Influence of normovolemic anemia on Doppler characteristics of the abdominal aorta and splanchnic vessels in Beagles

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Objective—To ultrasonographically evaluate hemodynamics in the abdominal aorta (AAo) and splanchnic vessels in dogs with experimentally induced normovolemic anemia.

Animals—11 healthy Beagles.

Procedure—The AAo, cranial mesenteric artery (CMA), celiac artery (CA), hilar splenic artery (HSA), and main portal vein (MPV) were evaluated in conscious dogs immediately before and after experimental induction of severe normovolemic anemia (Hct, 16%) and during recovery from moderate and mild anemia (Hct, 26% and 34%, respectively). Peak systolic velocity (PSV) or peak velocity (PV), time-averaged mean velocity (TAVmean), pulsatility index (PI), resistive index (RI), blood flow, congestion index (CI), and heart rate (HR) were recorded. Results were compared for anemic and control states.

Results—Severe anemia caused significant increases in HR (25% to 70%), PSV (AAo, 45.8%; CMA, 56.1%; and CA, 41.9%), PV (MPV, 84.2%), and TAVmean (AAo, 69.4%; CMA, 64.3%; CA, 29.7%; and MPV, 76.9%) and significant decreases in PI (AAo, 26.1%; HSA, 19.3%) and CI (MPV, 45.2%). There was no significant change in PI of the CMA or CA, portal blood flow, or RI of any artery. Significantly higher TAVmean persisted in all vessels during moderate anemia, but higher PSV persisted only in the CMA; PI (CMA and CA) and RI (CA) decreased significantly, but portal blood flow increased significantly. Significant increase in TAVmean (AAo and CMA) persisted during mild anemia, and PI (AAo, CMA, and HSA) but RI (CMA) were significantly lower.


Studies in dogs1-3 and rats4 conducted by use of invasive techniques have documented a hyperdynamic cardiovascular response to severe anemia characterized by increased cardiac output, reduced systemic vascular resistance, and increased blood flow (hyperemia) to various organs, including the abdominal splanchnic vascular bed. Variation in hemodynamic response is attributable to differing degrees of anemia, and there is variation in the hemodynamic response among vital organs, such as the heart and brain, and nonvital organs, such as the kidneys, liver, spleen, or gastrointestinal tract.5-25

In severely anemic human fetuses with RBC alloimmunization, noninvasive duplex Doppler ultrasonography (DUS) has been used to document increases in hemodynamic variables such as blood flow, time-averaged mean velocity (TAVmean), and peak systolic velocity (PSV) within various blood vessels, thereby supporting findings in studies conducted in other animals. Peak systolic velocity of the middle cerebral artery9,10 or main splenic artery11 and TAVmean of the middle cerebral artery12 are good DUS indices and have been proposed as clinical tests for use in the prediction, detection, and management of severe anemia in human fetuses. In nonhuman animals, a significant increase in cerebral blood flow has been reported in an anemic newborn lamb.13 To our knowledge, a hyperdynamic state in the abdominal splanchnic circulation in dogs with severe anemia has not been documented by use of noninvasive DUS. Reduction of splanchnic vascular resistance in hyperdynamic states has also not been determined by use of noninvasive techniques in humans or other animal species.

Clinicians at Onderstepoort Veterinary Academic Hospital, University of Pretoria, propose to use DUS to detect hemodynamic changes that may be associated with complicated babesiosis in dogs. Serious clinical consequences and therapeutic challenges are encountered in dogs with complicated babesiosis.14 Anemia is a common characteristic of the disease.14 Pathologic mechanisms underlying these complications are poorly understood but believed to be similar to that of cattle with complicated babesiosis or humans with complicated falciparum malaria.15-18 The mechanisms for these complications are believed to involve systemic...
inflammatory responses characterized by impaired perfusion and subsequently damage to 1 or multiple organs. Sequestration of RBCs within microvessels is most commonly blamed for impaired tissue perfusion and hypoxia, and congestion of capillary beds in various organs has commonly been reported during post-mortem examinations. Hypotension has also been reported in experimentally and naturally infected animals. Knowledge and ability to noninvasively detect hemodynamic changes associated with anemia in organs that are commonly involved in complicated babesiosis in dogs (eg, liver, spleen, and kidneys) may permit correct interpretation of DUS results in affected dogs, improve the understanding of pathophysiologic mechanisms, and be useful in predicting possible complications and monitoring clinical progress of dogs with babesiosis and related diseases, such as falciparum malaria.

