
http://dx.doi.org/10.1111/avj.12306


Copyright: © 2015 Australian Veterinary Association.
It is posted here for your personal use. No further distribution is permitted.
Preoperative factors associated with hypotension in young anaesthetised dogs undergoing elective desexing

RS Costa, AL Raisis*, G Hosgood and GC Musk

College of Veterinary Medicine, School of Veterinary and Life Sciences, Murdoch University, Murdoch, Western Australia, Australia

Abstract

Objectives

Document the proportion of dogs with perioperative hypotension and explore the association of sex, age and body mass and indices of hydration with mean arterial blood pressure (MAP) in two cohorts of young, healthy anaesthetised dogs.

Methods

Dogs were anaesthetised with a standardised protocol. The proportion of dogs with invasively measured MAP <60 mmHg for ≥10 min was recorded. The area under the MAP*time curve (MAP-AUC) was calculated for a standard perioperative period. The association of explanatory variables, including sex, age, body mass and indices of hydration (urine specific gravity (USG), packed cell volume and total solids) measured prior to surgery, with the MAP-AUC was explored using regression analysis in the first cohort (n = 71) and externally validated in the second cohort (n = 24).

Results

In cohort 1, 35 of 71 dogs (0.49, 95% confidence interval (CI) 0.37–0.61) dogs and 17/24 dogs in cohort 2 (0.71, 95% CI 0.53–0.89) developed hypotension. Regression analysis showed that age and
USG were significantly associated with MAP-AUC for cohort 1 (P = 0.0138). There was a positive association of MAP-AUC with age and a negative association with USG. The association of MAP-AUC with USG was supported in cohort 2, with a significant negative association (P = 0.014, r = −0.54)

**Conclusion**

The high frequency of hypotension in both cohorts supports blood pressure monitoring during anaesthesia of young, healthy dogs. USG, an index of hydration, appears negatively associated with MAP during anaesthesia, suggesting that subclinical dehydration may contribute to lower MAP during surgical anaesthesia.

**Keywords:** anaesthesia; blood pressure monitoring; dogs; hypotension

**Abbreviations:** ASA, American Society of Anaesthesiologists; CI, confidence interval; MAP, mean arterial blood pressure, MAP-AUC, area under the MAP*time curve; PCV, packed cell volume; TS, total solids; USG, urine specific gravity

Hypotension is the most commonly reported cardiovascular complication during anaesthesia of small animals,[1-3] with a frequency varying 7% to 46%.[1, 4, 5] The varying frequency may, in part, be related to the lack of a standard definition for hypotension,[6] which is commonly defined as mean arterial blood pressure (MAP) <60 mmHg,[7-9] but other definitions used in anaesthetised dogs include systolic arterial blood pressure <90 mmHg[4, 10] or <80 mmHg.[1] The use of either non-invasive (oscillometric and Doppler) or invasive techniques may also contribute to the variation in frequency, because inaccurate measurements, particularly with non-invasive methods, could result in inaccurate determination of hypotension. Further inconsistency in the anaesthetic drugs administered and the subjects' characteristics, particularly American Society of Anaesthesiologists (ASA) health status classification, could also contribute to discrepancies between studies. Unfortunately, none of the cited studies reported the influence of these factors on hypotension.
The first aim of our study was to document the proportion of young dogs developing hypotension (MAP < 60 mmHg) in two cohorts of ASA I dogs undergoing elective desexing. Our second aim was to explore the association between easily identified subject factors, including signalment (sex, age, body mass) and hydration status (assessed using packed cell volume (PCV), total solids (TS) and urine specific gravity (USG)) and perioperative MAP in the dogs during a surgical plane of anaesthesia.

We hypothesised that the proportion of dogs developing hypotension would be at least 0.40. We also hypothesised that when young dogs were maintained at an appropriate depth of anaesthesia for desexing, age would be positively associated with perioperative MAP and the indices of hydration (PCV, TS, USG) would be negatively associated with MAP.

**Materials and methods**

This study was approved by the Murdoch University Animal Ethics Committee (R2396/11).

