Closure of the epiploic foramen in the horse: an anatomical and clinical study

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In memory of

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List of abbreviations

μg	microgram
μL	microliter
μm	micrometre
3D	three-dimensional
AST	aspartate aminotransferase
BPM	beats pro minute
bwt	body weight
CI	confidence interval
cm	centimetre
EFE	epiploic foramen entrapment
FEMC	foramen epiploicum mesh closure
GGT	ɣ-glutamyltransferase
h	hour
HE	haematoxylin-eosin
HR	hazard ratio
IM	intramuscular
IU	international unit
IV	intravenous
kg	kilogram
L	litre
m	metre
mg	microgram
min	minute
mL	millilitre
mm	millimetre
mmHg	millimetres Mercury
OR	odds ratio
PCV	packed cell volume
POI	post-operative ileus
POC	post-operative colic
POR	post-operative reflux
RR	respiratory rate
s.d.	standard deviation
SAA	serum amyloid A
WBC	white blood cells

CHAPTER 1

General introduction and background of the thesis

“Winslow Foramen”, “Omental Foramen” or “Epiploic Foramen”?

In the Illustrated Veterinary Anatomical Nomenclature edited by Constantinescu and Schaller, which is widely considered “the bible of anatomical definitions” in the veterinary anatomical community, the “omental foramen” [epiploic foramen] is defined as *“the opening from the greater peritoneal sac to the omental vestibule that passes between the caudal vena cava dorsally, the portal vein that is included in the hepatoduodenal ligament ventrally, the caudal lobe of the liver cranially, and the pancreas caudally”* (Constantinescu and Schaller, 2012).

This slit-like opening is called the “Winslow foramen” in human literature, named after the French-Danish doctor and anatomist Jacob alias Jacques-Bénigne Winslow (1669-1760) who first described this enigmatic structure (Bellary et al., 2012). He was born in Denmark and was very dedicated to the Lutheran faith, as was the family tradition. During his theology studies he met a medical student with whom he frequently had long spiritual conversations. Winslow’s interest for medical studies emerged from these conversations and he decided to study medicine, whereas his friend was converted to theology studies. The name of his friend remains unknown in history, but the medical world owes one of the most famous anatomists to him (Orly, 1996; Bellary et al., 2012). Winslow’s ambitions brought him to Holland and later on to Paris. As a member of the Lutherian community he was financially supported for his studies not only by his family but also by the Danish Crown. However, in Paris he renounced his Lutheran faith for Catholicism under influence of the famous bishop of Meaux, Jaques Bénigne Bossuet (1627-1704), whose name he adopted from that moment on. Due to this conversion, he lost his scholarship and his family disowned him. However, from that moment on, he received contributions to support his study and work from Catholic patrons in Paris, which allowed him to build a very prolific career with numerous professional achievements (Bellary et al., 2012). He received his MD degree in 1703, was admitted in the “Académie des Sciences” in 1707, and 25 years later, he succeeded François Joseph Hunault to the chair of anatomy of the “Jardin du Roy”, which he held until 1758 (Orly, 1996).

Figure 1: Stipple engraving of Jacques-Bénigne Winslow. (Collection of the « Bibliothèque interuniversitaire de santé, Paris ».)

In 1715, Winslow described the aperture (foramen) which connects the greater and lesser sacs of the peritoneal cavity, and now bears his name. He published the first edition of his seminal work *“Exposition Anatomique de la Structure du Corps Humain”* in 1732. His work was recognized as the first anatomical treatise of descriptive anatomy, without addition of physiological details and hypothetical explanations beyond the scope of an anatomy text (Bellary et al., 2012). This manual started a new generation of anatomical handbooks influencing many anatomists all around Europe (Orly, 1996). It also included a description of the sympathetic nervous system which had a significant influence on the understanding of this controversial part of the nervous system (Orly, 1996).

The term “Winslow foramen” is not commonly used in veterinary medicine, despite Jacques-Bénigne Winslow’s enormous contribution to medical development. The term “epiploic foramen” is still accepted as an official alternative in the revised version of the 6th edition of the *Nomina Anatimica Veterinaria/NAV* [mentioned between square brackets] although “omental foramen” is preferred (World Association of Veterinary Anatomists, 2017). In fact “*épiploon*” is a synonym for “*omentum*”, and is used basically in Latin languages as for example French or Spanish.

Equine clinicians continue to use the term “epiploic foramen” despite the preference for “omental foramen” in the veterinary anatomical community. It was decided to use “epiploic foramen” throughout this text as the work was mainly conducted in light of clinical applications, and international veterinary clinical journals and literature do not accept “omental foramen” yet as the new terminology instead of “epiploic foramen”.

Embryologic development of the stomach and omenta in mammals

The complex positioning of the minor and major omenta and the epiploic foramen can be better understood when embryologic development of the region is considered (Figure 2). During embryonic development the stomach is suspended between the dorsal mesogastrium containing the developing spleen and the ventral mesogastrium containing the developing liver (Noden and De Lahunta, 1985; McGeady et al., 2006). The ventral mesogastrium anchoring the stomach at the level of the minor curvature, and the dorsal mesogastrium suspending the stomach at the level of the major curvature, undergo positional changes during the rotation of the stomach in the developing embryo (Noden and De Lahunta, 1985; McGeady et al., 2006). The dorsal mesogastrium lengthens considerably and displaces to the left together with a 90° left shift of the greater curvature and subsequent rotation to the left around the longitudinal axis of the stomach. Due to its lengthening, the dorsal mesogastrium forms a double fold constituting the greater omentum (Noden and De Lahunta, 1985; McGeady et al., 2006). The greater omentum containing the spleen is arranged as a sack-like structure which is the omental bursa (Noden and De Lahunta, 1985; McGeady et al., 2006). The latter bursa communicates with the abdominal cavity through the epiploic foramen (Noden and De Lahunta, 1985; McGeady et al., 2006). The part of the ventral mesogastrium between the minor curvature of the stomach and the liver develops toward the lesser omentum while the falciform ligament develops between the liver and the ventral abdominal wall (Noden and De Lahunta, 1985; McGeady et al., 2006).

After the 90° rotation of the stomach to the left in early embryologic life, a second gradual rotation occurs during the fetal and early postnatal period: the stomach rotates around a dorsoventral axis, over 90° in counter-clockwise direction when viewed from dorsal (Noden and De Lahunta, 1985), rendering the relative position of the involved structures even more complex.

