REVIEW

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Equine anaesthesia-associated mortality

Equine anaesthesia-associated mortality: where are we now?

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Abstract

Objectives To review the literature concerning mortality associated with general anaesthesia in horses and to assess whether there is evidence for a reduction in mortality over the 20 years since the Confidential Enquiry into Perioperative Equine Fatalities (CEPEF).

Databases used PubMed, Scopus, Google Scholar. Search terms used: horse; pony; equine; anaesthesia; anesthesia; recovery; morbidity, and mortality.

Conclusions The most recent studies, in which isoflurane and sevoflurane have been more commonly used for anaesthesia maintenance, report fewer intraoperative cardiac arrests than older studies in which halothane was favoured. Catastrophic fractures, however, have become the greatest cause of recovery-associated mortality.

Keywords anaesthesia, anesthesia, equine, mortality, recovery.

Introduction

Acknowledgement of changes in anaesthesia practice since the conclusion of the original Confidential Enquiry into Perioperative Equine Fatalities [CEPEF 1-3 (Johnston et al. 1995, 2002, 2004)] led to plans for a further study [(CEPEF 4 (Bettschart & Johnson 2011; Gent & Bettschart-Wolfensberger 2013; Wohlfender et al. 2015)], the final results of which are eagerly awaited. Until those results become available, however, it is appropriate to review the mortality associated with equine anaesthesia and to investigate the developments that have occurred over the two decades since the publication of the first reports.

Comparative mortality

Mortality associated with equine anaesthesia has been reported to be approximately 1% in healthy elective cases, but figures have ranged from 0.08% to 1.8%, depending upon study design (Mitchell 1969; Tevik 1983; Young & Taylor 1990, 1993; Johnston et al. 1995, 2002, 2004; Mee et al. 1998a, b; Bidwell et al. 2007) (Table 1). The number of postoperative days included, and whether or not anaesthesia was considered to be directly related to the outcome, affect the definition of 'mortality' [see below and Bidwell et al. (2007)]. Much higher mortality rates have been reported in emergency cases, particularly those requiring abdominal surgery for 'colic' (intra-abdominal conditions requiring surgical exploration) or Caesarean section, and range from 7.8% (Johnston et al. 2002) to 19.5%, even when animals with inoperable lesions are excluded (Mee et al. 1998b). The true contribution of anaesthesia to mortality in such cases is difficult to evaluate. Horses may survive emergency anaesthesia and colic surgery only to succumb to the complications of endotoxaemia and/or intractable postoperative ileus, or financial constraints may limit continued treatment in the early postoperative phase (Ducharme et al. 1983; Hunt et al. 1986).

The rate of ~ 1% that is considered to reflect the incidence of anaesthesia-associated mortality in healthy horses is between a hundred- and a thousand-fold greater than the incidences of mortality associated with anaesthesia in humans (0.01–0.001%) (Lunn & Mushin 1982; Jones 2001; Irwin & Kong 2014), 20-fold greater than that in dogs (0.05%), 10-fold greater than that in cats (0.11%), and not dissimilar from that reported for rabbits (0.73%) (Brodbelt et al. 2008). There is, therefore, much room for improvement.

Jones (2001) suggested that reductions in anaesthesia-related mortality, particularly for humans, had occurred over time as a result of the introduction of 'safer anaesthetic techniques' and attempts to reduce human error (through training and the use of existing and new monitoring devices). However, he also cautioned that the increasing complexity of surgery might offset some past and future improvements. In addition, Keats (1990) cautioned against the comparison of studies over time during which many factors were likely to change; he also suggested that anaesthetic mortality had not decreased 'because we create new mechanisms of mortality at the same rate we solve them'. Irwin and Kong (2014) reminded us that although human anaesthesia itself may now be relatively safe, surgery is not!

Equine mortality

Several studies evaluating mortality associated with general anaesthesia and surgery in horses have identified various risk factors which may help to inform case management and/or highlight increased risk (Table 1). The largest study to date has been the CEPEF [*n* = 41,824, CEPEF 1 and 2 (Johnston et al. 1995, 2002); *n* = 11,336, CEPEF-3 (Johnston et al. 2004)]. This series of multicentre studies spanned over 8 years (February 1991 to September 1999) of data collection and identified the most common causes of death, as well as several risk factors (Table 1).

74 The CEPEF studies reported mortality rates of 0.9% in healthy horses within 7 days of
75 anaesthesia and surgery, and 1.9% in all cases (including horses with colic or dystocia, foals,
76 and horses undergoing fracture repair) (Johnston et al. 2002). A third of the deaths were
77 attributed to intraoperative cardiac arrest or postoperative cardiovascular collapse, and around
78 another third to fractures (limb or neck) and post-anaesthesia myopathy (PAM).
79 Postoperative myopathy is associated with poor intraoperative muscle perfusion and oxygen
80 delivery (Grandy et al. 1987) and it is likely that at least some of the fractures occurred as a
81 consequence of myopathy-induced pain or weakness.
82 In addition to CEPEF, several smaller-scale, single-centre studies have reported mortality
83 rates between 0.08% and 1.5% in horses undergoing elective procedures (Mitchell 1969; Mee
84 et al. 1998a; Senior et al. 2007; Bidwell et al. 2007; Dugdale et al. 2015). These values
85 should be interpreted in the light of smaller sample sizes and differences in the horse
86 populations served by each centre, and with consideration of the inconsistencies in definitions
87 of 'mortality' between studies [see Senior (2013) for a recent review]. Furthermore,
88 comparison between studies is also hindered by variations in anaesthetist experience.
89 The largest single-centre study (n = 17,961) included almost half the number of horses in
90 CEPEF-1 and 2, but reported mortality of only 0.12% in a sample that included horses
91 undergoing emergency abdominal surgery (Bidwell et al. 2007). Half of these deaths were
92 caused by intraoperative cardiac arrest and the remainder by PAM, neuropathy or fracture
93 (Table 1). When all deaths occurring within the first 7 days post-surgery were included, the
94 mortality rate doubled to 0.24%, which is still comparatively low (Bidwell et al. 2007). The
95 majority of procedures, however, were of less than 1 hour in duration, which may have had a
96 major influence on the results.
97 The discrepancy between the mortality rates observed in the CEPEF study and those in the
98 single-centre study reported by Bidwell et al. (2007) probably reflects the differences

between the very wide range of different practices, clinics and hospitals included in the CEPEF study, with their differences in caseloads, anaesthesia protocols and both anaesthetic and surgical experience, and a study conducted in a highly efficient single centre performing primarily short routine procedures in a relatively homogeneous group of patients with a uniformly high standard of anaesthetic care, respectively. Furthermore, even within equine hospitals, there is likely to be variation in experience and training amongst clinicians. To date, there is no evidence that lack of experience adversely influences equine anaesthesia-associated mortality (Johnston et al. 2002). However, there is anecdotal evidence for the opposite, probably because the most experienced anaesthetists tend to be responsible for cases with the highest risk. Clearly, this requires further research.

