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1 **Prevalence of electrolyte disturbances and perianaesthetic death risk factors in**  
2 **120 horses undergoing colic surgery**

3  
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18  
19 **Abstract**

20 The objective of this study was to determine the prevalence of intraoperative  
21 electrolyte disturbances and risk factors associated with perianaesthetic death in horses  
22 undergoing colic surgery.

23 The files of 120 horses meeting the inclusion criteria were reviewed. Data retrieved  
24 from the medical records, including demographic data and the occurrence of  
25 electrolyte disturbances and other intraoperative complications, were analysed with a  
26 two step-approach by univariate and multivariate logistic regression models.

27 Hypocalcaemia was the most represented electrolyte disturbance (52.5%), followed by  
28 hypokalaemia (30.0%) that was associated with intraoperative administration of  
29 salbutamol ( $P = 0.045$ ). Perianaesthetic death occurred in 46 horses, accounting for an  
30 overall mortality rate of 38.3%. Risk factors associated with death were anaesthetic  
31 duration ( $P = 0.001$ ), body weight ( $P = 0.020$ ), presence of gastric reflux before  
32 anaesthesia ( $P = 0.021$ ), and intraoperative tachycardia ( $P = 0.043$ ) and acidosis ( $P =$   
33  $0.025$ ).

34 The mortality in the study population was comparable to previously reported findings.  
35 Based on the study findings, it is advisable to optimise haemodynamics prior to  
36 anaesthesia, in order to prevent intraoperative tachycardia that is associated with  
37 increased risk of death. Heavier horses and those with gastric reflux may have higher  
38 risk of fatalities, and intraoperative salbutamol administration may contribute to  
39 hypokalaemia.

40  
41 **Keywords** explorative laparotomy, equine, hypokalaemia, salbutamol, risk of  
42 perioperative death.

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## 51 1. Introduction

52 Ventral midline laparotomy is indicated in approximately 10% of horses  
53 presented due to colic [1,2]. Colic horses undergoing emergency laparotomy may  
54 experience perianaesthetic complications, usually require pre- and postoperative  
55 intensive care, and their management is expensive in terms of costs and human  
56 resources [2]. Updated information about the actual risk of fatalities would enable both  
57 owners and veterinarians to make informed management decisions.

58 There is a body of published work pertaining to perianaesthetic mortality of equine  
59 patients and related risk factors. However, to the best of the authors' knowledge, the  
60 majority of these studies either included both emergency and elective cases [3,4], or  
61 focused on a specific gastro-intestinal condition [2,5-7], or they were published more  
62 than a decade ago or earlier [1,2,8-11].

63 Within the last decade, much progress has been made in veterinary anaesthesia,  
64 owing to the development of sophisticated and modern anaesthetic techniques and  
65 equipment, as well as to the increased number of board-certified specialists  
66 worldwide. Based on this, it would be reasonable to update the current knowledge  
67 regarding equine perianaesthetic mortality with particular focus on critically ill horses  
68 undergoing surgical treatment of colic.

69 With respect to electrolyte disturbances, there is a number of publications focusing  
70 on their occurrence in horses with colic. Of these, some included horses undergoing  
71 medical management of colic [12-14], and one focused on the postoperative period  
72 after surgical treatment [15]. Several studies including horses undergoing emergency  
73 laparotomy specifically investigated the alteration of calcium and magnesium  
74 homeostasis during the anaesthetic [16-17].

75 Potassium serum concentration may also be affected by the anaesthetic, owing to  
76 starving and/or to the administration of catecholamines [18]. Moreover, salbutamol, a  
77 selective beta 2-adrenoreceptor agonist that is often used, in aerosolised form, in  
78 equine anaesthesia to improve the respiratory function [19], is known to decrease  
79 serum potassium in dogs [20] and may cause hypokalaemia in colic horses as well.  
80 Sodium homeostasis may be affected during the anaesthetic of colic horses due to  
81 dehydration, administration of hypertonic saline solution, or both. To the best of the  
82 authors' knowledge, these aspects have never been extensively investigated in colic  
83 horses undergoing anaesthesia and surgery.

