Article

Perioperative risk factors for mortality and length of hospitalization in mares with dystocia undergoing general anesthesia: A retrospective study

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Abstract — This study investigated associations between perioperative factors and probability of death and length of hospitalization of mares with dystocia that survived following general anesthesia. Demographics and perioperative characteristics from 65 mares were reviewed retrospectively and used in a risk factor analysis. Mortality rate was 21.5% during the first 24 h post-anesthesia. The mean ± standard deviation number of days of hospitalization of surviving mares was 6.3 ± 5.4 d. Several factors were found in the univariable analysis to be significantly associated ($P < 0.1$) with increased probability of perianesthetic death, including: low preoperative total protein, high temperature and severe dehydration on presentation, prolonged dystocia, intraoperative hypotension, and drugs used during recovery. Type of delivery and day of the week the surgery was performed were significantly associated with length of hospitalization in the multivariable mixed effects model. The study identified some risk factors that may allow clinicians to better estimate the probability of mortality and morbidity in these mares.

Résumé — Facteurs de risque périopératoires pour la mortalité et la durée d'hospitalisation chez les juments atteintes de dystocie subissant l'anesthésie générale : une étude rétrospective. Cette étude a étudié les associations entre les facteurs périopératoires et la probabilité de décès et la durée d'hospitalisation des juments atteintes de dystocie qui ont survécu après l'anesthésie générale. Les données démographiques et les caractéristiques périopératoires ont été examinées rétrospectivement et utilisées dans une analyse des facteurs de risque. Le taux de mortalité était de 21,5 % durant les 24 premières heures après l'anesthésie. La moyenne ± l'écart-type du nombre de jours d'hospitalisation des juments qui avaient survécu étaient de 6,3 ± 5,4 jours. Plusieurs facteurs ont été trouvés dans l'analyse à une variable comme présentant une association importante ($P < 0,1$) avec une probabilité accrue de mort péri-anesthésique, y compris : un taux total de protéines faible en stade préopératoire, une température élevée et une déshydratation grave à la présentation, une dystocie prolongée, de l'hypotension intra-opératoire et les médicaments utilisés pendant le réveil. Le type de mise bas et le jour de la semaine de l'intervention chirurgicale présentaient une association significative avec la durée d'hospitalisation dans le modèle des effets mixtes à variables multiples. L'étude a identifié certains facteurs de risque qui pourront permettre aux cliniciens de mieux prévoir la probabilité de mortalité et de morbidité chez ces juments.

(Traduit par Isabelle Vallières)

Can Vet J 2012;53:502–510

Introduction

Equine patients have a greater risk of mortality and morbidity related to general anesthesia than do other domestic species and humans (1). Several studies have been published over the past 20 y describing the perioperative mortality rates in equine patients (2–6). In the largest study of perioperative equine fatalities (CEPEF) the overall mortality rate within a 7-day window from the anesthetic event was 1.9% (6). In another study, the overall anesthetic mortality rate in a single private practice within a 7-day window was 0.24% (7). The mortality rate for horses undergoing emergency procedures has been shown to be as high as 31.4% for all emergencies (3),

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Previously presented as an abstract at the annual American College of Veterinary Anestheliogists (ACVA) meeting in San Antonio, Texas, September 2010.

Table 1. Descriptive statistics of continuous perioperative variables of mares with dystocia that died or survived

	Alive				Dead			
	n	Mean	SD	Range	*n*	Mean	SD	Range
Demographic data								
Age (y)	48	9.4	3.5	4.0–17.0	13	10.5	5.2	5.0–23.0
Weight (kg)	51	580.8	156.9	93.0–850.0	14	610.4	87.1	500.0–809.0
Preoperative data								
Heart rate (bpm)[a]	46	55.4	18.0	30.0–140.0	11	60.3	22.3	42.0–110.0
Respiratory rate (bpm)[b]	40	29.9	15.1	12.0–84.0	10	25.8	20.9	12.0–80.0
Temperature on presentation (°C)	26	36.8	1.2	34.7–39.3	6	38.3	0.94	36.9–39.7
PCV (%)	48	41.3	5.0	28.0–54.0	13	41.7	10.2	21.0–62.0
TP (g/L)	46	71.6	7.6	48.0–91.0	13	61.0	13.0	32.0–75.0
Sodium (mmol/L)	44	144.6	3.1	138.0–150.0	12	142.6	2.7	138.0–147.0
Potassium (mmol/L)	44	3.6	0.4	2.8–4.4	12	3.6	0.4	2.8–4.3
Chloride (mmol/L)	44	106.3	3.4	98.0–116.0	12	104.3	3.2	99.0–109.0
Dystocia duration pre-GA (h)	45	5.9	5.3	1.5–24.0	13	6.5	5.6	2.3–24.0
Intraoperative data								
Time from epidural to recovery (h)	21	3.4	1.9	1.2–7.5	4	5.6	3.9	2.0–11.0
Lowest value of potassium (mmol/L)	17	3.2	0.3	2.7–3.6	3	3.1	0.2	2.9–3.3
Lowest value of ionized calcium (mmol/L)	20	1.3	0.3	0.7–2.2	2	1.3	0.1	1.2–1.4
Ketamine (mg)	51	124.5	201.8	0–800.0	14	411.4	767.3	0–2620.0
Postoperative data								
Total recovery time (min)	47	62.9	44.3	20.0–300.0	5	86.0	44.4	25.0–140.0
Total anesthesia time (h)	51	2.2	1.2	0.3–5.0	14	1.7	1.3	0.2–4.8
Other								
Length of hospitalization (d)	50	6.3	5.4	1.0–36.0	0	—	—	—