Causes of death

Intraoperative cardiac arrest

The CEPEF studies, in agreement with others, reported that intraoperative cardiac arrest tended to occur early in the anaesthetic period, usually within the first 30 minutes. This was considered to possibly result from halothane-induced myocardial sensitization to catecholamines, which may increase the risk for arrhythmias, especially in the absence of premedication, and it was suggested that acepromazine may be protective against such arrhythmias (Johnston et al. 1995, 2002; Mee et al. 1998a; Gent & Bettschart-Wolfensberger 2013). Halothane was the most commonly used anaesthetic maintenance agent in several studies, including CEPEF-1 and 2 (Johnston et al. 1995, 2002; Mee et al. 1998a, b; Bidwell et al. 2007), which may have influenced the occurrence of adverse intraoperative cardiac events. In CEPEF-3, although overall mortality did not differ between isoflurane and halothane, fewer cardiac arrests occurred, especially in high-risk cases, when anaesthesia was maintained with isoflurane (Johnston et al. 2004).

In the most recent study, halothane was used only in occasional elective, healthy cases (Dugdale et al. 2015). Although no deaths attributable to cardiac arrest were reported, the study size was smaller (n = 1416) and contained few 'athletic' (racing or event-fit) horses, by contrast with that conducted by Bidwell et al. (2007), which reported four intraoperative cardiac arrests in mature 'athletic' horses originally deemed healthy.

Axial and appendicular skeletal fractures

Long bone, cervical or basal skull fractures during recovery have contributed to anaesthesia-related mortality through immediate euthanasia or instantaneous death (Young & Taylor 1993; Johnston et al. 2002, 2004; Bidwell et al. 2007; Dugdale et al. 2015). Fractures have been described as responsible for 26–64% of all anaesthesia-related fatalities, although in a study in which dislocations were included, this figure rose to 71% (Young & Taylor 1993; Johnston et al. 2002; Bidwell et al. 2007; Dugdale et al. 2015).

Horses undergoing internal fracture fixation are considered at greater risk for the sustaining of further fractures in recovery, but such patients constituted only a small proportion (2.3–5.0%) of the caseload in all the reports (Johnston et al. 1995, 2002; Bidwell et al. 2007; Dugdale et al. 2015). The reason for the differences in the incidence of fatal fractures among studies is unknown, and the sporadic nature of such occurrences may bias the data, especially in shorter-term studies which may simply be 'lucky' or 'unlucky'.

One potential explanation refers to whether or not assistance was provided during recovery. Bidwell et al. (2007), who reported the lowest incidence of mortality (eight of 17,961 cases, 0.04%), assisted the majority of their cases with head and tail ropes, whereas Dugdale and colleagues (2015) rope-assisted only two of their cases (both fracture fixations). In one of these, the technique was deemed dangerous for both horse and assistants during recovery.

The provision of rope-assisted recoveries was not reported in CEPEF. A more recent abstract

149 describing a study in which a rope recovery system was used for all horses reported that of
150 5854 horses anaesthetized, 30 (0.51%) suffered major complications resulting in mortality,
151 only two (0.03%) suffered fractures, and a single horse (0.02%) suffered a hock dislocation
152 (Chie Niimura et al. 2015).
153 Bidwell et al. (2007) emphasized that rope assistance cannot guarantee successful recovery,
154 but others have been more convinced about its benefits. For example, Wilderjans (2005)
155 reported no fractures, luxations or serious wounds in over 7000 non-fracture repair surgeries,
156 whereas Auer & Huber (2013) reported no significant difference in recovery quality when
157 horses were recovered with or without rope assistance following anaesthesia which
158 incorporated a partial intravenous (IV) anaesthetic technique. Whether rope assistance or
159 other forms of assistance can reduce the incidence of fracture remains to be unequivocally
160 proven (Kaestner 2010), but rope-assisted recovery techniques appear to be gaining
161 popularity.
162
163 *Post-anaesthesia myopathy*
164 Post-anaesthesia myopathy has been suggested to be a risk factor for the occurrence of
165 fractures during recovery by causing pain, muscular weakness and incoordination. The
166 importance of intraoperative cardiovascular monitoring and support, particularly the use of
167 dobutamine to maintain mean arterial blood pressure (MAP) above values likely to risk PAM,
168 has been highlighted by previous authors (Grandy et al. 1987; Richey et al. 1990; Young &
169 Taylor 1993; Johnston et al. 2004). The provision of such support has been accepted practice
170 in most equine hospitals since the early 1990s (Young & Taylor 1993). Indeed, partway
171 through this study, increased intervention to support arterial blood pressure (MAP
172 > 70 mmHg) resulted in fewer deaths and a reduction in the severity of PAM. This concurs
173 with the more recent studies and supports the conclusion of Duke et al. (2006) that

intraoperative treatment of hypotension may not always prevent PAM, but it can reduce its severity.

The occurrence of PAM, a form of compartment syndrome (with elements of ischaemia and later reperfusion injury), is associated with poor padding and positioning of the anaesthetized patient, a prolonged duration of anaesthesia, and hypotension, and has been extensively reviewed elsewhere (White & Suarez 1986; Grandy et al. 1987; Heppenstall et al. 1988; Lindsay et al. 1980, 1985, 1989; Richey et al. 1990; Taylor & Young 1990; Johnson 1993; Raisis 2005a, b). Although hypoxaemia would worsen tissue oxygen delivery already reduced by hypoperfusion/ischaemia, hypoxaemia itself has not yet been shown to be an independent risk factor for PAM (Trim & Wan 1990; Steffey et al. 1992; Whitehair et al. 1996). In recent years, muscular disorders, which often present with prolonged recumbency during recovery and should be differentiated from true ischaemic PAM, have been characterized. The reader is referred elsewhere for details of equine polysaccharide storage myopathy, hyperkalaemic periodic paralysis and malignant hyperthermia or hyperpyrexia (Valentine 2005; Spier 2006; Aleman 2008; Finno et al. 2009; Naylor 2015).

Spinal cord malacia/post-anaesthesia neuropathies

Post-anaesthesia spinal cord malacia (pseudonyms include spinal cord myelopathy, myelomalacia, haematomyelia and poliomyelomalacia) can be considered a form of central neuropathy. It is recognized as a non-painful ascending neurological dysfunction which initially affects the tail and pelvic limbs (so that paraplegic horses may appear to ‘dog-sit’), and progresses cranially. It is effectively an ischaemic necrosis of the spinal cord, most commonly starting in the thoracolumbar area, and is invariably fatal. Its occurrence is sporadic and although young male horses of larger breeds undergoing relatively short procedures in dorsal recumbency appear to be at the greatest risk, cases have been reported in

mature horses (Ragle et al. 2011), fillies (Schatzmann et al. 1979; Blakemore et al. 1984; Brearley et al. 1986), a pony (Lam et al. 1995), and following lateral recumbency (Raidal et al. 1997).