84 The main objectives of this retrospective investigation were:

- 85 • To determine the mortality risk and to identify the risk factors for  
86 perianaesthetic death in a population of 120 horses undergoing surgical  
87 treatment of colic in a large referral hospital;
- 88 • To define the prevalence of the intraoperative electrolyte imbalances –  
89 including calcium, potassium and sodium - in the study population, and
- 90 • To determine whether the intraoperative administration of aerosolised  
91 salbutamol was associated with changes in blood potassium concentration in  
92 the study population.

93

## 94 2. Materials and methods

95 The study was conducted under approval of the Social Science Ethical Review Board  
96 (SSERB) of the Royal Veterinary College (license number: URN SR: 2017-1030).

97

### 98 2.1. Case selection criteria and medical records review

99 The patient files of horses with colic admitted to the Equine Referral Hospital of the  
100 Royal Veterinary College between October 2012 and June 2018 were reviewed. The

101 case-specific key word-combinations entered in the database were “horse + colic”,  
102 “horse + colic + anaesthesia/anaesthetic”, and “horse + colic + abdominal  
103 surgery/laparotomy/ceiotomy”. The search was manually refined in order to include  
104 only patients that underwent surgery, and whose anaesthetic record was complete.  
105 Donkeys, mules and horses undergoing relaparotomy were excluded from the study.

106 Demographic variables, namely sex, age, breed, body weight (BW) and Body  
107 Condition Score (BCS; 0-9) [21] were collected and used for statistical analysis.  
108 Aspiration of stomach contents through a nasogastric tube prior to anaesthesia,  
109 reported either in the anaesthetic record or elsewhere in the medical file of the horse,  
110 was annotated as “gastric reflux”. The occurrence of intra-operative complications,  
111 namely hypotension, hypoxaemia, cardiac arrhythmias, metabolic acidosis, metabolic  
112 alkalosis and electrolyte imbalances, was extrapolated from the anaesthetic record.  
113 Intra-operative complications were defined as follows:

- 114 • Hypotension: mean arterial pressure, measured invasively, lower than 70  
115 mmHg for at least three consecutive 5 minute-interval readings [22];
- 116 • Hypoxaemia: PaO<sub>2</sub> lower than 60 mmHg in at least half of the measurements  
117 [22];
- 118 • Cardiac arrhythmias: any disturbance of the cardiac rhythm, as detected with  
119 electrocardiography, among ventricular premature contraction, atrial fibrillation,  
120 second degree atrio-ventricular (A-V) blocks, third degree A-V blocks, bradycardia  
121 (heart rate < 24 bt/min, either supraventricular or ventricular) and tachycardia (heart  
122 rate > 55 bt/min, either supraventricular or ventricular) [23-24];
- 123 • Metabolic acidosis: pH < 7.34 and HCO<sub>3</sub><sup>-</sup> < 22 mmol/L in at least half of the  
124 measurements [25-26];
- 125 • Metabolic alkalosis: pH > 7.43 and HCO<sub>3</sub><sup>-</sup> > 32 mmol/L in at least half of the  
126 measurements [25-26];
- 127 • Hypokalemia: K<sup>+</sup> blood concentration < 2.7 mmol/L in at least half of the  
128 measurements [12-27];
- 129 • Hyperkalemia: K<sup>+</sup> blood concentration > 5 mmol/L in at least half of the  
130 measurements [12];
- 131 • Hypocalcemia: iCa<sup>2+</sup> blood concentration < 1.4 mmol/L in at least half of the  
132 measurements [12];
- 133 • Hypercalcemia: iCa<sup>2+</sup> blood concentration > 1.7 mmol/L in at least half of the  
134 measurements [12];
- 135 • Hyponatremia: Na<sup>+</sup> blood concentration < 132 mmol/L in at least half of the  
136 measurements [12];
- 137 • Hypernatremia: Na<sup>+</sup> concentration > 146 mmol/L in at least half of the  
138 measurements [12].