[a] bpm — beats/min.
[b] bpm — breaths/min.
SD — standard deviation, GA — general anesthesia, PCV — packed cell volume, TP — total protein concentration.

and 11.7% for procedures involving only the abdominal cavity, including gastrointestinal emergency or caesarean section (C-section) (6).

Several factors have been associated with increased perioperative mortality risk, including last trimester of pregnancy, prolonged duration of anesthesia, type of surgery, emergency procedure, day and time of the day surgery is performed, lack of premedication and total inhalational technique (5,6). Weight can also affect perianesthetic mortality and morbidity as shown in draft horses undergoing surgery for colic (8).

Caesarean section for emergency dystocia is also associated with high perioperative mortality risk (6). Survival rates to discharge from hospital for mares undergoing C-section, including both elective and due to dystocia, have been reported to be between 82% and 89% (9–11). Mares undergoing elective C-section had 100% survival rate in one study (11) compared with mares undergoing emergency C-section due to dystocia, which had survival rates between 85% and 91% (11–13). Mares undergoing controlled vaginal delivery (CVD) under general anesthesia had a survival rate of only 71% in 1 center (11) and of 94% in another center (12).

The associated physiological changes endured during pregnancy together with the emergency nature of most dystocias result in stress, dehydration, potential acid-base and electrolyte abnormalities, weakness and pain, all of which may be responsible to a great extent for the high mortality rate of these cases. However, currently there is no objective information for this subpopulation of equine cases; therefore, it is important to describe the perianesthetic condition of mares with dystocia in an attempt to identify risk factors.

The objectives of the present study were to: 1) describe the perioperative characteristics, 2) determine risk factors associated with the probability of perianesthetic death, and 3) determine risk factors associated with the length of hospitalization, in adult mares with dystocia undergoing general anesthesia at a referral veterinary hospital.

Materials and methods

This retrospective case series was conducted using clinical records from medical archives of the Large Animal Surgery Service of the Veterinary Teaching Hospital, Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada. Medical records of 70 mares with dystocia requiring general anesthesia from 1995 to 2009 were analyzed.

Adult mares (> 2 years old) of any breed, weight, and purpose (race, work, breeding, companionship) undergoing general anesthesia for resolution of dystocia (either by CVD or C-section) were included in the study. Mares that were anesthetized after standing assisted vaginal delivery (AVD) had been unsuccessful or after successful standing AVD, which required general anesthesia for surgical repair of vaginal and/or uterine lacerations as a consequence of the traumatic delivery, were also included in the study. Mares with dystocia that died before general anesthesia and pregnant mares that required general anesthesia as a consequence of another illness (colic) and not primarily due to dystocia were excluded from the study. Mares came from a variety of locations and various referring veterinarians in southern Ontario. The mares were first received and treated by the Theriogenology Service and then transferred to the Large Animal Surgery Service if a C-section was required.

The data gathered from clinical records consisted of information collected during the interview with the patient's owner and information recorded by the theriogenologist, surgeon, and anesthetist. Data collected were grouped by category as follows:

1. **Demographic data:** age, weight, and breed.
2. **Preoperative data:** heart rate, respiratory rate, rectal temperature, percentage of dehydration, packed cell volume (PCV), total protein concentration (TP), venous sodium, potassium, chloride levels on presentation; crystalloid fluid administration (Lactated Ringer's) preoperatively; fetotomy performed before general anesthesia, delivery type, foal dead or alive at arrival, parturition time (early: $\geq$ 2 wk before due date, on time: within a 2-week window of due date, and late: $\geq$ 2 wk after due date), epidural use, epidural drugs, time between epidural administration and placement in recovery stall, duration of dystocia (between rupture of chorioallantoic membrane until general anesthesia).
3. **Intraoperative data:** premedication and induction drugs and dosage, maintenance protocol drugs and dosage, other drugs administered during surgery, presence of hypoxemia or hypercapnia, metabolic acidosis (based on base excess level below 0), hypocalcemia, hypokalemia, arrhythmias, hypotension and duration of hypotension ($\leq$ 1 h or $>$ 1 h).
4. **Postoperative data:** drugs used during recovery and dosage, recovery type, total recovery time (from turning off maintenance drugs to standing), total anesthesia time (from induction until turning off maintenance drugs either due to completion of the procedure or intraoperative death), recovery score (from 1 to 5; 1 being excellent and 5 being an accident leading to euthanasia), complications in recovery, survival to anesthesia and number of days in hospital until discharge of survivors.
5. **Other:** year, day of the week (weekday *versus* weekend), time of the day surgery was performed (morning from 7 am to 12 pm, afternoon from 12 pm to 22 pm and night from 22 pm to 7 am), and anesthetist.

Descriptive statistics of perioperative characteristics in mares with dystocia that died or survived were estimated and included in the computation of the mean, median, standard deviation, and range for continuous variables, and percentage of observations at each level for categorical variables.

Models were built for the following dependent variables: 1) mortality, modeled as a dichotomous variable (dead *versus* alive), and 2) number of days of hospitalization of surviving mares, modeled as a continuous variable. Deaths included mares that died during general anesthesia for any reason directly related to the dystocia or that were euthanized due to a complication related to anesthesia and/or surgery within 24 h of recovery from anesthesia. Deaths occurring more than 24 h after recovery from anesthesia were included in the "alive" group. Length of hospitalization was defined as the number of days an animal remained at the hospital and was recorded from the day of induction of general anesthesia until the day of hospital discharge.

Variables, model assumptions, and model fit were evaluated in simple logistic and linear regression models used to assess the association between perioperative factors and the probability of death and length of hospitalization, respectively. After multivariable simple (linear and logistic) main effects regression models were built, they were extended to mixed-effects regression models. Two- and three-level mixed regression models with random intercepts for primary anesthetist and year were built using the generalized linear latent and mixed model (gllamm) procedure (14) in a statistical software (Stata 10; StataCorp LP, College Station, Texas, USA). The two- and three-level hierarchical structure of these analyses consisted of cases nested by primary anesthetist and cases nested by anesthetist and anesthetist by year. The best fitting model was chosen based on the Akaike's Information Criterion (AIC) and Bayesian Information Criterion (BIC).

Results

A total of 65 records from patients meeting the inclusion criteria were reviewed. Five mares were excluded from the study because their clinical records were missing (n = 2) or because they had a C-section performed during colic surgery and not due to dystocia (n = 3). Of the 65 cases, 14 (21.5%) died during or after general anesthesia (first 24 h post-recovery). Causes of death or euthanasia included: fracture or luxated hips in recovery (n = 5); hemoabdomen (n = 3); cardiovascular collapse due to sepsis (n = 3); and euthanasia due to poor reproductive prognosis (n = 3). One additional mare died more than 24 h after recovery from anesthesia, within the following 7 d, which yields a total mortality rate of 23% in this subpopulation of horses.

Seventy-seven percent (50/65) of mares survived and remained hospitalized until discharge. The mean and median number of days of hospitalization were 6.3 and 5.5 d, respectively, with a standard deviation of 5.4 and a range of 1 to 36 d.

Descriptive statistics of all perioperative characteristics, indicating those significantly associated at the 20% level ($P < 0.20$) to the outcomes death and length of hospitalization in the unconditional analyses, are included in Tables 1 and 2, respectively.

Univariable associations between predictors and probability of death are included in Table 3. Variables significantly associated at the 5% level ($P < 0.05$) included: low preoperative plasma TP, no administration of oxytocin intraoperatively and low preoperative sodium levels. Only the preoperative level of plasma TP, measured on a continuous scale, remained significantly associated with the probability of death at the 5% significance level ($P < 0.05$) during model building. No evidence of confounding and no statistically significant interaction effects were identified ($P < 0.05$).

Univariable associations between perioperative characteristics and length of hospitalization are included in Table 4. After the main effects model was built, two-way scatter plots of the standardized residuals against the linear prediction of the outcome indicated a departure of the homoscedasticity assumption. Thus a square-root transformation of the outcome was performed.

