


# Recovery quality following a single post-anaesthetic dose of dexmedetomidine or romifidine in sevoflurane anaesthetised horses

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## Abstract

**Background:** Post-anaesthetic sedation is administered to horses to improve recovery quality from inhalant anaesthesia and reduce the risk of catastrophic injury. A single dose of dexmedetomidine for this purpose has not been evaluated clinically.

**Objectives:** To determine whether dexmedetomidine improves recovery quality from sevoflurane anaesthesia compared to a previously studied dose of romifidine.

**Study design:** Prospective, randomised, masked clinical trial.

**Methods:** Ninety-nine, adult, client-owned horses anaesthetised for elective procedures completed the trial. Anaesthetic protocol was standardised. Horses were randomly assigned to receive either dexmedetomidine 1 mcg/kg bwt (D) or romifidine 20 mcg/kg bwt (R) intravenously at their first spontaneous breath in recovery. Recoveries were reviewed and independently assigned subjective visual analogue scale (VAS) scores (0-100 mm, worst to best) for overall quality and standing ataxia scores (1-4, none to severe) by two anaesthesiologists blinded to treatment group. Objective anaesthesia and recovery data were also recorded. Comparisons were made using the Chi-square, Wilcoxon rank sum, linear models or Welch-Satterthwaite two-sample *t*-test ( $P \leq .05$ ). Predictors of VAS score were analysed independent of treatment group.

**Results:** There were no significant differences between groups except end-tidal sevoflurane (FE'Sevo) concentration and post-induction extra ketamine dosing. Including FE'Sevo and additional ketamine in the analysis as covariates, VAS scores and time to standing were not significantly different between groups. Increased age, not receiving a nerve block, increased duration of hypotension, and having a nervous temperament were significant predictors of VAS score.

**Main limitations:** No universal recovery scale exists for inter-study comparisons.

**Conclusions:** After sevoflurane anaesthesia, sedation with dexmedetomidine or romifidine provides clinically similar recovery time and quality.

## KEYWORDS

horse, anaesthesia, recovery, dexmedetomidine, romifidine

## 1 | INTRODUCTION

Maximising the quality of recovery from inhalant anaesthesia in horses by attempting to reduce emergence phenomena such as dysphoria, excitement, disorientation and lack of coordination is of interest because catastrophic injury in recovery is a significant contributor to equine peri-anaesthetic mortality.<sup>1</sup> Post-anaesthetic administration of an  $\alpha_2$ -adrenergic receptor agonist ( $\alpha_2$  agonist) has proven to positively influence recovery quality compared to recovery from inhalant alone.<sup>2-5</sup>

Experimental crossover studies have previously shown no difference in recovery time or quality between  $\alpha_2$  agonists xylazine, romifidine, and detomidine or xylazine and dexmedetomidine.<sup>5,6</sup> A large blinded clinical study, however, demonstrated superior recoveries from isoflurane anaesthesia with romifidine compared to xylazine.<sup>7</sup> Romifidine is a more  $\alpha_2$  selective than either xylazine or detomidine and is reported to cause less ataxia at sedative doses.<sup>8</sup> This may play a role in contributing to the recovery benefit observed in that study.

Dexmedetomidine, the active enantiomer of the racemic mixture medetomidine, is the most  $\alpha_2$ -selective and shortest acting  $\alpha_2$  agonist used in horses.<sup>9</sup> The employment of a balanced anaesthetic technique using a dexmedetomidine constant rate infusion has been shown to improve recovery quality and decrease number of attempts to stand in isoflurane anaesthetised horses.<sup>10</sup> It has also been shown to provide superior recovery quality as compared to an equivalent dose medetomidine infusion.<sup>11</sup> However, administration of dexmedetomidine as an infusion also maintains the negative effects of  $\alpha_2$  agonists, which include a significant decrease in cardiac output and gastrointestinal motility<sup>9,12</sup> for the duration of the anaesthesia.