139 All the aforementioned variables were measured during the anaesthetics, from  
140 whole arterial blood, with two different point-of-care analysers: a radiometer (IRMA  
141 Trupoint blood analysis system, Lifehealth MN USA) and a portable device with  
142 disposable cartridges (i-STAT blood analyser and cartridges CG8+, Abbott NJ USA),  
143 on a number of samples ranging from 3 to 7 per case. Electrolyte supplementation  
144 during surgery was noted. Other information extrapolated from the anaesthetic record  
145 included the American Society of Anaesthesiologists (ASA) risk classification (1-5E),  
146 the intra-operative administration of dobutamine, of noradrenaline and of beta 2-  
147 agonists (inhalational salbutamol), the indication for laparotomy, time to standing  
148 (defined as the minutes elapsed from arrival of the horse in the recovery box to  
149 standing), and the recovery score. Recovery scores were assigned by the anaesthetist

150 in charge, based on a simple descriptive scale ranging from 1 (excellent) to 5 (very  
151 poor) [28].

152 Indications for laparotomy were sub-categorised in ischaemic (large colon volvulus,  
153 small and large intestine volvuli, inguinal hernias, mesenteric hernias, and  
154 pedunculated lipomas causing strangulating obstruction) and non-ischaemic  
155 (obstructive: large colon impaction/displacement, ileal impaction, nephro-splenic  
156 entrapment, large colon enterolithiasis) conditions.

157 Perianaesthetic death was defined as a binary variable with two possible outcomes:  
158 survival or death, including euthanasia, from anaesthetic induction to 72 hours after  
159 the end of the anaesthetic.

160

## 161 2.2. *Statistical analysis*

162 The Kolmogorov-Smirnov and the Skewness and Kurtosis tests for normality  
163 were used to assess the distribution of discrete and continuous variables, respectively.  
164 Descriptive statistics was used to quantitatively describe the basic features of the data.

165 Univariate binary logistic regression, with perianaesthetic death set as dependent  
166 variable, was run separately for each of the following independent variables: sex,  
167 breed, BCS, ASA risk classification, indication for surgery, gastric reflux,  
168 hypotension, hypoxaemia, arrhythmias, metabolic acidosis, metabolic alkalosis, hypo-  
169 and hyperkalaemia, hypo and hypercalcaemia, hypo- and hypernatraemia, coexistence  
170 of more than one type of electrolyte imbalance, intraoperative calcium or potassium  
171 supplementation, ischaemic condition, intraoperative use of dobutamine, noradrenaline  
172 and/or salbutamol, duration of anaesthesia, time to standing and recovery score.

173 Univariate binary logistic regression was further used to determine whether there was  
174 an association between hypokalaemia and the intraoperative administration of  
175 salbutamol.

176 Variables showing significant association with the dependent variable ( $P < 0.05$ )  
177 were carried forward to be evaluated in a multiple logistic regression model, built  
178 using manual forward selection procedures. Odd ratios (OR) and associated 95%  
179 confidence intervals (CI) were estimated from the final logistic regression model and  
180 used as a measure to assess the quality of model fit, together with the goodness-of-fit  
181 test.

182 The Spearman correlation coefficient was used to investigate correlations between  
183 numerical discrete variables (recovery score versus time to standing, body weight and  
184 age, and time to standing versus body weight and age). Finally, in order to determine  
185 whether heavier, obese or older horses had a higher risk for perianaesthetic death,  
186 body weight, BCS and age were subcategorised ( $<500$  and  $\geq 500$  kg,  $<6$  and  $\geq 6$ , and  
187  $<120$  and  $\geq 120$  months, respectively) and analysed with either Chi-square or Fisher  
188 Exact test where appropriate.

189 Commercially available software was used for statistical analysis (Sigma Stat 4.0  
190 and Sigma Plot 14.0, Systat Software Inc., NV USA; IBM SPSS Statistics 24, UK).  
191 The level of significance was always defined as  $P < 0.05$ .

192

## 193 3. Results

194

### 195 3.1 *Demographic data*

196 Data are presented as either mean  $\pm$  SD or medians and ranges [min - max],  
197 depending on data distribution.

