Clinical features and management of equine postoperative ileus (POI)

Clinical Features and Management of Equine Postoperative Ileus (POI): Survey of Diplomates of the European Colleges of Equine Internal Medicine (ECEIM) and Veterinary Surgeons (ECVS)

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Ethical considerations: The University of Edinburgh School of Veterinary Medicine Ethical Review Committee approval was sought and granted for this study; the only potential ethical issues that this study might have raised laid in the proprietary information about the participants and data protection. To palliate to this, the researchers have ensured that the data collected from the survey were encrypted and remained anonymous.

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Owner informed consent: N/A: See ethical considerations above. This study surveyed clinicians regarding their perceptions and experiences with equine postoperative ileus; as such it did not examine individual case details/records and accordingly owner informed consent was not applicable.

Summary:

Reasons for performing the study: There is a need for an improved understanding of equine postoperative ileus (POI), both in terms of clinical definition and optimal management. Although the pharmacological strategies that are used to treat POI continue to evolve, little is known about the supplementary strategies used to prevent and manage this condition.

Objectives: To report the current strategies used to diagnose, prevent and manage POI following emergency abdominal surgeries.

Methods: An electronic survey invitation was sent by email to 306 European college diplomates (European Colleges of Equine Internal Medicine, ECEIM n = 120, and Veterinary Surgeons, ECVS n = 186).

Results*:* The response rate was 33% (100/306). The median reported estimated incidence of POI was 10-20%. The presence of reflux on nasogastric intubation was the main criterion used to define POI. Lesions involving the small intestine (SI) were thought to be the leading risk factors for developing POI. Anti-inflammatory drugs, antimicrobial drugs and intravenous fluids were the primary preventative strategies when managing patients at high risk for POI. Flunixin meglumine and lidocaine (lignocaine) were the drugs most commonly used to treat horses with POI. Supplementary POI preventative and treatment strategies included control of endotoxaemia, fluid therapy, early ambulation and judicious timing of post-operative feeding.

Conclusions: Appreciation of the potential risk factors associated with the development of POI appeared to have an impact on the choice of management strategies that are implemented. The majority of ECEIM and ECVS Diplomates in the survey used

flunixin meglumine and lidocaine, often in combination to treat horses with POI, likely reflecting the contributory role of inflammation in its pathophysiology. Various supplementary strategies were used to prevent and manage POI risk factors intra- and post-operatively.

Introduction

Ileus is the functional inhibition of propulsive bowel motility and frequently occurs in the period following abdominal surgery[1]. Progressive motility through the intestines relies upon complex interactions between a series of neurologic, vascular, hormonal and neuromuscular pathways. In horses, disruption of one or more of these pathways can lead to intestinal stasis or ileus[2,3,4]. The reported incidence of equine POI ranges from 10%-47% of colic surgery cases (regardless of lesion site) with an associated mortality rate as high as 86%[2,3,5]. It is reportedly caused by local inflammation and impaired neuromuscular function following mechanical manipulation of the gut with associated risk factors including the site and severity of the intestinal lesion and the duration of surgery [3,6,7,8,9].

The clinical definition of equine POI constitutes a debate amongst veterinary surgeons, with current discussions highlighting the fact that a provisional diagnosis based on one criterion alone (i.e. the reflux volume) might lead to an over-diagnosis of this condition[10]. In 2008, new suggestions for the diagnosis of ileus and POI were put forward with the intention of identifying more definitive diagnostic criteria, possibly avoiding unnecessary repeat surgery and improving the chances of successful recovery from abdominal surgeries[10].

The inflammatory response and the intrinsic neuromuscular function responsible for motility are considered as the main targets for POI management. As clinical studies evaluating pharmacological treatments in equids and other species continue to provide valuable insights into their use and efficacy[4,6,11,12,13], limited information is available regarding the non-pharmacological supplementary strategies implemented for preventing and managing POI.

This current survey aimed to report the current strategies used to diagnose, prevent and manage POI following emergency abdominal surgeries. To update and expand on a study performed in 2004[13], the current study was designed to survey both internists and surgeons on a broader spectrum of POI management strategies as well as assessing their understanding of the clinical features of POI.