Graphical assessment of Pearson and Deviance residuals showed 1 potential outlier among the lowest hierarchical level residuals in the multivariable simple linear regression model. This observation corresponded to a 12-year-old, 650-kg, Hanoverian mare that underwent a C-section and stayed 36 d in hospital due to infection of the incision. The removal of this

Table 2. Descriptive statistics of categorical perioperative variables of mares with dystocia that died or survived

	Total	Alive		Dead	
	n (%[a])	*n*	%[b]	*n*	%[b]
Demographic data					
Breed type[c]					
Hot-blood	49 (75.4)	39	79.6	10	20.4
Warm-blood	4 (6.2)	3	75.0	1	25.0
Draft	8 (12.3)	5	62.5	3	37.5
Miniature	4 (6.1)	4	100.0	0	0.0
Preoperative data					
Foal					
Dead on arrival	52 (80.0)	41	78.8	11	21.2
Alive on arrival	13 (20.0)	10	77.0	3	23.0
Time of parturition					
Early	16 (44.5)	12	75.0	4	25.0
On time	17 (47.2)	15	88.2	2	11.8
Late	3 (8.3)	3	100.0	0	0.0
Fetotomy before GA					
No	53 (81.5)	42	79.2	11	20.8
Yes	12 (18.5)	9	75.0	3	25.0
Dehydration on presentation					
Mild (0%–5%)	23 (46.9)	19	82.6	4	17.4
Moderate (6%–8%)	21 (42.9)	17	81.0	4	19.0
Severe (> 9%)	5 (10.2)	2	40.0	3	60.0
LRS before GA					
No	15 (23.1)	11	73.3	4	26.7
Yes	50 (76.9)	40	80.0	10	20.0
Delivery type					
Controlled vaginal	13 (20.0)	12	92.3	1	7.7
Fetotomy under GA	13 (20.0)	9	69.2	4	30.8
C-section	35 (53.8)	29	82.9	6	17.1
Other[d]	4 (6.2)	1	25.0	3	75.0
Epidural before GA					
No	33 (50.8)	26	78.8	7	21.2
Yes	32 (49.2)	25	78.1	7	21.9
Intraoperative data					
Anesthetic induction protocol					
A2/GG/K	20 (30.8)	15	75.0	5	25.0
A2/B/GG/K	6 (9.2)	6	100.0	0	0.0
A2/D/K	5 (7.7)	3	60.0	2	40.0
A2/B/D/K	1 (1.5)	1	100.0	0	0.0
A2/D/GG/K	18 (27.7)	14	77.8	4	22.2
A2/B/D/GG/K	14 (21.6)	11	78.6	3	21.4
B/D/Inhalant	1 (1.5)	1	100.0	0	0.0
Maintenance protocol					
Isoflurane only	37 (56.9)	30	81.1	7	18.9
Isoflurane + Medetomidine	12 (18.5)	9	75.0	3	25.0
Isoflurane + GXK	6 (9.2)	4	66.7	2	33.3
GXK only	2 (3.1)	2	100.0	0	0.0
Halothane only	7 (10.8)	6	85.7	1	14.3
Ketamine only	1 (1.5)	0	0.0	1	100.0
Opioid use					
No	28 (43.1)	22	78.6	6	21.4
Intraoperative	27 (41.5)	22	81.5	5	18.5
Recovery	8 (12.3)	6	75.0	2	25.0
Both intra-op and recovery	2 (3.1)	1	50.0	1	50.0
Lidocaine intraoperative					
No	55 (84.6)	44	80.0	11	20.0
Yes as bolus(es)	10 (15.4)	7	70.0	3	30.0
Atracurium intraoperative					
No	58 (89.2)	46	79.3	12	20.7
Yes	7 (10.8)	5	71.4	2	28.6
Catecholamine administration					
No	10 (15.4)	9	90.0	1	10.0
Dobutamine	47 (72.3)	37	78.7	10	21.3
Dobutamine + other	8 (12.3)	5	62.5	3	37.5
Fluids during GA					
LRS only	45 (70.3)	37	82.2	8	17.8
LRS + Dextran or pentastarch	8 (12.5)	7	87.5	1	12.5
LRS + Dextran + Plasma/blood	2 (3.1)	0	0.0	2	100.0
LRS + HS	7 (11.0)	5	71.4	2	28.6
LRS + Dextran + HS	2 (3.1)	1	50.0	1	50.0

Table 2. Descriptive statistics of categorical perioperative variables of mares with dystocia that died or survived *(continued)*

