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The influence of hypoxaemia, hypotension and hypercapnia (among other factors) on quality of recovery from general anaesthesia in horses

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CONTENTS

ZUSAMMENFASSUNG

Die Auswirkungen von Hypoxämie, Hypotonie und Hyperkapnie auf die Qualität der Aufstehphasen nach Allgemeinanästhesie bei Pferden wurde untersucht.

In die retrospektive Studie eingeschlossen wurden 1226 Pferde und Ponys, die mit einem balancierten Xylazin- oder Medetomidin-Isofluran-Anästhesieprotokoll anästhesiert wurden und bei denen ein vollständiges Anästhesieprotokoll vorlag. Die Aufstehphasen wurden basierend auf den verfügbaren Aufstehphasen-Scores in „gut“ und „schlecht“ unterteilt. Einfluss von Hypoxämie [$PaO2 < 60$ mmHg (7,99 kPa)], Hypotonie ($MAP < 70$ mmHg für mindestens 15 Minuten) und Hyperkapnie [$PaCO2 > 60$ mmHg (7,99 kPa)], Anästhesieprotokoll, Körpergewicht, Alter, Rasse, Geschlecht, Status der American Society of Anaesthesiologists (ASA), Art des Eingriffs, Notfall oder Nicht-Notfall, Dauer der Anästhesie, Lagerung, Zeit in Seiten- und Sternallage in Aufwachboxe, Zeit bis zum Aufstehen, nicht unterstützte oder unterstützte Aufstehphase gemäß dem Aufstehphasen-Score (gut/schlecht) wurden mithilfe einer generalisierten linearen Regressionsanalyse untersucht ($p < 0.05$).

Hypoxämie und eine längere Anästhesiedauer waren signifikant mit einer schlechten Aufstehphase assoziiert. Keine anderen Faktoren hatten einen signifikanten Einfluss auf die Qualität der Aufstehphase.

Klinisch hebt dies hervor, wie wichtig es ist, die Anästhesiezeit so kurz wie möglich zu halten, die Sauerstoffversorgung zu überwachen und Hypoxämie so schnell wie möglich zu behandeln.

Key words: anaesthesia, equine, hypercapnia, hypotension, hypoxaemia, recovery

ABSTRACT

The effect of hypoxaemia, hypotension and hypercapnia, among others, were investigated on quality of recovery from general anaesthesia in horses.

A retrospective single centre study including1226 horses and ponies anaesthetized using a xylazine or medetomidine-isoflurane balanced anaesthesia protocol and presenting a complete anaesthetic record was conducted. Recoveries were divided into ‘good’ and ‘bad’ based on the available recovery scores. Influence of hypoxaemia [PaO2 < 60 mmHg (7.99 kPa)], hypotension (MAP < 70 mmHg for at least 15 minutes) and hypercapnia [PaCO2 > 60 mmHg (7.99 kPa)], anaesthesia protocol, bodyweight, age, breed, sex, American Society of Anaesthesiologists (ASA) status, type of procedure, emergency or non-emergency, duration of anaesthesia, positioning, times spent in lateral and sternal recumbency during recovery, time until standing, non-assisted or assisted recovery on the assigned recovery score (good/bad) were investigated using generalized linear regression analysis ($p < 0.05$).

Hypoxaemia and prolonged duration of anaesthesia were significantly associated with a bad recovery score. No other factors had a significant influence on recovery quality.

Clinically, this highlights the importance of keeping anaesthetic time as short as possible and to monitor oxygenation and treat hypoxaemia as soon as possible.

Key words: anaesthesia, equine, hypercapnia, hypotension, hypoxaemia, recovery

SUBMITTED MANUSCRIPT

Influence of hypoxaemia, hypotension and hypercapnia (among other factors) on quality of recovery from general anaesthesia in horses

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MM: study design, data management, data interpretation, writing of manuscript KK: data management, input writing of manuscript IK: data management, input writing of manuscript PRT: statistics SKR: study design, data management, data interpretation, writing of manuscript

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Running head: Quality anaesthetic recovery horses - factors

Abstract

Objective To investigate the effect of hypoxaemia, hypotension and hypercapnia, among others, on quality of recovery from general anaesthesia in horses.

Study design Retrospective single centre study

Animals A sample of 1226 horses that underwent general anaesthesia between June 2017 and June 2021.

Methods Horses and ponies (> 200 kg, > 6 months) anaesthetized using a xylazine or medetomidine-isoflurane balanced anaesthesia protocol and presenting a complete anaesthetic record were included. Data were extracted from the clinic record system and from the original anaesthesia records. Recoveries were divided into 'good' and 'bad' based on the available recovery scores. Influence of hypoxaemia [$PaO_2 < 60$ mmHg (7.99 kPa)], hypotension (MAP < 70 mmHg for at least 15 minutes) and hypercapnia [$PaCO_2 > 60$ mmHg (7.99 kPa)], anaesthesia protocol, bodyweight, age, breed, sex, American Society of Anaesthesiologists (ASA) status, type of procedure, emergency or non-emergency, duration of anaesthesia, positioning, times spent in lateral and sternal recumbency during recovery, time until standing, non-assisted or assisted recovery on the assigned recovery score (good/bad) were investigated using generalized linear regression analysis ($p < 0.05$).