Material and methods

An electronic questionnaire using web-based proprietary software[a] was drafted and then piloted with a group of 6 surgeons and internists (not involved in preparation of the survey) to test for ease of use and question validation. Following adjustments, an invitation to participate in the survey was delivered via e-mail to all ECEIM (120) and ECVS (186) specialist veterinary clinicians listed under Large Animal Surgery (Total n= 306). A second and third reminder was sent at 2 weekly intervals if a response was not obtained. The responses included in this report are derived from fully completed questionnaires only. Individual responses were solicited; however it was possible that some practices were represented by one responder for the group. Ethical approval for the study was granted by the University of Edinburgh School of Veterinary Medicine Ethical Review Committee.

The questionnaire (see supporting information) consisted of 25 questions; open-ended (e.g. comments, descriptions) and closed-ended (e.g. Likert scales, multiple choices). The first set of questions aimed to determine the annual caseload and the cumulative incidence of POI following gastrointestinal (GI) surgery in the practice. The next series of questions identified the relative importance of different parameters used in the clinical definition of POI as well as the clinicians' opinions on factors contributing to POI. The participants were also asked about their own working definition of POI and whether protocols were in place in their institution for the pre-, intra- and postoperative prevention and treatment of POI. These were followed by questions about the clinicians' choices of POI pharmacological prevention and management strategies used in pre-, intra- and postoperative care. Other questions were designed to determine the additional and supplementary treatment modalities used to prevent and manage POI risk factors and whether and when a second laparotomy was considered.

Statistical analyses of the online survey included respondent numbers, percentages and frequency tables. Open questions comments were analysed by thematic analysis from which categories were generated. The percentages expressed in the results were rounded up to the nearest whole number. In order to facilitate further statistical analysis where necessary, data were exported into Minitab 16®[b]. Medians were calculated for the annual caseload and incidence of POI.

Results

Responses were obtained from 100 (48 ECEIM, 51 ECVS, 1 both colleges) out of the 306 invited participants (response rate = 33%). The median annual number of colic surgeries in the clinics of respondents was in the range of 41 to 60 (Figure1), with a median estimated POI cumulative incidence after colic surgery of 10-20% (Figure 2).

Fifty one percent of clinicians used a hospital/practice protocol for the definition of POI. The presence of reflux on nasogastric intubation was the main criterion (91% of respondents) used to define POI (Table 1) with a volume of >2 litres/hour (35% of respondents) on repeated intubation and ≥ 4 litres at any given intubation (31% of respondents) as the most common parameters adopted by clinicians when evaluating horses that reflux postoperatively (Figure 3).

Lesions involving the small intestine (SI) (73% of respondents) were considered 'extremely important' pre and intra-operative risk factors for developing POI (Table 2) with SI distension (74% of respondents) considered as the most important post-operative risk factor (Table 3).

The majority of respondents (64%) said that their hospital/practice used a set protocol to try to prevent POI, with anti-inflammatory drugs (96% of respondents), antimicrobial drugs (94%) and intravenous fluids (81%) being the primary POI preventative strategies, whereas the administration of opioid analgesics (49%) was used 'only in the minority of cases considered at risk for POI'. Flunixin meglumine (76% of respondents) and lidocaine (lignocaine) (50%) were the drugs most commonly used intra-operatively in surgical colic cases. Both flunixin meglumine (87% of respondents) and lidocaine (67%) were also drugs most commonly used predominantly postoperatively to prevent the development of POI, followed by butorphanol (39% of

respondents), metoclopramide (36%), erythromycin (27%), morphine (25%) and neostigmine (21%).

The majority of clinicians (72%) followed a hospital/practice protocol for the treatment of cases that have developed POI. Lidocaine (79%), flunixin meglumine (78%) and heparin (20%) were the main drugs used to treat POI "in all POI cases", followed by metoclopramide (27%) and polymyxin B (20%) "in a majority of POI cases" and by the opioids butorphanol (45%) and morphine (24%) ''in a few POI cases''.

When asked specifically about non-steroidal anti-inflammatory drugs (NSAIDs), flunixin meglumine (90% of respondents) was the most commonly selected in the treatment of horses with POI.

In an open question about their lidocaine dosage regimen in the treatment of POI, 98 respondents commented (2/100 respondents choose not to comment); the most common dosage strategy was bolus followed by continuous infusion (69/ 98 respondents) at doses of 1.3 mg/kg bolus with 0.05 mg/kg/min infusion (45/98 respondents). The second most common strategy was lidocaine by infusion at a rate of 0.02-0.05 mg/kg/min (10/98).