198 One hundred and twenty horses of various breeds were included in the study (Table  
199 1). Of these, 35.0% ( $n = 42$ ) were intact female, 40.8 % geldings ( $n = 49$ ), and the



200 remaining 24.2% (n = 29) intact males. Body weight, age and BCS were 510 [53-803]  
201 kg,  $161 \pm 75$  months and 5 [3-9], respectively. The ASA risk classification assigned to  
202 the horses was 4[3-5], with 17.5% (n = 21), 54.2 % (n = 65) and 28.3% (n = 34) of the  
203 horses classified as ASA 3E, 4E and 5E, respectively; all cases were classified as  
204 emergencies (E).

205

### 206 *3.2 Anaesthesia and perioperative period*

207 Preoperatively, stomach content was aspirated via nasogastric tube in 35% of the  
208 horses (n = 42). The indications for surgery, 30.0% of which (n = 36) were defined as  
209 ischaemic conditions, are listed in Table 2.

210 A team composed of one resident and one of four Diplomates of the European  
211 College of Veterinary Surgery (large animals) performed the surgeries. The  
212 anaesthetics were provided by a resident in Veterinary Anaesthesia, supervised by one  
213 of eight Diplomates of the European or American Colleges of Veterinary Anaesthesia  
214 and Analgesia.

215 Premedication was provided with an intravenous (IV) alpha 2 adrenoreceptor-  
216 agonist - either xylazine (Chanazine, Chanelle UK; dose: 1 [0.05 - 1.1] mg/kg) or  
217 romifidine (Sedivet, Boehringer Ingelheim UK; dose: 0.08 [0.05 - 0.08] mg/kg).  
218 Anaesthetic induction was achieved with IV ketamine (Ketamidol, Chanelle UK;  
219 dose: 2.2 [2.2 - 2.5] mg/kg) with either diazepam (Valium, Roche UK; dose: 0.05  
220 [0.05 - 0.1] mg/kg) or midazolam (Dormicum, Roche UK; dose: 0.05 [0.05 - 0.1]  
221 mg/kg), IV. Isoflurane (IsoFlo, Abbott UK) in either 100% oxygen or a mixture of  
222 air/oxygen, with or without an IV lidocaine infusion (Lidocaine Hydrochloride 0.2%,  
223 Fresenius Kabi UK; dose: 0.03 [0.02-0.05] mg/kg/min), was used for maintenance of  
224 anaesthesia. Intraoperatively, IV dobutamine (Dobutamine Concentrate, Hameln  
225 Pharmaceutical Germany; dose: 1 [0.5 - 2]  $\mu$ g/kg/min) and inhalational salbutamol  
226 (Ventolin, GlaxoSmithKline UK dose: 2 [0.5 - 2]  $\mu$ g/kg) were administered to 99.2 %  
227 (n = 119) and to 41.7% (n = 50) of the horses, respectively, while noradrenaline  
228 (Noradrenaline, Hospira UK; dose: 0.2 [0.1 - 0.4]  $\mu$ g/kg/min) to 40.0% (n = 48) of the  
229 horses. Analgesia was provided with either IV butorphanol (Alvegesic, Dechra UK;  
230 dose: 0.05 [0.04-0.05] mg/kg or IM morphine (Morphine Sulphate, Mercury  
231 Pharmaceuticals Ireland; dose: 0.1 [0.1-0.15] mg/kg, both given at 2 hour-intervals,  
232 starting from the beginning of surgery until standing. Intra-operative fluids were  
233 administered to each horse, with fluid types and volumes decided at the anaesthetists'  
234 discretion based on the patient requirement. The proportions and numbers of horses  
235 that experienced intraoperative complications are presented in Table 3.

236 Anaesthesia lasted  $146 \pm 63$  minutes, and time to standing was 41 [10 - 185]  
237 minutes. The quality of recovery was scored and recorded in 76 of 120 horses only;  
238 recovery score was 1, 2, 3 and 4 in 22.4% (n = 17), 36.8% (n = 28), 28.9% (n = 22)  
239 and 10.5% (n = 8) of the cases, respectively. Overall, recovery score from all horses  
240 was 2 [1-5]. There were statistically significant correlations between time to standing  
241 and recovery score (Spearman correlation coefficient = 0.47;  $P < 0.001$ ), and between  
242 age and recovery score (Spearman correlation coefficient = -0.24;  $P = 0.039$ ).

