Horses undergoing general anesthesia for elective procedures are at higher risk of death, compared with both small animals and humans. The Confidential Enquiry into Perioperative Equine Fatalities study, evaluating the outcome of 42,000 equine anesthetic events, found a total mortality rate of 1.9%; when laparotomies for colic and caesarean section were excluded, the mortality rate was 0.9%. Anesthesia technique and duration have been recognized as important risk factors.

Results—A mean ± SD end-tidal isoflurane concentration of 1.36 ± 0.16% was necessary to maintain a surgical plane of anesthesia in the isoflurane group. Mean infusion rates of 5.0 ± 1.3 μL/kg/min and 5.1 ± 0.8 μL/kg/min were necessary to maintain a surgical plane of anesthesia in the IRK and IGK groups, respectively. A lower need for ketamine as a rescue anesthetic was observed in the IGK group, compared with the isoflurane group. Higher blood pressure and lower heart rates were found at selected time points for the IRK group, compared with the IGK and isoflurane groups.

Conclusions and Clinical Relevance—Both PIVA protocols were satisfactory to maintain smooth and stable surgical anesthesia in horses. The present study supports previous findings in which PIVA has isoflurane-sparing effects. Furthermore, PIVA did not impair recovery quality. (Am J Vet Res 2012;73:959–967)
ics are delivered at low concentrations to reduce the occurrence of their cardiorespiratory depressant effects and are combined with IV agents to improve analgesia and anesthetic stability. Ketamine, combined with guaifenesin,16 lidocaine,17 medetomidine, and guaifenesin18 or medetomidine and benzodiazepines,19 has been the drug most commonly used for this purpose. Ketamine, a dissociative anesthetic agent, induces analgesic effects by antagonizing N-methyl-D-aspartate receptors,20,21 and low-dose infusions have been recommended to decrease nociception during surgery in horses.22,23 Among α1-adrenergic receptor agonists, romifidine provides longer lasting analgesia and less ataxia, compared with equipotent sedative doses of xylazine, detomidine, and romifidine.24,25 For this reason, it could represent a useful adjunct to ketamine for PIVA in horses.

The purpose of the study reported here was to investigate and compare the efficacy of either guaifenesin or romifidine together with ketamine as adjuncts to isoflurane to maintain anesthesia in horses undergoing surgery. The first hypothesis was that horses receiving the PIVA protocols would require less dobutamine and rescue anesthetics than would horses receiving only isoflurane to maintain the desirable anesthetic plane, with a lower concentration of anesthetic inhaled. The second hypothesis was that romifidine PIVA would be superior to guaifenesin PIVA regarding intraoperative stability and recovery quality.

**Materials and Methods**

**Animals**—45 client-owned horses (11 sexually intact males, 17 sexually intact females, and 17 geldings) referred to the Equine Clinic of the University of Bern were included in this prospective, randomized clinical study. Horses had to be scheduled for elective or emergency surgeries expected to last at least 60 minutes to be enrolled in the study.

**Experimental groups**—All horses were randomly assigned by lottery to 3 groups (n = 15/group). They received the same premedication and induction drugs but a different maintenance regimen. Anesthesia was maintained with isoflurane with a starting ETISO of 1.3% isoflurane alone (isoflurane group) or a 1% ETISO supplemented with an adjustable continuous infusion of romifidine and ketamine (IRK group) or ketamine and guaifenesin (IGK group).

**Experimental protocol**—Food, but not water, was withheld overnight from horses undergoing elective surgery. In each horse, a 14-gauge catheter was placed aseptically in the jugular vein for preoperative administration of antimicrobials and anesthetic drugs. At least 15 to 30 minutes before anesthesia, gentamycin (6.6 mg/kg) and sodium penicillin (20,000 U/kg) were administered IV. All horses were premedicated with romifidine (0.05 mg/kg) and L-methadone (0.05 mg/kg) given IV over 1 minute. General anesthesia was induced in an operating room equipped with a tilting table. An IV infusion of guaifenesin, administered by gravity drip to effect (maximal dose, 50 mg/kg) until muscle weakness was detected, was followed by a rapid injection of ketamine (2.2 mg/kg). The trachea was intubated with a cuffed rubber silicone endotracheal tube and connected to a large animal anesthetic machine with a circle breathing system filled with a mixture of isoflurane and oxygen.