The provision of a single dose of dexmedetomidine in the anaesthetic recovery period could negate consideration of these side effects if it proved to be equivalent or superior to other  $\alpha_2$  agonists. The authors are unaware of a large clinical study comparing a single post-anaesthetic dose of dexmedetomidine to another  $\alpha_2$  agonist. Therefore, the purpose of this clinical trial was to determine whether post-anaesthetic dexmedetomidine sedation conferred any recovery benefit over romifidine in horses undergoing elective procedures with a standardised anaesthetic protocol. We hypothesised that dexmedetomidine would provide a faster recovery of superior quality.

## 2 | MATERIALS AND METHODS

The study was a prospective, randomised and blinded clinical trial using client-owned horses receiving sevoflurane general anaesthesia for elective procedures of greater than 30 minutes duration at the Colorado State University Veterinary Teaching Hospital between July 2017 and December 2018.

### 2.1 | Horses

Horses qualified for the study if they were between the ages of 2 and 20 years, were of any breed (except heavy draught horses,

ponies and miniature horses), were systemically healthy based on physical exam, complete blood count and serum chemistry, and were assigned an American Society of Anesthesiologists (ASA) status of 1 or 2. Horses undergoing ophthalmic procedures, those requiring abdominal surgery, and/or those requiring a specific recovery technique (eg sling or ropes) were not included in the study. Even if client consent was obtained for qualified horses, they were excluded from the study at any point in time if the attending anaesthesiologist did not feel that the study's standardised anaesthetic protocol was suitable for the intended procedure. Power was calculated for the two-sample *t*-test ( $\alpha = 0.05$ ) based on data from a previous clinical trial comparing xylazine and romifidine.<sup>7</sup> A sample size of 45 horses per group was calculated to achieve 80% power.

### 2.2 | Anaesthesia

Horses were weighed before anaesthesia and drug doses were calculated according to actual weight. All were fasted prior to anaesthesia for a time dependent on the discretion of the attending surgeon. An intravenous (IV) catheter was placed with or without xylazine (AnaSed; Akorn Animal Health) sedation in either the right or left jugular vein the morning of the procedure. Prior to being brought to the anaesthesia induction area, horses received either potassium penicillin 22 000 IU/kg bwt (Pfizerpen; Pfizer) and gentamicin (VetOne) 6.6 mg/kg bwt or cefazolin (NovaPlus) 11 mg/kg bwt IV and either phenylbutazone (VetOne) 2.2 mg/kg bwt or flunixin meglumine 1.1 mg/kg bwt IV (Prevail; VetOne).

The horse's temperament was scored by the authors as a best fit of either 'calm/quiet', 'slightly nervous but easy to work with', 'nervous/reactive and difficult to work with' or 'aggressive/ill-tempered'. Following this assessment, xylazine was administered (0.7-1 mg/kg bwt IV) to clinical effect for sedation. The mouth was rinsed, and the horse was placed in a padded induction stall behind a swing door with its head held tethered to the wall by an experienced staff member using a halter and lead rope. Quality of sedation was graded immediately before induction on a scale of 1-4 (poor to marked) (Table S1).

Anaesthesia was induced with ketamine 2.5 mg/kg bwt (VetaKet; Akorn Animal Health) and midazolam (Alvogen) 0.07 mg/kg bwt IV. Anaesthetic induction quality was also graded on a scale of 1-4 (poor to excellent) (Table S1). Horses were intubated orotracheally and moved to the operating room on a cart. They were mechanically hoisted onto the surgical table and attached to a large animal anaesthesia breathing circuit (Mallard Medical 2800C; Mallard Medical) and maintained at a procedurally appropriate plane of anaesthesia with sevoflurane (VetOne) in 100% oxygen. If extra doses of IV ketamine were required to maintain anaesthesia, these were recorded.

Horses were placed in the recumbency suitable for the procedure and were provided with IV crystalloid fluids (Vetivex pHLyte; Dechra) at a targeted rate of 5-10 ml/kg bwt/h. Total fluid volume delivered was recorded. An arterial catheter was placed in either the facial, transverse facial, or dorsal metatarsal artery for measurement of direct arterial blood pressures. If mean arterial blood pressure (MABP)

fell below 70 mmHg, dobutamine (Hospira) was administered IV to effect (0.5-2 mcg/kg bwt/min) to maintain normotension. The duration of hypotension (considered as MABP <70 mmHg) was recorded and the average dobutamine dose used was calculated for each horse.

