Arterial blood pressure as a predictor of the response to fluid administration in euvoletic nonhypotensive or hypotensive isoflurane-anesthetized dogs

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Objective—To determine the effects of rapid small-volume fluid administration on arterial blood pressure measurements and associated hemodynamic variables in isoflurane-anesthetized euvoletic dogs with or without experimentally induced hypotension.

Design—Prospective, randomized, controlled study.

Animals—13 healthy dogs.

Procedures—Isoflurane-anesthetized dogs were randomly assigned to conditions of nonhypotension or hypotension (mean arterial blood pressure, 45 to 50 mm Hg) and treatment with lactated Ringer’s solution (LRS) or hetastarch (3 or 10 mL/kg [1.4 or 4.5 mL/lb] dose in a 5-minute period or 3 mL/kg dose in a 1-minute period [4 or 5 dogs/treatment; ≥ 10-day interval between treatments]). Hemodynamic variables were recorded before and for up to 45 minutes after fluid administration.

Results—IV administration of 10 mL/kg doses of LRS or hetastarch in a 5-minute period increased right atrial and pulmonary arterial pressures and cardiac output (CO) when dogs were nonhypotensive or hypotensive, compared with findings before fluid administration; durations of these effects were greater after hetastarch administration. Intravenous administration of 3 mL of hetastarch/kg in a 5-minute period resulted in an increase in CO when dogs were nonhypotensive. Intravenous administration of 3 mL/kg doses of LRS or hetastarch in a 1-minute period increased right atrial pressure and CO when dogs were nonhypotensive or hypotensive.

Conclusions and Clinical Relevance—Administration of LRS or hetastarch (3 or 10 mL/kg dose in a 5-minute period or 3 mL/kg dose in a 1-minute period) improved CO in isoflurane-anesthetized euvoletic dogs with or without hypotension. Overall, arterial blood pressure measurements were a poor predictor of the hemodynamic response to fluid administration. (J Am Vet Med Assoc 2014;245:1021–1027)

Hypotension in companion animals undergoing general anesthesia is a medical emergency and a key reason for initiating fluid administration.1–8 Hypotension, generally defined as SAP < 80 to 90 mm Hg or MAP < 60 mm Hg, is reported to develop in 7% to 38% of dogs during general anesthesia and is believed to be more prevalent in animals that are very young, old, or critically ill.1,5,7 Isoflurane, the most frequently administered inhalation anesthetic administered to dogs and cats, decreases arterial blood pressure when administered at clinically relevant concentrations (1.2% to 1.5%) and induces marked decreases in arterial blood pressure measurements and cardiac output when inhaled concentrations exceed 2.5%.9,10

Intravenous fluid administration and reduction of anesthetic drug administration are currently recommended for treatment of anesthesia-associated hypotension in dogs and cats. However, with regard to IV fluid administration in such situations, the optimal fluid choice, rate of fluid administration, and total fluid volume have not been established.3,11–13 Importantly, there is little to no evidence that conventional volumes or rates of IV fluid administration are effective for the treatment of anesthetic-associated hypotension in dogs. To the contrary, experimental evidence suggests that conventional (10 to 30 mL/kg/h [4.5 to 13.6 mL/lb/h]) or higher (60 to 80 mL/kg/h [27.3 to 36.4 mL/lb/h]) rates of IV isotonic crystalloid solution administration are ineffective for treatment of isoflurane-associated hypotension in euvoletic dogs.13,15 Potential explanations for these negative results include the rapid redistribution of crystalloid solutions into extravascular fluid compartments and an isoflurane-induced decrease in cardiac function or increase in venous vascular capacitance.12,13,16–20 Similarly, IV administration of a colloid solution (eg, hetastarch or dextran 70) during isoflurane anesthesia does not always improve arterial blood pressure in dogs.14,15,21 Further...
thermore, the rapid administration of large volumes (>20 mL/kg [9.1 mL/lb]) of hetastarch or dextran during isoflurane anesthesia are reported to result in adverse effects such as fluid overload, renal impairment, and blood clotting abnormalities.14,21–23