Lactated Ringer’s solution was delivered at a rate of 5 to 10 mL/kg/h. The infusion line was connected to three 3-way stopcock valves placed in parallel to allow for administration of rescue anesthetics, dobutamine, and anesthetic mixture; the latter was delivered via a low-resistance extension tube. Once the horse was properly positioned on the table, just briefly after the start of the isoflurane administration, the infusion of the anesthetic mixture was started by use of a peristaltic pump that was driven by a stepper engine controlled by a personal computer through purpose made software. The software allowed infusion rate control and recording together with anesthetic depth score over time.

A weekly calibrated infrared sidestream gas analyzer allowed a constant monitoring of inspired and expired gases (CO2, O2, and isoflurane) through a probe connected to the Y-piece of the breathing system. Three electrodes placed in apex-base configuration provided ECG trace and HR monitoring. Hemoglobin oxygen saturation was determined via a pulse oximetry infrared probe placed onto the tongue, which calculated HR as well. With the same multiparameter monitor, body temperature (measured through a nasoesophageal probe) and invasive blood pressure were continuously monitored and recorded every 5 minutes. Systemic arterial blood pressure was measured through a 20-gauge catheter placed in the facial or metatarsal artery. The arterial catheter was connected to a standard calibrated pressure transducer positioned at the level of the right atrium, through a nondistensible, low-resistance extension tube filled with heparinized saline (0.9% NaCl) solution. Arterial blood samples (approx 2.5 mL each) were anaerobically withdrawn into plastic heparinized syringes every 15 minutes from the time of catheterization and immediately analyzed. To maintain the desired ETISO throughout the procedure, intermittent positive-pressure ventilation was applied. The ventilator was set to deliver a tidal volume of 10 to 12 mL/kg, with a peak inspiratory airway pressure ≤ 30 cm H2O and an inspiration-to-expiration ratio of 1:2. Respiratory rate was set at 5 breaths/min and adjusted if hypoventilation was detected (Paco2 > 60 mm Hg). The initial oxygen flow was set at 7 L/min until the fraction of inspired oxygen was ≥ 0.8 or the starting ETISO was reached. Then, the oxygen flow rate was set at 10 mL/kg/min. The starting ETISO was 1%, corresponding to 0.8 MAC26 for IRK and IGK groups and 1.3%, corresponding to 1 MAC, for the isoflurane group. In each horse, reference values were recorded as soon as the desired ETISO was achieved and maintained for 5 minutes before starting surgical stimulation. In the IRK group, the anesthetic mixture included ketamine (6 mg/mL) and romifidine (0.06 mg/mL). The IGK group included ketamine (6 mg/mL) and guaifenesin (150 mg/mL). The initial infusion rate was set at 6.6 µL/kg/min for both anesthetic mixtures. This rate provided 39.6 µg of ketamine/kg/min, 0.396 µg of romifidine/kg/min, and 990 µg of guaifenesin/kg/min.