The aetiology of spinal cord ischaemia has not been elucidated and there are no recommended strategies for its prevention. Suggested initiating causes have included stretch ischaemia of the spinal cord during dorsal recumbency (possibly exacerbated by the haemodynamic consequences of dorsal recumbency and the associated increases in intra- and peri-spinal cord cerebrospinal fluid pressure), verminous arteritis, embolism (thrombo-, fibrocartilagenous or bone marrow), and vitamin E or selenium deficiency (Taylor et al. 1977; Schatzmann et al. 1979; Blakemore et al. 1984; Zink 1985; Brearley et al. 1986; Fuentealba et al. 1991; Stolk et al. 1991; Lerche et al. 1993; Gruys et al. 1994; Jackson et al. 1995; Lam et al. 1995; Raidal et al. 1997; Joubert et al. 2005; Brosnan et al. 2008; Ragle et al. 2011). It is difficult to explain why CEPEF-3 (Johnston et al. 2004) suggested that isoflurane was associated with more of these cases than halothane, although their dissimilar effects on systemic vascular resistance and myocardial contractility may be relevant (Grosenbaugh & Muir 1998; Durongphongtorn et al. 2006).

Peripheral neuropathy affecting the limbs, such as femoral nerve injury, especially if bilateral, may prevent the animal from standing up. This may impact on postoperative management and ultimately result in euthanasia (Dyson et al. 1988). In addition, as the dysfunction associated with pure neuropathy is usually more of a problem than pain, it is tempting to speculate that predisposition to fractures may increase as proprioception is impaired alongside motor and other sensory dysfunction. Furthermore, neuropathy may accompany myopathy (e.g. triceps myopathy accompanied by radial neuropathy), in which case pain and lameness or weakness may influence the outcome, as well as potentially increase the likelihood of a long bone fracture.

Facial neuropathy is another form of peripheral neuropathy and is usually unilateral. It rarely results in mortality, but morbidities such as impairment of food prehension and/or ocular protection may warrant supportive treatment.

Pure peripheral neuropathy usually results from neural trauma or ischaemia (caused by contusion, compression or stretch) and therefore careful patient positioning and padding, as well as good neural oxygen delivery (avoiding hypotension and hypoxaemia), should help to prevent it (Dyson et al. 1988; Johnson 1993). Over-extension of the head and neck during dorsal recumbency has been mooted as a cause of bilateral recurrent laryngeal nerve paresis or paralysis attributable to the stretching of these nerves, but the aetiology has not been fully determined (see below).

Post-anaesthesia respiratory obstruction

Post-anaesthesia respiratory obstruction (PARO) has been reported in several studies but at varying frequencies, including 3.7% in CEPEF (Johnston et al. 2002), 0.04–1.4% (Thomas et al. 1987), 0.3–1.5% (Senior et al. 2007), and 0.3% (Dugdale et al. 2015). This may reflect individual hospital-dependent factors, but may also refer to the inclusion of both non-fatal and fatal cases, which is not always clear in the published reports.

Horses are obligate nose-breathers and hence nasal mucosal congestion and dorsal displacement of the soft palate after tracheal extubation are common causes of transient upper respiratory tract partial obstruction during recovery from anaesthesia. These are usually easily recognized soon after tracheal extubation (by stertor), and most cases can be quickly remedied (by placing a nasopharyngeal or nasotracheal tube, or replacing the orotracheal tube, until the congestion resolves), negating fatal consequences. Prophylactic topical nasal decongestants (e.g. phenylephrine) administered before the horse enters the recovery box are

effective, although the timing of application of the decongestant is important (Lukasik et al. 1997).

Lethal consequences of PARO may follow severe (complete or near-complete) respiratory obstruction caused by either physical hindrance (e.g. secondary to nasal mucosal congestion or nostril occlusion if a patient becomes awkwardly positioned during recovery), or laryngospasm or bilateral laryngeal paresis or paralysis (Dixon et al. 1993). Severe respiratory obstruction rapidly (within one or two attempted breaths) causes pulmonary oedema by two mechanisms: negative intrapulmonary pressure (generated during frantic, stridorous inspiratory efforts), and neurogenic influences (the hyperadrenergic state created by a massive sympathetic response to profound hypoxaemia, hypercapnia and distress results in increased pulmonary capillary pressure and permeability) (Lang et al. 1990; Tute et al. 1996). Copious pink and frothy fluid emanates from the nostrils and mouth (during or shortly after relief of the obstruction) and the condition requires immediate treatment as soon as it is recognized to try to prevent fatality.

Factors suggested to be linked to PARO include stretch or ischaemia of the recurrent laryngeal nerves (secondary to head and neck over-extension during dorsal recumbency, especially that which is prolonged), hypoxaemia and prolonged anaesthetic duration (Thomas et al. 1987; Abrahamsen et al. 1990; Ball & Trim 1996). Although intra-laryngeal nerve damage has been considered unlikely, the exact aetiology remains to be determined (Rooney & Delaney 1970; Goulden et al. 1975; Holland et al. 1986; Thomas et al. 1987; Heath et al. 1989; Abrahamsen et al. 1990; Dixon et al. 1993; Ball & Trim 1996; Tute et al. 1996; Bradbury et al. 2008).

Although any nostril occlusion-type obstruction is likely to be witnessed during recovery, safe intervention is not always possible. By contrast, respiratory obstruction associated with suspected bilateral recurrent laryngeal nerve paresis or paralysis tends to be delayed in onset

and may not be witnessed in time to instigate treatment. Obstruction has been reported to occur some time (minutes to hours) after the horse has stood up (without incident), and appears to coincide with the need for increased respiratory effort (Southwood et al. 2003; Southwood 2004; Dugdale et al. 2015). This increased respiratory effort may simply derive from attempts to whinny to horses walking past the recovery box, or, more alarmingly, from attempts to vocalize to neighbouring horses made while the patient is being led back to its stable. This latter situation on the yard often occurs a long way from help, equipment and drugs; hence, treatment may be delayed, with fatal consequences (Dugdale et al. 2015).

Risk factors associated with mortality

Several published studies of equine anaesthesia-associated mortality have reported a variety of risk factors which, if amenable to manipulation, may help to reduce mortality (Table 1). The most commonly reported risk factors have been American Society of Anesthesiologists (ASA) physical status, age, surgery type (especially emergency abdominal and internal fracture fixation), prolonged duration of anaesthesia and out-of-hours surgery (Tevik 1983; Young & Taylor 1990, 1993; Johnston et al. 1995, 2002, 2004; Mee et al. 1998a, b; Chie Niimura et al. 2015; Dugdale et al. 2015).