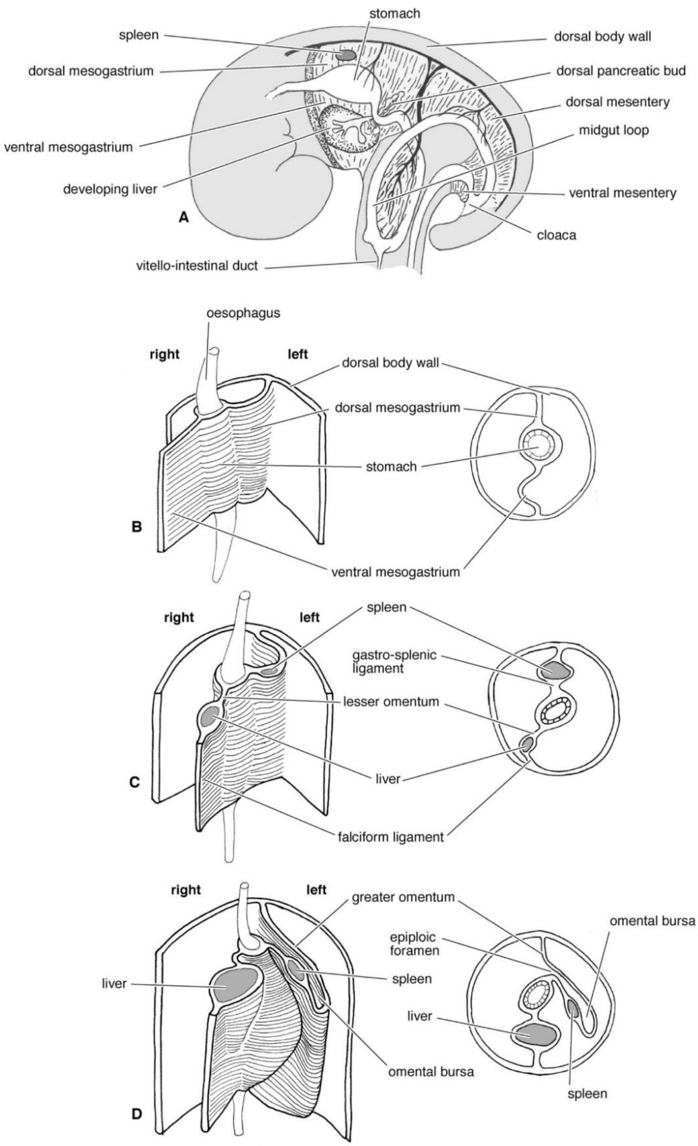

Figure 2: Lateral (A) and ventro-lateral cross-sectional views (B, C and D) through the abdominal region at the level of the stomach in a monogastric embryo. B: Developing stomach showing position of the dorsal mesogastrium and the ventral mesogastrium. C: Commencement of gastric rotation to the left and the position of the spleen in the dorsal mesogastrium and the liver in the ventral mesogastrium. D: Elongation of the dorsal mesogastrium and formation of the omental bursa. Growth of the liver in the ventral mesogastrium results in the formation of the lesser omentum dorsal to the liver and the falciform ligament ventrally. (Cahalan S. 2006. Digestive system, in: McGeady, T.A., Quinn, P.J., FitzPatrick, E.S., Ryan, M.T. (Eds.), Veterinary Embryology. Blackwell Publishing, Oxford, p. 210, reprinted with permission)

Anatomy of the epiploic foramen in the horse

The veterinary interspecies definition of the epiploic foramen is *"the opening from the greater peritoneal sac to the omental vestibule that passes between the caudal vena cava dorsally, the portal vein that is included in the hepatoduodenal ligament ventrally, the caudal lobe of the liver cranially, and the pancreas caudally"* (Constantinescu and Schaller, 2012). The omental vestibule is defined as *"the vestibule of the omental bursa enclosed by the minor omentum, the stomach and the liver"* and the omental bursa is defined as *"the potential space enclosed by the 2 omenta, the stomach and the liver"* (Constantinescu and Schaller, 2012).

Discrepancies exist in literature about the exact morphology and nomenclature of the equine epiploic foramen. Dissimilar descriptions of the equine epiploic foramen can be found throughout literature. The involvement of the lesser omentum, subdivided in the hepatoduodenal ligament and the hepatogastric ligament, in delineating the omental vestibule and the epiploic foramen has been described (Nickel et al., 1973; Barone, 1997). The epiploic foramen is mentioned as a slit-like opening, to the right of the median plane and ventral to the base of the caudate process of the liver (Nickel et al., 1973). The caudate process and caudal vena cava are described as the dorsal boundary, and the portal vein, the pancreas and the hepatoduodenal ligament as ventral boundary (Sisson, 1975). Another author describes the same boundaries of the epiploic foramen but also mentions the free border of the hepatoduodenal ligament instead of the hepatoduodenal ligament itself as a delineating structure (Nickel et al., 1973). The omental vestibule is described as the space that is delineated by the stomach on the left, by the gastrophrenic ligament ventrally, by the lesser omentum on the right, and by the gastropancreatic fold dorsally. This fold is attached to the dorsal border of the liver and to the caudal vena cava (Sisson, 1975). Two openings of the omental vestibule are reported, the smaller epiploic foramen on the right and a larger opening over the minor curvature of the stomach to the left (Sisson, 1975; Schmid et al., 1998). Both the *plica gastropancreaticoduodenalis* (Schmid, 1997) and the gastropancreatic fold (Schmid et al., 1998; Freeman and Pearn, 2015) have been identified by equine surgeons as structures that delineate the epiploic foramen and the omental vestibule ventrally. This is in contrast to the anatomic description in human anatomic literature (Putz and Pabst, 1994) and to the above mentioned veterinary anatomic interspecies definition (Constantinescu and Schaller, 2012).

The gastropancreatic fold is defined as "*a fold in the wall of the omental bursa containing the left gastric vessels"* and the hepatopancreatic fold as "*a fold in the wall of the omental bursa containing the hepatic artery"* (Constantinescu and Schaller, 2012). According to one author these two structures contribute to the formation of a large orifice which gives access to the large caudal recess of the omental bursa (Barone, 2001). Within the omental vestibule there is a dorsal recess that is defined as "*a minor diverticulum of the omental vestibule between the right crus of the diaphragm and the liver, and between the oesophagus and the caudal vena cava"* (Constantinescu and Schaller, 2012).

The epiploic foramen can become an internal hernia ring when viscera pass through, and provoke the formation of an internal hernia leading to strangulation (called epiploic foramen entrapment or EFE in horses), giving rise to abdominal pain necessitating emergency treatment.