Depth of anesthesia was adjusted (if indicated) every 5 minutes on the basis of a scoring system adapted from Endler et al17 by modifying either the infusion
rate of the 2 anesthetic mixtures for the IRK and IGK groups or the isoflurane concentration for the isoflurane group and administering ketamine or thiopental IV when indicated (Figure 1). In brief, scores ranged from –1 (deep anesthesia) to 3 (very light anesthesia), with 0 not necessitating any change (ideal), and were based on clinical and physiologic variables. The clinical variables included presence and quality of palpebral reflex, eye position, presence of nystagmus, tearing, and spontaneous movements of lips, ears, limbs, or neck. Among physiologic variables, only MAP was considered. If an MAP 10% lower than the reference value was

Figure 1—Flow chart representing the scoring system adopted to adjust anesthetic depth in a study of PIVA in horses. Answers to questions 1 through 4 provided a score and a modification of the isoflurane (ISO) concentration in the isoflurane group or the anesthetic mixture flow rate in the IRK and IGK groups together with the IV administration of ketamine (KET) or thiopental (THIO). A score of –1 represents too deep anesthetic depth, a score of 0 (not illustrated) represents ideal anesthetic depth, and scores of 1, 2, and 3 represent too light anesthetic depth.

Table 1—Data from horses anesthetized with isoflurane alone, IRK, or IGK (n = 15/group).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Isoflurane alone</th>
<th>IRK</th>
<th>IGK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>517 ± 99</td>
<td>491 ± 82</td>
<td>451 ± 127</td>
</tr>
<tr>
<td>Age (y)</td>
<td>7.6 ± 4</td>
<td>7.5 ± 5</td>
<td>8.5 ± 7.7</td>
</tr>
<tr>
<td>Elective surgeries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthopedic</td>
<td>6</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Head intervention</td>
<td>2</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Castration</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Wound repair</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Emergency surgeries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laparotomy</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Wound repair</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Recumbency position</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsal</td>
<td>7</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Right lateral</td>
<td>4</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Left lateral</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Turned position</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Anesthesia duration (min)</td>
<td>104.73 ± 33.40</td>
<td>126 ± 31.92</td>
<td>108.47 ± 45.86</td>
</tr>
<tr>
<td>Time to extubation (min)</td>
<td>8.46 ± 3.33</td>
<td>9.57 ± 5.65</td>
<td>9.57 ± 6.3</td>
</tr>
<tr>
<td>Time to extubation (min)</td>
<td>14.63 ± 2.3</td>
<td>18.75 ± 8.86</td>
<td>16.45 ± 6.12</td>
</tr>
<tr>
<td>Time to standing (min)</td>
<td>21.62 ± 8.3</td>
<td>26.33 ± 12.32</td>
<td>28.6 ± 11.44</td>
</tr>
<tr>
<td>Dobutamine infusion rate (µg/kg/min)</td>
<td>0.57 ± 0.33</td>
<td>0.47 ± 0.32</td>
<td>0.64 ± 0.43</td>
</tr>
<tr>
<td>Rescue anesthetics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine (mg/kg)</td>
<td>0.45 ± 0.36*</td>
<td>0.26 ± 0.35</td>
<td>0.11 ± 0.2</td>
</tr>
<tr>
<td>Thiopental (mg/kg)</td>
<td>0.9 ± 1.05</td>
<td>0.58 ± 0.86</td>
<td>0.49 ± 0.79</td>
</tr>
</tbody>
</table>

Data are expressed as number of horses or mean ± SD.
*Value is significantly (P = 0.01) different from that for the IGK protocol.
recorded, anesthetic depth was reduced according to the predefined protocol. Furthermore, whenever MAP was < 70 mm Hg, dobutamine was infused through a pump. The mean cumulative dose of ketamine and thiopental as well as the dobutamine administered to treat hypotension was finally calculated over the total anesthesia time. The incidence and types of cardiac arrhythmias were also recorded. Flunixin meglumine (1 mg/kg, IV) was administered at the end of surgery. At the end of anesthesia, considered as the time of discontinuation of administration of isoflurane or isoflurane plus anesthetic mixture, all horses received romifidine (0.01 mg/kg, IV). Horses were moved to a padded recovery box by means of a trolley and manually slid to the semihard floor in a quiet and dark environment. During recovery, oxygen was provided in a flow-by manner (15 L/min), and the endotracheal tube was removed after swallowing. Time to extubation, time to sternal recumbency, and time to standing were recorded. The recovery was always assisted, and its quality was graded on a numeric rating scale (Appendix) from 0 (excellent) to 4 (very poor).