Noninvasive DUS has been used in dogs to detect changes in abdominal splanchnic hemodynamic physiologic and pathophysiologic processes. Peak systolic velocity, end-diastolic velocity, mean velocity, pulsatility index (PI), resistive index (RI), blood flow, or the congestion index (CI) have been used to document hemodynamic changes associated with this function or chronic hepatic disorders. The purpose of the study reported here was to use noninvasive DUS to evaluate blood flow or mean flow velocities (peak and mean) and vascular resistance in the abdominal aorta (AAo) and splanchnic vessels of dogs with experimentally induced normovolemic anemia.

Materials and Methods

Animals—Eleven Beagles comprising 1 sexually intact male, 3 neutered males, and 7 sexually intact nonpregnant females were used in the study. Mean ± SD body weight was 12.0 ± 1.8 kg. Mean age of 4 males and 5 females was 2.63 ± 0.05 years; the exact age of 2 females could not be established. All Beagles were in good physical condition and appeared to be healthy. The dogs were part of the Onderstepoort Veterinary Academic Research Unit, Faculty of Veterinary Science, University of Pretoria. During the study, dogs were transported to the Onderstepoort Veterinary Academic Hospital, where they were housed in large kennels. In the first week of the study, 1 dog was entered into the study. Two dogs were entered into the study to obtain optimal image quality.

Experimental design—The study was conducted such that each dog served as its own control animal (hemodynamic and pathophysiologic processes). Peak systolic velocity, end-diastolic velocity, mean velocity, pulsatility index (PI), resistive index (RI), blood flow, or the congestion index (CI) have been used to document hemodynamic changes associated with this function or chronic hepatic disorders. The purpose of the study reported here was to use noninvasive DUS to evaluate blood flow or mean flow velocities (peak and mean) and vascular resistance in the abdominal aorta (AAo) and splanchnic vessels of dogs with experimentally induced normovolemic anemia.

ultrasonographic examinations—All examinations were performed by investigators (LMK). Food was withheld from dogs for 12 hours prior to ultrasonography. Dogs were not sedated or anesthetized for the examinations. The ventral and lateral portions of the abdomen and right lateral portion of the thorax from the 6th to 13th ribs were clipped, cleaned, and covered with acoustic gel. For general abdominal imaging, dogs were positioned in dorsal recumbency. Images of the spleen in parasagittal, transverse, and oblique planes were obtained in the left cranial quadrant of the abdomen, and images of the left kidney in dorsal, transverse, and oblique planes were obtained slightly caudal to the spleen. Dogs were then positioned in right lateral recumbency to enable us to obtain images of the AAo, cranial mesenteric artery (CMA), and celiac artery (CA) in the parasagittal or dorsal plane. Dogs were then positioned in left lateral recumbency to enable us to obtain images of the main portal vein (MPV) in dorsal, transverse, and oblique planes caudal to the liver via the 9th to 12th intercostal spaces.

All examinations were performed by use of an ultrasonic machine with a convex-array, linear-array, or phased-array transducer. The B-mode examination of the general abdominal cavity, organs, and AAo was conducted by use of a 5.0-MHz convex-array transducer; identification and evaluation of the CMA, CA, and hilar splenic artery (HSA) were performed by use of a 7.5-MHz linear-array transducer, although a convex-array transducer was used sometimes. The MPV was identified by use of a 6.0-MHz phased-array transducer. All machine settings, including overall gain, depth compensation gain, edge enhancement, focus, and line density, were adjusted during each examination to obtain optimal image quality.