Medical history of epiploic foramen entrapment

Epiploic foramen entrapment, still called "Winslow foramen hernia" in the human literature, was first described by Blandin in 1823 in a human post-mortem dissection (Blandin, 1837). In the second edition of his clinical anatomy book « Traité d'anatomie topograpique, ou anatomie des régions du corps humain » Blandin described his observation as follows: *« J'ai eu occasion d'observer, à l'hôpital de la Charité, un exemple fort remarquable de ce dernier genre d'étranglement intérieur : la plus grande partie du paquet de l'intestin grêle, après avoir remonté à droite, dans la région épigastrique, s'était introduite par l'hiatus de Winslow, dans l'arrière-cavité des épiploons; puis elle était sortie par une ouverture étroite, anormalement établie dans le mésocolon transverse; cette ouverture exerçait sur l'intestin une constriction forte, qui en avait déterminé le sphacèle.»* (Blandin, 1837). The first case encountered during explorative laparotomy on a living patient was reported in the medical journal "The Lancet" by Dr Treves from the London Hospital in 1888 (Treves, 1888). Exploratory laparotomy was undertaken eight days after the commencement of clinical signs. Small intestines, the caecum, the ascending colon and part of the transverse colon had passed through the Winslow foramen. During an attempt at reduction the hepatic artery could clearly be felt pulsating. Beside the small intestines that were reduced from the herniation further reduction was considered impossible. The patient died some 6 hours after he had been carried back to bed (Treves, 1888). The first patient recovering from this disease was described in “The Lancet” by Dr Neve in 1892 (Neve, 1892). A 17 years old Mohammedan Kashmiri was admitted to the Kashmir Mission Hospital with acute pain and absolute constipation of seven days duration. A large enema (4 pints) was given, and the patient was “*suspended by the heels and well shaken”*. Daily large enemas were performed and morphine was administered to relieve the pain. After 20 days it was decided to perform an exploratory laparotomy as the friends of the patient wished to remove him from the hospital unless more active treatment was undertaken. The colon had passed through the Winslow foramen, which acted as a strong “ring” leading to colonic distension. Freeing of the colon from the ring was impossible and Dr Neve (Neve, 1892) agreed with Dr Treves (Treves, 1888) that *“even modern abdominal surgery has not proved that the hepatic artery, the portal vein, and the bile duct can be divided simultaneously with impunity”* and that the constricting ring could not be incised. As traction had failed they could only hope that the handling would not lead to acute obstruction, and they proceeded to close the abdominal incision. On the second night after the operation the patient had a prolonged spasmodic pain for which a large enema was given and relief was obtained. The patient continued to improve and was discharged 26 days after the surgery. The author concluded that despite the unclear *modus operandi* of the cure of this patient, the patient undoubtedly owed his life to the operation performed and the first patient with herniation through the Winslow foramen was cured (Neve, 1892).

Winslow foramen hernia in man

Large case series are lacking in human literature as this condition is very uncommon in man. A case report from 1987 was accompanied by a literature review that identified 112 individual cases in the world literature until then. Organs herniated were small bowel (63%); caecum, ascending colon and terminal ileum (30%); and transverse colon (7%) (Valenziano et al., 1987). Of 25 cases reported since 1966, caecal herniation comprised two-thirds of these (Valenziano et al., 1987). The primary symptoms were pain originating from the herniated organ and hepatoduodenal ligament (Valenziano et al., 1987). Diagnosis may be made radiologically (Valenziano et al., 1987) or more recently by computed tomography (Sikiminywa-Kambale et al., 2014) and the treatment was surgical (Valenziano et al., 1987). The overall mortality rate up to 49% reported in the early literature was thought to be due mainly to delay in diagnosis and treatment as was concluded after collective review of the 90 earliest reported cases in 1967 (Erskine, 1967a). In the majority of these cases intestines were herniated from the abdominal cavity through the foramen into the omental bursa, as was the case during Blandins dissection (Blandin, 1837). In very rare cases intestines herniated into the omental bursa through traumatic or congenital rents with eventual re-entry into the general peritoneal cavity through the Winslow foramen in even more exceptional cases (Erskine, 1967a).

Authors were surprised by the rarity of herniation through this aperture and several assumptions explaining the occurrence of this type of herniation were made. Gross abnormalities were pointed out, such as an abnormally long mesentery and thus, abnormal mobility of the intestine or an enlarged Winslow foramen that admits more than one finger (Erskine, 1967a). Other gross variations described consisted of a funnel-like entrance from the abdominal cavity toward the Winslow foramen (Erskine, 1967a). A number of physiologic explanations have been proposed such as altered intra-abdominal pressure, eating a large meal and heavy lifting combined with contraction of the muscles of the abdominal wall exerting pressure which could push the intestines through the foramen (Erskine, 1967a).

Spontaneous closure of the Winslow foramen was reported in a case that necessitated revision of the performed intestinal anastomosis 1 month after surgery for intestinal herniation through the Winslow foramen (Erskine, 1967a). It was concluded that it is unclear how often nature can be relied on to close the aperture, but an inflammatory reaction at the level of the Winslow foramen should certainly be present in all patients after reduction of entrapped intestines (Erskine, 1967a). There is some discussion between authors on whether the Winslow foramen should be surgically closed after reduction of entrapped intestines to avoid recurrence of the condition. Lack of reported recurrent cases (Richardson and Anastopoulos, 1981; Saida et al., 2000) suggested that there is no direct need to close the Winslow foramen. Potential portal vein thrombosis or risk of trauma to the hepatic artery and biliary duct during the closure procedure made surgeons avoid closure of the Winslow foramen after intestinal reduction (Armstrong et al., 2007). Recently two cases of Winslow foramen herniation were reported in a case series of 14 internal hernias (11 peritoneal fossa, 2 Winslow foramen hernias and 1 pathologic orifice) (Armstrong et al., 2007). These intestinal hernias were easy to reduce, except for the 2 Winslow foramen hernia cases due to strangulation and congestion (Armstrong et al., 2007). In both cases patients died due to peritonitis illustrating that the prognosis for survival after Winslow foramen herniation is still not unequivocally positive in humans (Armstrong et al., 2007). Therefore some surgeons, despite the previously mentioned potential complications associated with epiploic foramen closure, tend to close the Winslow foramen to avoid recurrent herniation (Osvaldt et al., 2008). Closure was performed by direct suturing or by duodenal, colonic or omental pexy (Erskine, 1967a, 1967b; Osvaldt et al., 2008). Closure of the Winslow foramen with sutures at the end of the laparotomic procedure has recently been recommended if it can be done safely (Osvaldt et al., 2008). This could be performed laparoscopically with silk sutures if the herniated viscera could be reduced during the initial explorative laparoscopic procedure (Garg et al., 2016).

Other species

Reports of epiploic foramen herniation in other mammals, beside horses, are even more scarce. Three cases of small intestinal incarceration in the epiploic foramen in young calves were described by Deprez *et al.* (Deprez et al., 2006). These cases were diagnosed amongst 900 cattle referred with clinical signs of intestinal obstruction (0.3%) (Deprez et al., 2006). In 2 calves jejunum was herniated from left-to-right through the epiploic foramen and in 1 calf the herniation was from right-to-left resulting in the presence of herniated jejunum into the omental bursa (Deprez et al., 2006). Four cases of omental herniation of a variably sized portion of jejunal loops without passing through the epiploic foramen, but through an acquired omental rent, were identified amongst 712 cattle presented with mechanical ileus (0.6%) (Pardon et al., 2009).

To the best of my knowledge, epiploic foramen herniation has not been reported in other mammals beside humans, horses and young cattle.

Epiploic foramen entrapment in horses

In the equine veterinary literature the condition in which intestines are herniated through the epiploic foramen is called epiploic foramen entrapment or EFE. Epiploic foramen entrapment has been reported as an important cause of surgical colic in horses, in contrast to the limited occurrence in other mammalian species. A series of 15 cases reported in 1984 (Turner et al., 1984) demonstrated the high morbidity and mortality associated with this disease as 87% of horses with this condition died.