Horses were monitored with a base-apex electrocardiogram, pulse oximeter, capnograph and end-tidal sevoflurane analyser on a multi-parametric monitor (Mindray Passport 12; Mindray North America) calibrated weekly within the working range with sevoflurane standard gases (Air Liquide Healthcare America). An initial arterial blood gas sample was anaerobically collected approximately 15 minutes after placement of the horse on the surgical table to assess arterial partial pressures of oxygen (PaO<sub>2</sub>) and carbon dioxide (PaCO<sub>2</sub>). After this, horses were mechanically ventilated to maintain a target PaCO<sub>2</sub> of 45-55 mmHg.

Intraoperative peripheral nerve blocks with mepivacaine (Carbocaine-V; Zoetis) or bupivacaine (Clint Pharmaceuticals) and/or administration of intra-articular morphine (West Ward Pharmaceuticals [Hikma]) were performed in some horses at the discretion of the attending surgeon, and location and doses were recorded. If the anaesthetic plane was perceived as light or the horse moved, IV ketamine boluses were administered and doses were recorded. Horses receiving ketamine within 30 minutes of recovery were excluded from the study.

### 2.3 | Recovery

At the end of the procedure, mechanical ventilation was abruptly discontinued and horses were disconnected from the anaesthesia circuit and transported by cart to one of three padded recovery stalls (stalls one and two measuring 12' × 12' and stall three measuring 10' × 12'). End-tidal sevoflurane percentage (FE'Sevo) was recorded immediately prior to disconnection and corrected for the barometric pressure of the study location. Time of disconnection, time of placement on the recovery stall floor, recovery stall number and the presence of a limb bandage were recorded. Horses were placed in left or right lateral recumbency based on the surgical procedure (eg operated limb up), the dependent forelimb stretched forward, the endotracheal tube cuff deflated, and the endotracheal tube secured in place through the dental diastema with white tape extending to the horse's ear. Oxygen was insufflated through the endotracheal tube at 15 L/min. If the horse was apnoeic for 3 minutes as timed from placement in the recovery stall, an oxygen demand valve was used to provide two breaths per minute until the horse resumed spontaneous ventilation.

Either dexmedetomidine (Dexdomitor; Zoetis) 1 mcg/kg bwt IV (group D) or romifidine (Sedivet; Boehringer Ingeheim Vetmedica) 20 mcg/kg bwt IV (group R) was administered after the first spontaneous breath in recovery based on the horse's treatment group assigned by an online randomisation program (randomizer.org; Social Psychology Network Randomizer, Wesleyan University). The attending anaesthesiologist, surgeon, residents and veterinary students were blinded to the horse's treatment. Two nonblinded staff members were responsible for drawing up the appropriate drug in

secret, recording the drug and dose in a hidden folder, labelling the syringe only with the horse's case number, and providing it to the anaesthesiologist before recovery. At these doses, the volume of each drug is equivalent. Horses were allowed to recover unassisted. Personnel only entered the recovery stall in emergent situations, and this was documented. Horses were extubated once standing steadily for approximately 5 minutes.

Recovery was video recorded from arrival at the recovery stall until the horse was standing for 10 minutes and extubated. Two equine anaesthesiologists (R.C.H. and M.L.R.) blinded to treatment group reviewed the video recordings. Objective recovery values recorded included time to first movement, time to first attempt to sternal recumbency, number of attempts to sternal, time to successfully attain sternal recumbency, number of head bangs on the floor, time to first attempt to stand, time to successfully stand and number of attempts to stand. Both anaesthesiologists gave each horse a subjective visual analogue scale (VAS) score for overall recovery quality between 0 and 100 mm, with 0 being the worst possible recovery (ie catastrophic injury) and 100 being the best. Subjective scores on a scale of 1-4 (none to severe) (Table S1) were also given for limb paddling and ataxia at standing.