ASA physical status

Worsening physical status (ASA grade) has long been associated with an increased risk for mortality (Tevik 1983; Mee et al. 1998a, b; Johnston et al. 2004; Dugdale et al. 2015). Although horses suffering from colic with attendant hypovolaemia and endotoxaemia are readily assigned the higher ASA grades, Bidwell and colleagues (2007) reported increased mortality in horses presenting with pyrexia and/or increased white blood cell counts. These latter indicators of ill health may be either misinterpreted (e.g. pyrexia may be attributed to

stress or anxiety), or undiscovered (e.g. if full haematology does not form part of the pre-anaesthetic assessment in animals otherwise perceived as healthy), resulting in the assigning of falsely low ASA grades. Mares in the last trimester of pregnancy are also at increased risk for mortality and are often assigned higher ASA grades in view of their reduced physiological reserves during late gestation (Johnston et al. 1995). Brood mares, especially older and multigravida mares, appear to be particularly prone to long bone fractures, probably because of osteopaenia (Glade 1993; Johnston et al. 1995). In addition, heavily pregnant mares may present with signs of colic and/or exhaustion as a result of dystocia or other abdominal crises, which require emergency surgery, commonly outside of normal working hours.

Age

The association of older age with increasing risk for mortality has been reported in several studies (Johnston et al. 1995, 2002, 2004; Dugdale et al. 2015). However, CEPEF included sufficient younger animals to suggest that foals, particularly in the first month and if sick, were also at increased risk. This was especially clear if anaesthesia was induced with a volatile agent; halothane was the most commonly used agent at that time (Johnston et al. 1995, 2002, 2004).

Age may also influence fracture incidence during recovery because older animals are more likely to suffer comorbidities and to have osteoporosis, especially older brood mares (Jones 1989; Glade 1993). Furthermore, age may compound the effects of fatigue in older animals presenting for colic surgery (Johnston et al. 2002; Bidwell et al. 2007). Indeed, horses which suffer fractures in recovery do not all appear to have violent recoveries (Young & Taylor 1993). Hence, underlying muscle weakness or ataxia, of whatever cause, is thought to increase the torque experienced by the long bones which, in turn, may result in their structural failure.

Surgery type and recumbent position

Emergency abdominal surgeries and internal fracture fixation have been associated with greater mortality across a number of studies (Johnston et al. 1995, 2002, 2004; Dugdale et al. 2015). Part of this association, however, may reflect the prolonged anaesthesia time required by these more invasive surgical procedures (see below).

Mee et al. (1998a, b) reported mortality rates of 2.0% in non-colic emergencies and 4.3% in horses undergoing emergency exploratory coeliotomy. This greater mortality affecting horses with colic was considered a result of the probably pre-existing cardiovascular compromise and greater ASA grade. Although colic-related anaesthesia mortality seems to have improved more recently [1.6% (Dugdale et al. 2015)], this improvement may derive from the earlier referral of cases (fewer cases with high ASA grades), improved anaesthetic technique, and a greater incidence of intraoperative euthanasia based on increasing evidence regarding longterm prognosis (Proudman et al. 2002a, b, 2006). Colic cases with the poorest prognoses were more likely to be euthanized early in the course of anaesthesia; this would explain the association of non-resection colics and short periods of anaesthesia with increased mortality (Dugdale et al. 2015).

Dorsal recumbency, maintenance of anaesthesia with isoflurane or sevoflurane [compared with halothane, desflurane or total IV anaesthesia (TIVA); see below], and increasing age were initially associated with increased mortality in the recent Liverpool study, but these factors were also covariates with colic surgery (Dugdale et al. 2015). Confounding of dorsal recumbency and exploratory coeliotomy as potential explanatory or predictor variables for a poorer outcome has already been demonstrated in previous studies, which highlights the importance of multivariable statistical modelling for the interpretation of data (Johnston et al. 1995, 2002).

Recumbency has been variably linked with mortality and the dorsal position has usually been associated with the worst outcome (Johnston et al. 1995; Mee et al. 1998b; Dugdale et al. 2015). Recumbency is, however, a strong covariate of surgery type. Lateral recumbency and prolonged duration of anaesthesia were associated with increased risk for PAM, but not for mortality, in CEPEF-3 (Johnston et al. 2004) and were considered in detail by Young (1993).

Anaesthesia and surgery duration

Longer duration of anaesthesia has been associated with higher mortality in several studies [> 2 hours (Tevik 1983); 163 minutes *versus* 74 minutes (Young & Taylor 1990); > 2 hours and especially > 4 hours (Johnston et al. 1995)], possibly because it is linked with more complex surgical interventions. Two studies reported an association between a short duration of anaesthesia and increasing mortality, but this simply reflected early euthanasia in cases with poor prognoses (Mee et al. 1998b; Dugdale et al. 2015).

Longer anaesthesia leading to more time during which the concentration of anaesthetic in the brain is within a hypothetical 'ataxic range' would promote incoordination during recovery (Young & Taylor 1993). The generally shorter periods of anaesthesia (the majority were < 1 hour) reported by Bidwell et al. (2007) appear to have made a significant contribution to the relatively low immediate mortality (0.12%) identified by this group. By contrast with many other species, horses must stand up in the early postoperative period and there does not appear to be one fail-safe method to assist this process [for reviews, see Driessen (2005) and Clark-Price (2013)]. However, during the recent online survey conducted prior to CEPEF-4, a notable 40% of questionnaire respondents recorded the provision of some form of assistance during the recovery process (Wohlfender et al. 2015).

Out-of-hours procedures requiring general anaesthesia

Even after adjusting for emergency abdominal procedures such as colic-related interventions and Caesarean sections (i.e. in patients with higher ASA scores), mortality remained higher in out-of-hours procedures (Johnston et al. 1995, 2002). The recent attention to developing a 'safety culture' in the workplace has refocused attention on human factors. These include the reductions in vigilance, cognitive function and psychomotor skill performance (most notable at the time of a circadian nadir) associated with sleep deprivation, circadian rhythm disturbance and fatigue (Williamson & Feyer 2000; Ferguson et al. 2014). Around three-quarters of all critical incidents in aviation and anaesthesia are caused by human error and fatigue appears to contribute to the majority of these (Howard et al. 2002; Rampersad & Rampersad 2012). Longer-term consequences of shift work and chronic sleep deprivation include both mental and physical illness. We have, however, also to determine the impacts of anaesthesia and surgery on the patient at its own circadian nadir.