243

### 244 *3.3 Electrolyte disturbances*

245 The 79.2% (n = 95) of the horses experienced single (29.2%; n = 35) or multiple  
246 (50.8%; n = 61) electrolyte imbalances during surgery. Electrolytes were  
247 supplemented IV in 20.8% of the cases (n = 25); of these, 19 horses out of 25 received  
248 calcium gluconate (Calcium Gluconate 10%, Hameln Pharmaceutical Germany; dose:  
249 0.5 mL/kg, IV) and the remaining 6 potassium chloride (Potassium Chloride 7.45%,

250 Braun UK). The horses that received electrolyte supplementation during the  
251 anaesthetics had their  $iCa^{2+}$  and  $K^+$  blood concentrations below 0.9 and 2.7 mmol/L,  
252 respectively. Blood electrolytes were measured with the radiometer in 55% of the  
253 horses, and with the portable device and disposable cartridges in the remaining 45%.  
254 Hypocalcaemia (52.5%; n = 63) and hypokalaemia (30.0%; n = 36) were the most  
255 represented electrolyte imbalances. There was a significant association between the  
256 use of salbutamol during surgery and the development of intraoperative hypokalaemia  
257 (P = 0.045).

258

### 259 *3.4 Perianaesthetic death and risk factors*

260 Perianaesthetic death occurred in 46 horses, of which the 54.3% (n = 25) were  
261 euthanised during surgery, 10.9% (n = 5) died/ were euthanised during recovery and  
262 the remaining 34.8% (n = 16) were euthanised during the following 72 hours. This  
263 accounted for an overall mortality rate of 38.3%. Except for three horses that  
264 experienced a cardiopulmonary arrest in the recovery box and died spontaneously, all  
265 the study horses that died were euthanised. Euthanasia was performed when either the  
266 patient demanded further surgical intervention that was declined by the owner, or its  
267 clinical condition was so severe that the clinician in charge had no reasonable hope for  
268 a successful outcome.

269 Horses weighing  $\geq 500$  kg or aged  $\geq 120$  months had a higher risk of  
270 perianaesthetic death (P = 0.014 and P = 0.02, respectively). The univariate logistic  
271 regression indicated the following variables as significant risk factors for  
272 perianaesthetic death: duration of anaesthesia (P = 0.006), gastric reflux (P = 0.011),  
273 acidosis (P = 0.014), intraoperative tachycardia (P = 0.033) and body weight (P =  
274 0.037). The multivariate model confirmed these significances (Table 4).

275

### 276 *3.5 Suitability of the statistical model*

277 The confidence intervals were narrow for most variables, suggesting that the  
278 logistic regression model was overall accurate and fitted the data satisfactorily. The  
279 coefficient of determination  $R^2$  obtained with the goodness-of-fit test was equal to 0.8.

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284 **Table 1**285 Breeds of 120 colic horses undergoing laparotomy under general anaesthesia.

<b>Breed</b>	<b>Number of horses</b>	<b>% of total</b>
Crossbreed	44/120	36.7
Irish Sport	13/120	10.8
Thoroughbred	12/120	10.0
Welsh	10/120	8.3
Irish Cob	9/120	7.5
Shetland Pony	8/120	6.7
British Warmblood	6/120	5.0
Dutch Warmblood	3/120	2.5
Arabian	3/120	2.5
Hanoverian	3/120	2.5
Andalusian	3/120	2.5
New Forest Pony	2/120	1.7
Hackney	1/120	0.8
Oldenburg	1/120	0.8
Trakehner	1/120	0.8
Holstein	1/120	0.8