### 2.4 | Data analysis

Statistical analysis was performed using SAS 9.4. For categorical variables, the Chi-square test was used to compare proportions for the two treatments. For numeric variables, normality was assessed by visual inspection of residual diagnostic plots and the Welch-Satterthwaite two-sample *t*-test was used to compare means for the two treatments. Nonparametric comparisons were made using the Wilcoxon rank sum test. Linear models and Poisson regression were used to compare treatments accounting for co-variables. Models were fit separately for each response variable. Differences were considered statistically significant at  $P \leq .05$ . Ataxia and VAS scores were analysed for each observer separately and also as an average. Agreement between observers for VAS, limb paddling, and ataxia scores was analysed using the Pearson, intraclass correlation (ICC), and/or weighted kappa.

Independent of treatment group, selected variables with potential effects on recovery quality (sex, breed, colour, bodyweight, age, temperament, sedation score, total xylazine dose, induction score, total anaesthesia time, duration of hypotension, extra ketamine dose, FE'Sevo, procedure type, intra-articular morphine use, nerve block use and the presence of a limb bandage) were further analysed as predictors of VAS score using two techniques. Prior to formal model fitting, pairwise scatterplots and Pearson correlation values were considered for the subset of nine numeric variables plus VAS score. In the first approach, a backwards elimination model was used in which each of the variables were sequentially eliminated until all terms remaining were significant at the  $P \leq .05$  level. In the second approach, a series of models was fit using VAS as the response and testing for treatment differences. Each model contained one of the predictors and was adjusted for

treatment, FE'Sevo and extra ketamine dosing. After model fitting, residual diagnostic plots were used to evaluate assumptions of normality and equal variance.

### 3 | RESULTS

Numerical results and statistical analyses for horse, anaesthesia and procedural comparisons can be found in Table S2.

#### 3.1 | Horses

A total of 105 cases were enrolled in the study. Five horses were subsequently excluded for receiving ketamine within 30 minutes of recovery. One horse was inadvertently enrolled a second time 7 months after first completing the study, and the data from his second anaesthesia were excluded from analysis. Therefore, group D contained 49 horses and group R contained 50 horses. There were no statistically significant differences between groups with respect to horse breed, age, colour, weight, sex or temperament. The study population consisted primarily of Quarter Horses.

#### 3.2 | Anaesthesia and procedure

Pre-anaesthetic xylazine dose, sedation score and induction score were not statistically significantly different between groups, but horses in group D received significantly more additional post-induction ketamine than horses in group R (mean  $\pm$  standard deviation  $0.25 \pm 0.34$  mg/kg bwt vs  $0.12 \pm 0.23$  mg/kg bwt;  $P = .03$ ). The elective procedures were primarily orthopaedic in nature (arthroscopy/tenoscopy). There were no statistically significant differences between groups in procedure type, total anaesthesia time and number of horses receiving a nerve block or intra-articular morphine.

Anaesthetic complications that occurred with no significant difference between treatment group in incidence included hypotension and an increased alveolar-to-arterial  $PO_2$  gradient. No horses were hypoxaemic ( $PaO_2 < 60$  mmHg). Average dobutamine dose and crystalloid fluid administration rate was similar between groups. However, a significant difference was found in FE'Sevo concentrations at the time of circuit disconnection, with horses in group D requiring a higher dose of inhalant anaesthetic than horses in group R (mean  $\pm$  standard deviation  $2.9 \pm 0.5\%$  vs  $2.4 \pm 0.3\%$ ;  $P < .001$ ).

#### 3.3 | Recovery

Recovery data are presented in Table 1. Horses were divided evenly between recovery stalls, and a similar number of horses in each group had a distal limb bandage. All horses recovered without injury except

for one horse, a 20-year-old Warmblood gelding from group D that had undergone a right front biaxial palmar digital neurectomy (total anaesthesia time of 91 minutes). This horse suffered an open, comminuted right radial fracture attempting to stand in an otherwise uneventful recovery, was re-anaesthetised, and was subsequently humanely subjected to euthanasia. All recovery data for this horse, except time to standing and standing ataxia score, were included in the study.

VAS scores ranged from 0 to 99 mm for RCH and 0 to 100 mm for MLR and were not found to be significantly different between groups. Agreement between observers was good (Pearson correlation 0.85, ICC 0.74). Too few horses exhibited head bangs on the floor or limb paddling to adequately analyse this data.