Inconsistent clinical signs were held responsible for delayed surgery and subsequent reduced prognosis (Turner et al., 1984). Entrapment from the abdominal cavity through the epiploic foramen into the omental bursa (right-to-left) was encountered in 12 cases and an opposite direction (left-to-right) was reported in only 3 cases (Turner et al., 1984). Another 15 cases were reported in 1988 (Vasey, 1988). Entrapment from the abdominal cavity through the epiploic foramen into the omental bursa (right-to-left) was reported in all of these cases (Vasey, 1988). Epiploic foramen entrapment accounted for 5% of the surgically treated horses referred with colic in the referral institution where the latter case series was conducted (Vasey, 1988). The ileum was involved in the entrapment in 14/15 cases (93%) (Vasey, 1988). Only 3/11 horses (27%) that underwent surgery survived (Vasey, 1988). Over time, reported survival rates increased. Seventy-four percent of operated horses were alive 1 month after surgery and 63% were alive at the time these were written up (3 to 45 months post-surgery with a mean of 17.2 ± 7.2 months) in a series of 19 surgically treated EFE cases reported in 1993 which included horses of variable ages and breeds (Engelbert et al., 1993). The first large case series was reported in 1995 and summarized details of 53 EFE cases (59% Thoroughbred horses) (Vachon and Fischer, 1995). Seventy-nine percent of the horses that were recovered from anaesthesia survived until hospital discharge (35/44) and 70% survived for at least 1 year post-operatively (31/44) (Vachon and Fischer, 1995). Proudman *et al.* identified EFE as carrying a worse prognosis for long-term survival compared to other strangulating small intestinal lesions (Proudman et al., 2002a). Epiploic foramen entrapment was significantly associated with decreased survival of surgical colic cases (Proudman et al., 2002b). The same authors offered evidence that some of the increased risk of death associated with EFE cases is due to lower pre-operative plasma total protein values and longer surgery times in these horses (Proudman et al., 2005). Horses that had suffered EFE were more than 4 times more likely to undergo re-laparotomy compared to other horses undergoing colic surgery (French et al., 2002). In the latter studies, rates of survival were relatively poor which contrasts with work by Freeman and Schaeffer where short-term survival rates were better for EFE cases compared to strangulation by lipoma and miscellaneous strangulations (Freeman and Schaeffer, 2005). Twenty of 21 horses that recovered from anaesthesia (95%) were discharged despite the ileum being involved in significantly more cases (81%) compared to strangulation by lipoma (31%) and miscellaneous strangulations (46%) (Freeman and Schaeffer, 2005). Of note, a high number of EFE patients that required bowel resection and anastomosis underwent jejunocaecostomy (9/13, 69%) compared to jejunoileostomy (2/13, 15%) and jejunojejunostomy (2/13, 15%), and it was suggested that the avoidance of end-to-end jejunoileostomy in case of ileal involvement could improve the outcome following surgery for EFE (Freeman and Schaeffer, 2005). This in agreement with the findings of Steenhaut *et al.* who found that 10/23 (43%) horses survived to discharge after an end-to-end anastomosis (no distinction made between jejunojejunostomy and jejunoileostomy) compared to 12/19 (63%) survivors after an end-to-side jejunocaecostomy during EFE colic surgery (Steenhaut et al., 2004). The disparity in wall thickness between the jejunum and ileum and considerable cuff formation that can result from an inverting suture pattern in the thicker ileal wall could be responsible for problematic short-term outcomes with end-to-end jejonoileostomy (Stewart et al., 2014). More horses undergoing jejunoileostomy underwent repeat laparotomy during the hospitalisation period compared to horses that underwent jejunojejunostomy or jejunocaecostomy in a population of horses that recovered from general anaesthesia following resection and anastomosis for treatment of a small intestinal obstruction (Stewart et al., 2014). However, there was no difference in short-term outcome between groups, whereas horses with a jejunocaecostomy were more likely to have long-term complications with colic (Stewart et al., 2014).

The caecum is involved in a large percentage of human cases of Winslow foramen herniation (Valenziano et al., 1987). This is in contrast to equine EFE, where, except for a few reported cases of herniation of the large colon (Foerner et al., 1993; Steenhaut et al., 1993; Segura et al., 1999) and one recently reported case of herniation of the apex of the caecum (Grzeskowiak et al., 2017), all herniations consisted of herniated small intestines. The ileum has been consistently to be reported to be involved in around two thirds of EFE cases: 10/15 cases (66.7%) (Vasey, 1988), 12/19 cases (63.2%) (Engelbert et al., 1993), 37/53 cases (69.8%) (Vachon and Fischer, 1995) and in 47/71 cases (66.2%)(Archer et al., 2004b). In the study by Freeman and Schaeffer the ileum was involved in a greater proportion (81%) (Freeman and Schaeffer, 2005). Thirty hours delay before surgery was tolerated in an exceptional case because there was only a parietal hernia involving the antimesenteric portion of the ileum (left-to-right) (Hammock et al., 1999). The horse recovered fully after reduction of the entrapped intestinal segment without resection (Hammock et al., 1999).

Archer and co-workers have performed several epidemiologic studies within specific equine populations to identify factors associated with EFE, in light of the very high occurrence of this disease in horses compared to other mammalian species. In a first retrospective study they were able to confirm their clinical observation that there is an association between windsucking/crib-biting and EFE (Archer et al., 2004a). Crib-biting/windsucking is a stereotypic behaviour where horses contract the strap muscles of the ventral throat and draw air into the cranial oesophagus with or without grasping a horizontal fixed object with their incisor teeth (Waters et al., 2002; Albright et al., 2009). In a subsequent case-control retrospective study including 71 cases, EFE horses were significantly more likely to have a history of crib-biting/windsucking than the control group (OR 7.9, 95% CI 4.1-15.3) and the condition occurred more often between October and March, which could be explained by increased stereotypic behaviour during this stabling period (Archer et al., 2004b). Thoroughbred and Thoroughbred-cross horses were overrepresented (Archer et al., 2004b). In a subsequent, international, prospective, case-control study crib-biting/windsucking behaviour was associated with increased risk for EFE (OR 67.3, 95% CI 15.3–296.5) as was history of colic in the previous 12 months (OR 4.4, 95% CI 1.5–12.7) and horses of greater whither height (OR 1.05, 95% CI 1.01–1.08) (Archer et al., 2008a). Other factors associated with altered risk of EFE included the person(s) responsible for the horses' daily care (owner/relative/spouse not involved in daily care OR 5.5, 95% CI 2.3–13.3) and a number of behavioural features, including response to a stimulus causing fright (easily frightened OR 0.4, 95% CI 0.1–1.0) or excitement (sweats up easily/occasionally OR 0.3, 95% CI 0.1–0.8), reaction to their surroundings (inquisitive OR 0.4, 95% CI 0.2–0.8) and feeding behaviour when stressed (goes off food in full/part OR 0.3, 95% CI 0.1–1.0) (Archer et al., 2008a). A prospective unmatched, multicentre case-control study performed by the same group demonstrated that crib-biting/windsucking was associated with the largest increase in likelihood of EFE (Archer et al., 2008b). A history of colic in the previous 12 months, increased stabling in the previous 28 days and greater wither height increased the likelihood of EFE to a smaller extent (Archer et al., 2008b). Horses with access to a mineral/salt lick, horses that are easily frightened and horses not fed at the same time as others were at reduced risk for EFE (Archer et al., 2008b).