	Total	Alive		Dead	
	n (%[a])	*n*	%[b]	*n*	%[b]
Oxytocin administration during GA or recovery					
No use	40 (61.5)	27	67.5	13	32.5
Use	25 (38.5)	24	96.0	1	4.0
Hypoxemia based on blood gas					
No $PaO_2 > 70$ mm Hg	46 (85.2)	37	80.4	9	19.6
Yes $PaO_2 \leq 70$ mm Hg	8 (14.8)	6	75.0	2	25.0
Hypercapnia based on blood gas					
No $PaCO_2 < 60$ mm Hg	47 (87.0)	39	83.0	8	17.0
Yes $PaCO_2 \geq 60$ mm Hg	7 (13.0)	4	57.1	3	42.9
Metabolic acidosis					
No BE ≥ 0	10 (18.9)	10	100.0	0	0.0
Yes BE < 0	43 (81.1)	32	74.4	11	25.6
Calcium administration during GA					
No	42 (64.6)	33	78.6	9	21.4
Yes	23 (35.4)	18	78.3	5	21.7
Potassium chloride administration during GA					
No	61 (95.3)	48	78.7	13	21.3
Yes	3 (4.7)	2	66.7	1	33.3
Hypotension during GA					
No (MAP ≥ 60 mmHg)	36 (63.2)	31	86.1	5	13.9
Yes (MAP < 60 mmHg)	21 (36.8)	14	66.7	7	33.3
Arrhythmias during anesthesia					
No arrhythmias	10 (15.6)	8	80.0	2	20.0
Sinus tachycardia (> 40 bpm)	51 (79.7)	41	80.4	10	19.6
Other[e]	3 (4.7)	1	33.3	2	66.7
Postoperative data					
Recovery drugs					
A2 only	26 (44.8)	25	96.2	1	3.8
GXK	2 (3.4)	1	50.0	1	50.0
A2/K	15 (25.9)	11	73.3	4	26.7
Acepromazine/A2/K	3 (5.2)	3	100.0	0	0.0
None	12 (20.7)	11	91.7	1	8.3
Recovery type					
Unassisted	44 (78.6)	39	88.6	5	11.4
Assisted head and tail rope/tilt table	12 (21.4)	10	83.3	2	16.7
Recovery score					
Euthanized during GA	7 (12.5)	0	0.0	7	100
Score 1	21 (37.5)	21	100.0	0	0.0
Score 2	10 (17.9)	10	100.0	0	0.0
Score 3	7 (12.5)	7	100.0	0	0.0
Score 4	4 (7.1)	4	100.0	0	0.0
Other[f]	7 (12.5)	0	0.0	7	100.0
Complications in recovery					
None	39 (68.4)	39	100.0	0	0.0
Wounds or tongue bite	2 (3.5)	2	100.0	0	0.0
Focal myositis	1 (1.7)	1	100.0	0	0.0
Fracture	3 (5.3)	0	0.0	3	100.0
Other	12 (21.1)	8	66.7	4	33.3
Other					
Day of the week					
Weekday	42 (64.6)	32	76.2	10	23.8
Weekend day	23 (35.4)	19	82.6	4	17.4
Time of the day					
Morning	23 (35.4)	19	82.6	4	17.4
Evening	16 (24.6)	12	75.0	4	25.0
Night	26 (40.0)	20	76.9	6	23.1

[a] Percentage of the total number of animals accounted for the specific variable.
[b] Percentage of the number of animals included in a specific category within the variable.
[c] Breed type: Hot-blood — American Quarter horse, Standardbred, Thoroughbred; Warm-blood — Hanoverian, Trakehner; Draft — Belgian, Clydesdale, Friesian, Percheron; Miniature — Miniature donkey, miniature horse.
[d] Other: fetotomy under GA + caesarean section or re-anesthetized after assisted vaginal delivery.
[e] Other: ventricular tachycardia and/or ventricular fibrillation and/or atrial fibrillation.
[f] Other: score 6 (accident during recovery) or euthanized during recovery due to systemic poor condition.
A2 — alpha 2 adrenergic agonist; GG — guaifenesin; D — diazepam; B — butorphanol; K — ketamine; GXK — guaifenesin + xylazine + ketamine; LRS — lactated Ringer's solution; HS — hypertonic saline solution; PaO_2 — arterial partial pressure of O_2; $PaCO_2$ — arterial partial pressure of CO_2; BE — base excess; MAP — mean arterial blood pressure. For other abbreviations see legend for Table 1.

Table 3. Univariable associations[a] at the 20% level between perioperative predictors and death of mares with dystocia undergoing general anesthesia