Doppler examinations of the AAo and MPV were performed at a Doppler frequency of 3.5 MHz. The sample window was obtained anywhere along the length of the AAo cranial to the origin of the left renal artery. Sample window for the MPV was obtained at the best location within the vessel, which was typically immediately caudal to the liver, a point at which a long-axis vessel-beam intercept angle of ≤ 60° could be obtained by use of the intercostal space. Evaluation of the CMA, CA, and HSA was performed at a Doppler frequency of 5.2 MHz, although we also used a frequency of 3.5 MHz for the CMA and CA. The sample window for the CMA or CA was obtained within each vessel approximately 5 mm from the vessel’s origin from the aorta. For the HSA, the sample window was obtained approximately 5 mm from the splenic hilus, within or outside the parenchyma. Use of a 7.5-MHz frequency for B-mode examinations and color Doppler ultrasonography facilitated the determinations for the sample windows.

In the AAO and MPV, 1 cursor of the Doppler gate was placed close to an inner surface of the vessel wall and the sec-
ond on the opposite surface as a modification of the technique of uniform insonation. This maintained the size of the sample window within at least two thirds of the vessel diameter and avoided wall artifacts or spectral contamination from adjacent vessels. In the CMA, CA, or HSA, the cursors were oriented transversely across the vessel diameter as it coursed toward the transducer. In all vessels, except for the HSA, vessel-beam alignment was subjected to an angle-correction procedure before the spectral tracing was recorded. Angle correction was assisted by manual adjustment of the transducer and the electronic steering capacity of the linear-array transducer. The vessel-beam angle was recorded. Machine settings were optimized for high-sensitivity imaging in the Doppler mode. In 1 animal, heart rate (HR) could not be determined during the control period because the dog was intolerant to the placement of ECG pads. In addition, the HR, together with Doppler measurements of the CA and HSA, was not obtained in 1 dog each, and the HR with Doppler measurements of the MPV was not obtained in 4 dogs for various reasons.

Data analysis—Abdominal organs were subjectively evaluated by use of B-mode ultrasonography. Measurement of the thickest area of the spleen was used to estimate its size. Echogenicity of the spleen, liver, and kidneys was subjectively compared with each other. Diameter of the largest branch of the splenic vein in the body of the spleen was measured at the splenic hilus (long-axis view) and the cross-sectional area calculated. The largest cross-sectional area of the MPV was obtained by cine looping an image (short-axis view) and measuring it by use of the elliptical program of the onboard computer. This minimized errors attributable to variation in the cross-sectional area with time caused by respiration. Doppler spectra of each vessel were evaluated for flow patterns by the use of a concurrent ECG. The instantaneous HR for each Doppler cycle was computed from the preceding R–R interval on the ECG. Because an R–R interval is the number of milliseconds that elapses during 1 cardiac cycle, the total number of cardiac cycles (ie, HR) that would be completed within 1 minute (ie, 60,000 milliseconds) was computed as HR = 60,000/R–R interval.

During each experiment, measurements were obtained from spectral cycles in which preceding R–R intervals were approximately equal, excluding obvious sinus arrhythmias. Values recorded for HR, PI, RI, PSV, TAVmean, peak velocity (PV), MPV PV, TAVmean, blood flow, and CI were obtained by averaging 3 measurements or calculations from 3 ECG or spectral Doppler cycles. Doppler variables were measured by use of the onboard computer.