Fluids for IV administration possess unique pharmacokinetic and pharmacodynamic properties that are dependent on their chemical and colliagative properties and on the circumstances (eg, the animal’s condition and fluid requirements) that exist when they are administered.24–25

Both crystalloids and colloids redistribute into extravascular fluid compartments, suggesting that the rate of fluid administration is more important than the amount or type of fluid administered.26 A fluid challenge, defined as rapid IV administration of small volumes (3 to 10 mL/kg [1.4 to 4.5 mL/lb] administered in a 2- to 20-minute interval) of crystalloid or colloid preparations, is used in human critical care settings to identify patients that are fluid responsive and likely to benefit from fluid therapy.27–29 Results of a clinical study30 conducted in anesthetized and critically ill humans suggest that a fluid challenge reduces the risk associated with more liberal fluid administration and is useful for determining preload reserve and fluid responsiveness, provided that appropriate physiologic variables are monitored. Peer-reviewed manuscripts and current fluid therapy guidelines for dogs and cats recommend the equivalent of a fluid challenge as treatment for hypotension during anesthesia.31–33

The purpose of the study reported here was to determine the effects of rapid small-volume fluid administration on arterial blood pressure measurements and associated hemodynamic variables in isoflurane-anesthetized euclidean dogs with or without experimentally induced hypotension. We hypothesized that treatment with such a fluid-challenge equivalent would improve SAP in isoflurane-anesthetized nonhypotensive or hypotensive euclidean dogs.

Materials and Methods

Animals—All procedures were reviewed and approved by the Institutional Animal Care and Use Committee at QTest Labs and complied with federal guidelines for the care and use of laboratory animals. Thirteen purposebred adult Beagles or mixed-breed dogs were acclimated to the animal facility. The dogs’ mean ± SD weight was 11.0 ± 2.1 kg (24.2 ± 4.62 lb). All dogs were determined to be in good health on the basis of results of a physical examination; core body temperature and respiratory activity were within 10% of each other. Under conditions of nonhypotension (MAP > 60 mm Hg), each dog was considered to be in a light plane of anesthesia but did not move, did not respond to touch or sound, possessed minimal jaw tone, and did not resist mechanical ventilation. The isoflurane concentration was increased, under conditions of hypotension, to maintain MAP at 45 to 50 mm Hg. Each dog was stabilized for approximately 30 minutes before fluid administration.

Dogs (equipped with radiotelemetry units) were randomly selected from the dog colony, anesthetized, and randomly assigned to conditions of hypotension or nonhypotension and to be administered 1 of 3 doses of LRS5 or hetastarch6: a 3 mL/kg dose in a 5-minute interval, a 10 mL/kg dose in a 5-minute interval, or a 3 mL/kg dose in a 1-minute interval. Thus, there were 12 combinations of experimental conditions and treatments; each of the 12 treatment groups included a minimum of 4 dogs with hypotension or 4 dogs without hypotension.

Each dog was allowed to recover from anesthesia after each experiment, and the IV catheter and thermocouple were removed. The dog was returned to the animal facility. An interval of at least 10 days was allowed to elapse before use of a given dog in another experiment.

Data collection—Heart rate, RAP, PAP, SAP, DAP, and MAP were continuously monitored for each dog during each anesthetic episode. These variables along with core body temperature and cardiac output (L/min)
were recorded at baseline (immediately before fluid administration performed at 0 minutes), immediately after fluid administration, 15 minutes after fluid administration, and between 30 and 45 minutes after fluid administration. An increase in MAP ≥ 10 mm Hg was considered to be clinically relevant.