Results Hypoxaemia and prolonged duration of anaesthesia were significantly associated with a bad recovery score. No other factors had a significant influence on recovery quality.

Conclusion and clinical relevance Hypoxaemia and prolonged anaesthesia duration have a negative effect on quality of anaesthetic recovery in horses. Clinically, this highlights the importance of keeping anaesthetic time as short as possible and to monitor oxygenation and treat hypoxaemia as soon as possible.

Keywords anaesthesia, equine, hypercapnia, hypotension, hypoxaemia, recovery

Introduction

Mortality in equine anaesthesia remains very high compared to other species (Gozalo-Marcilla et al. 2021). To date, the largest multicentre study revealed mortality rates of 0.9% in non-colic cases and 1.9% if colic cases were included (Johnston et al. 2002). A more recent literature review concerning mortality associated with general anaesthesia in horses, stated that of all fatal incidents, one third were related to recovery and postoperative complications (Dugdale & Taylor 2016). Therefore, improving the safety of recovery is crucial. Many factors affecting recovery after general anaesthesia in horses have been investigated (Gozalo-Marcilla & Ringer 2021, Loomes & Louro 2022a, b). American Society of Anesthesiologists (ASA) status, body weight, prolonged anaesthesia duration, type of intervention, out of hours and emergency surgery have been identified among others, to be risk factors for an unsafe recovery (Gozalo-Marcilla & Ringer 2021; Santiago-Llorente et al. 2021). Furthermore, choice of anaesthesia protocol and medication can affect quality of recovery (Gozalo-Marcilla & Ringer 2021; Santiago-Llorente et al. 2021; Loomes & Louro 2022a, b)

Rüegg et al. (2016) showed that hypoxaemia in horses undergoing colic surgery increases the risk of an unsafe recovery for the horse. However, this has never been confirmed in a larger study population or in non-colic cases. In general, the influence of intraoperative complications such as hypoxaemia, hypotension and hypercapnia on the quality of recovery are insufficiently investigated (Gozalo-Marcilla & Ringer 2021).

Therefore, the goal of the present study was to investigate the effect of hypoxaemia, hypotension and hypercapnia on quality of recovery from general anaesthesia in horses. The main hypothesis was that hypoxaemia during anaesthesia has a negative effect on quality of recovery. A further hypothesis was that also hypotension could influence quality of recovery.

Material and methods

This study was a single centre retrospective study evaluating records of 1226 horses that underwent general anaesthesia at the Equine Hospital of the Vetsuisse Faculty University of Zürich. Owners consent to use medical files for research purposes was signed upon admission of each horse to the hospital.

The reporting in this study conformed to the Strengthening the Reporting of Observational Studies (STROBE) guidelines (Supplementary Table S1).

Case selection

Horses and ponies that underwent general anaesthesia between June 2017 and June 2021 were included in the study. Inclusion criteria were body weight > 200 kg, age > 6 months as well as a complete anaesthesia record including invasive blood pressure monitoring and at least one arterial blood gas analysis. Donkeys, mules and other equids were excluded. Horses anaesthetized with a different anaesthetic protocol than that described below were also disregarded.

Standard anaesthetic protocols and monitoring

Food but not water was withheld for 8–12 hours in horses undergoing anaesthesia for elective procedures.

All horses were weighed prior to anaesthesia. Premedication consisted of antibiotics - Penicillin (Penicillin Natrium Streuli ad us. vet.; Streuli Pharma AG, Switzerland; 30`000 IU kg^{-1} intravenously (IV)] and gentamycin (Genta 10%; CP-Pharma, Switzerland; 10 mg kg^{-1} IV) or amoxicillin-clavulanic acid (Synulox Suspension ad us. Vet.; Zoetis Schweiz GmbH, Switzerland 8.75 (7 mg kg^{-1} amoxicillin; 1.75 mg kg^{-1}clavuranic acid) mg kg^{-1} intramusculary (IM) and either: flunixin (Fluniximin ad us. vet.; Graeub AG, BE Switzerland; 1.1 mg kg^{-1}) or phenylbutazone (Butadion ad us. vet.; Streuli Pharma AG, SG, Switzerland; 4 mg kg^{-1}) injected IV 30–60 minutes prior to anaesthesia. Acepromazine (Prequillan ad us vet.; Arovet AG, Switzerland; 0.03 mg kg^{-1}) was given IM at the same time as the premedication if there were no contraindications to its administration such as unstable or unknown cardiovascular status, emergency laparotomies, risk of major bleeding or history of seizures.