Pulsatility index was determined by use of the following equation:

$$PI = \frac{PSV - \text{end diastolic velocity}}{TAV\text{mean}}.$$  

Resistive index was determined by use of the following equation:

$$RI = \frac{PSV - \text{end diastolic velocity}}{PSV}.$$  

Blood flow was computed by use of the following equation:

$$\text{Blood flow} = \text{cross-sectional area} \times TAV\text{mean}.$$  

Congestion index was calculated by use of the following equation:

$$CI = \frac{\text{cross-sectional area}}{TAV\text{mean}}.$$  

Results of each experiment were entered into a computer spreadsheet program on a personal computer. All ultrasonographic procedures were recorded on videotape for possible reevaluation and future reference. All data were tested for normality by use of the Shapiro-Wilk test. Values of data that were normally distributed were reported as mean ± SD, and those that were not normally distributed were reported as median and range. Values for Doppler variables for dogs in each anemic state were compared with the value for the physiologic (control) state by use of paired t tests for data that were normally distributed or the Wilcoxon signed rank test for data that were not normally distributed. Differences were considered to be significant at $P \leq 0.05$. A statistical software program was used to perform the data analysis.

Results

Severe acute anemia—Mean ± SD Hct was 16.0 ± 0.77% after blood removal for 3 to 5 days. Dogs were lethargic, and a few had a reduced appetite during a 12-hour period. Dogs had extremely pale mucous membranes and a fast and weak pulse, but rectal temperature was within the reference range. The spleen was significantly ($P = 0.005$) thinner (mean thickness was 17.0 ± 1.9 mm and 13.9 ± 0.0 mm for the control state and severe anemia, respectively [18.1%]; Figure 1). Subjectively, splenic echogenicity was frequently increased. There was a significant ($P = 0.025$) reduction in mean cross-sectional area of the HSV (control state, 0.046 ± 0.021 mm²; severe anemia, 0.024 ± 0.009 mm²; 47.8%). There was no significant change in mean cross-sectional area of the MPV. There was a significant reduction in mean HR for all observations during severe anemia (25.2% to 70.1%; Figure 2; Table 1).

Spectral Doppler patterns of the AAo, CMA, CA, and MPV during severe anemia resembled the corresponding patterns for clinically normal dogs described elsewhere. However, adjacent arterial systolic peaks were more regularly and closely spaced (Figures 3 and 4). Overall duration of the cardiac cycle, particularly that of the diastolic phase, was remarkably shortened. Frequently, a single conical velocity pattern was the only feature that formed the diastolic segment of

![Figure 1](image1.jpg)
the Doppler spectrum because any extra horizontal or conical segment had been lost. In 1 case, only half of a cone representing an increasing diastolic velocity remained toward the end of the diastolic phase; therefore, a biphasic (instead of triphasic) velocity pattern was seen in the aortic Doppler spectrum. A triphasic velocity pattern was seen less frequently in the CMA spectrum of anemic dogs than in that of control dogs.

We detected a significant increase in mean PSV (AAo, 45.8%; CMA, 56.1%; and CA, 41.9%), mean PV (MPV, 84.2%), and mean TAVmean (AAo, 69.4%; CMA, 64.3%; CA, 29.7%; and MPV, 76.9%; Figure 3). A significant decrease in mean PI was seen only in the AAo (20.5%) and HSA (19.3%), whereas mean PI in the CMA and CA was unchanged (Figure 6). No significant change was found in mean RI of any artery. Mean CI was significantly reduced (45.2%). Portal flow increased by 67.7%, although this was not a significant change.

**Moderate anemia**—Mean ± SD Hct was 26.3 ± 0.74% after dogs were allowed to recover for 5 to 7 days. Dogs were active and physically strong. Mucous membranes were pale to pale pink, and pulse was slightly weak and fast. Rectal temperature was within the reference range. Splenic echogenicity was subjectively increased, but we did not detect a significant change in splenic thickness or cross-sectional area of the HSV or MPV. Significantly higher mean HR was observed during some measurements (20%; Table 1).