**Statistical analysis**—An unbalanced ANOVA appropriate for unpaired data with repeated measures and Bonferroni correction was used to evaluate differences between dogs with and without experimentally induced hypotension and assess the effects of the various fluid administrations. If the time-by-treatment interaction was significant, an all pairwise comparison (Tukey test) of treatment effects was conducted. Additionally, given a time-by-treatment interaction, within-treatment time effects were assessed by comparing 0-minute values against values collected after 0 minutes. If no interaction existed, the main effect of time was investigated, and again an all pairwise approach was used. Values of P < 0.05 were considered significant.

**Results**

All dogs were considered to be in excellent health before and after the completion of the study. Seven dogs were each used in 5 experiments, 3 dogs were each used in 3 experiments, and 1 dog was used in 4 experiments. All IV catheters were percutaneously placed, and no surgical procedures were performed during anesthesia. Oxygen saturation as determined by pulse oximetry was > 93% in all dogs during the experiments. The end-tidal isoflurane concentration after the stabilization period and before fluid treatment ranged from 1.3% to 1.9% when dogs were nonhypotensive dogs and 2.1% to 3.2% when dogs were hypotensive. Notably, small changes in end-tidal isoflurane concentration (≤ 0.2%) resulted in changes in MAP (≥ 5 mm Hg) requiring prolongation of the equilibration period. End-tidal isoflurane data were not obtained at the 15-minute time point after fluid administration except for hypotensive dogs administered 3 mL of LRS or hetastarch in a 1-minute interval.

Baseline RAP was significantly increased in hypotensive dogs and baseline systemic arterial blood pressure values and cardiac output were significantly decreased, compared with baseline values in nonhypotensive dogs (Tables 1 to 4). There were no changes from baseline in heart rate or rhythm or SAP, DAP, or MAP after administration of either LRS or hetastarch administered at 3 mL/kg over 5 minutes when dogs did not receive fluid.

### Table 1—Hemodynamic effects of LRS (n = 4) and hetastarch (5) administered at a dose of 3 or 10 mL/kg (1.4 or 4.5 mL/lb) in a 5-minute interval in isoflurane-anesthetized euclidean dogs with and without experimentally induced hypotension.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment</th>
<th>Dose (mL/kg)</th>
<th>Nonhypotensive conditions</th>
<th>Hypotensive conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Baseline</td>
<td>End dose</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>LRS</td>
<td>3</td>
<td>110 ± 3</td>
<td>114 ± 25</td>
</tr>
<tr>
<td></td>
<td>LRS</td>
<td>10</td>
<td>103 ± 19</td>
<td>110 ± 17</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>3</td>
<td>5 ± 3</td>
<td>6 ± 2</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>10</td>
<td>4 ± 2</td>
<td>6 ± 3</td>
</tr>
<tr>
<td>RAP (mm Hg)</td>
<td>LRS</td>
<td>3</td>
<td>5 ± 3</td>
<td>8 ± 4</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>10</td>
<td>5 ± 3</td>
<td>8 ± 4</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>LRS</td>
<td>3</td>
<td>107 ± 14</td>
<td>110 ± 14</td>
</tr>
<tr>
<td></td>
<td>LRS</td>
<td>10</td>
<td>113 ± 6</td>
<td>118 ± 9</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>3</td>
<td>107 ± 13</td>
<td>120 ± 12</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>10</td>
<td>101 ± 17</td>
<td>103 ± 14</td>
</tr>
<tr>
<td>DAP (mm Hg)</td>
<td>LRS</td>
<td>3</td>
<td>71 ± 17</td>
<td>73 ± 19</td>
</tr>
<tr>
<td></td>
<td>LRS</td>
<td>10</td>
<td>80 ± 4</td>
<td>84 ± 7</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>3</td>
<td>72 ± 12</td>
<td>82 ± 14</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>10</td>
<td>67 ± 15</td>
<td>68 ± 13</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>LRS</td>
<td>3</td>
<td>86 ± 17</td>
<td>89 ± 19</td>
</tr>
<tr>
<td></td>
<td>LRS</td>
<td>10</td>
<td>95 ± 5</td>
<td>100 ± 8</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>3</td>
<td>88 ± 12</td>
<td>91 ± 11</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>10</td>
<td>82 ± 17</td>
<td>84 ± 15</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>LRS</td>
<td>3</td>
<td>1.6 ± 0.5</td>
<td>2.0 ± 0.53</td>
</tr>
<tr>
<td></td>
<td>LRS</td>
<td>10</td>
<td>1.8 ± 0.4</td>
<td>2.3 ± 0.47</td>
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<tr>
<td></td>
<td>Hetastarch</td>
<td>3</td>
<td>1.7 ± 0.4</td>
<td>2.0 ± 0.44</td>
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<tr>
<td></td>
<td>Hetastarch</td>
<td>10</td>
<td>1.8 ± 0.5</td>
<td>2.3 ± 0.47</td>
</tr>
</tbody>
</table>