All horses were anaesthetized with either a xylazine- or a medetomidine-isoflurane balanced anaesthesia protocol. Therefore, horses were sedated with either xylazine (Xylazin 2%; Streuli Pharma AG, Switzerland; 1.1 mg kg^{-1}; xylazine protocol) or medetomidine (Medetor ad us. Vet.; Virbac AG, Switzerland; 7 µg kg^{-1}; medetomidine protocol) IV. The dose was modified at the anaesthetist's discretion to provide an adequate level of sedation for the induction of anaesthesia. Anaesthesia was induced with ketamine (Ketanarkon 100 ad us. vet.; Streuli Pharma AG, Switzerland; 2.2 mg kg^{-1}) and diazepam (Valium 10 mg; Roche Pharma AG, Switzerland; 0.02 mg kg^{-1}) IV. Once recumbent, the horses were endotracheally intubated and connected to a large animal anaesthetic machine: Mallard 2800C-P (Mallard Medical, CA, USA/AB Medical Technologies Inc.), Tafonius (Hallowell Engineering & Manufacturing Corp., MA, USA) or Tafonius Junior (Hallowell Engineering & Manufacturing Corp., MA, USA). Anaesthesia was maintained using isoflurane (IsoFlo; Provet AG, Switzerland) in oxygen and air with the inspired fraction of oxygen (FIO_2) (0.5–1) adjusted to maintain an arterial partial pressure of oxygen (PaO_2) > 80 mmHg (10.66 kPa). Initial (start of inhalant anaesthesia to first blood gas measurement) FIO_2 settings were adjusted based on pulse oximetry readings to obtain an oxygen saturation (SpO_2) > 90%. Horses were allowed to breathe spontaneously, but mechanical ventilation was started if considered necessary by the anaesthetist. This decision was made individually for each case and taking into account several factors including arterial partial pressure of CO_2 ($PaCO_2$), end-tidal CO_2 ($P\grave{E}CO_2$), respiratory rate (f_R), tidal volume (VT), oxygenation, and cardiovascular function of the horse. No cut-off values to start mechanical ventilation were pre-defined. Isoflurane was titrated to maintain a sluggish palpebral reflex and a constant rate infusion (CRI) of either xylazine (0.7 mg kg^{-1} $hour^{1}$; xylazine protocol) or medetomidine (3.5 µg kg^{-1} $hour^{-1}$; medetomidine protocol) was started at the same time as isoflurane. Based on the occurrence of nystagmus or sudden movements, horses received boli of ketamine (0.1–0.2 mg kg^{-1} IV) or thiopental (Thiopentalum natricum; Spedalia AG, Switzerland; 0.5–1 mg kg^{-1} IV), respectively to adjust the plane of anaesthesia to an adequate level. Throughout anaesthesia, all horses received a CRI of lactated Ringer's solution starting with a rate of 5–10 mL kg^{-1} $hour^{-1}$. Fluid administration was continuously adapted to the horse's cardiovascular state, estimated blood loss and urinary output (measured with a urinary catheter). All horses received a CRI of dobutamine (Dobutrex; Teva Pharma AG, Switzerland) to maintain a mean arterial blood pressure (MAP) between 70 and 90 mmHg. Dobutamine was started at the same time as the horse was connected to the anaesthetic machine, with an initial rate of 0.6 µg kg^{-1} $minute^{-1}$. Salbutamol (Ventolin; GlaxoSmithKline AG, Switzerland; 2 µg kg^{-1}) was administered intratracheally, if PaO_2 was < 60 mmHg (7.99 kPa), and the horse was declared as non-food producing. At 20–40 minutes before the end of surgery, all horses received morphine (Morphine HCL, Sintetica SA, Switzerland; 0.1 mg kg^{-1}) intramuscularly (IM).

Standard monitoring during anaesthesia included presence of nystagmus and palpebral reflex, mucous membrane colour and capillary refill time, respiratory gas analysis (PE`CO_2 and isoflurane (FE´Iso), FIO_2, f_R, VT, pulse rate (PR), electrocardiography (ECG), invasive arterial blood pressure, pulse oximetry, and urinary output every 5 minutes. The first blood gas analysis was performed as soon as an arterial catheter was available and then repeated hourly. If blood gas abnormalities were present or in horses presenting a critical medical status, the analysis was repeated every 30 minutes.

For recovery, a padded helmet was fitted to the horse's head and phenylephrine 0.15% (Phenylephrin hydrochloridum; G. Streuli & Co. AG, Switzerland; 0.03 mg kg^{-1}) was administered bilaterally into the ventral meatus of the nose before moving to a padded recovery box. All horses received IV sedation with either 0.3 mg kg^{-1} xylazine (xylazine protocol) or 2 µg kg^{-1} medetomidine (medetomidine protocol) for recovery. At the discretion of the anaesthetist in charge, the dose of sedation could be increased. During recovery, oxygen was supplied (15 L $minute^{-1}$) via the endotracheal tube and - after extubation - intranasally. Elective cases were extubated 10–15 minutes after the end of isoflurane; horses undergoing exploratory laparotomy for colic or emergencies that had not been starved were only extubated once the swallowing reflex was evident. Generally, horses were allowed to recover freely, but were assisted with ropes or manually for certain indications (e.g., prolonged colic surgery, geriatric horses, horses with casts, and horse undergoing Caesarean section). In case of rope-recovery, one rope was attached to the head protector or halter and a second rope was tied to the tail. Each rope was operated by a separate person. All horses were left undisturbed in lateral recumbency for 1 hour. If a horse remained in lateral recumbency after that time, it was stimulated by noise and touch to move into a sternal position. If the horse did not react to stimulation, further assessment was made to determine whether the horse should receive additional fluids or glucose containing fluids.