Arterial and portal vein spectral Doppler patterns were similar to corresponding patterns described elsewhere in clinically normal dogs. A significant increase

![Figure 2—Mean ± SD heart rate (HR) in dogs during various states of anemia. *Value differs significantly (P < 0.001) from the value for the control state.](image)

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Control state</th>
<th>Severe anemia</th>
<th>Moderate anemia</th>
<th>Mild anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAO HR (beats/min)</td>
<td>103.3 ± 19.8</td>
<td>136.2 ± 18.7</td>
<td>110.7 ± 10.7</td>
<td>105.9 ± 10.5</td>
</tr>
<tr>
<td>PSV (cm/s)</td>
<td>127.1 ± 33.7</td>
<td>185.3 ± 40.4</td>
<td>149.1 ± 24.0</td>
<td>145.1 ± 29.4</td>
</tr>
<tr>
<td>$TAV_{max}$ (cm/s)</td>
<td>22.9 ± 7.6</td>
<td>39.8 ± 11.8</td>
<td>32.8 ± 3.3</td>
<td>32.0 ± 5.5</td>
</tr>
<tr>
<td>PI</td>
<td>3.22 ± 0.91</td>
<td>2.38 [0.24-3.51]</td>
<td>2.47 ± 0.49</td>
<td>2.23 [2.13-3.20]</td>
</tr>
<tr>
<td>RI</td>
<td>0.84 ± 0.04</td>
<td>0.64 ± 0.04</td>
<td>0.82 ± 0.04</td>
<td>0.83 ± 0.02</td>
</tr>
<tr>
<td>CMA HR (beats/min)</td>
<td>106.6 [57.0-117.6]</td>
<td>133.5 ± 12.1</td>
<td>108.0 ± 11.4</td>
<td>114.7 [87.8-124.1]</td>
</tr>
<tr>
<td>PSV (cm/s)</td>
<td>103.4 ± 20.2</td>
<td>161.4 ± 17.2</td>
<td>123.9 ± 19.8</td>
<td>114.3 ± 14.0</td>
</tr>
<tr>
<td>$TAV_{max}$ (cm/s)</td>
<td>21.0 ± 5.8</td>
<td>34.5 ± 6.4</td>
<td>31.4 ± 7.8</td>
<td>29.4 ± 5.0</td>
</tr>
<tr>
<td>PI</td>
<td>2.66 ± 0.63</td>
<td>2.06 [1.78-3.61]</td>
<td>2.10 ± 0.56</td>
<td>2.01 ± 0.31</td>
</tr>
<tr>
<td>RI</td>
<td>0.82 ± 0.04</td>
<td>0.83 ± 0.04</td>
<td>0.81 [0.69-0.87]</td>
<td>0.79 ± 0.03</td>
</tr>
<tr>
<td>CA HR (beats/min)</td>
<td>96.7 ± 16.2</td>
<td>137.4 [99.4-142.6]</td>
<td>114.0 [96.1-118.4]</td>
<td>106.7 ± 13.7</td>
</tr>
<tr>
<td>PSV (cm/s)</td>
<td>115.2 ± 27.8</td>
<td>163.5 ± 34.6</td>
<td>129.9 ± 17.9</td>
<td>112.6 ± 17.0</td>
</tr>
<tr>
<td>$TAV_{max}$ (cm/s)</td>
<td>25.9 ± 9.0</td>
<td>33.6 ± 6.2</td>
<td>30.8 [27.0-46.3]</td>
<td>26.8 ± 5.3</td>
</tr>
<tr>
<td>PI</td>
<td>2.25 ± 0.51</td>
<td>2.23 ± 0.52</td>
<td>1.78 ± 0.27</td>
<td>2.03 ± 0.47</td>
</tr>
<tr>
<td>RI</td>
<td>0.79 ± 0.04</td>
<td>0.82 ± 0.06</td>
<td>0.75 ± 0.04</td>
<td>0.78 ± 0.06</td>
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<tr>
<td>HSA HR (beats/min)</td>
<td>91.9 ± 22.7</td>
<td>133.7 ± 14.0</td>
<td>94.2 ± 12.4</td>
<td>104.7 ± 23.6</td>
</tr>
<tr>
<td>PI</td>
<td>1.35 ± 0.45</td>
<td>1.09 ± 0.25</td>
<td>1.11 ± 0.22</td>
<td>1.07 ± 0.21</td>
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<tr>
<td>RI</td>
<td>0.66 ± 0.10</td>
<td>0.84 ± 0.07</td>
<td>0.80 ± 0.05</td>
<td>0.82 ± 0.09</td>
</tr>
<tr>
<td>MPV HR (beats/min)</td>
<td>81.1 ± 20.1</td>
<td>138.5 ± 22.0</td>
<td>96.3 ± 15.6</td>
<td>80.0 ± 18.5</td>
</tr>
<tr>
<td>PV (cm/s)</td>
<td>19.0 [15.1-45.7]</td>
<td>42.0 ± 14.8</td>
<td>34.5 ± 16.5</td>
<td>22.7 ± 9.2</td>
</tr>
<tr>
<td>$TAV_{max}$ (cm/s)</td>
<td>10.6 ± 2.8</td>
<td>19.1 ± 7.3</td>
<td>18.7 ± 8.8</td>
<td>13.5 ± 3.8</td>
</tr>
<tr>
<td>BF (mL/min/kg)</td>
<td>36.6 ± 13.0</td>
<td>61.2 ± 38.7</td>
<td>65.1 ± 36.3</td>
<td>46.4 ± 21.4</td>
</tr>
<tr>
<td>CI</td>
<td>0.066 ± 0.019</td>
<td>0.034 ± 0.013</td>
<td>0.044 ± 0.021</td>
<td>0.051 ± 0.016</td>
</tr>
</tbody>
</table>