Data are reported as mean ± SD.

Dogs were randomly selected from a group of 13 research dogs, anesthetized, and randomly assigned to conditions of hypotension (MAP, 45 to 50 mm Hg) or nonhypotension (MAP, > 60 mm Hg) and to be administered 1 of the 2 doses of LRS or hetastarch. The 13 dogs were used in 3, 4, or 5 experiments; an interval of at least 10 days was allowed to elapse before use of a given dog in another experiment. Under conditions of nonhypotension, 4 dogs received 3 mL of LRS/kg and 4 dogs received 10 mL of LRS/kg; 5 dogs received 3 mL of hetastarch/kg and 5 dogs received 10 mL of hetastarch/kg. Under conditions of hypotension, 5 dogs were included in each experiment. Variables of interest were assessed at baseline (immediately before fluid administration performed at 0 minutes), immediately after completion of fluid administration (end dose), 15 minutes after fluid administration, and between 30 and 45 minutes after fluid administration.

*For a given variable within a fluid treatment, value is significantly (P < 0.05) different from baseline value when dogs were hypotensive. tValue is significantly (P < 0.05) different from baseline value when dogs were nonhypotensive. TFor a given variable within a fluid treatment, value is significantly (P < 0.05) different from baseline value when dogs were nonhypotensive. ND = Not done.
or did not have hypotension. Similar findings were observed after administration of either LRS or hetastarch administered at 10 mL/kg over 5 minutes except that heart rate was decreased from baseline immediately after administration of LRS and increased from baseline at 30 to 35 minutes after administration of hetastarch when dogs were hypotensive.

Cardiac output was significantly increased from baseline in dogs that were not hypotensive immediately after administration of the 3 mL/kg dose of LRS in a 5-minute interval (Table 1). The RAP, PAP, and cardiac output were significantly increased from baseline values in dogs that were not hypotensive immediately after administration of the 10 mL/kg dose of LRS in a 5-minute interval. Cardiac output was significantly increased from baseline in dogs that were not hypotensive immediately and at 30 to 45 minutes after administration of a 3 or 10 mL/kg dose of hetastarch in a 5-minute interval. The RAP and PAP were significantly increased from baseline at all time points after hetastarch administration of a dose of 10 mL/kg in a 5-minute interval when dogs were not hypotensive; cardiac output was significantly increased from baseline immediately and at 30 to 45 minutes after that fluid administration. Cardiac output was significantly increased from baseline in hypotensive dogs immediately after LRS or hetastarch administration at a dose of 10 mL/kg in a 5-minute interval.

Administration of LRS or hetastarch at a dose of 3 mL/kg in a 1-minute interval resulted in a significant increase in RAP and cardiac output immediately after fluid administration, compared with baseline values, when dogs were and were not hypotensive (Tables 3 and 4). Administration of hetastarch at a dose of 3 mL/kg in a 1-minute interval caused PAP to increase significantly from baseline values when dogs were and were not hypotensive. Cardiac output remained significantly increased at 30 to 45 minutes after completion of hetastarch treatment when dogs were not hypotensive. Cardiac output was not increased after hetastarch administration at the 30- to 45-minute time point when dogs were hypotensive. We did not observe a clinically relevant increase (≥ 10 mm Hg) in MAP following any of the fluid administrations in any dog with experimentally induced hypotension.