Data collection

Horse data were extracted automatically from the clinic record system into a Microsoft excel (Microsoft corporation, WA, USA) sheet. Information considered crucial for the present study, i.e. complications during anaesthesia (hypoxaemia, hypotension, hypercapnia), anaesthetic protocol, urgency status, duration of anaesthesia and data concerning the recovery phase were manually compared and double checked with the archived anaesthesia records and completed.

Horse Data

The following demographic information of each horse was collected: breed, age, bodyweight and sex. Breed of the horses was assigned to one of 10 different groups: Ponies, Warmbloods (e.g., Swiss Warmblood, Irish Sport Horse, Holsteiner), American Horses (e.g., Quarter

Horse, Paint Horse), Arabians (e.g., Shagya-Arabian, Partbred Arabian), Draught horses (e.g., Shire Horse), small draught horses (e.g., Swiss Freiberger, Haflinger, Fjord Horse), Thoroughbreds, Baroque horses (e.g., Andalusian, Pura Raza Espagnol, Lusitano, Lippizan, Friesian), Icelandic horses and Unknown.

Procedural data

The following general information about the procedure was collected: ASA status of the horse, emergency or non-emergency procedure, recumbency (lateral or dorsal recumbency), type of procedure and duration of anaesthesia.

Procedures were grouped into eight categories: abdominal surgery (e.g., colic surgery or Caesarean section), orthopaedic surgery other than fracture repair, fractures, ophthalmologic surgery, soft tissue surgery other than abdominal (e.g., tumour resection, umbilical hernias), head and throat surgery (e.g., tie back, tooth extractions), diagnostic imaging (e.g., computed tomography (CT), magnetic resonance imaging (MRI), myelography), and others (procedures that could not clearly be classified as one of the previously named groups).

Intraoperative complications

Each anaesthetic record was checked manually for occurrence of hypoxaemia [defined as $PaO_2 < 60$ mmHg (7.99 kPa) in at least one arterial blood gas analysis], hypotension (defined as a MAP < 70 mmHg for at least 15 minutes) and hypercapnia [defined as $PaCO_2 > 60$ mmHg (7.99 kPa) in at least one arterial blood gas analysis].

Recovery Data

The time in lateral and sternal recumbency was noted, as well as the time until standing, defined as the time from end of inhalation anaesthesia until the horse stood on all four feet. Whether recovery was assisted (head-and-tail ropes or manually) or not, was also recorded.

The recovery scoring system used at the institution consisted in a numeric score with a range from 1-5 (Table 1). For the present evaluation, the recovery scores extracted from the anaesthetic records were grouped into two categories: good (scores 1–3 of the previously described scale) or bad (scores 4–5) recovery score.

Statistical Analysis

Statistical analysis was performed using R 0 (R Core team 2022). A generalized linear regression (glm) analysis was performed to evaluate factors affecting recovery (good or bad recovery score). For this analysis it was a binomial glm with a logit link: i.e., logistic regression. Investigated factors included hypoxaemia, hypotension, hypercapnia, anaesthesia protocol (xylazine or medetomidine), bodyweight, age, breed, sex, ASA status, type of procedure, emergency or non-emergency, duration of anaesthesia, positioning, times spent in lateral and sternal recumbency during recovery, time until standing, non-assisted or assisted recovery. A backward selection procedure was used with factors using a *p* value cut off of 0.156 to eliminate non-significant factors from the multivariable analysis. Variables remaining in the final model were selected using *Akaike information criterion (AIC) (Akaike 1974).*

Results

A total of 1226 cases matched the inclusion criteria of the study and their data was used for the analysis.

Descriptive data

Overall, 1071 horses (87.4%) had a good, whereas 155 (12.7%) had bad anaesthetic recovery scores. A horse suffered a fatal injury during recovery and had to be euthanized due to a metacarpal fracture. An additional three horses were assigned a recovery score 5 because they had poor recoveries leading to skin or mucosal wounds; however, these injuries had no influence on the clinical outcome. Meaning that in the present study one horse (0.08%) died while attempting to stand.

Demographic data and information related to the anaesthetic protocol, positioning, and type of intervention are summarized in Tables 2 and 3, respectively. A total of 9.4%, 10.9% and 29.9% of the horses presented hypoxaemia, hypotension and hypercapnia, respectively (Table 4). Some horses developed more than one complication; 11 horses had concurrent hypoxaemia and hypotension, 57 horses had concurrent hypoxaemia and hypercapnia and seven had concurrent hypoxaemia, hypotension and hypercapnia.

The first blood gas analysis was performed 30 (20–40) minutes [median (interquartile range)] after induction of anaesthesia. Hypoxaemia was detected in 115 horses. Median (range) PaO_2 of all the hypoxaemic blood gas values was 52.0 (30.0–59.9) mmHg [6.76 (3.99–7.98) kPa], and the median (range) PaO_2 of all horses that were hypoxaemic and presented a bad recovery was 49 (33-59) mmHg [6.41 (4.39-7.86) kPa]. A total of 69 horses showed hypoxaemia once, 23 horses in two, and 23 horses in three or more blood gas analyses. In 50 of the 115 horses with hypoxaemia, it was present at the beginning of anaesthesia but resolved with treatment. Nomoxaemia was present in 22 horses at the beginning on anaesthesia, which developed hypoxaemia during the procedure that resolved by the end of anaesthesia. Hypoxaemia developed in 19 horses during anaesthesia which remained until the end. While 24 horses were hypoxaemic throughout the whole procedure.