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292 **Table 2**

293 Indication for surgery for 120 colic horses undergoing laparotomy under general  
 294 anaesthesia.

<b>Indication for surgery</b>	<b>Number of horses</b>	<b>% of total</b>
Strangulation	39/120	32.5
<ul style="list-style-type: none"> <li>• Pedunculated lipoma (n = 37)</li> <li>• Foreign body (n = 2)</li> </ul>		
Small intestine entrapment	20/120	17.0
<ul style="list-style-type: none"> <li>• Nephrosplenic space (n = 6)</li> <li>• Epiploic foramen (n = 11)</li> <li>• Inguinal hernia (n = 1)</li> <li>• Diaphragmatic hernia (n = 1)</li> <li>• Gastrosplenic ligament (n = 1)</li> </ul>		
Large colon impaction	18/120	15.0
Dorsal colon displacement	17/120	14.2
<ul style="list-style-type: none"> <li>• Right (n = 12)</li> <li>• Left (n = 5)</li> </ul>		
Large colon <b>volvulus</b>	10/120	8.3
Ileus/inflammation	8/120	6.7
Intestinal lymphoma	2/120	1.7
Intestinal rupture	3/120	2.5
Gastric ulceration	1/120	0.8
Ileocaecal intussusception	1/120	0.8
Intra-abdominal mass	1/120	0.8

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300 **Table 3**

301 Intraoperative complications occurring in 120 colic horses undergoing laparotomy  
 302 under general anaesthesia.

<b>Intraoperative complication</b>	<b>Number of horses</b>	<b>% of total</b>
Hypotension	106/120	88.3
Tachycardia	63/120	52.5
Hyponatraemia	2/120	1.7
Hypernatraemia	7/120	5.8
Hypokalaemia	36/120	30
Hyperkalaemia	6/120	5
Hypocalcaemia	63/120	52.5
Hypercalcaemia	1/120	0.8
Acidosis	12/120	10
Alkalosis	55/120	45.8

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310 **Table 4**

311 Details of multiple logistic regression and significant risk factors associated with  
 312 perioperative death in 120 colic horses undergoing laparotomy under general  
 313 anaesthesia.

<b>Variable</b>	<b>Coefficient</b>	<b>Standard Error</b>	<b>P value</b>	<b>OR (95% CI)</b>
Body weight (kg)	0.004	0.004	0.020	1.00 (1.00 - 1.01)
Tachycardia (y/n)	0.908	0.452	0.043	2.48 (1.03 - 5.96)
Acidosis (y/n)	1.925	0.857	0.025	6.86 (1.28 - 36.76)
Gastric reflux (y/n)	1.048	0.525	0.021	2.85 (1.03 - 7.87)
Duration of anaesthesia (min)	-0.012	> 0.001	0.001	0.99 (0.98 - 0.99)

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#### 317 4. Discussion

318 The main findings of this retrospective study were that in the study population  
319 hypocalcaemia and hypokalaemia were the most common electrolyte disorders, and  
320 that perianaesthetic mortality was comparable to what has been reported previously in  
321 horses undergoing colic surgery [4,10], with heavier horses, presence of gastric reflux,  
322 longer anaesthetics and the occurrence of intraoperative tachycardia and acidosis being  
323 significant risk factors.

324 Similarly as found by other studies [12,17], in the study population  
325 hypocalcaemia and hypokalaemia were the most common intraoperative electrolyte  
326 imbalances.

327 Possible causes of hypocalcaemia are endotoxaemia, sepsis and diarrhoea,  
328 although the use of volatile anaesthetics has also been associated with a decrease in  
329 calcium serum concentrations [16,29,30].

330 Regarding hypokalaemia, its origin in horses with colic may be multifactorial,  
331 with altered intake and absorption and excess loss from the gastrointestinal tract due to  
332 diarrhoea being the most common causes [31].

333 Beta-adrenergic stimulation is known to increase the uptake of potassium into  
334 cells [32]. Interestingly, a significant association was found in the study population  
335 between the intraoperative use of a beta-2 agonist, salbutamol, and the occurrence of  
336 hypokalaemia. This finding should be critically interpreted, considering that two  
337 different point-of-care analysers were used to measure blood potassium concentration.  
338 The reference ranges for blood potassium concentration provided by the manufacturer  
339 of the i-Stat (1.9-4.1 mmol/L) [33] are considerably lower than those reported in the  
340 literature [12,27]. This represents a drawback which might limit the validity of our  
341 findings. Nevertheless, one study comparing the i-Stat with a radiometer whose  
342 measuring principles are similar to the one used in the current study found very good  
343 agreement between the two devices with respect to blood potassium concentration in  
344 horses, with excellent correlation of the measured values [27]. Moreover, the min-max  
345 i-Stat values for equine blood potassium concentrations reported in this study were  
346 2.7-5.9 mmol/L, suggesting that horses with concentrations lower than 2.7 mmol/L, as  
347 measured by the i-Stat, are likely to suffer from actual hypokalaemia [27]. Overall,  
348 these aspects seem to indicate that our findings are relevant, and that the intraoperative  
349 administration of salbutamol may contribute to the development of hypokalaemia.  
350 Whether such hypokalaemia would be clinically relevant, however, remains debatable.  
351 Although both hypokalaemia and hypocalcaemia may potentially increase  
352 perioperative morbidity by causing muscle weakness, ileus and tachycardia [13-14],  
353 we failed to demonstrate their association with mortality in the study population. This  
354 could be because, in the sample population, in many cases the anaesthetist in charge  
355 chose to supplement the electrolytes whenever they felt this was indicated, an action  
356 that could have prevented the complication from worsening the outcome.