### Discussion

The data obtained in the present study indicated that MAP was a poor predictor of responsiveness to a fluid challenge (ie, rapid IV administration of a small volume of fluid) in euvolemic dogs anesthetized with isoflurane. Administration of LRS or hetastarch in fluid volumes (3 or 10 mL/kg) and at rates (0.6 to 3 mL/kg/min [0.27 to 1.4 mL/lb/min]) recommended for the treatment of hypotension did not result in clinically relevant (ie, ≥ 10 mm Hg) increases in MAP in isoflurane-anesthetized euvolemic dogs with experimentally induced hypotension (MAP approx 50 mm Hg). In most instances, cardiac output increased immediately in response to each fluid challenge when dogs were nonhypotensive or hypotensive, suggesting that monitoring cardiac output or stroke volume is more predictive of a response to fluid therapy in euvolemic dogs during isoflurane anesthesia. The RAP and PAP were increased, compared with baseline values, after administration of LRS or hetastarch at dose of 10 mL/kg in a 5-minute interval when dogs were or were not hypotensive. Immediately after administration of LRS or hetastarch at a dose of 3 mL/kg in a 1-minute interval, RAP was increased, compared with baseline values, when dogs were or were not hypotensive; PAP was increased at that time point after that hetastarch challenge. These effects on RAP and PAP were typically of longer duration following hetastarch administration.

Perioperative hypotension can be caused by hypovolemia, poor cardiac function (eg, heart failure and cardiac arrhythmias), anesthesia, or a combination of these factors. Hypovolemia may be absolute (eg, dehydration and hemorrhage) or relative (increased venous capacitance) and is a natural consequence of surgical

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**Table 2—Hemodynamic effects of LRS and hetastarch administered at a dose of 3 mL/kg in a 1-minute interval in isoflurane-anesthetized euvolemic dogs with and without experimentally induced hypotension.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment</th>
<th>Nonhypotensive conditions</th>
<th>Hypotensive conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>End dose 15 min</td>
<td>30–45 min</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>LRS</td>
<td>101 ± 21</td>
<td>101 ± 20</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>116 ± 19</td>
<td>115 ± 22</td>
</tr>
<tr>
<td>RAP (mm Hg)</td>
<td>LRS</td>
<td>4 ± 2</td>
<td>6 ± 21</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>5 ± 2</td>
<td>7 ± 34</td>
</tr>
<tr>
<td>PAP (mm Hg)</td>
<td>LRS</td>
<td>13 ± 2</td>
<td>14 ± 3</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>15 ± 4</td>
<td>17 ± 31</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>LRS</td>
<td>101 ± 25</td>
<td>102 ± 23</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>97 ± 14</td>
<td>98 ± 16</td>
</tr>
<tr>
<td>DAP (mm Hg)</td>
<td>LRS</td>
<td>64 ± 10</td>
<td>65 ± 9</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>65 ± 6</td>
<td>63 ± 9</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>LRS</td>
<td>78 ± 15</td>
<td>80 ± 14</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>77 ± 10</td>
<td>78 ± 12</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>LRS</td>
<td>1.8 ± 0.4</td>
<td>2.1 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>Hetastarch</td>
<td>2.2 ± 0.5</td>
<td>2.6 ± 0.8</td>
</tr>
</tbody>
</table>