Statistical analysis—All response variables, reported as mean ± SD, were normally distributed and underwent a Levene test to evaluate the homogeneity of variances. For the variables with homogeneous variance, data were evaluated with 1-way ANOVA, followed by the Bonferroni test. For those with nonhomogeneous variance, data were evaluated with a Welch ANOVA, followed by a Tamhane test for multiple comparisons. All analyses were performed with statistical software. Continuous response variables, which included MAP, HR, oxygen saturation, end-tidal concentration of carbon dioxide, and blood gas values (Pao2, Paco2, alveolar-arterial difference in Pao2, pH, base excess, and HCO3− concentration), were evaluated with ANOVA, followed by the least significant difference t test; recovery scores were analyzed with the Fisher exact test. Values of P < 0.05 were considered significant.

Results

Weight, age, rescue anesthetics, anesthetic depth score of 2, and recovery quality resulted in homogeneous variance, whereas anesthetic depth scores of –1, 1, and 3 resulted in nonhomogeneous variance. No significant differences were found in terms of weight, age, and sex among the horses of the 3 groups. Mean duration of anesthesia was 113 ± 38 minutes, without significant differences among the isoflurane (104 ± 33 minutes), IRK (126 ± 32 minutes), and IGK (108 ± 46 minutes) groups. Emergency surgeries were performed in 12 horses, including 3 isoflurane, 6 IRK, and 3 IGK group horses (Table 1). Anesthetic mixture infusion was ≥ 70 mm Hg. If an MAP 15% or 25% greater than the reference value was recorded, anesthetic depth was increased according to the predefined protocol. The mean cumulative dose of ketamine and thiopental as well as the dobutamine administered to treat hypotension was finally calculated over the total anesthesia time. The incidence and types of cardiac arrhythmias were also recorded. Flunixin meglumine (1 mg/kg, IV) were administered at the end of surgery. At the end of anesthesia, considered as the time of discontinuation of administration of isoflurane or isoflurane plus anesthetic mixture, all horses received romifidine (0.01 mg/kg, IV). Horses were moved to a padded recovery box by means of a trolley and manually slid to the semihard floor in a quiet and dark environment. During recovery, oxygen was provided in a flow-by manner (15 L/min), and the endotracheal tube was removed after swallowing. Time to extubation, time to sternal recumbency, and time to standing were recorded. The recovery was always assisted, and its quality was graded on a numeric rating scale (Appendix) from 0 (excellent) to 4 (very poor).
rates were progressively reduced during the procedure (Figure 2) in the IRK (mean, 5.0 ± 1.3 µL/kg/min) and IGK (5.1 ± 0.8 µL/kg/min) groups. In the IRK group, mean infusion rates of romifidine and ketamine were 0.3 ± 0.1 µg/kg/min and 30 ± 8 µg/kg/min, respectively. In the IGK group, mean infusion rates of guaifenesin and ketamine were 765 ± 120 µg/kg/min and 31 ± 5 µg/kg/min, respectively. Mean ETISO necessary to maintain a surgical plane was 0.98 ± 0.02% and 0.97 ± 0.06% in IRK and IGK groups (0.75 MAC), respectively, and 1.36 ± 0.16% (1.05 MAC) in the isoflurane group. There was a significant (P < 0.001) difference among groups, with a significant difference between the isoflurane group and both IRK (P = 0.01) and IGK (P = 0.01) groups; however, no difference between the 2 PIVA protocols was detected (P = 0.3).

Stability of anesthesia, as defined through the scoring system, was evaluated and compared in terms of percentage of the total anesthesia time spent by horses of each group at a given depth score and was significantly higher in the 2 PIVA groups (Figure 3), with lower occurrence of purposeful movements than in the isoflurane group. A score of −1 was recorded more often in the IRK and IGK groups than in the isoflurane group (P < 0.001). A score of 2 was recorded more often in the isoflurane group than in the IGK group (P = 0.08).