357 The current study identified a mortality rate of 38.3%, which also included  
358 horses euthanised intraoperatively. These results are comparable to those of two  
359 studies that included large numbers of equine patients. Johnston and colleagues found  
360 that perioperative fatalities, including euthanasia, occurred in 1843 out of 5330 horses  
361 undergoing colic operation, which represents the 35% of all cases [4]. Similarly, in  
362 792 horses anaesthetised for surgical colic the risk of death or euthanasia was 35.5%  
363 [10]. Another study that included 300 horses identified a short-term mortality rate to  
364 discharge, following a single laparotomy, of 29.3% [2]. Proudman and colleagues  
365 reported a lower mortality rate and found that 88 out of 774 horses [11], equal to 13%  
366 of the total, died or were euthanised intraoperatively. However, this number did not

367 include the postoperative deaths. The results of the current investigation might indicate  
368 that the quality of anaesthesia delivered to equine patients has not improved over the  
369 last decade. Alternatively, they could also reflect a tendency to offer to the horse  
370 owners more advanced treatment options than in the past, and therefore to be more  
371 prone to attempt surgery in patients that are critically ill.

372 The current study found that heavier horses are at higher risk for perianaesthetic  
373 mortality. This is in agreement with the findings of previous investigations. Proudman  
374 and others found that heavier breeds carried a higher risk of postoperative fatalities  
375 and hypothesised that the size may be a more likely risk factor than any specific breed  
376 susceptibility [11]. Besides the specific problems of colic horses, heavier horses may  
377 be predisposed to various complications, namely post-anaesthetic myopathies and  
378 neuropathies. Interestingly, correlation statistics found an association between older  
379 age and mortality; however, this finding was not confirmed by regression, which  
380 questions its actual significance.

381 In contrast with another study [11], which found no association between  
382 nasogastric reflux and the outcome, in the current study population horses with  
383 nasogastric reflux were at higher risk of death. It is challenging to provide a  
384 reasonable explanation for this finding. The presence of nasogastric reflux may reflect  
385 an increased intragastric pressure that could potentially account for impaired  
386 cardiovascular function during dorsal recumbency. However, possibly owing to  
387 stomach decompression and IV fluids administration prior to anaesthesia, in the  
388 current study no significant association was found between the presence of reflux and  
389 intraoperative tachycardia or hypotension. As an alternative explanation, nasogastric  
390 reflux might predispose to aspiration of gastric content during induction or recovery of  
391 anaesthesia, with consequent impairment of the respiratory function [34]. Although  
392 none of the horses experienced post-operative respiratory distress, undetected  
393 aspiration of gastric content may have accounted for some intraoperative deaths by  
394 causing hypoxaemia, hypercapnia and potentially adrenergic response.

395 With respect to the duration of anaesthesia, the current work confirms the  
396 findings of previously published work, which identified this variable as a risk factor  
397 for death of both colic and non-colic horses, and found that the longer the duration of  
398 the anaesthetic or of the operation, the higher the risk for perioperative fatalities  
399 [4,9,10].