Data are reported as mean ± SD. Dogs were randomly selected from a group of 13 research dogs, anesthetized, and randomly assigned to conditions of hypotension (MAP, 45 to 50 mm Hg) or nonhypotension (MAP > 60 mm Hg) and to be administered a dose of either LRS or hetastarch. Under conditions of nonhypotension or hypotension, 4 dogs were included in each experiment. See Table 1 for remainder of key.
trauma, open body cavities, and the vasodilatory effects of anesthetic drugs. Relative hypovolemia caused by anesthesia is characterized by hypotension. The dogs in the present study were in good health, were not in heart failure, were euvoicmic, and had minimal blood loss during anesthesia because no surgical procedures were performed. Abnormalities in cardiac rate or rhythm were not observed during isoflurane anesthesia. Therefore, we attributed hypotension to relative hypovolemia caused by propofol- and isoflurane-induced vasodilatation and decreases in cardiac function, considering that both propofol and isoflurane are known to have negative inotropic effects and blunt baroreceptor reflex activity, inhibit sympathetic vasoconstriction, and increase vascular capacitance.

In contemporary human medicine, the type (crystalloid or colloid), volume (liberal or restricted), and rate of fluid administration during the perioperative period have become controversial issues. The problems, as summarized in several reviews, include LRS-induced proinflammatory effects, saline (0.9% NaCl) solution–induced hyperchloremic metabolic acidosis and impairment of renal blood flow, minimal plasma expansion after crystalloid administration, prolonged clotting times and impaired renal function after colloid administration, and acute kidney injury and loss of the protective vascular endothelial surface layer (glycocalyx) associated with fluid overload. The potential for fluid retention and edema are further aggravated by isoflurane-associated hypotension, which has been shown to promote interstitial fluid accumulation, decrease interstitial colloid osmotic pressure, and increase vasopressin secretion, which decreases urine output and the excretion of excess fluid. Studies have revealed that isotonic crystalloids are rapidly eliminated from the intravascular (central) fluid compartment during isoflurane anesthesia and that IV fluid redistribution to peripheral tissues (interstitial tissue) is independent of the volume of fluid infused and markedly influenced by hypotension.

Published reviews and guidelines for intraoperative fluid therapy suggest that crystalloid or colloid administration is effective for the treatment of hypotension during inhalation anesthesia. Recent evidence suggests that conventional rates or high volumes of isotonic crystalloid administration for the treatment of inhalation anesthetic–induced hypotension (relative hypovolemia) are unlikely to result in substantial improvement in arterial blood pressure and that reducing the inhalation anesthetic concentration is key to its improvement. However, conventional crystalloid fluid therapy can improve cardiac output during inhalation anesthesia in dogs.

Results of a study conducted in isoflurane-anesthetized euvolemic, nonhypotensive dogs indicated that conventional fixed-rate fluid administration (10 to 30 mL/kg/h) did not increase arterial blood pressure but did improve cardiac output. Other studies have also identified that the administration of isotonic crystalloid solutions has dilutional effects resulting in decreases in Hct, total protein concentration, colloid osmotic pressure, select (crystalloid-dependent) electrolyte disturbances, and blood viscosity and an increase in cardiac output. Furthermore, results of 2 previous studies indicated that higher volumes and rates (60 and 80 mL/kg/h) of isotonic crystalloid fluids (an isotonic electrolyte solution [60 mL/kg/h] and LRS [80 mL/kg/h]) administration for 1 hour did not restore MAP to baseline values in isoflurane-anesthetized euvolemic, hypotensive (MAP, 40 to 50 mm Hg) dogs and resulted in clinical signs of fluid overload (vomiting, facial edema, and nasal discharge) during recovery from anesthesia. Reduction of the end-tidal isoflurane concentration to approximately 1.6% during the last 15 minutes of a 1-hour infusion of the isotonic electrolyte solution (60 mL/kg/h) restored arterial blood pressure and blood flow to values greater than baseline, suggesting that isoflurane-induced depression of compensatory responses is responsible for the lack of a response to fluid infusion. We did not determine whether a decrease in isoflurane concentration would have improved the response to fluid administration among the dogs used in the present study, but results from that other study suggest that this would have occurred.