Of the 115 horses presenting hypoxaemia during anaesthesia 27 were assigned a bad recovery score. From these 27, 12 horses were only hypoxaemic at the beginning of anaesthesia, six at the end of anaesthesia, four in the middle of anaesthesia (normoxaemic at the beginning and end) and five throughout the whole procedure.

Of all hypoxaemic horses, 89 received salbutamol which resolved hypoxaemia definitively in 55 and temporarily in four horses. In seven horses, blood gas analysis was not repeated after salbutamol administration because anaesthesia finished. Of the 23 horses that did not improve with salbutamol, four (17.4%) showed a bad recovery. Of the 55 horses that improved with salbutamol 13 (23.6%) were assigned a bad recovery score. In contrast, of the 26 hypoxaemic horses that did not receive salbutamol (restrictions for food producing animals in Switzerland), eight horses improved to a PaO_2 > 60 mmHg (7.99 kPa).

A total of 365 horses presented hypercapnia; 252 were allowed to breath spontaneously, in 10 horses spontaneous ventilation was supported with continuous positive airway pressure (CPAP), and 105 horses required mechanical ventilation.

Data concerning recovery are presented in Table 5. Out of 1226 recoveries, 496 were scored by the same anaesthetist. The other cases were scored by the respective anaesthetist in charge.

Table 1 Recovery scoring system used at the institution and recovery score used in the present study

Recovery score recorded on the protocol	**Recovery scoring assigned for evaluation**
1: calm recovery, successfully stands on first attempt	Good recovery
2: calm recovery, successfully stands on second attempt	
3: > 2 attempts for standing horse remains calm	
4: several attempts to stand with the horse in danger of injury	Bad recovery
5: horse injured	

Table 2 Demographic data of 1226 horses that underwent general anaesthesia using a xylazine or medetomidine-isoflurane balanced anaesthesia protocol. Recoveries were divided into 'good' and 'bad' based on the available recovery scores. Data are presented as mean ± standard deviation or number [*n* (%)].

Variable	**Good recovery** *n* **= 1071**	**Bad recovery** *n* **= 155**	**Total** *n* **= 1226**
Age (years)	11.0 ± 6.3	10.8 ± 6.1	11 ± 6.3
Sex			
Male	144 (13.4)	22 (14.2)	166 (13.5)
Male castrated	492 (46.0)	76 (49.0)	568 (46.3)
Female	433 (40.5)	56 (36.1)	489 (39.9)
Unknown	2 (0.1)	1 (0.6)	3 (0.3)
Weight (kg)	502.4 ± 109.2	505.6 ± 99.6	502.8 ± 108
Breed			
WB	569 (53.1)	91 (58.7)	660 (53.8)
IH	102 (9.5)	8 (5.2)	110 (9.0)
SDH	94 (8.8)	12 (7.7)	106 (8.6)
Pony	50 (4.7)	4 (2.6)	54 (4.4)
Arabian	44 (4.1)	9 (5.9)	53 (4.3)
AH	66 (6.2)	14 (9.0)	80 (6.5)
BH	86 (8.0)	7 (4.5)	93 (7.6)
DH	11 (1.0)	1 (0.6)	12 (1)
TB	19 (1.8)	5 (3.2)	24 (2)
Unknown	30 (2.8)	4 (2.6)	34 (2.8)

AH = American horse, BH = Baroque horse, DH = draught horse, IH = Icelandic horse, SDH = small draught horse, TB = thoroughbred, WB = Warmblood

Table 3. Anaesthesia and procedure related data of 1226 horses that underwent general anaesthesia using a xylazine or medetomidine-isoflurane balanced anaesthesia protocol. Recoveries were divided into ‘good’ and ‘bad’ based on the available recovery scores. Data are presented as median (interquartile range) or number [*n* (%)].

Variable	**Good recovery** *n* **= 1071**	**Bad recovery** *n* **= 155**	**Total** *n* **= 1226**
Anaesthetic protocol			
Xylazine	490 (45.8)	66 (42.6)	556 (45.4)
Medetomidine	581 (54.2)	89 (57.4)	670 (54.6)
Premedication with acepromazine			
Yes	714 (66.7)	95 (61.3)	809 (66)
No	357 (33.3)	60 (38.7)	417 (34)
Positioning			
Dorsal recumbency	487 (45.5)	91 (58.7)	578 (47.1)
Lateral recumbency	514 (48.0)	51 (32.9)	565 (46.1)
Unknown	70 (6.5)	13 (8.4)	83 (6.8)
Procedure			
Laparotomy	133 (12.4)	32 (20.6)	165 (13.5)
Orthopaedic surgery	377 (35.2)	54 (34.8)	431 (35.1)
Fractures	74 (6.9)	8 (5.2)	82 (6.7)
Ophthalmologic	109 (10.2)	10 (6.5)	119 (9.7)
Soft tissue	166 (15.5)	19 (12.3)	185 (15.1)
Head and throat	72 (6.7)	8 (5.2)	80 (6.5)
Diagnostic imaging	25 (2.4)	5 (3.2)	30 (2.4)
Several	42 (3.9)	3 (1.9)	45 (3.7)
Unknown	73 (6.8)	16 (10.3)	89 (7.2)
Duration anaesthesia (minutes)	141.5 (110 - 187)*	170.5 (133 - 127)*	146 (110 - 190)
Emergency	236 (22.0)	53 (54.6)	289 (23.6)