The mean dose of thiopental required to deepen anesthesia was higher, albeit not significantly, in the isoflurane group than either IRK or IGK groups, whereas that of ketamine was significantly (P = 0.009) higher in the isoflurane group than in the IGK group (Table 1). No significant (P = 0.4) difference among groups was detected in terms of dobutamine infusion (Figure 4).

Although HR remained within reference range in the isoflurane (31 to 34 beats/min), IRK (33 to 36 beats/min), and IGK (34 to 49 beats/min) groups, HR was significantly higher in the IGK group, compared with the IRK group at 55 minutes (P = 0.02), and in the IGK group, compared with both isoflurane (P = 0.037) and IRK (P = 0.01) groups at 60 minutes. Mean arterial blood pressure was significantly higher in the IRK group, compared with the IGK group, at 25 (P = 0.01), 30 (P = 0.014), 35 (P = 0.006), and 40 (P = 0.001) minutes; furthermore, at 45 and 60 minutes, MAP was significantly lower in the IGK group, compared with both isoflurane (P = 0.012) and IRK (P = 0.010) groups (Figure 5).

No significant differences in oxygen saturation, PaCO₂, PaO₂, alveolar-arterial difference in PO₂, base excess, HCO₃⁻ concentration, and pH were found among groups. These variables were kept within physiologic ranges for anesthetized horses throughout anesthesia.

One horse in the isoflurane group, referred because of colic, was euthanized during surgery after 90 minutes of anesthesia and therefore excluded from statistical analysis of the recovery phase. There were no significant (P = 0.46) differences among groups regarding recovery times and quality. Quality was excellent (score 0) in 23 horses, good (score 1) in 13, fair (score 2) in 6 (3 in the isoflurane group, 2 in the IRK group, and 1 in the IGK group), and poor (score 3) in 2 in the IGK group (Figure 6). One horse in the isoflurane group developed postanesthetic myopathy of the right triceps muscle 7 hours after standing but recovered...
without complications within the next 24 hours. One horse in the IRK group developed second-degree atrioventricular block during the first 10 minutes of anesthesia, which ceased without treatment.

**Discussion**

Surgical anesthetic depth is usually considered to be reached at 1.2 to 1.5 MAC. In the present study, horses receiving isoflurane alone were adequately anesthetized with a mean isoflurane concentration close to the published MAC value. Furthermore, horses receiving PIVA protocols were successfully anesthetized with a mean ETISO corresponding to 0.75 MAC. This substantial reduction in isoflurane requirements suggests that a consistent contribution to anesthetic depth is provided by ketamine with either guaifenesin or romifidine.

In the present study, mean infusion rate of either romifidine-ketamine or guaifenesin-ketamine was approximately 5 µL/kg/min, providing 30 µg of ketamine/kg/min with both PIVA protocols. In previous clinical reports on the use of similar ketamine infusion rates, a plasma concentration of 0.8 µg/mL was estimated. Such a concentration is expected to provide analgesia with only minor effects on recovery quality. Guaifenesin was chosen as an adjunct to ketamine to provide additional muscle relaxation. It has been described as a safe and adequate drug for PIVA in horses receiving halothane. Despite its wide therapeutic range, guaifenesin possibly provokes hemolysis, thrombosis, and thrombophlebitis as well as a decrease in CO and blood pressure and an increase in HR when an overdose is administered or accumulation occurs. In the present study, the mean infusion rate of the guaifenesin-ketamine anesthetic mixture provided approximately 765 µg of guaifenesin/kg/min, far less than the infusion rates typically used during TIVA in horses. Nevertheless, horses receiving guaifenesin had higher HR, lower MAP, and slightly higher dobutamine requirements, compared with the other groups. Moreover, 2 horses of this group had a poor recovery (score 3), with severe ataxia probably related to persisting muscle weakness.