Survival to hospital discharge of recovered horses after surgery for EFE ranges between 79 and 85% in larger case series (Vachon and Fischer, 1995; Archer et al., 2004b, 2011). Although short-term survival has been defined as “survival to hospital discharge after recovery from surgery”, it is important to acknowledge that this percentage does not take euthanasia during surgery in account and therefore “overall survival of horses undergoing surgery” should also be considered. Steenhaut *et al.* reported 49% survival until discharge amongst the total population of horses that underwent surgery for EFE (44/90) (Steenhaut et al., 2004). When horses are included that did not survive the surgery, overall survival percentages until discharge range between 66 and 69% in the previously cited publications (Vachon and Fischer, 1995; Archer et al., 2004b, 2011). Long-term survival is difficult to compare between studies due to different definitions (Vachon and Fischer, 1995; Archer et al., 2004b, 2011). Long-term survival of 70% (defined as survival for at least 1 year post operatively), long-term survival of 700 days (defined as the time where 50% of horses discharged from the hospital are still alive) and long-term survival of 397 days (defined as the time where 50% of all horses undergoing surgery are still alive) have been reported (Vachon and Fischer, 1995; Archer et al., 2004b, 2011). Increased Packed Cell Volume (PCV), increased length of small intestine resected, and post-operative ileus (POI) have been associated with increased likelihood of mortality of EFE cases in the international prospective multicentre study by Archer and co-workers (Archer et al., 2011). The existing epidemiologic studies on survival after surgery for EFE originate from the United Kingdom or North America (apart from the study from Steenhaut (Steenhaut et al., 2004)) and are mainly conducted in Thoroughbred dominated equine populations. The study from Steenhaut was conducted on the European continent within a study population of mainly Warmblood horses (67%) and reported a slightly lower survival to hospital discharge of the horses that underwent surgery compared to the larger United Kingdom and North American case series (Steenhaut et al., 2004).

Horses undergoing surgical repositioning of entrapped intestines can die due to uncontrollable intra-operative haemorrhage from the larger vessels surrounding the epiploic foramen or at the base of the entrapped mesentery. Such uncontrollable intra-operative haemorrhage occurred in 1/15 cases (7%) (Vasey, 1988), in 3/26 cases

(12%) (Livesey et al., 1991), in 3/53 cases (6%) (Vachon and Fischer, 1995), in 3/71 cases (4%) (Archer et al., 2004b) and in 3/90 cases (3%) (Steenhaut et al., 2004). Haemorrhage was due to a longitudinal tear in the portal vein in the 3 cases described by Livesey *et al.* (Livesey et al., 1991). In 2 of their cases a considerable amount of serosanguinous fluid was present within the abdomen before reduction of the intestines. A sudden drop in blood pressure leading to death occurred after reduction suggesting that a small spontaneous tear was present before reduction and was partially occluded by the entrapped intestines (Livesey et al., 1991). In the third case uncontrollable intra-operative haemorrhage occurred after an attempt to dilate the epiploic foramen manually to facilitate intestinal reduction (Livesey et al., 1991). In the 3 cases a longitudinal tear ranging from 0.8 to 3 cm was present in the dorsal aspect of the portal vein adjacent to the most cranial point of entry into the liver where the hepatoduodenal ligament is reflected from the portal vein (Livesey et al., 1991). The authors concluded that portal vein lacerations in this region may occur spontaneously as a result of tension exerted by incarcerated small intestines on adjacent structures, or by manual dilation of the epiploic foramen, which the authors recommended not to perform (Livesey et al., 1991). Repair of a lacerated portal vein is considered impossible because of surgical inaccessibility of the latter structure (Livesey et al., 1991). Hypoglycaemia and hepatic ischemic necrosis have been reported in a horse after small intestinal incarceration through the epiploic foramen (Davis et al., 1992). Necropsy of the liver of that one and only horse that died after a post-operative episode of hypoglycaemia and related neurological signs, revealed grossly visible thrombi in the portal vein and in adjacent “other large vessels” (Davis et al., 1992). Contiguous lobuli had moderate to severe centrilobular necrosis (Davis et al., 1992). Potential hepatic artery implication was not mentioned.

Pathophysiology of equine epiploic foramen entrapment

Historically, it was hypothesised that EFE occurs more frequently in older horses, due to enlargement of the epiploic foramen induced by geriatric liver atrophy (Rooney and Robertson, 1996). This hypothesis was refuted later on during several investigations (Freeman and Schaeffer, 2001; Archer et al., 2004b). Furthermore, the description of a case of EFE (right-to-left) in a 4 months old foal without any signs of liver atrophy, wasn’t in favour of this geriatric liver atrophy hypothesis (Murray et al., 1994). Albanese *et al.* demonstrated a significant increase in intra-abdominal pressure during and after cribbing in a cribbing cohort of 8 horses compared to a non-cribbing cohort of 8 horses (Albanese et al., 2013). Increased intra-abdominal pressure observed during and after crib-biting/windsucking could be associated with the occurrence of EFE (Freeman and Pearn, 2015) as this stereotypic behaviour has been associated with EFE in horses (Archer et al., 2004a, 2004b, 2008a, 2008b). Freeman and Pearn performed several cadaveric dissections and they suggested that the funnel-like shape of the equine omental vestibule, as it tapers toward the more fixed epiploic foramen, acts as a trap that allows intestines to enter the wide opening of the omental vestibule, and then move through it from the left to the right toward the smaller epiploic foramen, where intestines become entrapped (Freeman and Pearn, 2015). The increased intra-abdominal pressure during and after crib-biting (Albanese et al., 2013) could possibly dilate the omental vestibule and potentially force intestine into it (Freeman and Pearn, 2015). In contrast to human reports and early reports in horses (Turner et al., 1984; Vasey, 1988), EFE is described from the left to the right through the epiploic foramen in the vast majority of horses in more recent publications (53/53 (100%) (Vachon and Fischer, 1995), 69/71 (97.2%) (Archer et al., 2004b) and 46/47 (97.9%) (Steenhaut et al., 2004)). This left-to-right entrapment implies that the omental bursa inverts together with the intestines into the omental vestibule and that at some point in this process the greater omentum ruptures.