Although most of us have little control over our working days, recognition of one's own chronotype (morning lark or night owl), and awareness of the onset of one's own or others' fatigue can at least warn of the increasing level of risk associated with continued working. Fatigue can be assessed using the Samn Perelli Fatigue Checklist or the Karolinska Sleepiness Scale (Richter et al. 2005), the use of which may also increase the chance that team members will look out for one another (Caldwell et al. 2008; Toff 2010). In addition, tactics to help maintain vigilance are worth investigating and include strategies such as regular intake of healthy meals or snacks, regular intake of water to maintain hydration, intake of caffeine (although this may have only short-term effects as tolerance can develop), exercise if possible, napping if possible, the use of bright lights in theatre, the use of checklists and the use of appropriately set, alarmed monitoring devices (Ferguson et al. 2014; Gregory & Edsell 2014). The importance of teamwork and good communication was

emphasized in a special issue of the British Journal of Anaesthesia (Hardman & Moppett 2010) devoted to human factors. We should try to accept that we are all human, embrace modern, mindful views of 'professionalism' (Armitage-Chan 2014), and keep in mind this warning from Weinger & Ancoli-Israel (2002): 'Physicians must recognize that it is neither unprofessional nor weak to admit sleepiness or fatigue when on the job and make efforts to mitigate the potential consequences to patient care.'

Anaesthetic agents, techniques and monitoring

Although most of the patient- and surgery-related factors associated with mortality are not amenable to manipulation, anaesthetic-related factors may be. Mitchell (1969) suggested that premedication was beneficial and Johnston et al. (1995) reported that lack of premedication was associated with increased mortality. After cases of colic surgery and Caesarean section were excluded from analysis, Johnston et al. (2002) later reported that the inclusion of acepromazine reduced mortality.

Mortality was also reduced when TIVA was employed (Johnston et al. 2002; Bidwell et al. 2007; Dugdale et al. 2015). Although many instances of TIVA were likely to have been applied in less complicated procedures of relatively short duration, these are not universal features and may reflect a true benefit of injectable anaesthetic agents. In support of this, TIVA techniques have been associated with a reduced stress response (Taylor 1989, 1990; Taylor et al. 1995).

The protective effects of acepromazine presumably include its anxiolytic actions, which reduce circulating catecholamines that might otherwise favour the development of cardiac dysrhythmias. In addition, its mild sedative effects may reduce anaesthetic induction and maintenance requirements and may contribute to calmer recoveries. Benefit from acepromazine is also apparent when it is included in protocols in which α_2-agonists are used

(Marntell et al. 2005). In such circumstances, tissue perfusion is improved through enhanced cardiac output because of reduced systemic vascular resistance and increased heart rate. This potential increase in tissue oxygen delivery is probably somewhat offset by a reduction in haematocrit caused by the splenic sequestration of erythrocytes (Marntell et al. 2005), but this may improve blood flow as a result of the reduced viscosity (Stone et al. 1968; Spier & Meagher 1989). The reduction in haematocrit is probably attributable to both the acepromazine and the α_2-agonist (Parry & Anderson 1983; Kullman 2011). The reduction in systemic vascular resistance, however, may make hypotension more likely during anaesthesia (Parry et al. 1982).

Hypotension is a known causative factor for PAM and arterial blood pressure monitoring has been associated with a reduction in the severity of PAM; thus the importance of arterial blood pressure monitoring and support cannot be overemphasized (Young & Taylor 1993; Duke et al. 2006). Furthermore, arterial blood pressure monitoring appears to reduce mortality caused by intraoperative cardiac arrest (Johnston et al. 2004), possibly by increasing the vigilance of the haemodynamic status of the patient.

Although isoflurane has been found to be associated with a lower incidence of cardiac arrest than halothane, an apparent increase in the number of spinal cord malacia cases with isoflurane (compared with halothane) implies the absence of any overall difference in mortality between these two agents [CEPEF-3 (Johnston et al. 2004)]. Dugdale and colleagues (2015) reported greater mortality with isoflurane and sevoflurane in comparison with all other maintenance agents. This is most probably attributable to their more frequent general usage and a preference for their use over other agents in sicker horses undergoing long procedures.

Volatile anaesthetic agents are convenient for maintenance of prolonged anaesthesia, but the more fat-soluble compounds (halothane, sevoflurane) accumulate in adipose tissue and can

prolong recovery time (i.e. they have context-sensitive decrement times) in a manner somewhat reminiscent of the way in which injectable agents can accumulate (i.e. they have context-sensitive half times). Nevertheless, hepatic metabolism offers an alternative elimination strategy for halothane (of which ~ 20% is metabolized) and sevoflurane (of which ~ 2% is metabolized), which can, to some degree, offset the effect of their greater fat solubility on prolonging the recovery from anaesthesia. The hepatic metabolism of isoflurane (~ 0.2%) and desflurane (~ 0.02%) has a negligible effect on recovery. Volatile agents also produce marked dose-related cardiopulmonary depression and a related profound stress response. Despite the fact that the halo-ethers isoflurane and sevoflurane have replaced halothane (a halo-hydrocarbon) for anaesthetic maintenance, isoflurane in particular has been associated with poorer recovery quality compared with halothane (Grosenbaugh & Muir 1998; Matthews et al. 1998; Donaldson et al. 2000), and the quality of recovery following sevoflurane may not always be superior to that following isoflurane (Leece et al. 2008). The influence of desflurane, another halo-ether but with very low blood and fat solubility, on recovery quality has also been equivocal (Jones et al. 1995; Clarke et al. 1996; Tendillo et al. 1997; Valente et al. 2015). It seems that the replacement of halothane with halo-ethers, particularly isoflurane, has reduced the incidence of intraoperative cardiac arrest at the price of producing more complications during recovery, especially fractures, which currently appear to represent the leading cause of fatality.

The current vogue for ‘partial/supplemental IV anaesthesia’, which is intended to provide balanced anaesthesia and analgesia with better preservation of cardiopulmonary function and a less marked stress response, by using injectable agents to reduce the required dose of inhalation agents, also reflects efforts to improve the quality of recovery (Auckburally & Flaherty 2011; Gozalo-Marcilla et al. 2014, 2015). It remains to be seen, however, whether

this approach will reduce the morbidity and mortality associated with equine anaesthesia and surgery.