Romifidine as adjunct to ketamine had some advantages over guaifenesin in the present study, probably because of its sedative, muscle relaxant, and analgesic effects, which could be antagonized if needed. Indeed, the analgesic and sedative efficacy of romifidine could have contributed to both the hemodynamic stability and better recoveries. Cardiopulmonary effects of romifidine infusion have not been investigated in detail so far. McMurry et al observed that horses receiving TIVA had higher blood pressures than those in which anesthesia was maintained with halothane. Considering that CO was similar in the 2 groups, higher SVR was suspected as the cause of the higher blood pressure recorded. This hypothesis is supported by other studies on α-adrenergic receptor agonists. In standing horses, a detomidine CRI led to an increase in MAP and SVR and to a decrease in HR and CO; similarly, during isoflurane anesthesia, medetomidine CRI led to lower HR and cardiac index and higher MAP than did lidocaine CRI. On the other hand, infusion of either medetomidine-midazolam-ketamine or medetomidine-guaifenesin-ketamine as an adjunct to sevoflurane enabled maintenance of optimal CO and MAP, without increase in SVR, possibly because of the low medetomidine dose administered as well as the lower l-phenylalanine-related vasodilative effect.

More recently, a romifidine CRI of 40 µg/kg/h as an adjunct to isoflurane did not alter cardiac index and SVR, compared with isoflurane alone, in horses undergoing surgery.

In equine patients, maintenance of adequate cardiovascular variables is extremely important because decreased peripheral perfusion can lead to myopathies caused by reduced muscular blood flow. One horse in the isoflurane group developed myopathy after recovery, but no signs of myopathy were observed in the horses that received PIVA. It remains unclear whether this adverse event was linked to the anesthetic technique rather than to an inappropriate body position during surgery. In fact, this horse, a 5-year-old female weighing 480 kg, was placed in lateral recumbency for 120 minutes for a tooth extraction and surprisingly had a mean MAP of 83 mm Hg (range, 69 to 92 mm Hg) throughout the procedure.

Dobutamine is currently infused to prevent or treat hypotension and cardiac depression during anesthesia. Almost all horses in the present study received dobutamine to maintain arterial blood pressure > 70 mm Hg. Mean infusion rate of dobutamine was not significantly different among the 3 groups; however, horses in the IRK group had significantly higher MAPs. This could be the result of the drug combination administered to this group or the algorithm used to deliver dobutamine. In fact, according to the scoring system, if an MAP 10% less than the reference value was detected, anesthetic depth was reduced before dobutamine rate was increased; horses in the PIVA groups had a significantly higher incidence of a score of −1 during the first hour, compared with the other groups. Because the reduction of the anesthetic mixture infusion rate, expected to increase blood pressure back to the reference value in the PIVA groups, did not provide immediate effects, a higher incidence of a score of −1 was observed for the IRK and IGK groups, compared with the isoflurane group.

Bradycardia and atioventricular blocks are usually more intense in the first minutes after α-adrenergic receptor agonist administration, last longer after romifidine administration than after xylazine or detomidine administration, and are dose dependent. In the present study, no bradycardia was detected, but 1 horse in the IRK group developed transient second-degree atrioventricular block, which resolved without treatment. Interestingly, horses in the IGK group had a gradual increase over time in HR, which became significant at the end of the measurements. This may reflect the sympathomimetic actions of ketamine. The strong vagal effects of romifidine potentially prevented similar sympathetic effects in the IRK group. Alternatively, these sympathomimetic actions could simply reflect an autonomic response to the reduced MAP observed in this group.
When comparing IV anesthesia with inhalation anesthesia, it is difficult to ensure that comparable anesthetic depth is obtained. Although the end-tidal concentration is easily measured for inhalation agents, the plasma concentration of each drug administered IV is impractical to quantify in real time. An attempt to standardize anesthetic depth with a predefined objective tool was meant to reduce the subjectivity of judgment and possibly improve reliability between observers. Previous reports have described the maintained spontaneous activity of cranial nerves during TIVA because nystagmus, active palpebral reflex, tearing, swallowing, and ear movement are usually present even at surgical anesthetic depth. On the other hand, autonomic responses to noxious stimulation such as increased blood pressure and HR as well as the presence of brisk palpebral reflex, nystagmus, sweating, and tearing during inhalation anesthesia indicate superficial anesthe-