Surgical techniques to prevent recurrence of colic

Surgical techniques to prevent recurrence of specific colic types have been described. Laparoscopic nephrosplenic closure techniques, either by suturing dorsomedial splenic capsule to the dorsal portion of the nephrosplenic ligament (Marien et al., 2001) or by polypropylene mesh application (Epstein and Parente, 2006), were developed to avoid recurrent nephrosplenic entrapment of the large colon, because recurrence rates of up to 21-23% have been reported for this condition without surgical recurrence prevention (Röcken et al., 2005; Nelson et al., 2016). Recurrence of large colon displacement or volvulus has been prevented by large colon resection (Pezzanite and Hackett, 2017) or colopexy (Trostle et al., 1998). Exact percentages for inguinal hernia recurrence in horses are not known, but it is generally agreed that inguinal re-herniation is likely to occur and preventive measures, such as castration or inguinal hernioplasty, are recommended. Several techniques for inguinal hernioplasty have been described: laparoscopic suturing under general anaesthesia (Fischer et al., 1995), laparoscopic

cylindrical mesh application on the standing sedated horse (Mariën, 2001), laparoscopic peritoneal flap techniques either under general anaesthesia (Rossignol et al., 2007) or in the standing sedated horse (Wilderjans et al., 2012), and laparoscopic cyanoacrylate gluing combined with helical titanium coil tacking on the standing sedated horse (Rossignol et al., 2014).
Preventive closure of the epiploic foramen had not been described prior to the start of the present study. Nevertheless, recurrence of EFE in horses has been reported in several case series (1/53 (2%) (Vachon and Fischer, 1995), 2/71 (3%) (Archer et al., 2004b) and 1/7 (14%) (Freeman et al., 2014)). This is in contrast to human literature where reports of recurrent Winslow foramen hernias are lacking. However, according to recent human literature and taking the severity of the pathology into account, the Winslow foramen may be closed after surgical reduction of a Winslow foramen hernia in humans, if it can be performed safely (Osvaldt et al., 2008).

The epiploic foramen in the horse is not visible and can only be palpated during standard ventral midline laparotomy. It is inaccessible for conventional open techniques due to its dorsal location within the abdomen and the large volume of the abdomen in horses. Closure of the epiploic foramen with sutures or by means of duodenal, colonic or omental pexy-techniques, as described in humans after reduction of intestines from the Winslow foramen (Erskine, 1967a, 1967b; Osvaldt et al., 2008), is therefore not achievable during equine colic surgery.

During the course of this work, Munsterman *et al.* described a laparoscopic technique for preventive epiploic foramen closure on the standing sedated horse (Munsterman et al., 2014). The epiploic foramen was closed by means of 4 to 10 helical titanium coils inserted into the gastropancreatic fold and the caudate lobe of the liver in 6 experimental horses (Munsterman et al., 2014). This technique resulted in epiploic foramen closure by a thin tissue fold in 5/6 of these experimental horses.

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CHAPTER 2

Aims of the thesis

Epiploic foramen entrapment (EFE) is an important cause of colic in horses and requires surgical correction. Despite its importance, there is still a widespread misunderstanding about this pathology amongst equine practitioners and surgeons. Discrepancies exist in literature about the anatomic description of the epiploic foramen in horses and knowledge is lacking about the specific surgical anatomic landmarks and 3D configuration of the epiploic foramen which is needed for the development and description of novel surgical techniques in the region. Knowledge is lacking about the pathophysiology of this disease in horses and why it occurs so often in horses compared to humans and other animals. Spontaneous closure or preventive surgical closure of the foramen after EFE has been sporadically reported in the human literature. Despite large case series of EFE in horses publications about spontaneous or surgical epiploic foramen closure are lacking in veterinary literature except for one recent experimental study on surgical epiploic foramen closure (Munsterman et al., 2014).

The general aims of this thesis are to explore and enhance knowledge about the anatomy of the equine epiploic foramen, to create opportunities to prevent herniation of intestines through the epiploic foramen and to evaluate the outcome of EFE colic in horses.

The specific aims were:

- To describe the precise anatomy of the equine epiploic foramen and omental vestibule in accordance with anatomic interspecies definitions, to quantify the dimensions of the equine epiploic foramen and to relate these findings to laparoscopic images **(Chapter 3)**.
- To describe the laparoscopic Foramen Epiploicum Mesh Closure (FEMC) technique and its outcome in experimental horses **(Chapter 4)**.
- To determine whether spontaneous epiploic foramen closure occurs in horses after EFE **(Chapter 5)**.
- To determine whether the FEMC technique can also be performed through a ventral midline laparotomy under general anaesthesia **(Chapter 6)**.

Finally, an epidemiologic study is performed as the large majority of existing epidemiologic studies on survival after surgery for EFE in horses originate from the

United Kingdom and North America and are mainly conducted in Thoroughbred dominated populations, with the aim:

- To document peri-operative variables of EFE surgeries in a referral hospital on the European continent and to identify short- and long-term survival and variables associated with survival **(Chapter 7)**.

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CHAPTER 3

A topographic anatomical study of the equine epiploic foramen and comparison with laparoscopic visualisation

Adapted from:
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Abstract

Reasons for performing study: There are no previous studies correlating the anatomy of the equine epiploic foramen and its defining structures with laparoscopic images.

Objectives: The purpose of this study was to describe the precise anatomy of the epiploic foramen and the omental vestibule, to quantify the dimensions of the epiploic foramen and to relate these findings to laparoscopic images.

Study design: Descriptive study of equine cadaver material and laparoscopic images.

Methods: Thirty-two horses euthanized for reasons unrelated to colic were studied. Two cadavers were used to make vascular casts of the coeliac artery and portal vein. In 30 cadavers the epiploic foramen and omental vestibule were casted with a polyurethane prepolymer immediately after euthanasia. The cast served as a landmark during dissection and the circumference of the epiploic foramen was measured from these casts. Histology was performed on structures defining the epiploic foramen in two horses. Laparoscopic images from 6 standing right flank procedures were reviewed.

Results: The defining structures of the equine epiploic foramen and omental vestibule are the hepatoduodenal ligament, the hepatogastric ligament and the gastropancreatic and hepatopancreatic folds. The hepatoduodenal ligament has a secondary fold which forms the ventral border of the epiploic foramen, consisting of a central connective tissue core of mainly elastin fibres. The hepatic artery for part of its course is incorporated in the hepatoduodenal ligament. All these structures are clearly visible laparoscopically. The mean circumference of the epiploic foramen is 11.6 ± 2.6 cm and its circumference is positively correlated with body weight but is unrelated to age or sex.

Conclusions: Several clinically relevant structures delineate the equine epiploic foramen. Its defining structure consists, in part, of elastin fibres. Anatomical and laparoscopic knowledge may assist surgeons in developing interventions to treat diseases involving the epiploic foramen.

Introduction

The epiploic foramen is an important structure for the aetiology of equine colic because of the high prevalence of intestinal epiploic foramen entrapment (EFE) (Freeman and Schaeffer, 2001; Archer et al., 2004). The lack in understanding of the 3-dimensional (3D) anatomy of this structure, specifically relating to the laparoscopic anatomy, is an impediment to development of surgical techniques which could be used to prevent EFE (Freeman and Pearn, 2015).