Larger volumes of intraoperative crystalloid fluid administration were associated with increased mortality in one study (Young & Taylor 1990), but prolonged duration of anaesthesia was also reported as a risk factor that would have influenced the total fluid volume administered. Nevertheless, excessive crystalloid fluid administration, resulting in widespread tissue congestion and oedema, is associated with increased human and feline morbidity (Holte et al. 2002; Grocott et al. 2005; Cotton et al. 2006; Brodbelt et al. 2007). Fluid therapy guidelines have been recently reviewed for small animals (Davis et al. 2013), and are currently under renewed scrutiny for people (National Institute for Health and Care Excellence 2013). Much of the debate regarding perioperative fluid therapy surrounds the interactions of different types of fluid with the endothelial glycocalyx and their immunomodulatory effects (Boldt 2000; Gosling 2003; Lang et al. 2003; Chappell et al. 2008; Muir 2009; Boldt & Ince 2010). Colloids, such as hydroxyethyl starches, and hypertonic saline can have useful effects in the face of a systemic inflammatory response, although the timing of administration may be important (Gosling 2003; Strandvik 2009). However, colloids, especially the hydroxyethylated starches, have recently been blamed for causing nephrotoxicity when used for haemodynamic support in critically ill humans, although they were, in these instances, used in huge, and repeated, doses (Chan et al. 1983; Allen et al. 1986; Mythen 2005; Brandstrup 2006; Lobo et al. 2006; Santry & Alam 2010; Nolan & Mythen 2013). Although colloids remain indicated for the treatment of acute hypovolaemia or oncotic support, the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency recommends monitoring renal function (Myburgh 2015). Nephrotoxicity may also result from the administration of crystalloid fluids containing high chloride concentrations, partly because the resultant

hyperchloraemia/hyperchloraemic acidosis causes renal vasoconstriction (Schneider & Bellomo 2013). For further information about current research and controversies in fluid therapy, the reader is referred to the various proceedings of the annual 'Great World Fluid Debates' held by the Congress in Evidence-Based Perioperative Medicine (EBPOM).

Recovery quality

Only one study has reported an association between recovery score and mortality (Young & Taylor 1990). This is probably because horses that die during anaesthesia or never stand up during recovery cannot be assigned a recovery quality score. Furthermore, although it is tempting to presume that the recovery of horses that suffer a catastrophic fracture must have been violent, this is clearly not always the case (Young & Taylor 1993). Only one other group has investigated recovery score as a potential factor influencing mortality, but found no association (Mee et al. 1998a, b), possibly because its analysis included intraoperative deaths. Recovery quality is influenced by the same factors that affect mortality [age, ASA physical status, surgery, body position, anaesthesia duration and out-of-hours surgery (Young & Taylor 1990; Taylor & Young 1993; Dugdale et al. 2015)]. Increasing body mass, which has been considered an important factor for some time (Johnston 1992), has recently been shown to be associated with recovery quality (Franci et al. 2006; Dugdale et al. 2015), as has horse temperament (Leece et al. 2008).

The longer the period of anaesthesia maintenance with volatile agents, the less likely the anaesthetic induction agents are to affect the course of anaesthesia and recovery (Taylor & Yong 1993). A recent abstract reported poorer recoveries in six horses when midazolam was used in conjunction with ketamine for anaesthesia induction than when propofol was used in conjunction with ketamine, before 1 hour of isoflurane anaesthesia (Jarrett et al. 2015). Poorer recovery scores following midazolam–ketamine anaesthesia inductions were

associated with a higher residual percentage of midazolam in the plasma at the start of recovery compared with propofol, but the dose of midazolam used (0.1 mg kg^{-1}) was also higher than is commonly described. The influence of sedative agents given at the time of premedication on recovery quality has yet to be fully determined, but TIVA techniques and sedation in early recovery may improve recovery quality (Santos et al. 2003; Ida et al. 2013; Woodhouse et al. 2013; Dugdale et al. 2015).

Conclusions

We are still a long way from greatly reducing the mortality associated with equine anaesthesia. Improvements have been made, such as in the monitoring and supporting of the cardiovascular system, so that anaesthesia itself is less likely to be fatal; however, we still lose horses after anaesthesia to a range of catastrophes that would not occur if the horse were not anaesthetized. Probably the most notable development is the increased emphasis on fractures that occur during the recovery period and necessitate euthanasia.

Authors' contributions

AHAD contributed to the preparation of the manuscript. PMT contributed to the preparation of the manuscript. Both authors contributed to the critical revision of the manuscript.

Conflicts of Interest

The authors have no conflicts of interest.

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864 Zink MC (1985) Postanesthetic poliomyelomalacia in a horse. Can Vet J 26, 275–277.

865 **Table 1** Mortality and reported risk factors associated with equine anaesthesia in studies published between 1969 and 2015, and morbidity

866 prevalence and associated risk factors in a four-centre UK study published in 2007

Study	Mortality	Causes of death	Excluded risk factors	Identified risk factors
Mitchell (1969) Single centre, included emergency and elective cases Exact postoperative follow-up time not documented (Data collected Jan 1962 to Dec 1969)	7/473 (1.5%) Deaths thought solely due to anaesthetic problems: 4/473 (0.85%)	Two cardiac arrests (one followed acepromazine premedication and thiopental induction; one followed promazine premedication and thiopental/suxamethonium induction) One chloroform overdose One malposition and occlusion of head/neck blood flow	No statistical evaluations performed; purely descriptive	Note that most procedures were of 20–50 minutes in duration Pre-anaesthetic medication was suggested to be desirable to smooth the anaesthetic process

		One paraplegic pony died under GA when manoeuvred, possibly as a result of disturbance of the fracture site One pathological femoral fracture and massive haematoma that developed during recovery following pelvic radiographs (horse severely lame beforehand) One pony with grass sickness had C-section for delivery of premature foal but died 24 hours later		

Tevik (1983) Single centre, included emergency and elective cases Time frame of postoperative horse observation not specified, but > 24 hours (Data collected 1965 to 1981)	33/1216 (2.7%) Anaesthesia considered main cause of 10 deaths occurring within first 24 hours of surgery 10/1216 (0.8%) However, a further eight animals died from PAM within the following 36–96 hours post-surgery: 18/1216 (1.5%)	*Deaths during anaesthesia and in the first 24 hours post-surgery:* CVR depression, *n* = 7 Cardiac arrest after suxamethonium administration, *n* = 2 Asphyxiation after ETT removed too early, *n* = 1 Others, *n* = 13 *Deaths > 24 hours post-surgery:* PAM, *n* = 8 Peritonitis, *n* = 1 Ruptured ventricle, *n* = 1	Age	Poorer ASA physical status Surgery/anaesthesia of > 2 hours 'Good risk' patients noted to be at particular risk for PAM