Because the difference in FE'Sevo and extra ketamine doses could have affected recovery times, VAS score, and ataxia score, the data were analysed using a linear model with both as co-variables. Number of attempts to sternal and number of attempts to stand did not satisfy assumptions of normality, and a Poisson regression was used to interpret these values. Based on the co-variate model, standing ataxia score became significantly different for one observer (R.C.H.) and the average of both observers. Agreement between observers was moderate for ataxia score (weighted kappa 0.46).

#### 3.4 | Predictors of VAS score

Backwards elimination was used to identify a subset of variables that were predictive of VAS score. Increased age and not receiving a nerve block were associated with decreased VAS score. Variables were sequentially eliminated until all terms remaining were significant at the  $P < .05$  level. This resulted in a model including just age and nerve block ( $R^2 = .175$ ). The estimated slope corresponding to age is  $-1.382$  ( $P < .001$ ). The estimated average difference in VAS score comparing nerve block vs no nerve block is found to be  $+13$  mm ( $P < .001$ ).

A series of models were fit using VAS as the response and adjusting for treatment, FE'Sevo and extra ketamine dose. In addition, each of the models included exactly one additional predictor as above. Of these predictors, the following were significant at the  $P < .05$  level: increased age, increased duration of hypotension, not receiving a nerve block and being of slightly nervous vs calm temperament. The estimated slope corresponding to age was  $-0.968$  ( $P = .02$ ) and  $-0.420$  ( $P = .03$ ) for duration of hypotension. Horses receiving nerve blocks scored a mean VAS of  $86 \pm 10$  as compared to  $73 \pm 20$  for horses not receiving nerve blocks ( $P = .02$ ). The mean VAS score for calm horses was  $81 \pm 16$  vs  $71 \pm 22$  mm for nervous horses ( $P = .04$ ).

### 4 | DISCUSSION

The results of this study demonstrate that a single dose of dexmedetomidine (1 mcg/kg IV) for post-anaesthetic sedation provides clinically equivalent recovery time and quality to horses receiving a single dose of romifidine (20 mcg/kg IV) after elective procedures under

**TABLE 1** Mean  $\pm$  SD (standard deviation), numeric value, and median, range recovery data in 99 horses receiving either intravenous dexmedetomidine (1 mcg/kg bwt) or romifidine (20 mcg/kg bwt) in recovery after a standardised general anaesthetic protocol

Variable	Dexmedetomidine n = 49	Romifidine n = 50	Between group comparison
General recovery variables (number of horses)	32 Stall 1 14 Stall 2 2 Stall 3 32 Limb bandaged 5 Demand valve	32 Stall 1 17 Stall 2 1 Stall 3 33 Limb bandaged 9 Demand valve	Chi-square P = .7 P = .9 P = .3
Time to first movement (mean $\pm$ SD)	30 $\pm$ 9 min	26 $\pm$ 8 min	Linear model P = .2
Time to first attempt to sternal recumbency (mean $\pm$ SD)	33 $\pm$ 9 min	28 $\pm$ 9 min	Linear model p = 0.06
Time to sternal recumbency (mean $\pm$ SD)	34 $\pm$ 11 min	32 $\pm$ 13 min	Linear model P = .3
Number of attempts to sternal recumbency (mean $\pm$ SD) (median, range)	2.0 $\pm$ 1.6 1, 1-8	2.2 $\pm$ 1.8 1, 1-7	Poisson regression P > .9
Time to first attempt to stand (mean $\pm$ SD)	37 $\pm$ 13 min	35 $\pm$ 15 min	Linear model p = 0.2
Time to standing (mean $\pm$ SD)	43 $\pm$ 12 min	40 $\pm$ 16 min	Linear model P = .5
Number of attempts to stand (mean $\pm$ SD) (median, range)	5 $\pm$ 4 3, 1-29	5 $\pm$ 4 4, 1-23	Poisson regression P = .7
VAS score (mean $\pm$ SD) (median, range)	RCH: 70 $\pm$ 23 mm 77, 0-98 mm MLR: 81 $\pm$ 21 mm 90, 0-100 mm Average: 76 $\pm$ 21 81, 0-99	RCH: 72 $\pm$ 18 mm 74, 13-99 MLR: 81 $\pm$ 18 mm 86, 28-100 mm Average: 76 $\pm$ 17 77, 24-100	Linear model P = .8 (RCH) P = .3 (MLR) P = .5 (average)
Standing ataxia score (mean $\pm$ SD) (median, range)	RCH: 2.7 $\pm$ 0.9 3, 1-4 MLR: 2.7 $\pm$ 1.1 3, 1-4 Average: 2.7 $\pm$ 0.9	RCH: 3.0 $\pm$ 0.8 3, 1-4 MLR: 2.7 $\pm$ 0.8 3, 1-4 Average: 2.9 $\pm$ 0.8	Linear model P = .03* (RCH) P = .1 (MLR) P = .04* (average)