Comments about supplementary strategies used to prevent intra-operative risk factors for POI or other complications included: the prevention of post-operative adhesions (80%) with carboxymethylcellulose and careful/minimal manipulation of the gut, the prevention of inflammation (67%) with anti-inflammatory drugs, and the prevention of infection (76%) with antibiotics (used both intravenously and for intra-abdominal lavage).

The supplementary postoperative strategies to prevent and manage POI were, in decreasing order of frequency: decompression with nasogastric tube (93%), hand-

214 walking exercise (86%), use of antibiotics (85%), judicious timing of feeding (85%),
215 control of endotoxaemia (83%), fluid therapy (71%) and other strategies (25%). When
216 asked to comment further on the 'judicious timing of feeding', the respondents (91)
217 stated: feeding within 12-24 hours or as soon as possible or in small amounts at
218 first/grazing (47/91), feeding at 24-48 hours postoperatively (14/91), feeding when no
219 signs of reflux are apparent or when motility was regained (11/91), use hay net outside
220 the stall /or muzzle (4/91).

221 The majority of clinicians aimed for maintenance rates in fluid therapy (64%), and
222 most (81%) used polyionic resuscitation fluids. When adding supplements to fluids, the
223 most common were: magnesium (76% of respondents), calcium (67%), and potassium
224 (59%). In the post-operative period, most clinicians (70%) placed the nasogastric tube
225 only as required. In POI cases, 26% of respondents used total parenteral nutrition
226 (TPN) in a few cases, 73% of respondents never used TPN and 51% used partial
227 parenteral nutrition (PPN), but only in a few cases.

228 In POI cases, the majority of clinicians (88%) said they would consider a second
229 (laparotomy) surgery. If clinicians decided to perform a second surgery, 46% of those
230 expressed their preference as operating within 2 to 4 days following the first surgery.

231

232 **Discussion**

233 The overall response rate of 33% was deemed satisfactory when considered in light of
234 response rates between 13 and 52% from surveys performed on similar populations in
235 the past 10 years[13,14,15,16] and was considered to accurately reflect the views of the
236 overall population approached at the outset (within a 90-95% confidence interval).

Respondents were recruited exclusively from members of speciality colleges to ensure that clinics with accredited expertise only were included.

Accurate phenotypic definition is essential if meaningful conclusions are to be drawn from any disease-related study. Although the results of the current survey failed to support the adoption of a universal definition of POI amongst respondents, the most commonly employed criterion was the presence of reflux on nasogastric intubation, in agreement with the results of previous studies[2,10,17]. This criterion was followed by, in order of decreasing frequency, ultrasonographic evidence of small intestinal distension, mild to severe abdominal discomfort, tachycardia, transrectal palpation of small intestinal distension and the absence of intestinal sounds, inclusion criteria which may reflect their increased use in the definition of POI as suggested by Merritt & Blikslager (2008)[10]. Also, respondents used different reflux volume criteria to diagnose POI. Although the majority used a volume of >2 litres/hour on repeated intubations or ≥4 litres at any given intubation as their definition of POI, one quarter of respondents defined POI based on a reflux volume of > 2 litres at any given intubation, a definition which likely dates back to some of the earliest definitions reported in the literature[2,17]. Although this early reported criterion could contribute to an overdiagnosis of the condition[10], median range of POI prevalence (10-20%), based on the responses, were similar to the ranges derived from previous studies (18.4-21 %)[2,3] on POI after small and large intestinal colic surgery.

Despite the limitations of survey-based questionnaires, the methodology used was considered to be appropriate to fulfil the objectives of this study. Also, the substantial reduction in response rate to a request for more factual data (i.e. clinical audits, case details etc.) often results in incomplete data sets and lower inclusion numbers[18].

It is recognised that clinicians may be guided and informed by their knowledge of the literature on POI. In order to minimize the influence of this information obtained from the literature pertaining to different specialties and focus more on the clinical experience of the respondents, this survey pooled and summarized perceived best practice from experts in both medicine and surgery.