Young & Taylor (1990) (preliminary data) Single centre Time frame of postoperative horse observation not specified, but appeared to be up to 3 days	Overall mortality: 9/498 (1.8%)	PAM, *n* = 6 Neuropathy, *n* = 1 Fracture, *n* = 1 Halothane overdose, *n* = 1		Prolonged anaesthesia time (163 minutes for 'disasters' *versus* 74 minutes) Low pulse rate during maintenance (29 beats minute^{-1} *versus* 34 beats minute^{-1}) Low diastolic pressure Low breathing rate Age (10.4 years *versus* 6.1 years) Volume of crystalloids administered (7.7 L *versus* 1.4 L) Type of surgery Recovery quality Time to achieve sternal recumbency in recovery (43 minutes *versus* 28 minutes)
Young & Taylor (1993) (definitive data)	Overall mortality (colics excluded): 9/1314 (0.68%)	PAM, *n* = 6 (associated with re-fractures, *n* = 2) Cervical fracture*, *n* = 1	Factors investigated for potential associations with recovery score as an	Improved recoveries were noted to occur with: shorter GA duration; less invasive surgery (a covariate of the above); longer recovery time;

Single centre, excluded emergency colics Time frame of postoperative horse observation not specified, but appeared to be up to 3 days (Data collected 1984 to 1990)	Total morbidity: 19/1314 (1.4%)	Patella luxation*, *n* = 1 Femoral nerve neuropathy, *n* = 1 Transient (~ 2 hours) blindness, *n* = 1 Halothane overdose, *n* = 1 (Further cases of PAM recovered, *n* = 8) *Not noted as a particularly violent recovery	acknowledgement of the recovery phase as the period during which many problems arise or become apparent	lower pulse rate at induction, and higher pulse rate and breathing rate during maintenance Although treatment of hypotension had no effect on recovery quality or PAM occurrence, it did decrease the severity of PAM
Johnston et al. (1995) (preliminary CEPEF-1) Multicentre	All perioperative until 7 days post-surgery: 102/6255 (1.6%)	Not specified by cause	Sex Many breeds: Thoroughbreds; Thoroughbred crosses;	Age (foals aged < 3 months and horses aged > 12 years at increased risk compared with referent category of 2–4 year-olds) Last trimester of pregnancy associated with increased risk

Time frame of postoperative horse observation included the first 7 days post-surgery (Data collected Feb 1991 to Mar 1993)	Perioperative deaths until 7 days post-surgery, excluding emergency abdominal surgeries: 46/5220 (0.9%)		Warmbloods; Hunters; Arabs; ponies, and Shires	'Cob' breed associated with increased risk Emergency abdominal surgery associated with increased risk Internal fracture fixation associated with increased risk Dorsal recumbency associated with greater risk than either lateral* Duration of surgery (> 120 minutes and especially > 240 minutes increase risk)*† Out-of-hours surgery increases risk, especially during 18.00–09.00 hours compared with referent category of 08.01–13.00 hours* Season (Oct–Dec decreased risk compared with referent category of Apr–Jun) No premedication increased risk* Xylazine premedication increased risk*

				Acepromazine premedication appeared protective* Inhalation induction with halothane increased risk, especially in foals, compared with referent category of GG + thio Induction with GG + ketamine increased risk compared with referent category of GG + thio* *All potentially confounded by colics and emergency abdominal procedures †Fracture fixation surgeries are likely to confound anaesthetic duration
Mee et al. (1998a) Single centre, elective cases Horses followed post-surgery until hospital discharge	Elective cases (included some re-laparotomies) 8/1279 (0.63%)	Cannon bone fracture, *n* = 1 Postoperative haemorrhage at surgical site, *n* = 1	Age Sex Breed Use of horse Body mass Duration of anaesthesia	Physical status: increasing illness increased risk for mortality

(maximum of 3 weeks) (Data collected Feb 1991 to Dec 1995)	Anaesthesia alone blamed for 1/1279 (0.08%)	Repeat laparotomies with shock-related deaths, *n* = 3 Cardiac arrest possibly related to unforeseen hyperkalaemia, *n* = 1 Respiratory arrest at 8 hours after thoracotomy, *n* = 1 Intraoperative respiratory then cardiac arrest unresponsive to resuscitation, *n* = 1	Body position Recovery quality	
Mee et al. (1998b) Single centre, emergency cases	4/203 operable non-colic emergencies (2.0%)	*Emergency non-colic deaths:*	*Between non-colics and colics:* Age	*Between non-colics and colics:-* Physical status – increasing ASA grade increased risk of mortality

Horses followed post-surgery until hospital discharge (maximum of 3 weeks) (Data collected Feb 1991 to Dec 1995)	124/635 operable colics (19.5%)	Intraoperative cardiac arrest (ruptured bladder foal), *n* = 1 Postoperative haemorrhage (guttural pouch mycosis; pelvic abscess), *n* = 2 Unknown, died 5 days post-surgery for over-reach injury, *n* = 1 *Emergency colic intraoperative deaths:* Cardiac arrests, *n* = 13 Ventricular fibrillation, *n* = 2 Haemorrhage, *n* = 2	Sex Breed Use of horse Body mass Duration of anaesthesia Recovery quality *Within 'colics':* Age Sex Breed Use of horse Body mass Body position Recovery quality	Body position (but probably confounded by 'colic') *Within 'colics'* Physical status: increasing ASA grade increased risk for mortality. Duration of anaesthesia (short GA associated with higher mortality but confounded by early euthanasia of cases with poor prognoses)

		Emergency colic postoperative deaths: Failed to stand, *n* = 1 Shock, *n* = 12 Postoperative ileus, *n* = 1 Unknown, *n* = 3 *Emergency colic postoperative euthanasias:* Fractures in recovery, *n* = 2 PAM/N, *n* = 4 Shock, postoperative ileus, laminitis, *n* = 52 Peritonitis/rupture, *n* = 16 Diarrhoea, *n* = 6		

		'Unusual' causes, *n* = 10		
Johnston et al. (2002) (CEPEF-1 and 2) Multicentre Time frame of postoperative horse observation included the first 7 days post-surgery (Data collected Feb 1991 to Mar 1994 for CEPEF-1, and Apr 1994 to Feb 1997 for CEPEF-2)	All perioperative deaths up to 7 days post-surgery: 785/41,824 (1.9%) Perioperative deaths up to 7 days post-surgery, excluding emergency abdominal surgeries: 328/35,978 (0.9%) Perioperative deaths up to 7 days post-surgery in colics/emergency abdominal surgeries:	*Deaths in non-emergency abdominal surgeries:* Intraoperative cardiac arrest/postoperative CV collapse, *n* = 109 Fractures, *n* = 84 PAM, *n* = 23 Abdominal, *n* = 43 CNS/spinal cord malacia, *n* = 18 Respiratory complications, *n* = 12 Postoperative haemorrhage, *n* = 4 Found dead, *n* = 15	Sex Breed Body position (too many confounders) Season (too many confounders)	Age (< 1 month suggested to be associated with increased risk in abstract but not supported by statistical model; ≥ 14 years showed some increase in risk but not quite statistically significant; > 12 months to 5 years associated with least risk; referent category 5 years to < 14 years) Fracture repair surgeries associated with greatest risk compared with referent ENT surgeries Out-of-hours surgery (any time outside the referent category of 06.00–13.00 hours increased risk; but worst was 00.00–06.00 hours Acepromazine premedication suggestive of reduced risk but did not reach statistical significance

