from our study dogs correlated with ECG tracings. During the study, increasing familiarity with features of the waveforms allowed identification of each wave, even without the ECG reference; however, when exaggerated respiratory movements caused marked translational motion artifact during inspiration, the ECG tracing was necessary to reliably identify the specific waves.

To the authors' knowledge, this is the first quantitative study of hepatic venous velocities in dogs. Quantitation of hepatic venous velocities is well described in humans. In dogs, the a-, S-, and D-wave velocities were approximately half and v-wave velocity was approximately double the corresponding values in humans.[2] These differences between species may simply represent subtle differences in pressure gradients that develop between the abdominal systemic veins and the right atrium. Alternatively, other factors such as differences in venous compliance or intra-abdominal pressure may be involved.

The overall appearance of the Doppler-derived hepatic waveforms remained relatively consistent in the different hemodynamic states (including cardiovascular depression and hyperdynamic circulation) created in the study dogs. The main quantitative change observed during periods 3 and 4 was an increase in size of the S-wave, compared with that of the D-wave. Compared with baseline data, volume overload in conditions of cardiovascular depression was associated with an increase in S-wave velocity and in S:D ratio. This likely represented a greater difference between hepatic venous pressure and RAP during ventricular systole. It was surprising that the D-wave amplitude did not increase during period 3, despite the marked increase in systemic venous pressures. This suggested that conduit flow across the right atrium and through the opened tricuspid valve was diminished, despite the high filling pressures. Impaired right ventricular relaxation or limitations of ventricular distensibility in response to high RAP might be invoked to explain this finding. Conversely, during period 4, the D-wave increased in velocity. Although the increment was small, this might have represented enhancement of ventricular diastolic function under the influence of the catecholamine dobutamine. Furthermore, cardiac filling pressures decreased to near baseline values during period 4 and may not have encroached on the compliance limits of the right ventricle.

The movement of blood across hepatic veins depends in part on the pressure gradient established between the abdominal venous pressure and the right atrium. Although RAP did correlate with S-wave velocity, neither univariate nor multivariate regression identified a hemodynamic variable that strongly predicted the hepatic venous velocities. The direct effects of the drugs administered to the study dogs on vasomotor tone might represent an additional influence on the hepatic venous flow and velocity, but aside from calculation of systemic vascular resistance (which predictably decreased under high doses of isoflurane), vascular function was not addressed in our study.

The general consistency of hepatic vein velocity waveforms among the different experimental periods suggested that assessment of qualitative or quantitative alterations in velocity waveforms might be useful clinically in dogs. This supposition remains to be evaluated. Furthermore, in terms of quantitative aspects of hepatic venous velocity, it remains to be determined whether any consistent abnormality can be identified in dogs with altered cardiac output, cardiac failure, or hypervolemia. The S:D ratio has been used to assess right-sided heart disease in humans; ratios of < 0.6 have been associated with tricuspid valve regurgitation.[2] Normal ratios in humans range from 2.4 to 0.8 (mean value, 1.5). Our results indicated that in healthy isoflurane-anesthetized dogs during different hemodynamic states, the S:D ratio ranged from 1.0 to 1.86 (mean value, 1.27). A ratio may be used to normalize wave velocities and allow comparisons of data from different sample volume locations and among patients. Because the S:D ratio was only weakly correlated to the hemodynamic variables, additional factors that influence hepatic venous flow should be examined.

Our study had a number of limitations, and the following issues deserve consideration when interpreting these data. It is certainly possible that waveform velocities are different in awake versus anesthetized dogs. Anesthesia of the dogs was necessary in our study to maintain a controlled environment for hemodynamic manipulation, and further studies in healthy awake dogs are needed. Also, body position or other

factors that influence intra-abdominal pressure may affect the hepatic venous waveforms or velocities. Venous tone was not measured in the study dogs, and it would have been optimal to measure the instantaneous pressure gradient between systemic abdominal veins and the right atrium with a more sophisticated system involving micromanometer-tipped catheters. Although ventricular systolic function was estimated by cardiac output and stroke volume, ventricular diastolic function also influences the pressure gradient that drives blood from systemic veins towards the heart, but this was not quantified. The small number of dogs used in our study may have influenced statistical assessment of the significance of differences detected; however, pilot studies and initial power calculations suggested that 10 subjects would allow for detection of clinically relevant changes from baseline values (ie, differences of > 25%). Potential errors in velocity measurement may have been introduced by the use of Doppler angle correction. Doppler angle allows the user to correct the angle between the ultrasound beam and the direction of the blood flow to obtain accurate Doppler velocity values. Potential errors occur when the placement of the cursor is not precisely oriented parallel to the vessel wall and when the angle of correction is > 60°. It is generally accepted that the calculated flow velocity will be acceptably accurate if the angle of correction is < 60°. In the study of this report, great care was taken to align the Doppler angle cursor precisely parallel to the vessel wall because the alignment is a critical component in the accurate determination of velocities. Micromanipulation of the transducer was performed to achieve the optimal Doppler signal while Doppler angle cursor placement parallel to the vessel lumen was maintained. Observation of the vessel in B-mode with frequent image updates and careful observation of the Doppler waveform allowed the maximal velocities to be recorded. However, the relationship of the interrogating Doppler signal in the third dimension (azimuthal or z-plane) cannot be accounted for. Finally, acute alterations of hemodynamic variables in clinically normal dogs do not necessarily correspond to those that develop in dogs with spontaneous disease.

Despite these limitations, results of the study of this report may be useful in the investigation of hepatic venous flow and evaluation of dogs with heart cardiac disease, liver disease, or iatrogenic fluid overload. For example, compared with clinically normal humans, a decrease in the size of the S-wave and a decrease in the S:D ratio are observed in patients with tricuspid insufficiency. In severe tricuspid valve insufficiency, the S-wave may reverse direction and become positioned above the waveform baseline. Hepatic venous waveform alterations also are described in humans with various hepatic parenchymal diseases, such as fibrosis, lipidosis, and metastasis.[11-14] Waveforms in these patients may be dampened because of the decreased compliance of the hepatic vessels. In the study dogs of this report, volume overload was associated with a significant increase in the S:D ratio, compared with baseline values.

In conclusion, hepatic vein waveform velocities were identified and quantified in a group of healthy anesthetized dogs and were similar to qualitative findings reported in humans and dogs. Systolic S-wave and diastolic D-waves were most prominent in these dogs, but a- and v-waves were also recorded consistently in different hemodynamic conditions.

[a]Swan-Ganz thermodilution catheter, Baxter Healthcare Corp, Irvine, Calif.
[b]Marquette Instruments Inc, Milwaukee, Wis.
[c]Micropuncture pediatric introducer set, Cook Inc, Bloomington, Ind.
[d]Technos, Biosound Esaote Inc, Indianapolis, Ind.
[e]Brevibloc, esmolol hydrochloride (10 mg/mL), Baxter Healthcare Corp, Deerfield, Ill.
[f]Dobutamine injection USP (250 mg/20mL), Abbott Laboratories, North Chicago, Ill.
[g]SigmaStat 2.03, SPSS Inc, Chicago, Ill.

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