This survey provided additional information on the clinicians' perception of the relative importance of the factors contributing to POI. The most important pre- and intra-operative factors were lesions involving the small intestine, intestinal resection and anastomosis, endotoxaemia and extensive bowel handling. The most important post-operative factors were small intestinal distension, inflammation and postoperative adhesions. The administration of opioids in the pre-, intra- and/or postoperative periods was largely perceived as "not very important" as a risk factor for the development of POI [see table 3], and this is consistent with a lack of published data currently to identify this as a risk in horses.

Despite the lack of an overall consensus on management recommendations in the equine clinical literature for peri-operative care in relation to abdominal surgery, the survey results supported a tendency amongst the respondents to follow a defined hospital/practice protocol for the prevention and particularly the management of POI. Whether or not such a protocol is in place, the management approach to POI amongst the respondents largely fell into 2 categories: pharmacological intervention and supportive care. Consistent with previously reported results[13] and despite the conflicting evidence in the literature relating its prokinetic properties, lidocaine was the most common choice under 'prokinetic' drugs. The administration protocols (i.e. bolus IV with continuous infusion; 69 respondents) and dosage regimens (i.e. 1.3 mg/kg IV with continuous infusion 0.05mg/kg/min; 45 respondents) were comparable to those

mentioned in other studies[13]. Other prokinetic drugs used intra- or post-operatively in an attempt to prevent POI included, in a decreasing order, metoclopramide, erythromycin and neostigmine, findings which were consistent with the study of Van Hoogmoed et al, although that particular study revealed erythromycin to be second to lidocaine as the most popular choice[13].

The use of anti-inflammatory drugs was a more commonly adopted means of POI prevention compared with prokinetic drug use. The common use of flunixin meglumine, a potent non-steroidal anti-inflammatory drug with a specific indication for the treatment of pain associated with gastrointestinal inflammation[21], likely reflects the perception that inflammation plays a key role in the development of POI. Indeed, for a number of years, research has highlighted the pivotal role of intestinal inflammation in the pathophysiology of POI[9]. Little variation was evident in relation to the doses of flunixin meglumine used (1.0-1.1mg /kg IV; 43% of respondents) and the dosing regimen employed (q8h to q12h).

In the human literature, the Enhanced Recovery After Surgery (ERAS) Group recommended the use of NSAIDs and the avoidance of opioids for peri-operative analgesia, to preserve gastrointestinal motility[22]. This present survey demonstrated that the majority of clinicians failed to perceive the use of opioids pre-, intra-, and post-operatively as constituting an important risk factor for POI, even employing their use as part of preventative and treatment strategies. Although no definitive conclusions on the risks and benefits of opioid treatment can be drawn from this study, it was noted that 87% of the respondents that reported a POI incidence greater than the median range of 10-20% used opioids as a prevention or treatment strategy. Indeed, a number of equine studies have demonstrated that the μ-opioid receptor antagonist (naloxone)[c] to have a stimulatory effect on large intestinal motility[23,24,25]. Furthermore, alvimopan

311 (Entereg ®)[d], a selective μ-opioid receptor antagonist, is an emerging treatment for
312 human POI [11] and is recommended for the perioperative management of intra-
313 abdominal surgeries[22]. Such classes of drugs were not used as POI prevention or
314 management strategies by the majority of respondents (75%).

315

316 In addition to prokinetic and anti-inflammatory drug use, supportive care constituted a
317 significant component of POI treatment. Intravenous fluid therapy forms the mainstay
318 of such support; however differences between respondents were evident with regard to
319 the volume administered. The majority of respondents (64%) provided fluid
320 maintenance requirements, with almost one third administering volumes in excess of
321 maintenance requirements. With regard to electrolyte supplementation, the survey
322 results showed that the majority (81%) of respondents supplemented the polyionic
323 fluids with calcium borogluconate, magnesium sulphate and potassium chloride when
324 indicated by the results of blood electrolyte analysis. Magnesium and calcium (76 and
325 67% of respondents, respectively) were supplemented more commonly than potassium
326 (59% of respondents). Horses that have surgical colic often present peri-operatively
327 with magnesium and calcium concentration levels lower than normal ranges; this is
328 especially true in horses with strangulating GI lesions [26]. Low ionised calcium
329 concentrations in venous blood have been associated with both a greater risk of POI and
330 fatality in hospitalised colic cases [26,27].