The epiploic foramen is defined as *“the opening from the greater peritoneal sac to the omental vestibule that passes between the caudal vena cava dorsally, the portal vein that is included in the hepatoduodenal ligament ventrally, the caudal lobe of the liver cranially, and the pancreas caudally”* (Constantinescu and Schaller, 2012). The omental vestibule is defined as *“the vestibule of the omental bursa enclosed by the minor omentum, the stomach and the liver”* and the omental bursa is defined as *“the potential space enclosed by the 2 omenta, the stomach and the liver”* (Constantinescu and Schaller, 2012). The involvement of the lesser omentum, subdivided into the hepatoduodenal ligament and the hepatogastric ligament, in delineating the omental vestibule and the epiploic foramen has been previously reported (Nickel et al., 1973; Barone, 1997). The epiploic foramen is described as a slit-like opening to the right of the median plane and ventral to the base of the caudate process of the liver (Nickel et al., 1973). The caudate process and caudal vena cava are described as the dorsal boundary and the portal vein, the pancreas and the hepatoduodenal ligament as the ventral boundary (Sisson, 1975). Nickel *et al.* described the same boundaries of the epiploic foramen but also described the free border of the hepatoduodenal ligament rather than the hepatoduodenal ligament itself as a delineating structure (Nickel et al., 1973). The omental vestibule is described as the space delineated by the stomach on the left, by the gastrophrenic ligament ventrally, by the lesser omentum on the right and by the gastropancreatic fold dorsally. This fold is attached to the dorsal border of the liver and to the caudal vena cava (Sisson, 1975). Two openings of the omental vestibule have been reported, the smaller epiploic foramen on the right and a larger opening over the minor curvature of the stomach to the left (Sisson, 1975; Schmid et al., 1998). Both the *plica gastropancreaticoduodenalis* (Schmid, 1997) and the gastropancreatic fold (Schmid et al., 1998; Freeman and Pearn, 2015) have been identified as structures that delineate the epiploic foramen and the omental vestibule.

The *plica gastropancreatica* is defined as a *"fold in the wall of the omental bursa containing the left gastric vessels"* and the *plica hepatopancreatica* as a *"fold in the wall of the omental bursa containing the hepatic artery"* (Constantinescu and Schaller, 2012). According to Barone, these two structures contribute to the formation of a large orifice which gives access to the large caudal recess of the omental bursa (Barone, 2001). Within the omental vestibule there is a dorsal recess defined as a *"minor diverticulum of the omental vestibule between the right crus of the diaphragm and the liver, and between the oesophagus and the caudal vena cava"* (Constantinescu and Schaller, 2012). The ability to visualise the epiploic foramen laparoscopically has been previously reported (Galuppo et al., 1995) but, so far, no detailed descriptions of the laparoscopic anatomy of this region are available.

The purpose of our study was to 1) describe the exact topographical location of the epiploic foramen and omental vestibule, 2) determine the dimensions of the epiploic foramen and 3) relate these anatomical findings to images from the region obtained during standing right flank laparoscopy. This study was performed as the first step in the development of a laparoscopic technique to close the epiploic foramen to prevent EFE.

Material and methods

Anatomical study

Two animals (one foal and one pony), subjected to euthanasia for reasons unrelated to colic, were initially studied. The cadavers were embalmed with a mixture of 20 L zinc chloride 42%[a] and 200 mL formaldehyde 25.4% (Arthil 25)[b] after perfusion with physiologic solution immediately after euthanasia. The coeliac artery and the portal vein were injected with 20 mL coloured polymethyl methacrylate (Batson)[c]. Dissection on horizontally suspended cadavers was performed 24 h later.

We developed and used a polyurethane casting model recently described in dogs to define omental structures (Doom et al., 2016). Thirty horses subjected to euthanasia for reasons unrelated to colic were used. Immediately after euthanasia, the horses were suspended in a 4 sling system. Two slings in the axillary regions were attached to a first tackle and two slings in the inguinal regions were attached to a second tackle to suspend the cadaver in an upright position. A vertical incision of approximately 20 cm was made caudal to the last right rib to open the peritoneal cavity. Under manual guidance, a 0.5 cm diameter silicone tube was inserted into the epiploic foramen and attached to a commercially available pressurized can containing 250 mL polyurethane-based prepolymer foam (Hubo PU foam)[d]. Following foam injection into the epiploic foramen, the tube was withdrawn and the flank incision closed in a routine fashion. The cadavers were left suspended for at least 3 hours to allow the prepolymer to cure, prior to dissection of the cadavers. The polyurethane cast served as a guide in dissecting relevant structures. The polyurethane casts were collected and used as a replica mould of the epiploic foramen and omental vestibule showing the outlines of the delineating structures. The circumference, length and height of the epiploic foramen was measured on the casts and circumference was related to weight, age and sex. The normality of continuous datasets was assessed and variables were transformed logarithmically where necessary. Univariate correlations were calculated using Pearson correlation coefficients. A P value <0.05 was considered statistically significant.

Histology

In 2 cadavers specific structures delineating the epiploic foramen and omental vestibule were sampled for histological analysis during the anatomical dissection. Omental structures were pinned on cardboard before formaldehyde fixation to prevent sample deformation. Haematoxylin and eosin, Masson trichrome, Van Gieson trichrome, elastic fibre and reticular fibre staining's were performed on 7 μm thick sections of 3.5% formaldehyde fixated and paraffin embedded tissue samples.

Laparoscopy

Data from the dissection studies were related to laparoscopic images recorded during standing right flank laparoscopy in 6 clinical cases undergoing routine laparoscopy for ovariectomy (n=5) and cryptorchidectomy (n=1). Horses were sedated with 10 μg/kg bwt detomidine intravenously (IV) (Domosedan)[e] + 0.1 mg/kg bwt morphine IV (Morphine HCl)[f] and sedation was maintained by constant rate infusion of 6 μg/kg/h detomidine IV (Domosedan)[e]. Local analgesia was provided by flank infiltration of 60 mL mepivacaine (Scandicaine)[g]. Further analgesia and sedation were obtained by epidural infiltration of 0.2 mg/kg bwt xylazine (Xyl-M)[k] and 0.1 mg/kg bwt morphine (Morphine HCl)[e]. A 58 cm 30° laparoscope[l] was introduced in the right flank through a laparoscopic cannula that was placed between the last rib and the *tuber coxae*, just dorsal to the internal oblique abdominal muscle. Mepivacaine (Scandicaine)[g] was injected into the testicle or mesovarium and, while waiting for its effect, the laparoscope was directed cranially to visualise the region of interest. Intra-abdominal pressure was maintained at 15 mmHg by means of a carbon dioxide insufflator[l].

Results

Anatomical findings

The following description is based on the dissection of 2 embalmed cadavers with casted vasculature (Figure 1) and the 30 polyurethane casts of the epiploic foramen and omental vestibule which all demonstrated similar anatomy (Figure 2). Only the epiploic foramen and omental vestibule were identified and described since the omental bursa was not a focus of our studies. The structure that delineates the omental vestibule ventrally is the lesser omentum, subdivided into the hepatogastric ligament (medially) and the hepatoduodenal ligament (laterally). The hepatoduodenal ligament had two attachments to the liver forming a funnel narrowing to the right of the median plane (Figure 1 and 2). The narrowest part of this funnel was located at the level of the base of the caudate process of the liver. At this level a fold protruding from the hepatoduodenal ligament was palpable as a firm band, was laparoscopically visible (Figure 3B) and was forming the caudoventral delineation of the epiploic foramen. After delineating the epiploic foramen, the hepatoduodenal ligament fanned out to its duodenal attachment on the right. The ovoid-shaped epiploic foramen was orientated obliquely in a cranioventral-caudodorsal direction (Figure 1A, Figure 3B). The epiploic foramen was delineated craniodorsally by the base of the caudate process of the liver. More aboral the duodenum was attached to the dorsal abdominal wall by the mesoduodenum which was a continuation of the hepatoduodenal ligament (Figure 1A).