The dose and infusion rate of remifidine were adapted from Davies and Swan. During PIVA, it is more difficult to evaluate the typical clinical-physiologic signs than it is during inhalation anesthesia alone, and to the authors’ knowledge, correlation between reflex activity and anesthetic depth has not been investigated.

In the present study, horses receiving isoflurane alone were more easily aroused by surgical stimulation than those receiving PIVA, as confirmed by the higher need for ketamine throughout surgery. Furthermore, the higher proportion of negative scores in the PIVA groups could indicate that the initial anesthetic mixture infusion rates, in addition to 1% ETo4, were too high. The dose and infusion rate of remifidine were adapted from Davies and Swan. In the present study, mean infusion rate of remifidine-ketamine provided approximately 18 µg of remifidine/kg/h, which was 25% of the dose administered by McMurphy et al. In that study, remifidine was infused, together with guaifenesin and ketamine, in a TIVA regimen. A second hypothesis could be that PIVA may suppress cranial reflexes more than does isoflurane alone, given that most of the negative scores in these groups were attributable to lack of palpebral reflex.

In the present study, a computerized algorithm was used to determine the necessity of administration of additional anesthetics and to increase or decrease the infusion rates of the anesthetic mixture and the administration of isoflurane. The algorithm facilitates a rational approach to drug delivery and eliminates personal bias. A similar concept has been introduced in human anesthesia in which drug delivery follows evaluation of the pharmacokinetic variables of the drug via computerized pumps and the anesthetic depth of the patient. A drawback of the present drug delivery algorithm could be that it does not include pharmacokinetic variables in the overall calculation of the infusion rates and administered boluses and may lead to accumulation of drugs or metabolites with anesthetic potency (ie, ketamine).

Recovery is a known critical phase of equine anesthesia, and poor recoveries resulting in fractures represent slightly more than a quarter of all anesthetic-associated fatalities. All horses in the present study received remifidine at the end of surgery, and this can explain the calm recovery observed in most of them and the lack of differences in recovery times and quality among groups. In conclusion, both PIVA techniques were adequate to maintain surgical anesthesia in horses. As expected, they exerted an isoflurane-sparing effect with a lower need for rescue anesthetics and a more stable anesthetic depth, without worsening recovery quality.

References

11. McMurphy RM, Young LE, Marlin DJ, et al. Comparison of the cardiopulmonary effects of anesthesia maintained by continu-


Appendix appears on the next page
**Appendix**

Description of scores for quality of recovery from anesthesia in horses.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (good)</td>
<td>1 to 2 quiet, coordinated attempts to sternal and standing positions; no or light ataxia (excellent) once standing</td>
</tr>
<tr>
<td>1 (fair)</td>
<td>1 to 2 quiet, slightly uncoordinated attempts to sternal and standing positions; mild ataxia once standing</td>
</tr>
<tr>
<td>2 (poor)</td>
<td>&gt; 2 quiet attempts to sternal and standing positions; mild to considerable ataxia once standing</td>
</tr>
<tr>
<td>3 (very poor)</td>
<td>Uncoordinated and excited attempts to sternal and standing positions, with or without minor injuries (ie, superficial lacerations); severe ataxia once standing</td>
</tr>
<tr>
<td>4 (very poor)</td>
<td>Multiple attempts to sternal or standing resulting in major or life-threatening injuries (ie, fractures) or prolonged recumbency or unable to stand 2 hours after the end of anesthesia</td>
</tr>
</tbody>
</table>