Variable	OR	OR 95% CI	*P*-value
Preoperative TP	0.89	0.81–0.97	0.006
Per 10 g/L increase	0.30	0.13–0.70	0.006
Oxytocin administration			
No	ref	ref	ref
Yes	0.09	0.01–0.71	0.023
Preoperative sodium			
≤ 144.2 (mmol/L)	ref	ref	ref
> 144.2 (mmol/L)	0.17	0.03–0.85	0.031
Ketamine intraoperative	1.002	0.999–1.003	0.073
Per 50 mg administered	0.08	−0.007–0.16	0.073
Temperature on presentation			
≤ 37.11°C	ref	ref	ref
> 37.11°C	8.0	0.81–78.8	0.075
Preoperative chloride	0.83	0.67–1.06	0.085
Hypotension during GA			
No (MAP ≥ 60 mmHg)	ref	ref	ref
Yes (MAP < 60 mmHg)	3.1	0.84–11.49	0.090
Hypercapnia based on blood gas			
No ($PaCO_2$ < 60 mmHg)	ref	ref	ref
Yes ($PaCO_2$ ≥ 60 mmHg)	3.66	0.68–19.60	0.130
Recovery drugs			5.39[b] (0.146)
A2 only	ref	ref	ref
GXK	25	0.82–762.18	0.065
A2/K	9.09	0.91–90.96	0.060
none	2.27	0.13–39.73	0.574
Total anesthesia time			5.37[b] (0.147)
< 0.8 h	ref	ref	ref
≥ 0.8 to < 2.25 h	2.8	0.57–13.75	0.205
≥ 2.25 to < 3 h	0.27	0.02–2.90	0.278
≥ 3 h	0.86	0.15–5.06	0.865
Age			3.78[b] (0.151)
4 to 7 y	ref	ref	ref
8 to 11 y	3.20	0.72–14.2	0.127
> 12 y	0.80	0.12–5.43	0.819
Dehydration on presentation			3.71[b] (0.156)
Mild (0% to 5%)	ref	ref	ref
Moderate (6% to 8%)	1.12	0.24–5.17	0.887
Severe (> 9%)	7.13	0.88–57.55	0.065
Dystocia duration before GA			3.54[b] (0.170)
< 4.5 h	ref	ref	ref
≥ 4.5 to < 6.5 h	4.00	0.91–17.55	0.066
≥ 6.5 h	1.50	0.29–7.81	0.630

Ref: referent (reference category); for other abbreviations see key of Tables 1 and 2.
[a] Arranged by level of significance.
[b] Chi-squared test (*P*-value) for significance of all categories of the variable.
OR — odds ratio.
CI — confidence interval.

outlier from the model changed the significance of 2 of the main effects; therefore, we decided to remove this observation and re-fit the model.

In the final multivariable linear regression model, after the outlier's removal, the variables delivery type and day of the week anesthesia was performed were significantly associated with the square-root of the number of days of hospitalization, after accounting for primary anesthetist, which was included as a random intercept (Table 5). No evidence of confounding effect or significant interaction terms was found ($P < 0.05$). Results of this final multivariable linear regression model suggest that performing general anesthesia on a weekend day decreased the number of days of hospitalization compared to performing the procedure on a weekday and that delivery through fetotomy under general anesthesia decreased the number of days of hospitalization compared with CVD. However, C-section increased the number of days of hospitalization compared with controlled vaginal delivery.

Discussion

Some perioperative characteristics of mares with dystocia that required general anesthesia, divided into those that survived and those that died are described. Possible associations between perioperative characteristics and perioperative mortality, as well as length of hospitalization among surviving mares are investigated.

The perioperative mortality of mares in our study (23%) seems greater than that reported in the CEPEF study for emergency abdominal procedures (11.7%); however, that study included only emergency C-sections and not CVD or fetotomies under anesthesia (6). The survival rates per type of delivery obtained in our study were 92.3% for CVD, 69.2% for fetotomy, and 82.9% for C-section, which are similar to those reported in previous studies (11,12).

Higher levels of preoperative plasma TP and sodium were found to decrease the odds of death of mares with dystocia undergoing general anesthesia. Plasma proteins are very important for several reasons: 1) they, especially albumin, provide the oncotic pressure or colloid osmotic pressure inside the capillaries that prevents filtration of water from the blood into the interstitial space, which prevents edema formation (15); 2) globulins possess enzymatic and immune functions (15); 3) fibrinogen is essential in the coagulation cascade (15); and 4) most anesthetic drugs are highly protein bound, and only the unbound fraction is pharmacologically active; therefore, the lower the TP the greater the fraction of active drug, possibly resulting in greater clinical effect (16). Hence, it is not surprising that hypoproteinemic mares with dystocia are at increased risk of death, especially when other physiologic functions are also disturbed. It is not clear why lower preoperative TP levels were found in mares that died. Blood was obtained on arrival before any fluids were administered, but some mares, especially those that were very dehydrated, might have received fluids before referral; this could have caused lower TP levels. Alternatively, mares with acute hemorrhage might have had lower TP without a significant change in PCV due to splenic contraction. Six mares had presenting TP values less than 60 g/L in this study, 4 of which died due to hemoabdomen, which may also explain the association between this variable and probability of death.

The fact that a greater level of preoperative sodium was protective is counterintuitive since one of the possible causes of hypernatremia is dehydration, which if severe enough could lead to shock. In fact, presence of severe dehydration (> 9%) increased the risk of death. Nonetheless, the difference in sodium levels between survivors and non-survivors were clinically insignificant and the OR values were very small despite being significant.