The Hct for the various states of anemia were as follows: control state, 45% to 52%; severe anemia, 15% to 17%; moderate anemia, 25% to 27%; and mild anemia, 31% to 37%.

*For each variable, P values represent comparison with the control state; values were considered significant at P ≤ 0.05. Values reported are median (range) because the data were not normally distributed as determined by use of the Shapiro-Wilk test.

AAo = Abdominal aorta. CMA = Cranial mesenteric artery. CA = Celiac artery. HSA = Hilal splenic artery. MPV = Main portal vein. HR = Heart rate. PSV = Peak systolic velocity. PV = Peak velocity. $TAV_{max}$ = Time-averaged mean velocity. BF = Blood flow. PI = Resistivity index. RI = Resistive index. CI = Congestion index.

Table 1—Comparison of heart rate and Doppler variables for the abdominal aorta and splanchnic vessels in 11 Beagles during various states of experimentally induced anemia.
in mean PSV persisted only in the CMA (19.8%), whereas the AAo, CA, and MPV did not have significant changes (Table 1). Mean TAVmean remained significantly higher in all vessels (AAo, 47.6%; CMA, 50.0%; CA, 26.7%; and MPV, 76.4%). There was significant reduction in mean PI of the CMA (21.2%) and CA (21.0%); however, there was no significant change in mean PI of the AAo or HSA. Mean RI of the CA (4.8%) was significantly reduced, but we did not detect a change in mean RI of the AAo, CMA, or HSA. There was a significant increase in mean portal blood flow (77.9%) but no significant change in mean CI.

Mild anemia—Mean ± SD Hct was 34.4 ± 1.9% after dogs were allowed to recover for 12 to 16 days. Dogs were active and physically strong. Mucous membranes were pale to pale pink. Pulse and rectal temperature were within the reference ranges. Splenic echogenicity was still subjectively increased. Arterial and venous Doppler spectra were similar to those obtained during the control state.

Mean TAVmean remained significantly increased in the AAo (42.8%) and CMA (40.0%), but there was no significant change in the CA or MPV (Table 1). Significant reduction in mean PI was evident in the
flow velocities of various vessels have been reported. Observations of the human fetus during severe anemia have revealed significant increases in blood flow of the umbilical vein. Similar observations were made by use of invasive techniques in dogs with normovolemic anemia that reportedly caused increased blood flow in the Aa0 and various splanchnic vessels or vascular beds during severe anemia. Failure to detect a significant change during severe, moderate, or mild states of anemia in the study reported here may have been attributable to a small sample.