Cohort 1 consisted of young, healthy dogs being desexed by supervised undergraduate veterinary students in neutering laboratories at Murdoch University Veterinary Hospital between 2011 and 2012. Cohort 2 consisted of young, healthy dogs being desexed by veterinarians in a general practice clinic at Murdoch University Veterinary Hospital between February and July 2012. Anaesthesia of dogs in both cohorts was supervised by experienced veterinarians.

All dogs included in this study were classified as ASA I based on clinical examination and preoperative blood tests. Dogs were excluded if the standard anaesthetic protocol could not be used because their temperament prohibited blood sample collection without extra restraint or the use of the standard anaesthetic protocol, or their body condition score (>6/9) prevented accurate determination of lean body weight for calculation of drug doses.
The dogs in cohort 1 were admitted to hospital the day before surgery and their sex, age and body mass were recorded. Clinical examination and collection of urine and blood samples were performed on admission (day 1) and repeated prior to premedication on the day of surgery (day 2). The dogs from cohort 2 were admitted on the day of surgery and their sex, age and body mass were recorded. Clinical examination and collection of blood and urine samples were performed prior to premedication on the same day.

Urine was collected by free catch. If the dog did not urinate on the day of surgery (day 2 for cohort 1), a sample was collected immediately following induction of anaesthesia by manually expressing the urinary bladder. USG was determined using refractometry.

Blood for PCV and TS determination was collected from the jugular vein, placed directly into heparinised microcapillary tubes and measured using a microhaematocrit reader (Clements Medical Equipment, NSW, Aust) and refractometry, respectively.

Anaesthesia was performed in all dogs using a standardised protocol. All dogs were fasted overnight and water was provided until premedication, which comprised 0.03 mg/kg of acepromazine (ACP2, Ceva Animal Health, NSW, Australia) and 0.3 mg/kg of morphine (DBL® Morphine Sulfate Injection, Hospira, VIC, Australia) administered IM 30 min prior to induction of anaesthesia. Anaesthesia was induced with 4–6 mg/kg of propofol IV (Fresofol 1%, Fresenius Kabi, NSW, Australia) titrated until sufficient depth of anaesthesia allowed intubation of the trachea without a response. Anaesthesia was maintained with isoflurane (Veterinary Companies of Australia, NSW, Australia) delivered in up to 100% oxygen using a non-rebreathing system for animals less than 10 kg body weight and a rebreathing (Bain) system for animals weighing more than 10 kg. Hartmann's solution (Baxter Compound Sodium Lactate, Baxter Healthcare Corporation, IL, USA) was administered at 10 mL/kg/h IV and active warming was performed using warm air blowers.

Postoperative analgesia was provided using meloxicam (0.2 mg/kg; Metacam®, Boehringer Ingelheim Vetmedica Inc., MO, USA) administered SC at the end of anaesthesia. Additional postoperative analgesia was provided using tramadol (0.2 mg/kg; Tramal®, CSL Biotherapies, VIC, Australia) IM every 12 h if required.
Heart rate, respiratory rate, oxygen saturation, end-tidal carbon dioxide tension, body temperature (oesophageal probe) and invasive blood pressure were monitored using the Surgivet V9203 multivariable monitor (PolymountGCX® Corporation, CA, USA). Depth of anaesthesia was monitored clinically. Appropriate depth of anaesthesia was considered present during surgery if eye position was ventral, the palpebral reflex was absent and muscle tone was relaxed.[11] Isoflurane vaporiser settings were adjusted to the minimum that could achieve these clinical signs. In addition, vaporiser settings were decreased incrementally as required to maintain the respiratory rate at >10 breaths/min and/or end-tidal carbon dioxide tension <60 mmHg and heart rate >60 beats/min) in all dogs. All dogs that remained hypotensive (MAP < 60 mmHg) despite decreasing the administered dose of isoflurane, received a maximum of three increments of 10 mL/kg of Hartmann's solution administered over 10–15 min until MAP was >60 mmHg. No other treatment was provided. The vaporiser setting required to produce an appropriate depth of anaesthesia in each dog was recorded.