ASA Score			
ASA I	85 (7.9)	14 (9.0)	99 (8.1)
ASA II	640 (59.8)	82 (52.9)	722 (58.9)
ASA III	113 (10.6)	20 (12.9)	133 (10.8)
ASA IV	99 (9.2)	21 (13.6)	120 (9.8)
ASA V	18 (1.7)	4 (2.6)	22 (1.8)
Unknown	116 (10.8)	14 (9.0)	130 (10.6)

*Significant difference between good and bad recovery scores ($p < 0.05$), ASA: American Society of Anesthesiologists.

Table 4 Data regarding anaesthesia related complications (hypoxaemia [$PaO_2 < 60$ mmHg (7.99 kPa)], hypotension (mean arterial pressure < 70 mmHg for at least 15 minutes), hypercapnia [$PaCO_2 > 60$ mmHg (7.99 kPa)] of 1226 horses that underwent general anaesthesia using a xylazine or medetomidine-isoflurane balanced anaesthesia protocol. Recoveries were divided into 'good' and 'bad' based on the available recovery scores. Data are presented as number of horses [*n* (%)].

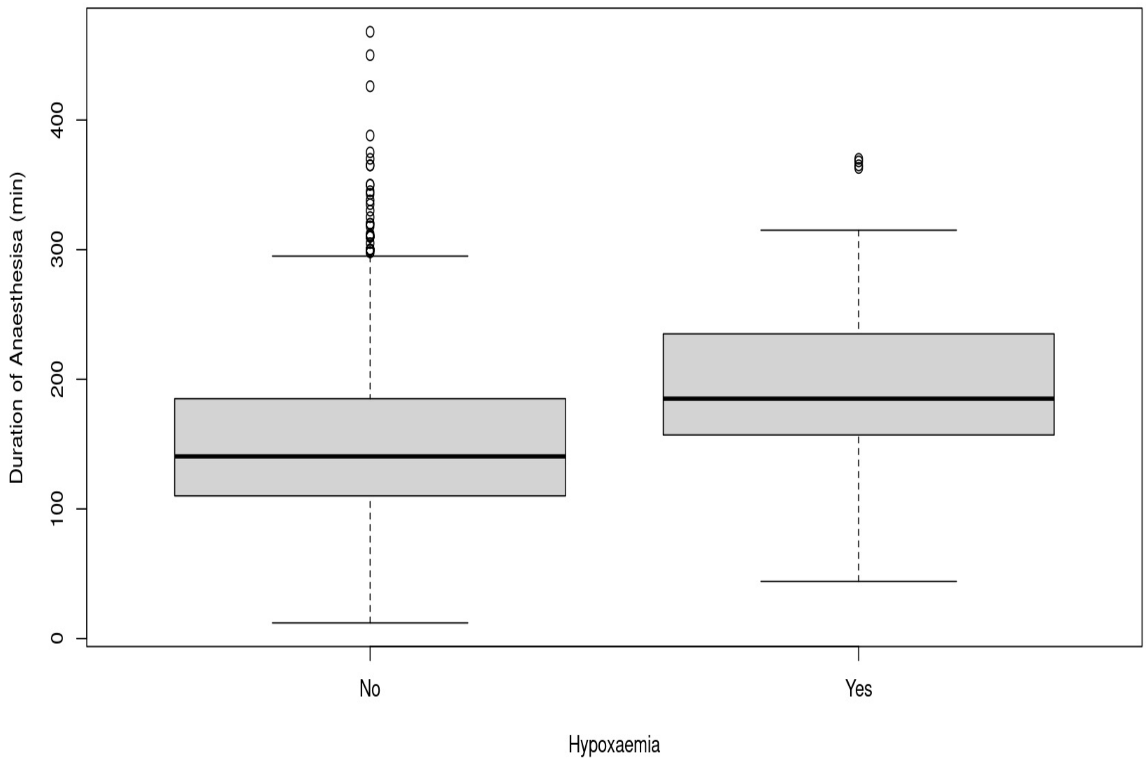
Variable	**Good recovery** ***n* = 1071**	**Bad recovery** ***n* = 155**	**Total** ***n* = 1226**
Hypoxaemia	86 (8.0)*	29 (18.7)*	115 (9.4)
Hypercapnia	304 (28.4)	63 (40.6)	367 (29.9)
Hypotension	107 (10.0)	27 (17.4)	134 (10.9)

*Significant difference between good and bad recovery score ($p < 0.05$)

Table 5 Recovery characteristics of 1226 horses that underwent general anaesthesia using a xylazine or medetomidine-isoflurane balanced anaesthesia protocol. Recoveries were divided into 'good' and 'bad' based on the available recovery scores. Assisted recoveries include head-and-tail rope as well as manually assisted recovery. Recovery time is defined as the time from end of isoflurane until the horse stands on all four feet. Data are presented as median (interquartile range) or number of horses [*n* (%)].