Few Doppler evaluations conducted in human fetuses with anemia have investigated vascular resistance by use of PI or RI. No significant change has been found in PI or RI of the umbilical or uterine artery, but RI of the splenic artery in hydropic fetuses (severe anemia) is significantly increased. The increase in splenic RI is believed to be attributable to congestion of the splenic capillary bed with trapped RBCs. Analysis of results of our study revealed a reduction in vascular resistance during severe anemia in the Aa0, HSA, and MPV, as indicated by a significant reduction in PI or CI. A reduction in vascular resistance in the CMA and CA was detected later, as indicated by a significant reduction in PI or RI. The reason for this delayed reduction in resistance is not clear, but it may have been associated with redistribution of blood from the splanchnic bed during the acute onset of severe anemia. Variation was also observed with regard to the specific resistance index that changed in response to anemia. A significant reduction in PI was the major finding, whereas a reduction in RI was seen in fewer instances (CMA and CA).

Arterial flow velocity and direction are sensitive to peripheral vascular resistance. When resistance is decreased, forward flow velocity is increased and reverse flow velocity is decreased in a linear relationship, and vice versa. In the study reported here, the transformation of an aortic or CMA velocity pattern from triphasic to biphasic, increase of systolic and diastolic velocities, and increase in TAVmean support observations of other investigators. A significant increase in portal vein TAVmean with no change in cross-sectional area resulted in a significant reduction in CI, further suggesting that flow resistance by the portal vein was also reduced.

Two mechanisms are probably involved in the reduction of vascular resistance. First, a reduction in RBC mass leads to a significant decrease in blood viscosity in dogs. Second, reduced hemoglobin content during anemia results in increased activity of an endothelial-derived relaxing factor (ie, nitric oxide), leading to arteriolar vasodilation. Theoretically, increased perfusion pressure or blood volume can cause similar changes in vascular resistance and blood velocity, although a significant change in mean arterial pressure was not found in patients with normovolemic or hypervolemic anemia. There is no evidence to suggest that the circulating blood volume or arterial press-
A remarkable degree of regularity and shortening in R–R intervals during severe anemia, correlating with a regular cardiac rhythm and significant increase in HR, was found in the dogs of our study. The exception of approximately 20% of the observations during moderate anemia, these changes did not persist beyond the severely anemic state. An echocardiographic study evaluating left ventricular function performed in the same dogs revealed a significant increase in cardiac output, fractional shortening, ejection fraction, and HR during the severely anemic state (data not shown). These observations conform to findings of other investigations that used invasive techniques and revealed an increase in HR and cardiac output as components of the hyperdynamic cardiovascular response during acute and chronic severe normovolemic anemia in dogs. Increased cardiac output has also been documented in humans with severe chronic anemia. In 1 study, investigators found that an increase in HR provided a greater contribution to an increase in cardiac output, compared with the contribution provided by an increase in stroke volume. However, in hemodilution experiments in which dextran or other similar fluids were exchanged for blood without a volume deficit, a hyperdynamic state was created without any significant change in HR. It is believed that the increase in cardiac output in severe anemia is the result of reduced total systemic vascular resistance resulting in increased venous return. Heart rate reportedly influences Doppler variables. In 1 study, investigators found an inverse relationship between HR and PI of the descending aorta and other arteries in growth-retarded human fetuses. Significant reduction in PI of the AAo and HSA was seen in the study reported here, with a significant increase in HR in severely anemic dogs. However, although HR began to return to values obtained during the normal physiologic state and HR during the moderately anemic state was no longer significantly different from that during the control state. This may have contributed to failure to detect significant changes, especially those with a marginal value for significance. Measurements to confirm normal circulating blood volume and arterial pressure were not performed following induction of anemia because the study was designed along a clinical line intended to conform, as much as possible, to routine clinical practice at our facility. A deficit in circulating volume or arterial pressure would decrease blood flow and flow velocities and increase values of resistive indices. There was no evidence to suggest that dogs had such a deficit. Instead, lack of a significant reduction in cross-sectional area of the portal vein suggested that there was a normal circulating blood volume during all anemic states.