Arterial blood pressure was measured using a 20–22g metatarsal arterial catheter connected via fluid-filled extension tubing to a transducer (DTXPlus™, Becton Dickinson Critical Care Systems, Singapore) that interfaced with the multivariable monitor. Prior to the start of anaesthesia, the transducer was checked for linearity using a water manometer. The transducer was positioned at the thoracic inlet, the approximate position of the heart base in dorsal recumbency, and zeroed to atmospheric pressure. A rapid flush test was performed before the start of measurement to subjectively assess the level of damping of the measurement system, and invasive measurement of blood pressure was started after the dog was moved into the operating room. Blood pressure calculated from the average of 10 consecutive measurements was recorded every 5 min. At the end of anaesthesia, the transducer was reopened to the atmosphere to confirm absence of baseline drift during the study.

Statistical analysis

Hypotension was considered present if MAP was <60 mmHg for ≥10 min despite decreasing the vaporiser setting or increasing surgical stimulation. The proportion of dogs classified as hypotensive was the criterion of interest and the point estimate and 95% confidence interval (CI) was calculated.
using methods for proportions (statistical software: SAS v9.3, SAS Institute, NC, USA). For each
dog, the time at which hypotension was first recorded relative to the start of surgery was identified
and the mean and 95% CI were determined.

The mean (95% CI) percent isoflurane vaporiser setting was calculated from the observation time
points during the standardised perioperative period common to males and females (10 min before start
of surgery to 40 min after start of surgery for cohort 1; 5 min before start of surgery to 30 min after
start of surgery for cohort 2). The proportion of animals using a rebreathing (circle) breathing system
or non-rebreathing breathing system was also determined.

All continuous data (age, body mass, PCV, TS, USG, anaesthesia duration, surgery duration) were
tested for normality using D'agostino and Pearson omnibus normality test (GraphPad Prism 5, CA,
USA). All continuous variables except age and body mass were normally distributed and the mean
and 95% CI were calculated. Age and body mass were each summarised as median and interquartile
interval. For the purpose of analysis, USG was modified as (USG − 1) × 1000; therefore, USG of
1.040 would be 40. For cohort 1, the mean USG, PCV and TS were compared across days 1 and 2
using a paired t-test with significance determined at P ≤ 0.05 (GraphPad Prism 5). Categorical
variables (sex) were described as proportions with 95% CI.

To investigate subject factors that influenced MAP during anaesthesia, the area under the MAP versus
time curve (MAP-AUC-10–40 and MAP-AUC-5–30 for cohorts 1 and 2, respectively) during the
standardised perioperative period common to males and females (see above) was calculated using the
trapezoidal method (GraphPad Prism 5).

For cohort 1, the association of explanatory variables including sex, age, body mass, USG (day 2),
PCV (day 2) and TS (day 2) with the MAP-AUC-10–40 was explored using multiple regression. If data
for day 2 were missing, the USG, PCV and TS values for day 1 were used by default. Regression
analysis was performed with backward selection. All variables were entered into the model and
retained with a level of significance P < 0.15. Inclusion was set at P < 0.15 to avoid premature
exclusion of possible associations between explanatory variables and outcome. This reduced our
chance of prematurely dismissing an explanatory factor from cohort 1 that may be important and preclude further testing in cohort 2.

The model of best fit was based on the Mallow's C(p) criterion and the coefficient of determination (R2), including variables that created the smallest C(p) closest to the number of variables in the model (p), and the largest coefficient of determination (R2). For variables with significant association with MAP-AUC, the estimated regression coefficient was reported. For a model with a single explanatory variable, the correlation coefficient (r) was reported.

The model was then externally validated against the second similar but unique cohort. The intent of this study was not to develop a predictive model from cohort 1, but rather to detect associations between subject factors and MAP, and then verify that similar findings could be repeated in a second, similar, but unique, cohort. Thus, regression analysis was performed for cohort 2, modelling age and USG against MAP-AUC, as described above.