400 The occurrence of intraoperative tachycardia was identified as another  
401 significant risk factor for perianaesthetic death in the current investigation. Whilst  
402 other types of arrhythmias, namely sinus bradyarrhythmias and A-V blocks, may be  
403 interpreted as a more benign alteration of the equine dromotropism [23], in this species  
404 tachycardia is more likely to reflect a certain degree of cardiovascular instability –  
405 although during surgery it may also result from inadequate analgesia or dobutamine  
406 overdose. Increased heart rate has been interpreted by various authors as a sign of  
407 cardiovascular compromise in colic horses, possibly resulting from endotoxaemia  
408 and/or hypovolaemia [35-36] and has been reported to increase the risk of death in  
409 horses undergoing colic operation [11]. Tachycardia may be blunted in the awake  
410 colic horses under the effect of previously administered alpha 2-agonists and become  
411 evident only during general anaesthesia. Moreover, mechanical ventilation and dorsal  
412 recumbency are likely to worsen the venous return to the heart and hence further  
413 decrease the cardiac output. In this scenario, optimizing the cardiovascular function  
414 before anaesthesia with adequate fluid therapy may help to improve the outcome and  
415 decrease the risk of mortality.

416 In colic horses, acidosis may impair cardiac function by altering the inotropism,  
417 and worsen the vasodilation caused by endotoxaemia. The occurrence of metabolic  
418 acidosis during anaesthesia was found a significant risk factor for mortality in the  
419 horses of this study. However, this finding should be interpreted cautiously, owing to  
420 both the intrinsic limitations of the variable and its associated large CI obtained from  
421 the multivariate regression model –which indicates a low accuracy of the model with  
422 respect to this specific variable. Serum bicarbonate concentrations and pH were both  
423 evaluated with the purpose of identifying all the cases of metabolic acidosis.  
424 Nevertheless, without a full electrolyte panel, which would have allowed a more  
425 comprehensive evaluation of the acid-base status, the presence of mixed electrolyte  
426 disorders could not be completely ruled out. Therefore, there could have been cases  
427 with a normal blood pH and yet undetected acidosis, or alkalosis, or even both.

428 In the horses of this study, recovery score was negatively correlated to age and  
429 positively correlated to time to standing. In other words, the younger the horses and  
430 the more time they took to stand, the worse was the quality of their recovery. Whilst  
431 the association between duration and quality of recovery was somewhat expected,  
432 geriatric horses would be expected to have a worse recovery than younger ones, as  
433 they may more easily develop muscular weakness and fatigue. However, recovery  
434 from anaesthesia is a process that is likely to be affected by learning behaviour, and it  
435 is reasonable to assume that older horses, owing to a quieter temperament and possibly  
436 previous experience of anaesthesia, may cope better with the situation [37].

437 In the current study, the ASA classification was not found a significant risk  
438 factor for perianaesthetic death. One reason for this finding may be that data  
439 distribution affected the statistical modelling process for this specific variable; since  
440 only colic horses were included in the study, an ASA grade 4 was assigned to most  
441 patients while ASA grades 1 and 2 were not represented in the study population.

442 This study has two important limitations. Each referral centre represents a  
443 unique set-up and, since this study was not designed as multicentric, the study sample  
444 may not represent well the entire equine population. However, it is worth considering  
445 that the Royal Veterinary College is a referral centre with an international background  
446 and generational diversity, including specialists who come from all over the world and  
447 were trained in either Europe or the US.

448 Another study limitation is that this study included a considerably smaller number of  
449 horses compared to previous studies that investigated equine perianaesthetic mortality.  
450 However, the suitability of the statistical model, together with the selection of a  
451 specific, presumably relatively small sub-population (colic horses undergoing  
452 surgery), suggest that our findings may be useful to implement the scientific  
453 knowledge pertaining to equine perianaesthetic mortality.

454

## 455 **5. Conclusions**

456 To date, there is no evidence that the mortality rate of colic horses undergoing  
457 surgery may be lower than in the past years, despite the increased number of  
458 anaesthesia specialists. Heavier horses and those with preoperative gastric reflux may  
459 carry a higher risk of fatalities. In the attempt to prevent intraoperative tachycardia,  
460 which was associated with increased risk of death in the study horses, the  
461 cardiovascular function should be optimised prior to anaesthetic induction and during  
462 anaesthetic maintenance. During anaesthesia, hypokalaemia may develop – or worsen  
463 - as a result of aerosolised salbutamol administration.

464

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