\*Denotes significant difference between groups.

sevoflurane anaesthesia. In addition, four factors identified as predictors of poor recovery quality were not receiving an intraoperative nerve block, duration of hypotension (defined as MABP <70 mmHg), increased age and having a slightly nervous vs calm temperament before anaesthesia.

A head to head comparison of equipotent doses of dexmedetomidine and romifidine has not been made in horses to the authors' knowledge, but the doses selected were considered to be equivalent based on previous comparisons to xylazine. When medetomidine was compared to xylazine in horses, 10 mcg/kg appeared equivalent to 1 mg/kg.<sup>13</sup> As compared to medetomidine, dexmedetomidine is administered at half the dose to equal sedative effect.<sup>14</sup> Doses of romifidine that have been used as a 1-1.1 mg/kg xylazine equivalent range from 80 to 120 mcg/kg.<sup>5,15,16</sup> Therefore, 100 mcg/kg romifidine and 5 mcg/kg dexmedetomidine (and

thus 20 mcg/kg and 1 mcg/kg, respectively) were considered equivalent.

Sedation has previously been shown to significantly prolong the time to first movement after inhalant anaesthesia in horses.<sup>17</sup> Inhalant anaesthetic elimination and therefore recovery time is influenced by a number of factors including blood-gas solubility of the inhalant, total anaesthesia time, minute ventilation and cardiac output. An increase in mean respiratory frequency in recovery hastens isoflurane clearance in horses.<sup>18</sup> Sedative drugs with respiratory depressant effects (such as  $\alpha_2$  agonists) would be expected to slow inhalant elimination,<sup>4</sup> although elimination kinetics when  $\alpha_2$  agonists are administered at the first spontaneous breath in recovery are not described in horses. A comparison of post-anaesthetic sedation with xylazine, detomidine or romifidine showed there were no differences in time to standing between either of these  $\alpha_2$  agonists.<sup>5</sup> Our study

similarly (and contrary to the hypothesis) did not show a difference in overall recovery times between groups, even though romifidine has a much longer duration of peak sedation, longer half-life and slower clearance than dexmedetomidine in conscious horses. Despite these differences in pharmacokinetics, dexmedetomidine and romifidine have comparable cardiovascular and respiratory depressant effects in the first 30 minutes after administration, which could explain their similar effect on duration of recovery from inhalant anaesthesia.<sup>9,19</sup>

Despite randomisation, horses in group D required more post-induction additional ketamine and had a higher FE'Sevo concentration at disconnection from the anaesthetic circuit than the horses in group R. Although this was not statistically significant, fewer horses in group D received a nerve block than horses in group R. The superior intraoperative analgesia may at least in part explain the differences in anaesthetic requirement.

Once standing, horses in group D were scored as significantly less ataxic than horses in group R (Table 1). Statistically, this is primarily related to the scores from one of the two observers. However, agreement between observers for ataxia score was rated only as moderate, so this finding should not be over-interpreted. Based on the simple scale used for ataxia grading, there is likely no clinically relevant difference between fractions of a score, and a definitive qualitative statement cannot be made.