**Results**

Cohort 1 included 71 dogs (48% male, 52% female) (Table 1). The mean start time for recording invasive blood pressure was 30 min (95% CI 28–31) after the induction of anaesthesia, which was 10 min (95% CI 9–11) prior to the start of surgery. Of the 71 dogs, 35 (49%; 95% CI 37–61) developed hypotension during general anaesthesia (Table 1). Of these, 34 (97%) developed hypotension within the standardised period; 19/35 hypotensive dogs required one increment, 11 dogs required two increments and 5 dogs required three increments of IV fluids to achieve a target MAP >60 mmHg.

Cohort 2 included 24 dogs (33% male, 67% female) (Table 1). The mean start time for recording blood pressure was 24 min (95% CI 21–27) after the induction of anaesthesia and 7 min (95% CI 4–9) prior to the start of surgery. A total of 17 (71%) dogs developed hypotension during general anaesthesia (Table 1), all within the standardised period. Of these dogs, 7 required one increment, 7
required two increments and 3 required three increments of IV fluids to achieve a target MAP >60 mmHg.

A circle breathing system with a standard fresh gas flow of 2 L/min was used in 56/71 dogs (79%) in cohort 1 and 18/24 dogs (75%) in cohort 2. A Bain breathing system was used in the remaining 15 dogs (21%) and 6 dogs (25%) in cohorts 1 and 2, respectively (Table 1).

For cohort 1, USG, PCV and TS data were not obtained for all dogs, because of haemolysis of some samples (Table 2). There was no significant difference in PCV (P = 0.586, n = 58) and TS (P = 0.258, n = 58) between day 1 or day 2; USG was significantly higher on day 2 (P < 0.001, n = 35 paired values). The PCV, TS and USG data were available for 20 dogs in cohort 2 (Table 2).

Discussion

This study showed that the proportion of dogs with hypotension was at least as high as the hypothesised estimate of 40% and that the combination of age and USG best explained the cumulative MAP over the perioperative period. The USG appeared to be the most robust explanatory variable, being verified in the second cohort.

The intent of the study of the first, larger cohort was to explore associations and that of the second cohort was to verify the findings in a similar yet unique group. External validation is indicated in predictive modelling, where a regression model is derived from a cohort, and then its ability to predict outcomes in a separate, similar but often smaller, cohort is tested.[12] Our intent was not to develop a predictive model of MAP, but to explore its association with easily identifiable subject factors that the practitioner could recognise and perhaps manipulate. It was, however, thought important to verify the findings from the first cohort in a second cohort. Our combined findings from both cohorts support our conclusion of an association of MAP in the perioperative period with USG.

The negative association of USG with MAP indicates how hydration status may affect MAP. In the first cohort, the significant increase in USG between admission and the day of surgery suggests the
development of dehydration in these dogs.[13] It is probable that voluntary water intake was inadequate during hospitalisation, resulting in reduced urinary water excretion in an attempt to preserve body water. Reduced water intake can be attributed to both the stress of an unusual environment and fasting. At least 70% of the total water intake is consumed just before, during and immediately after meals;[14] thus, overnight fasting could contribute to dehydration.[15] Typically, small decreases in body water associated with subclinical dehydration would not be expected to affect blood volume significantly. However, when combined with drug-induced vasodilation and increased vascular volume, it is possible that even small decreases in total body water could contribute to reduced blood volume and thus blood pressure.[16]

The proportion of dogs with hypotension in cohort 1 was similar to that reported in several previous studies[2, 5, 10] of anaesthetised dogs. Two studies report lower frequencies of 7%[1] and 22%.[4] Factors such as different definitions of hypotension used,[6] the utilisation of non-invasive methods for measuring MAP[1] and variability in anaesthetic drugs and patient characteristics such as ASA scores may have contributed to the discrepancies between studies. Gaynor et al. defined hypotension as systolic arterial blood pressure <80 mmHg measured using the Doppler technique,[1] which could have resulted in its overestimation[17] and thus underestimation of the frequency of hypotension. In our study, MAP was measured invasively in all dogs to minimise inaccurate estimation of the proportion of dogs with hypotension.[18, 19] We also attempted to reduce variability by using a cohort of young healthy dogs undergoing an elective procedure using a standardised anaesthetic protocol.