Table 4. Univariable associations[a] at the 20% level between perioperative characteristics and the number of days of hospitalization (on its original scale) of mares with dystocia undergoing general anesthesia

Variable	Coefficient	95% CI	*P*-value
Type of delivery			16.17[b] (< 0.001)
Controlled vaginal	ref	ref	ref
Fetotomy under GA	−0.47	−1.08–0.14	0.128
Caesarean section	0.88	0.41–1.36	0.001
Total anesthesia time (h)	1.99	0.82–3.16	0.001
Time between epidural administration and recovery start from GA			
< 3.77 h	ref	ref	ref
> 3.77 h	0.31	0.09–0.53	0.009
Breed type[c]			4.75[b] (0.006)
Hot-blood	ref	ref	ref
Warm-blood	10.52	4.64–16.39	0.001
Draft	−1.82	−6.48–2.85	0.437
Miniature	0.18	−4.97–5.34	0.943
Oxytocin administration			
No	ref	ref	ref
Yes	2.863	−0.14–5.86	0.061
Day of the week			
Weekday	ref	ref	ref
Weekend day	−2.40	−5.52–0.71	0.128
Preoperative PCV (%)	−0.22	−0.53–0.10	0.182
Preoperative TP			1.70[b] (0.194)
≤ 67 g/L	ref	ref	ref
> 67 to ≤ 73 g/L	−3.567	−7.72–0.59	0.091
> 74 g/L	−3.067	−7.22–1.09	0.144

[a] Arranged by level of significance.
[b] F-test (*P*-value) for all categories of the predictor.
[c] For breed type see legend for Table 2.
CI — confidence interval.
For abbreviations see legend for Table 1.

Table 5. Final multivariable mixed effects[a] linear regression model of the association between perioperative characteristics and the square root of the number of days of hospitalization in mares with dystocia undergoing general anesthesia (model after removal of outlier)

Variable	Coefficient	95% CI	*P*-value
Delivery type[b]			
Controlled vaginal	ref	ref	ref
Fetotomy under GA	−0.50	−0.88–−0.11	0.012
Caesarean section	0.74	0.43–1.05	< 0.001
Day of the week			
Weekday	ref	ref	ref
Weekend day	−0.30	−0.57–−0.03	0.030
Random effect			
Variance (cov) Anesthetist	3.40 e^{-12} (3.27 e^{-07})		
Variance (cov) Case	0.20 (0.04)		

[a] Clustering was controlled for by including a random intercept for primary anesthetist.
[b] Delivery type: χ^2 (2) = 57.6, $P < 0.001$.
GA — general anesthesia.
CI — confidence interval.

Administration of intraoperative oxytocin was protective, which could be explained by the fact that half of the mares that died did so during surgery due to a severe complication (e.g., hemoabdomen, intestinal perforation or extensive uterine wall laceration with poor future reproductive prognosis); consequently, those mares were probably very ill and no oxytocin was administered to them, causing the spurious effect that administering this drug had a protective effect on the probability of death.

Some factors did not reach statistical significance but showed a tendency towards a significant association with the outcome death ($P < 0.1$) and are worth discussing due to their clinical significance. Firstly, mares that had a rectal temperature on presentation of more than 37.11°C tended to be

8 times more likely to die. Body temperature has been shown to fluctuate in periparturient mares, rapidly decreasing below normal values between the 3 h prior to and the time of parturition; the lowest temperature recorded at the time of parturition was 36.58°C ± 0.16°C (17). A supranormal increase in body temperature has also been demonstrated, beginning at 1 h post-partum and peaking at 6 h post-partum to values of 38.02°C ± 0.08°C (17). It is possible that mares presenting with body temperatures higher than 37.11°C were already at a later stage of labor, and the duration of the dystocia had been longer, and therefore they were systemically more advanced in their illness. In fact, dystocia duration longer than 4.5 h was associated with increased odds of death. Further investigation into the possible correlation between rectal temperature and probability of death is warranted.

Secondly, mares that were hypotensive during anesthesia tended to be 3 times more likely to die. All mares that died during surgery due to uterine artery rupture and hemoabdomen had hypotension and cardiovascular collapse, and those that died in the recovery stall due to cardiovascular collapse had hypotension during anesthesia. Some mares were euthanized due to problems in recovery (e.g., fractures or inability to stand); these mares probably had muscular weakness, which could be associated with different predisposing factors, one of them being hypotension during anesthesia. Hypotension during equine anesthesia has been associated with increased risk of myopathy due to muscle hypoperfusion (2,18,19). Other possible reasons for muscular weakness are electrolyte imbalances, such as hypokalemia and/or hypocalcemia, which could potentially impact the recovery quality in horses if they are not normalized beforehand. Mares presenting with dystocia undergoing CVD or C-section have lower ionized calcium levels than normal horses, but potassium and magnesium levels are within normal limits (20). However, in this subpopulation of horses we did not observe a significant association between level of ionized calcium and the probability of death.