331 Nasogastric intubation in equine POI is required and the majority of respondents (70%)
332 elected to place the nasogastric tube only “as required” after surgery. This approach in
333 equine patients may have been adopted due to a perceived association between the
334 presence of in-dwelling tubes and POI, despite several equine studies failing to identify

335 such a practice as a common risk factor for postoperative complications related to colic
336 surgeries[5,17,20].

337 Approximately half of the respondents considered the timing of feeding following
338 surgery to be “quite important” with regard to its contribution to the development of
339 POI. Further comments indicated that postoperative feeding should only start after
340 resumption of normal peristaltic function and be implemented in small amounts at first
341 (e.g. start with handful of grass/hay). Some respondents commented that they hang hay
342 nets outside the stall, a ‘sham feeding’ strategy in some ways akin to giving chewing
343 gum to human patients in early recovery, a practice thought to stimulate vagal
344 activity[28].

345 With regard to nutritional support during necessary periods of starvation, the survey
346 revealed that the majority of clinicians seldom use parenteral nutrition (PN). Fifty one
347 percent used partial PN “in a few POI cases” and 73% “never use” total PN. It is likely
348 that the selection of the few cases which receive PN is based on a variety of criteria,
349 including duration of POI and consequently starvation. One study showed that the
350 routine post-operative use of PN had no beneficial effect on either time of first oral
351 feeding, duration of hospitalization or short-time survival in 30 horses recovering from
352 strangulating SI resection and anastomosis[29]. The high costs associated with PN were
353 also identified as a limiting factor to its use in comments by 11 respondents.

354

355 It has been suggested that the compelling evidence for the beneficial effects of early
356 ambulation on tissue recovery postoperatively in human medicine could be applied to
357 equine medicine[30]. Although the potential benefits of such a practice remain

358 unknown, 86% of respondents in the current survey did adopt hand walking as an early
359 post-operative care strategy aimed partly at minimising the risk of POI.

360 Results from this current survey showed that the majority of respondents would
361 consider a repeat laparotomy (88%) as part of their therapeutic approach to POI, with
362 46% of those advocating such an approach within a 2 to 4 day timeframe following the
363 first surgery in refractory cases. Despite the reported low short-term (36.4%) and long-
364 term (22.2%) survival rates associated with a repeat laparotomy[31,32], there are
365 diagnostic, prognostic and therapeutic advantages of this approach. Additionally, seven
366 respondents commented on the importance of small intestinal and caecal decompression
367 as a means of reducing risk of POI, rating them as either 'extremely' or 'quite
368 important'. Clinical reports also exist which support the benefits of small intestinal
369 decompression in cases of POI[5,33].

370 In conclusion, this survey highlighted a variety of issues in relation to equine POI.
371 Firstly, there is a requirement for a more precise definition of the condition, the
372 universal adoption of which may help to characterize the syndrome more fully.
373 Secondly, there appears to be good awareness within the European specialist colleges,
374 of published risk factors for POI which are used to different degrees in the design of
375 POI preventative protocols at the practice/hospital level. However, a more universally
376 adopted approach, based on these factors, could form the basis of a more standardised
377 treatment protocol that could then be objectively assessed in future prospective studies.
378 Thirdly, there is good agreement amongst specialist equine clinicians with regard to the
379 appropriate treatment of POI; however there remains a need to critically assess the
380 effectiveness of such therapeutic approaches on a wider multi-centre scale.

381

Manufacturer's address:

[a] Survey Monkey® , Palo Alto, California, USA.

[b] Minitab 16®, State College, Pennsylvania, USA.

[c] Naloxone was developed by Sankyo in the 1960s, the patent has expired. It is available in generic form.