Value	**Good recovery** ***n* = 1071**	**Bad recovery** ***n* = 155**	**Total** ***n* = 1226**
Assisted recovery	137 (12.8)	19 (12.3)	156 (12.7)
Unassisted recovery	934 (87.2)	136 (87.7)	1070 (87.3)
Recovery time (minutes)	55 (42–70)	56 (41.5–70.5)	55 (42–70)
Time in lateral (minutes)	43 (31–55)	38 (28.8–53)	42 (31–55)
Time in sternal (minutes)	10 (2–22.5)	10 (2–22)	10 (2–22)

Figure 1



Logistic regression

Owing to missing data, 15 of the 1226 horses were excluded from the regression analysis. Logistic regression revealed that anaesthetic duration and hypoxaemia independently predict bad recoveries. However, hypoxaemia was also associated with increased duration of anaesthesia (Fig. 1). Logistic regression showed that the best fitting model included duration of anaesthesia and hypoxaemia as predictor variables (AIC 833.81). Duration of anaesthesia was significantly associated with bad recovery scores (odds of bad recovery score increased by a factor of 1.006 [Confidence Interval (CI) 1.003–1.008] for each unit (minute) increase in duration of anaesthesia, $p < 0.0001$)) and this was independent from the presence of hypoxaemia. Also, hypoxaemia itself was associated with a bad recovery score (odds of bad recovery score in the presence of hypoxaemia were 1.89 [CI 1.10–3.11] times that of the odds in the absence of hypoxaemia $p = 0.020$).

For demographic data (age, sex, weight, breed), type of procedure, ASA status, the anaesthetic protocol (xylazine *versus* medetomidine), recumbency during procedure, time in lateral recumbency during recovery, time in sternal recumbency during recovery, time until standing, assisted *versus* unassisted recovery, emergency procedures, hypotension and hypercapnia no significant statistical influence on quality of recovery (good/bad recovery score) was detected.

Discussion

This study evaluated multiple factors that influence quality of recovery in horses with a specific assessment of intraoperative hypoxaemia, hypotension and hypercapnia. The results showed that only anaesthesia duration and hypoxaemia were identified as risk factors for a bad recovery score.

Prolonged anaesthesia is a predictor of bad recovery, which agrees with previous studies (Trim et al. 1989; Young & Taylor 1993; Johnston et al. 2002; Santiago-Llorente et al. 2021; Loomes & Louro 2022a). Prolonged anaesthesia is probably associated with complex procedures implicating a more critical medical status (e.g., more complicated colic surgeries, complex fracture repair) of the horse and therefore a higher risk of poor recovery. Also, accumulation of anaesthetics over time will lead to a longer duration of drug elimination, and therefore more ataxia if the horse tries to stand up during this time. Further, muscle and nerve compression during prolonged anaesthesia might affect quality of recovery due to the resulting pain, paresis or weakness (Richey et al. 1990).

The statistical analyses showed an association between hypoxaemia and increased duration of anaesthesia. However, hypoxaemia alone affected quality of recovery. Although hypoxaemia has been described as a risk factor for death in colic horses (Trim et al. 1989), very little literature is available about the effect of hypoxaemia on recovery. Dupont et al.

(2018) suspected hypoxaemia to be the main factor for prolonged recovery after anaesthesia in a draught horse. While a retrospective study investigating recoveries after emergency laparotomy demonstrated a significant association between hypoxaemia during anaesthesia and bad recoveries (Rüegg et al. 2016). However, to the authors' knowledge this has never been confirmed in a larger study population and in non-emergency cases. Conversely, use of salbutamol, a short acting β_2-adrenoceptor agonist, used to treat hypoxaemia in anaesthetized horses, has been related to poorer recovery scores, and identified as a risk factor for catastrophic fractures or luxation's during recovery (Kälin et al. 2021; Bennell et al. 2022). Although salbutamol is used routinely for the treatment of hypoxaemia, neither of the two studies identified hypoxaemia itself as a risk factor. In the present study, hypoxaemia was a negative factor for good recovery. Atelectasis and ventilation/perfusion mismatch are recognised problem in horses undergoing general anaesthesia (Nyman & Hedenstierna 1989; Nyman et al. 1990). With prolonged time in recumbent position, this condition deteriorates, and hypoxaemia may develop. The exact mechanism by which hypoxaemia affects recovery quality in horses was not explained in the present study. In humans, hypoxaemia results in the impairment in the speed of information processing, executive function, psychomotor speed and overall cognitive function (Turner et al. 2015). Similar effects might be relevant in horses and consequently lead to worse recoveries. However, to the authors' knowledge, altered cognition in horses experiencing hypoxaemia has never been investigated. Then again, reduced oxygenation of muscle and nerve tissue could also diminish muscle strength and therefore affect quality of recovery. Alternatively, the effects of hypoxaemia on drug metabolism could be relevant. In humans and rabbits, presence of hypoxaemia leads to altered expression of the cytochrome (CYP) 450 enzymes (du Souich & Fradette 2011). Acute hypoxaemia downregulates different isoforms of CYP and therefore results in reduced clearance of certain drugs and increases the probability of drug toxicity. Similar processes may occur in equine patients and slowing the metabolism of anaesthetic agents leading to accumulation and therefore worse recoveries. Especially after prolonged anaesthesia.