Crystalloids pass easily through endothelial and capillary membranes into the interstitium, minimizing their potential plasma volume-expanding effects, whereas colloids are believed to remain in the blood stream for a longer period. The potential benefit of colloid fluid therapy is generally attributed to their molecular weight and an increase in the plasma effective colloid osmotic pressure. The clinical relevance of these attributes remains controversial and requires further investigation, particularly during inhalation anesthesia or in animals with hemorrhage, trauma, or sepsis, given that the penetration capacity of a colloid into the interstitial space is not only dependent on the individual colloids molecular weight but also its electrical charge, shape, effective radius, and interaction with the endothelial glycocalyx. Regardless, and in contrast to the effect of crystalloids, MAP was increased from baseline values 15 minutes after administration of hetastarch (80 mL/kg/h) to isoflurane-anesthetized euvolemic hypotensive (MAP, 40 to 50 mm Hg) dogs. One study investigating the effects of fluid administration to euvolemic, hypotensive (MAP, 50 mm Hg) dogs anesthetized with isoflurane (mean end-tidal isoflurane concentration, 2.43 ± 0.23%) revealed that dextran 70 at a dose of 7 mL/kg (3.18 mL/lb) administered at a rate of 30 mL/kg/h (0.5 mL/kg/min [0.23 mL/lb/min]) increased MAP by only 4 to 6 mm Hg within 10 to 15 minutes. The volumes and rates of crystalloid or colloid administration used in the present study encompassed these values as well as those currently recommended for the treatment of isoflurane-associated hypotension in dogs and did not result in predictable increases in MAP in dogs with or without experimentally induced hypotension. The MAP did increase minimally when dogs were hypotensive after administration of LRS or hetastarch at a dose of 3 mL/kg in a 1-minute interval, but this observation was not significant.

Our study and previous investigations in isoflurane-anesthetized nonhypotensive dogs did detect increases in cardiac output in response to fluid administration. Increases in cardiac output that occurred following the administration of either LRS or hetastarch in the present study were variable in duration and were consistent in isoflurane-anesthetized dogs with experimentally
induced hypotension immediately after a fluid dose of 10 mL/kg in a 3-minute interval or 3 mL/kg in a 1-minute interval was administered. Increases in cardiac output are indicative of a beneficial response to fluid therapy and have been attributed to an increase in preload (increase in end-diastolic volume without a change in afterload or cardiac contractility), a decrease in ventricular end-systolic volume, an increase in cardiac contractility, and a decrease in blood viscosity.51-55 A 200-ml fluid challenge (2.5 mL/kg/min [1.14 mL/lb/min]) to euvolemic pigs anesthetized with thiopental (7 mg/kg/h) and fentanyl (30 µg/kg/h) did not induce proportional increases in hepatic and renal blood flow, compared with blood flow in other tissue beds, suggesting that responses to fluid therapy–associated volume expansion may be tissue specific.50 Results of the present study indicated that bolus fluid administration (ie, a fluid challenge) for the treatment of hypotension caused by isoflurane anesthesia (relative hypovolemia) does not induce predictable increases in systemic arterial blood pressure variables in isoflurane-anesthetized nonhypotensive dogs with or without experimentally induced hypotension. We did not evaluate the effect of surgical stimulation but empirically believe that this would have confounded the results by increasing heart rate, cardiac output, and arterial blood pressure. The administration of vasoactive drugs (ie, dopamine or phenylephrine) or alternative options for anesthesia (eg, dissociative anesthesia) and analgesia (eg, opioid infusion) should be considered if a fluid challenge is ineffective for treating hypotension during isoflurane anesthesia in dogs, particularly if the isoflurane concentration cannot be reduced or when fluid administration is contraindicated (ie, heart failure).21,39,60 Importantly, the study findings do not apply to conscious or anesthetized dogs that become hypotensive from blood loss (absolute hypovolemia). Animals with hemorrhage retain a larger volume of infused fluid within the vasculature compartment and have a beneficial blood pressure response to fluid therapy.21,61,62

References