[d] ENTEREG®. Cubist Pharmaceuticals, Inc.; Lexington, MA

Supporting item: Survey questionnaire

Figures:

Figure 1: ECVIM and ECVS Diplomates' approximate annual number of colic surgeries in practice from an online questionnaire of the Clinical Features and Management of Equine Postoperative Ileus, completed by 100 respondents

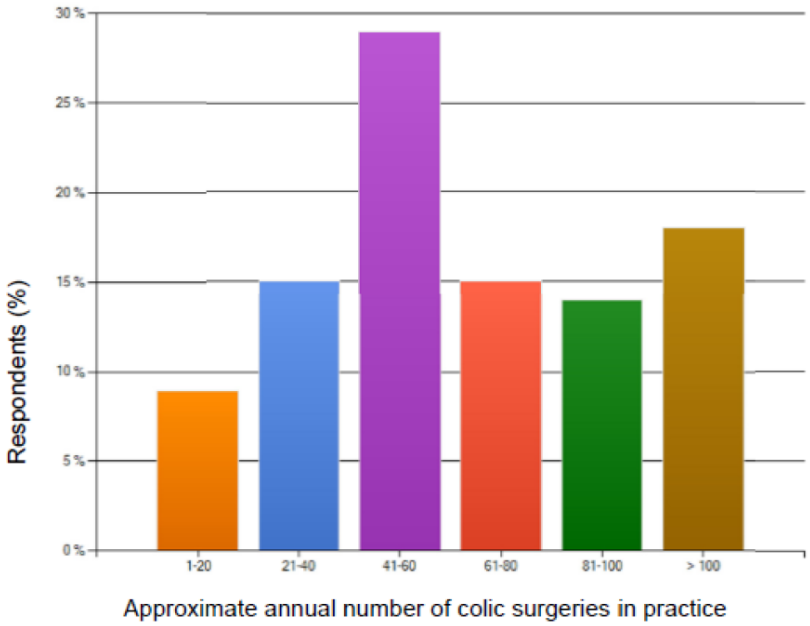


Figure 2: ECVIM and ECVS Diplomates' estimated incidence (%) of POI cases in practice from an online questionnaire of the Clinical Features and Management of Equine Postoperative Ileus, completed by 100 respondents

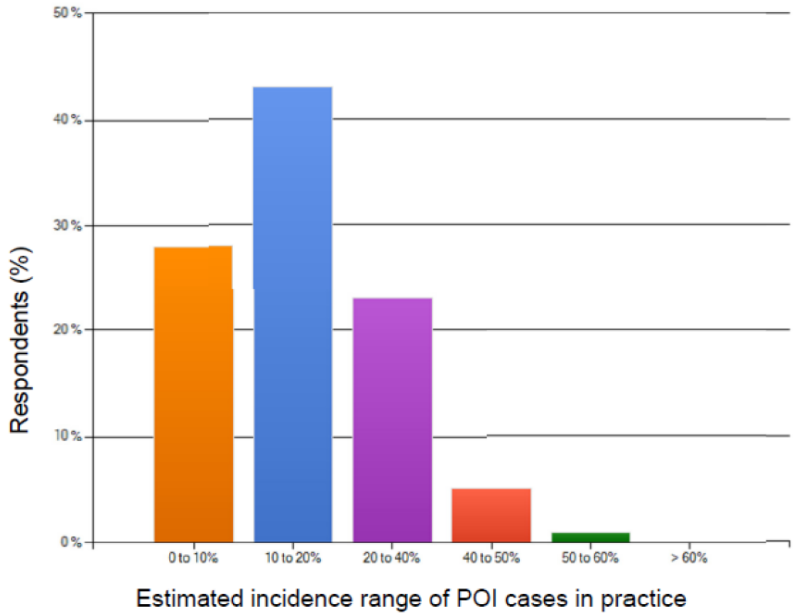
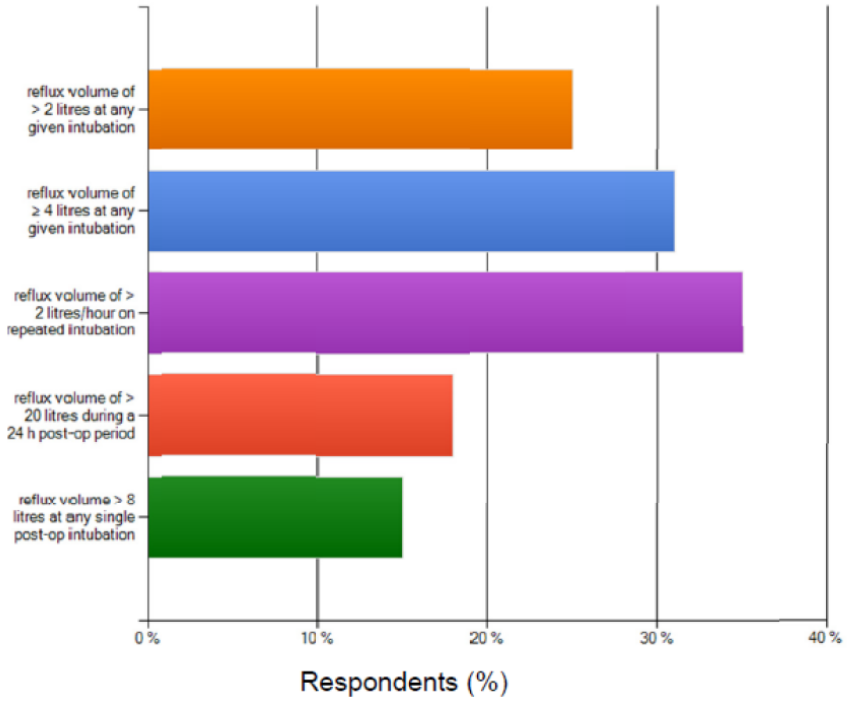