	457/5846 (7.8%)	Other, *n* = 20		TIVA protective but total inhalational technique associated with increased risk, when compared with referent category of IV induction with IH maintenance (TIVA anaesthetics tended to be of < 90 minutes in duration) Duration of anaesthesia was not modelled because of early intraoperative deaths in which cardiac arrest occurred. However, the authors suggest that prolonged procedures were associated with greater risks and internal fracture fixation surgeries are amongst the longest
Johnston et al. (2004) (CEPEF-3) Multicentre	All perioperative deaths up to 7 days post-surgery: 134/8242 (1.6%)	Cardiac arrests, *n* = 43 Fractures, *n* = 31 PAM‡, *n* = 10 Respiratory complications, *n* = 6		Physical status: worsening grade associated with increased risk for death and particularly for cardiac arrest Blood pressure monitoring reduced the risk for cardiac arrest-related death

Time frame of postoperative horse observation included the first 7 days post-surgery (Data collected May 1997 to Sept 1999)	Excluding emergency abdominal procedures, mortality: Unknown numerator and denominator (0.9%)	Abdominal, *n* = 17 CNS/spinal cord malacia, *n* = 5 Other, *n* = 22 ‡Non-fatal PAM was more common (*n* = 57)		Surgery type: emergency abdominal surgery associated with increased risk but fracture fixations associated with the highest risk of mortality Age: mortality was lowest overall in yearlings No overall difference between isoflurane and halothane for overall mortality or non-fatal perioperative complications, except: isoflurane was associated with lower overall mortality and fewer non-fatal perioperative complications in horses aged 2–5 years, and with fewer cardiac arrest-related deaths, especially for horses of worse physical status. However, isoflurane had an apparent association with an increased risk for CNS/spinal cord malacia-associated death

				Regarding PAM: increased duration (> 90 minutes) of anaesthesia and lateral recumbency increased risk
Bidwell et al. (2007) Single centre, included emergency and elective cases Horses were observed throughout the immediate recovery period and also for 7 days (Data collected 1997 to 2001)	21/17,961 (0.12%) Including those which died or were euthanized within 7 days of surgery: 42/17,961 (0.24%)	*Immediate perioperative deaths:* Intraoperative cardiac arrests, *n* = 10 (five sick foals, one sick mature horse, four athletic mature horses originally deemed healthy, although two had signs of mild infection preoperatively: two preceded by AV block, initially responsive to atropine; one preceded by	Only descriptive statistics performed	Authors warned of horses with preoperative evidence of systemic infection (pyrexia; increased white blood cell count) Majority of recoveries were rope-assisted but this did not always prevent problems Duration of most anaesthetics was < 60 minutes with a limited number of anaesthetic protocols No fatalities were reported for cases maintained by TIVA techniques It was noted that seven of the eight horses to suffer fractures were aged 9–18 years; three had presented for colic and three for dystocia. Body mass in these seven horses was 400–650 kg

		VPCs and ventricular tachycardia which became unresponsive to lidocaine; one arrested upon tracheal intubation) Fractures, *n* = 8 PAM/N, *n* = 3 *Deaths within the 7 days post-surgery:* Colon ruptures, *n* = 11 Peritonitis, *n* = 6 Uterine artery rupture, *n* = 3 Sepsis, *n* = 1		
Senior et al. (2007)	2/861 (0.2%)	*Mortalities:*		

Multicentre (all UK), excluded colics Horses were observed throughout the immediate recovery period and also for 72 hours post-surgery (Data collected Apr 2004 to Jun 2005)	The two fatal fractures occurred at one of the centres, for which the mortality rate was therefore: 2/257 (0.8%)	Fractures, *n* = 2 (one cervical spine, one humerus) *Morbidities:* PAC, *n* = 45 Prolonged recoveries, *n* = 37 (> 30 minutes hour^{-1} of GA) Thrombophlebitis, *n* = 8 Pyrexia, *n* = 6 Wounds sustained in recovery, *n* = 6 Lameness/PAM/N, *n* = 5 Carpal chip fracture, *n* = 1 Colitis/diarrhoea, *n* = 5		

		PARO, *n* = 3		
Dugdale et al. (2015) Single centre, included emergency and elective cases Horses were only observed throughout the recovery period, until they left the recovery box (Data collected May 2010 to end Dec 2013)	14/1268 (1.1%) overall mortality 7/782 (0.9%) for healthy, elective cases 7/450 (1.6%) for colic emergencies 0/36 (0%) for non-colic emergencies	*Mortality* *In healthy cases:* Fractures, *n* = 5 PAM, *n* = 1 Spinal cord malacia, *n* = 1 *In colics:* Fractures, *n* = 4 Carpal dislocation, *n* = 1 PARO, *n* = 2 *In non-colic emergencies:* 0	Breed Body mass Sex Note: increasing body mass was found to be a risk factor for poorer recovery quality	Physical status: increasing ASA grades associated with greater risk Age: increasing age associated with increasing risk Dorsal recumbency associated with increased risk compared with either lateral* Anaesthetic maintenance with isoflurane/sevoflurane increased risk compared with halothane, desflurane or TIVA* Shorter anaesthetic duration increased risk* Colic surgeries without resection were at greater risk* *Colic was a confounder of dorsal recumbency; colics were more likely to have had anaesthesia maintained with isoflurane or sevoflurane, and colics euthanized early during surgery, therefore

				without resections, confounded shorter duration anaesthetics *Worse recoveries were noted to occur with:* Greater ASA physical status* Increasing body mass† Short duration of anaesthesia* Out-of-hours anaesthesia *Age was a covariate of ASA physical status and colic surgery; cases with poor prognoses tended to be euthanized early under anaesthetic †Breed type was a covariate of body mass

ASA, American Society of Anesthesiologists [classification of physical status from 1 (healthy) to 5 (moribund and not expected to survive > 24 hours)]; AV, atrioventricular CEPEF, Confidential Enquiry into Perioperative Equine Fatalities; CNS, central nervous system; C-section, Caesarean section; CV, cardiovascular; CVR, cardiovascular and respiratory ENT, ear, nose, throat; ETT, endotracheal tube; GA, general anaesthesia; GG, guaiphenesin (pseudonym: glyceryl guaiacolate ether) IH, inhalation IV, intravenous; OOH, out of hours; PAC, post-

anaesthesia colic; PAM/N, post-anaesthesia myopathy/neuropathy; PARO, post-anaesthesia respiratory obstruction; TIVA, total intravenous anaesthesia; VPC, ventricular premature complex/contraction. *†‡Indicate associated information within the same row (study).