Despite standardisation of the anaesthetic and surgical procedure, a much greater proportion of dogs in cohort 2 developed hypotension compared with cohort 1. Investigation of the differences between the two cohorts revealed that the age of dogs in cohort 2 was significantly lower than in cohort 1. Furthermore, although age showed a strong association with MAP in the cohort 1, a similar association was not verified in cohort 2. It is possible the significantly younger age combined with a smaller spread of ages in cohort 2 prevented such an association from being detected. An association between age and blood pressure is consistent with reports of higher frequency of anaesthesia-related
hypotension in younger dogs,[5] children[20] and foals[21, 22] compared with older subjects. Studies in conscious dogs also report lower MAP in younger (<12 months) dogs compared with older (>12 months) dogs,[23, 24] with a mean MAP of 79.2 mmHg reported in 6-month-old dogs and a mean MAP of 92.9 mmHg in dogs aged 12–24 months.[23] These findings could be caused by age-related changes in cardiovascular function. Sympathetic nervous system activity is immature in young dogs (21–40 days old), but improves as the animal ages.[25] Cardiac contractility, thus cardiac function, is also reported to increase in dogs from 3 to 9 months of age.[26] Reduced cardiac function may exacerbate the cardiovascular effects of sedatives and anaesthetic agents, resulting in lower blood pressures during anaesthesia in younger animals compared with older animals. Our study did not include geriatric dogs and thus the relationship between blood pressure and age in a much older cohort of dogs may differ from that observed in our study.

**Study limitations**

Several aspects of this study should be acknowledged. First, invasive measurement of blood pressure in our study commenced after the dogs were moved into the operating room, so no data were obtained in the preparation room, which could have resulted in underestimation of the frequency or duration of hypotension. Furthermore, all dogs with MAP <60 mmHg for ≥10 min were treated with increased rates of IV fluid administration, which should increase MAP over time. Although this may have reduced the ability to detect associations between MAP and the explanatory variables, it is more likely that it would have underestimated the importance of variables such as age and USG.

The missing data for some variables could affect the association between these variables and perioperative MAP. In cohort 1, the inclusion of data for six dogs from day 1 allowed us to maximise the number of dogs in the analysis and is, if anything, likely to have biased the result away from our hypotheses. Although there was no difference in the PCV or TS values between day 1 and day 2, USG was significantly lower on day 1. Thus, the influence of USG on MAP may have been underestimated.
In our study, the calculation of AUC allowed for a global assessment of the MAP across time and created one response variable that allowed exploration using association analysis (regression). This avoids finding spurious results at multiple, individual, arbitrary time points, a consequence of increased type I error. The MAP-AUC assessed the cumulative MAP over the common time period of −10 to 40 min (cohort 1) and −5 to 30 min (cohort 2), which allowed standardised comparison across males and females. Sex was included in the initial regression analysis to account for any differences that the procedures (stimulus, open abdomen) might have on the MAP, but no association was found. It was also considered that this period likely represented the time in which MAP would be more likely to be influenced by subject factors and not factors related to effects of prolonged anaesthesia such as decreasing body temperature and increasing evaporative water losses from the pulmonary system[27] and peritoneum (females only).[28] It is also important to note that, of the dogs that developed hypotension, all developed hypotension at least once during this standardised period; therefore, data collected after the standard period would likely not add much information.

Lastly, this study was designed to assess subject factors that could influence measured blood pressure when anaesthesia was maintained at an appropriate clinical depth for the desexing procedure being undertaken. The dose of isoflurane required in each animal was not determined in this study because end-tidal agent monitoring was not available. As a circle breathing system was used in most dogs, we acknowledge that the inspired concentration of isoflurane may be slightly lower than the vaporiser setting in those cases. Thus we cannot rule out the possibility that the administered dose of isoflurane also influenced the measured blood pressure. The results of our study show that regardless of the dose of isoflurane required, when anaesthesia is maintained at an appropriate depth, USG was the subject factor that had the strongest association with the measured MAP.