Figure 3: ECVIM and ECVS Diplomates' postoperative reflux volume corresponding most to respondents' own working definition of POI from an online questionnaire of the Clinical Features and Management of Equine Postoperative Ileus completed by 100 respondents.



TABLES:

TABLE 1: ECVIM and ECVS Diplomates' rating of the importance of different parameters in the diagnostic classification of POI from an online questionnaire of the Clinical Features and Management of Equine Postoperative Ileus, completed by 100 respondents

Parameter	% of respondents rating factor as 'Extremely Important'	% of respondents rating factor as 'Quite Important'	% of respondents rating factor as 'Not very Important'	% of respondents rating factor as 'Not important at all'
Presence of reflux on nasogastric intubation	**91**	9	0	0
Ultrasonographic evidence of multiple fluid distended small intestinal bowel loops	**68**	29	3	0
Evidence of multiple fluid distended small intestinal loops on rectal examination	**47**	42	11	1
Deterioration of cardiac parameters (tachycardia)	35	**50**	15	1
Absence of gut sounds	22	**46**	31	4
Mild to moderate signs of abdominal discomfort	21	**61**	16	3
Fever	3	14	**63**	31

Bolded: most common answer(s)

TABLE 2: ECVIM and ECVS Diplomates' rating of the importance of potential pre- and intraoperative risk factors for the development of POI from an online questionnaire of the Clinical Features and Management of Equine Postperative Ileus, completed by 100 respondents

Risk factor	% of respondents rating factor as 'Extremely Important'	% of respondents rating factor as 'Quite Important'	% of respondents rating factor as 'Not very Important'	% of respondents rating factor as 'Not important at all'
Lesions involving the small intestine	**73**	26	1	0
Intestinal resection and anastomosis	**59**	35	6	0
Endotoxaemia	**50**	46	4	0
Increased amount of bowel handling	**49**	40	11	0
Long-time course between referral and admission of colic case	39	**48**	12	1
Long anaesthesia and surgery duration	32	**50**	16	2
Increased packed cell volume (PVC) at admission	19	**44**	31	4
Increased blood lactate level pre-op	16	**62**	22	1
High albumin and protein serum concentration pre-op	4	32	**59**	5
Administration of opioids as pain medication pre and/or intra-op	3	9	**55**	32

Bolded: most common answer(s)

TABLE 3: ECVIM and ECVS Diplomates' rating of the importance of potential postoperative risk factors for the development of POI from an online questionnaire of the Clinical Features and Management of Equine Postoperative Ileus, completed by 100 respondents

Risk factor	% of respondents rating factor as 'Extremely Important'	% of respondents rating factor as 'Quite Important'	% of respondents rating factor as 'Not very Important'	% of respondents rating factor as 'Not important at all'
Small intestinal distension	**74**	26	0	0
Inflammation	**65**	31	3	1
Post-op adhesions	**40**	36	21	3
Abdominal pain	20	**60**	18	2
Gastric distension	26	**58**	12	4
Interval to commencement of post-op feeding	14	**53**	25	8
Infection	24	**48**	27	1
Postoperative pain medication (opioids)	7	22	**59**	12
Interval to commencement of post-op exercise	5	27	**43**	25
Volume and type of intravenous fluids given	10	37	**43**	10

Bolded: most common answer(s)

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