However, horses in the present study were anaesthetised with isoflurane which is eliminated by ventilation and not by metabolism. Xylazine and medetomidine are not expected to negatively influence recovery quality, nor are low intraoperative doses of ketamine and thiopental (Loomes & Louro 2022a), even if metabolism would be slightly decreased.

In the present study, most hypoxaemic horses nevertheless presented a good recovery, indicating that quality of recovery is influenced by multiple factors and that hypoxaemia alone is not sufficient to predict a bad recovery.

Hypotension was not identified as a risk factor for bad recovery. Other studies reported that hypotension during anaesthesia can prolong the duration of recovery (Voulgaris & Hofmeister 2009) and generally affect survival rate in horses with colic (Trim et al. 1989). In the present study, only a few (10.9%) horses developed hypotension, and this generally was not severe. The small number of hypotensive horses was probably attributed to the immediate start of dobutamine, i.e., simultaneously with isoflurane and even before invasive blood pressure measurements were available.

Hypercapnia was not associated with bad recovery scores. To the authors' knowledge this is the first study that investigated the influence of hypercapnia on recovery quality in horses. As flight animals, horses seem to tolerate hypercapnia well (Taylor 1999). Carbon dioxide produces an increase in cardiac index, stroke index, mean blood pressure, mean pulmonary artery pressure, haematocrit, haemoglobin, arterial oxygen content, mixed venous oxygen content, and oxygen delivery from which horses might benefit during general anaesthesia (Khanna et al. 1995).

In agreement with previous studies, there was no difference in recovery scores for xylazine- *versus* medetomidine-isoflurane balanced anaesthesia, and the two protocols seem to have no impact on recovery quality (Kälin et al. 2021; Wiederkehr et al. 2021).

Contrary to previous studies, no influence of ASA physical status, age, weight, breed and type of surgery (emergency procedure or not) on quality of recovery was detected

(Johnston et al. 2002; Gozalo-Marcilla & Ringer 2021; Loomes & Louro 2022a, b). A main difference between our study and previous studies, was the dichotomization of recovery scores in to “good” and “bad” instead of using a numerical scoring system, which may have influenced our results. In the authors’ opinion, this dichotomization seems reasonable based on its clinical relevance, whereby good or bad quality, seems to be more important than a numerical score or the number of attempts to reach standing position. Other authors have used a similar approach previously (Rüegg et al. 2016; Kälin et al. 2021; Santiago-Llorente et al. 2021). However, recovery is without doubt the most critical phase of equine anaesthesia and even a calm coordinated recovery can lead to life-threatening injuries in horses.

Beyond this, differences in study design and anaesthesia protocol might lead to different results. For example, the present study only included α_2-adrenoceptor agonist balanced anaesthesia and disregarded other protocols like total intravenous anaesthesia.

This study has several limitations. Different anaesthetists were involved which leads to bias in the subjective scoring of recoveries. However, of the 1226 horses 496 recoveries were judged by the same person in context of a concurrent study (Kälin et al. 2021). Further, although the numerical scoring system used in the present study seems more subjective than others, a substantial agreement **(**κ = 0.69) between scorers **has been shown** in a previous study (Kälin et al. 2021). To the authors’ knowledge, there is no validated scoring system recommended for prospective studies investigating anaesthetic recovery in horses (Vettorato et al. 2010; Suthers et al. 2011). A further limitation of this study was the lack of an objective scoring system for assessing the plane of anaesthesia since different anaesthetists participated in this study. FE´Iso, although continuously monitored, was not included in the statistical analysis because a previous study using exactly the same anaesthetic protocols did not detect an influence on recovery quality (Kälin et al. 2021). The same reasoning applies to the use of low intraoperative doses of ketamine and thiopental.

Also, the possible influence of acepromazine was not investigated in the present study. The effect of perianaesthetic acepromazine on recovery quality is difficult to predict and studies evaluating its impact are not consistent (Loomes & Louro 2022b). This is probably due to the fact that the use of acepromazine is strongly linked to the ASA status of the horse and to the type of intervention.

The present study did not investigate the impact of additional medical treatment during recovery e.g., intravenous fluids or glucose supplementation. Those measures could influence quality of recovery but this information was not accessible for every horse and the authors chose not to include incomplete data.

Another limitation is that the study was conducted at a single centre and using two standardized α_2-adrenoceptor agonist balanced anaesthesia protocols, therefore extrapolation of the results should be done carefully. Finally, due to the retrospective nature of the present study a prospective sample size calculation was not possible. Consequently, the number of horses included in this study might have been too low to detect a potential influence of some variables.

Conclusion

In conclusion, the main hypothesis of the study could be partially confirmed. The present study shows that horses undergoing prolonged anaesthesia and horses experiencing hypoxaemia have an increased risk for bad recovery. In a clinical aspect this highlights the importance of keeping the anaesthetic time as short as possible and avoiding or treating low PaO_2 levels adequately.

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