Irrespective of drug, we identified several factors that were predictive of poor VAS score. These have all been identified directly or indirectly in prior research. In adult horses, increasing age has previously been shown to increase the risk of peri-anaesthetic mortality.<sup>1</sup> Similarly, it is not surprising that nervous horses have poorer recoveries than calm horses. In paediatric medicine, the more anxious a child is prior to surgery with sevoflurane-based anaesthesia, the more likely they are to experience emergence delirium, anxiety and pain during anaesthetic recovery.<sup>20</sup>

It is also well known that prolonged periods of hypotension (MAPB <60 mmHg) have profound effects on recovery quality.<sup>21</sup> In our study, however, the average duration of hypotension for each group was short (Table S2) and hypotension was defined as MABP <70 mmHg. At no point in time was MABP recorded as <60 mmHg in any horses. It seems as though even very subtle decreases in MABP have more of an influence on recovery quality than previously considered. While it is true that horses having longer durations of hypotension could potentially have had longer total anaesthesia times, duration of anaesthesia did not influence VAS score in any analysis. It is possible that even very short periods of decreased muscle blood flow under anaesthesia have a notable impact and a higher ideal MABP should be targeted.

In addition, pain has been associated with poor recovery in other equine studies.<sup>22</sup> Although the majority of our procedures could be considered by some to be relatively 'simple' orthopaedic surgeries not traditionally necessitating a nerve block, intraoperative nerve blocks are increasingly employed at our institution in these cases. The association of not receiving a nerve block and low VAS score in this study supports their continued use in this scenario. Interestingly, intra-articular morphine administration was not similarly predictive of VAS score. This is possibly related to the

time course of analgesia provided by the intra-articular morphine. In our cases, it was always administered after the joint was closed and just a few minutes before the horse was moved to recovery. In an experimental model, intra-articular morphine did not exert significant reduction in pain scores 30 minutes after administration but did after 1.5 hours and up to 24 hours.<sup>23</sup> Since our average standing time was around 40 minutes, it is likely that the morphine would not have had sufficient time to influence pain in the recovery stall. The combination of a nerve block and intra-articular morphine, however, would provide both immediate and long-lasting post-operative benefits.

Limitations are present in all studies and equine anaesthetic recovery studies in particular. There is no universal recovery scoring system that has been adopted by all researchers, making comparing conclusions between studies difficult. The VAS score was chosen in this study because the methods were designed to replicate a previous clinical trial comparing romifidine and xylazine.<sup>7</sup> Although agreement between scorers was good in our study, the fact remains that VAS scoring is extremely subjective. A standardised anaesthetic protocol, while scientifically necessary to minimise variation between groups, also may not necessarily reflect a day-to-day clinical case scenario. Adjustments are usually made in pre-anaesthetic and intraoperative drug selection, dosing, and patient handling based on subjective assessment by the anaesthetist, which arguably plays at least some role in the quality of an individual horse's recovery. Finally, a control group receiving no post-anaesthetic sedation was not included. Post-anaesthetic sedation is the standard of care at our institution based on ample evidence to support its use.<sup>2-5</sup> Additionally, a control group was unnecessary to answer the question posed by the study.

## 5 | CONCLUSION

A single dose of dexmedetomidine (1 mcg/kg bwt IV) is clinically equivalent to a single dose of romifidine (20 mcg/kg bwt IV) sedation in the recovery period from sevoflurane anaesthesia in horses. Future prospective studies should be performed to follow-up on the findings that local anaesthetic nerve blocks positively influenced recovery and that subtle, short-duration decreases in MABP had a negative effect on recovery quality.

### ETHICAL ANIMAL RESEARCH

This study was approved by the Colorado State University Veterinary Teaching Hospital Clinical Review Board (Veterinary Clinical Study #2017-068).

### OWNER INFORMED CONSENT

Informed consent for inclusion in the trial was obtained from all horse owners.

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## AUTHOR CONTRIBUTIONS

R. Hector, M. Rezende and K. Mama contributed equally to the design and implementation of the study. R. Hector and M. Rezende independently scored recovery videos. A. Hess completed the statistical analyses. R. Hector is responsible for the integrity of the original data and the accuracy of analysis. R. Hector drafted the first draft of the manuscript. All authors edited and approved the final manuscript.

## CONFLICT OF INTEREST

The authors have declared no competing interests.

## DATA ACCESSIBILITY STATEMENT

The data that support the findings of this study are openly available in at <https://figshare.com/s/b88489d89e7f197597b4>.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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