Thirdly, mares receiving guaifenesin + xylazine + ketamine or alpha-2 adrenergic agonist + ketamine during the recovery from anesthesia tended to have 25 and 9 times higher odds of death, respectively, than those receiving only an alpha-2 adrenergic agonist agent. This association could be due to a greater level of sedation and ataxia during recovery from anesthesia in these mares already predisposed to muscular weakness when more drugs than just an alpha-2 adrenergic agonist were used during this period. Alternatively, it is possible that more systemically ill mares were maintained at a more superficial plane of inhalant anesthesia and therefore additional drugs were required to transfer them to the recovery stall and avoid early attempts to stand, giving the spurious impression that the use of these drugs was associated with an increased risk of mortality. It has been previously shown that administration of an alpha-2 adrenergic agonist drug during recovery from inhalant anesthesia in horses prolongs and improves the recovery quality (21). Administering a combination of ketamine and xylazine in the recovery for a period of 30 min after discontinuation of the inhalant did not improve the recovery quality of horses; however, it did not worsen it either (22).

Lastly, mares which were presented with severe dehydration (> 9%) and dystocia duration between 4.5 and 6.5 h, tended to have 7 times and 4 times greater odds of death, respectively, compared with mares that had mild dehydration and dystocia duration of < 4.5 h. Mares experiencing dystocia for a longer period of time are more likely to be systemically ill and dehydrated. Severe dehydration causes intravascular hypovolemia and shock; therefore, it is not surprising that severely dehydrated mares are at greater risk of perioperative mortality. Moreover, foals are more likely to be delivered alive when the duration of stage II of delivery is shorter (23). Therefore, it is important for both mare and foal survival to implement strategies to expedite resolution of the dystocia.

Mean duration of anesthesia was longer in the surviving mares than in mares that died (2.2 *versus* 1.7 h, respectively), in contrast with the results of the CEPEF study, in which prolonged anesthesia was associated with increased risk of perioperative mortality (5,6). However, in the present study this mean time was calculated pooling results from mares that died or were euthanized intraoperatively and mares that died in recovery after completion of the procedure. The mean anesthesia time of mares that completed the procedure was in fact very similar to that of surviving mares (2.6 h).

Performing a C-section was associated with a longer length of hospitalization than was the case with a CVD. Caesarean section involves opening of the abdominal cavity and thus the time for total recovery from surgery is longer than when other methods of dystocia resolution are used (e.g., fetotomy or CVD). Mares that had a fetotomy done under anesthesia, however, had shorter hospital stays than those that had CVD, which might seem counterintuitive since more trauma to the reproductive tract could potentially be done during fetotomy, thus requiring longer recovery times. Trauma to the reproductive tract of the mare was likely responsible for the much higher mortality rates of mares undergoing fetotomy compared with those undergoing CVD in this and previous studies (12). It is likely that mares surviving fetotomy had less trauma to the reproductive tract than those that died; therefore, the hospital stay was shorter in these mares than in those undergoing CVD. The skills of the person performing the fetotomy may also determine the amount of trauma done to the reproductive tract and affect the outcome.

When dystocia occurred on a weekend day the length of hospitalization of survivors was shorter. This variable was not significantly associated with the probability of perioperative mortality. In contrast, in the CEPEF study, when anesthesia was performed during a weekend day the odds of mortality increased (6). In this subpopulation of mares in our study, it is possible that during the weekend, submission to the referral clinic was done much faster than during a weekday, thereby decreasing the duration of dystocia and the obstetrical manipulations at the farm before referral. This could have significantly reduced the amount of trauma, allowing faster recoveries of the mares referred over weekends.

We acknowledge the limitations of the present study. The retrospective study involves inherent variability due to the lack of control over certain variables and some missing information in the clinical records of patients. In addition, the small effective

sample size, especially for the outcome mortality (n = 14), prevented us from using a multivariable mixed effects model, and thus, only those risk factors associated unconditionally with the outcome were presented. Furthermore, we reviewed cases from only 1 referral hospital, in which some practices and procedures might differ from those of other centers; therefore, these results might only be extrapolated to similar referral clinics. However, cases were submitted from a wide variety of referring veterinarians as well as horse breeds and owners, which may improve the internal validity of our results by better representing the general population of horses in this area. In addition, various anesthetists with different levels of experience were involved in the anesthetic management of these mares, avoiding excessive clustering of cases.

In conclusion, we found that the perianesthetic mortality rate in dystocia mares is very high and that preoperative systemic conditions and some perianesthetic management practices are contributing factors of mortality and morbidity. Studies with a greater number of cases and clinics, however, are still needed.

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