**Conclusion**

The high proportion of young dogs with hypotension in this study supports the routine use of blood pressure monitoring in young, healthy dogs. Of the subject factors assessed in this study, USG was
verified in both cohorts to be associated with the cumulative MAP, suggesting that subclinical dehydra
tion that occurs because of fasting and hospitalisation could increase the sensitivity of such dogs to the effects of anaesthetic agents on the cardiovascular system.

Acknowledgements

The authors acknowledge the assistance of the staff involved in the student neutering clinics and the general practice clinicians at Murdoch University Veterinary Hospital.

References


Figure 1. Fit plot for urine specific gravity (USG) and cumulative mean arterial blood pressure (MAP) calculated from 5 min before to 30 min after start of surgery (MAP-AUC.5-30) in 20 young, healthy dogs undergoing elective desexing in a general practice clinic. The regression line (solid line), and the 95% confidence interval (dotted lines) of the fitted line are depicted (P = 0.014, r = −0.54).
Table 1. Medians (interquartile intervals) of age and body mass and means (95% confidence interval) of general anaesthesia (GA) duration, surgery duration, dose of isoflurane (ISO), cumulative mean arterial blood pressure and numbers of dogs developing hypotension in two cohorts of young, healthy dogs undergoing elective desexing

<table>
<thead>
<tr>
<th>Table 1. Medians (interquartile intervals) of age and body mass and means (95% confidence interval) of general anaesthesia (GA) duration, surgery duration, dose of isoflurane (ISO), cumulative mean arterial blood pressure and numbers of dogs developing hypotension in two cohorts of young, healthy dogs undergoing elective desexing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Table 1. Medians (interquartile intervals) of age and body mass and means (95% confidence interval) of general anaesthesia (GA) duration, surgery duration, dose of isoflurane (ISO), cumulative mean arterial blood pressure and numbers of dogs developing hypotension in two cohorts of young, healthy dogs undergoing elective desexing</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Age (months)</strong></td>
</tr>
<tr>
<td><strong>Body mass (kg)</strong></td>
</tr>
<tr>
<td><strong>GA duration (min)</strong></td>
</tr>
<tr>
<td><strong>Surgery duration (min)</strong></td>
</tr>
<tr>
<td><strong>ISO concentration (%)</strong></td>
</tr>
<tr>
<td><strong>MAP-AUC, area under the MAP*time curve</strong></td>
</tr>
<tr>
<td><strong>No. developing hypotension (%)</strong></td>
</tr>
</tbody>
</table>

*Significantly different from cohort 1 (P = 0.0016, t-test).

*Calculated from 10 min before to 40 min after start of surgery (MAP-AUC-10–40) for cohort 1 and from 5 min before to 30 min after start of surgery (MAP-AUC-5–30) for cohort 2.

MAP-AUC, area under the MAP*time curve.
Table 2. Means (95% confidence interval) of urine specific gravity (USG), packed cell volume (PCV) and total solids (TS) in two cohorts of young, healthy dogs undergoing elective desexing

<table>
<thead>
<tr>
<th></th>
<th>Cohort 1 (n = 71)</th>
<th>Cohort 2 (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
</tr>
<tr>
<td>USG</td>
<td>1.035 (1.032–37)</td>
<td>1.041* (1.038–43)</td>
</tr>
<tr>
<td>n</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>PCV (L/L)</td>
<td>0.41 (0.40–0.42)</td>
<td>0.41 (0.39–0.42)</td>
</tr>
<tr>
<td>n</td>
<td>58</td>
<td>65</td>
</tr>
<tr>
<td>TS (g/L)</td>
<td>74 (72–76)</td>
<td>76 (74–78)</td>
</tr>
<tr>
<td>n</td>
<td>58</td>
<td>65</td>
</tr>
</tbody>
</table>

*Significantly different from day 1 (n = 35 pairs, P < 0.001).