The large number of vessels examined, including those for which data were not reported here; the need for a precise sample collection technique; and differences in patient cooperation resulted in time constraints that may have influenced accuracy of certain measurements. In 1 dog, HR could not be determined...
during the control state because the dog would not tolerate placement of ECG pads. In addition, the HR, together with Doppler measurements of the CA and HSA, was not obtained for 1 dog each, and the HR with Doppler measurement of the MPV for 4 dogs was not obtained because of various reasons. In the case of the CA, it was obscured by gastrointestinal gas. Examination of the HSA represented a special problem because the spleen moved constantly during normal respiratory excursions. Splenic mobility worsened in dogs that struggled. For these conditions, it was impossible to obtain good spectral tracings because the splenic artery was oscillating in and out of the sample window. Obtaining 3 consecutive cycles of the Doppler spectrum of the HSA was particularly difficult. Sometimes we obtained only 1 cycle of the spectrum with varying intensity or even an incomplete cycle of the spectrum. A poor spectral tracing may yield inaccurate measurements of Doppler variables.

The MPV was usually evaluated last, and it was evaluated in fewer dogs because of time constraints. Additionally, examining the MPV required considerable effort when manipulating the transducer within a limited intercostal space to obtain an optimal insonation angle. The procedure was often uncomfortable to the dogs, which caused them to move. Vessel movements also were evident with respiration, and vessels were sometimes obscured by gastrointestinal gas.

Other limitations and sources of systematic and random errors encountered with Doppler hemodynamic measurements despite technologic advances in ultrasonic equipment include estimation of vessel cross-sectional area, angle of insonation, and mean velocity from which Doppler blood flow measurements are derived.\(^{28,30,34}\) In the study reported here, estimation of cross-sectional area was required for measurement of portal vein blood flow and CI. The problem of small vessel size was not encountered, and there was good resolution of the inner circumference of the MPV in the cross-sectional view. However, the MPV was not perfectly circular in cross section, the diameter of the MPV varied with respiratory movements, and gas from the stomach or lungs sometimes made viewing difficult. The optimal technique used for estimating portal cross-sectional area may have resulted in overestimation of blood flow and CI of the MPV because the true mean cross-sectional area would have been less than the estimated value.

Cross-sectional area of the HSV was estimated only for comparison of vessel size between control and anemic states. Cross-sectional area was calculated from the diameter measured by use of a long-axis view because it was difficult to obtain images of the vessel in a short-axis view.

Variation was evident between 0° and 60° for the estimated intersection angle between the ultrasound beam and long axis of each vessel when obtaining a Doppler spectrum. Moreover, it was unlikely that the scan plane and long-axis plane of a vessel were always aligned when estimating the insonation angle.\(^{28}\) Random and systematic errors in estimation of the insonation angle may have contributed to variation in estimating the angle and blood flow velocities. The modified technique of uniform insonation used in the study reported here may have further resulted in overestimation of TAV mean and blood flow because some low-velocity components of flow may have been excluded.

Despite the assumptions and modifications made in measurements and limitations of the DUS technique, the changes reported in this study appear to reflect the true influence of normovolemic anemia on Doppler variables. Collection of data from a homogeneous population by the same investigator and use of the same machine for all evaluations greatly minimized variations attributable to those factors. However, caution should be exercised for use of these data because they are likely to vary with the study population, equipment, and techniques used.

Noninvasive Doppler ultrasonography documented hyperdynamic circulation in the AAO and splanchic vessels in dogs with experimentally induced normovolemic anemia. Analysis of the results indicates that anemia significantly reduces arterial and venous DUS resistance indices and increases blood velocities and blood flow. This should be taken into consideration when interpreting results of DUS investigations of any physiologic or pathologic state with concurrent anemia. Lack of DUS evidence of abdominal splanchic hyperdynamic circulation or evidence of a change in the opposite direction (eg, an increase in RI or PI) in dogs with conditions that have coexisting anemia, such as babesiosis, should raise the suspicion for other important pathologic processes.

References


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