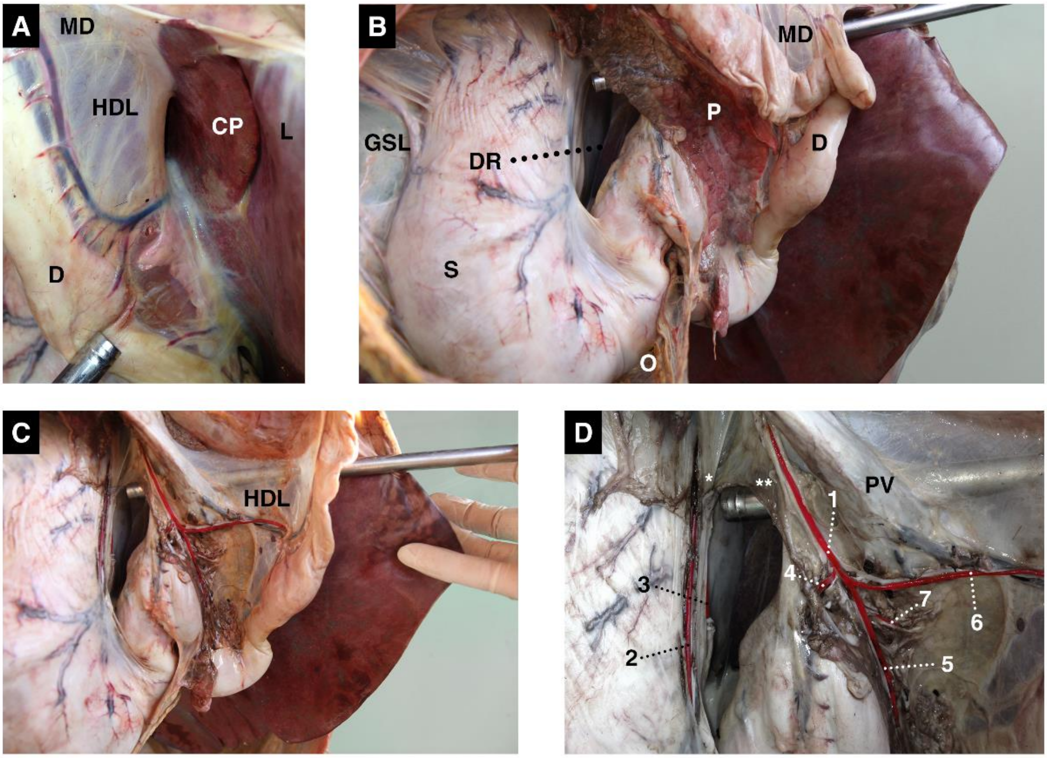

Figure 1: Dissection of an embalmed cadaver with casted coeliac artery and portal vein. A) Right-to-left view with the laparoscope ready to be introduced in the epiploic foramen, B) caudo-cranial view on the same preparation; the omental bursa is opened and the laparoscope introduced through the epiploic foramen into the omental vestibule, C) same view as B) with the pancreas removed and the duodenum lifted up, and D) filtered image highlighting the casted vasculature.
D = duodenum; MD = mesoduodenum; HDL = hepatoduodenal ligament; L = liver; CP = caudate process; GSL = gastrosplenic ligament; S = stomach; P = pancreas; O = greater omentum; DR = dorsal recess; PV = portal vein
1 = trunk of hepatic artery; 2 = visceral branch of left gastric artery; 3 = parietal branch of left gastric artery; 4 = right gastric artery; 5 = right gastroepiploic artery; 6 = gastroduodenal artery; 7 = proper hepatic artery
* = gastropancreatic fold; ** = hepatopancreatic fold

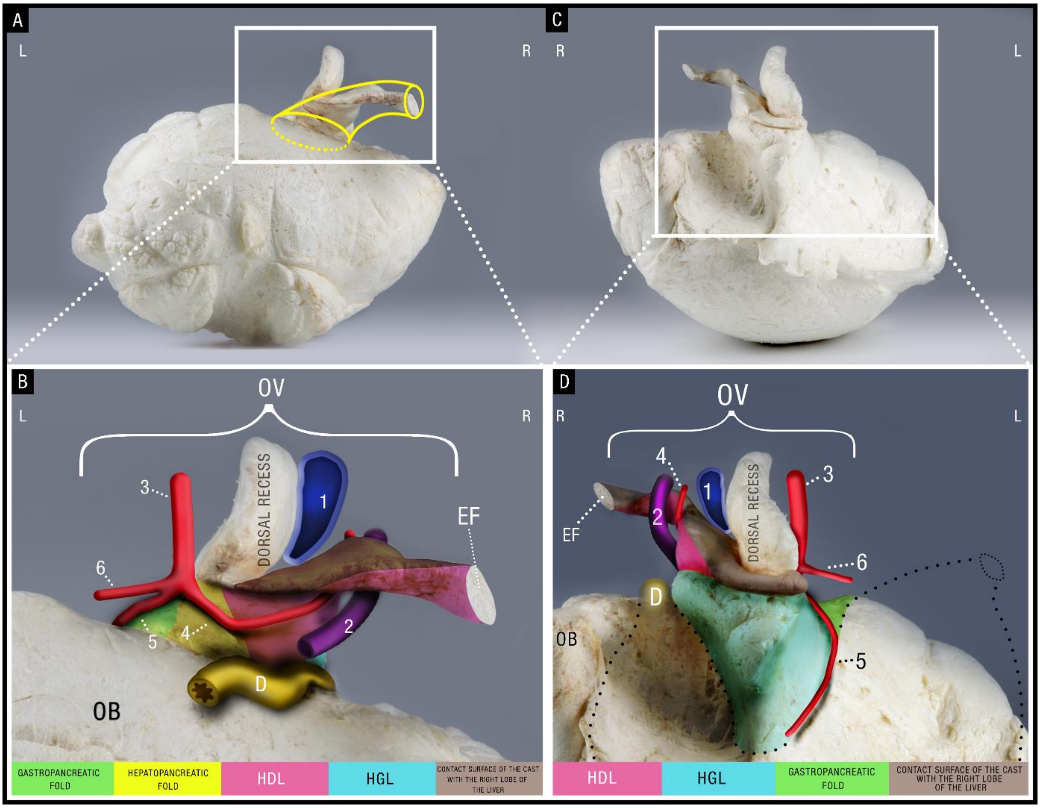

Figure 2: Polyurethane cast of the epiploic foramen (EF), omental vestibule (OV) and omental bursa (OB) with schematic representation of the surrounding structures.

A) Caudoventral-craniodorsal view with schematic presentation of the funnel-like shape of the omental vestibule,
B) Detail of caudoventral-craniodorsal view,
C) Cranioventral-caudodorsal view and
D) Detail of cranioventral-caudodorsal view. The dotted line in Figure 2D represents the contour of the stomach.

L = left; R = right; D = duodenum; HDL = hepatoduodenal ligament; HGL = hepatogastric ligament; 1 = caudal vena cava; 2 = portal vein; 3 = coeliac artery; 4 = hepatic artery; 5 = left gastric artery; 6 = splenic artery

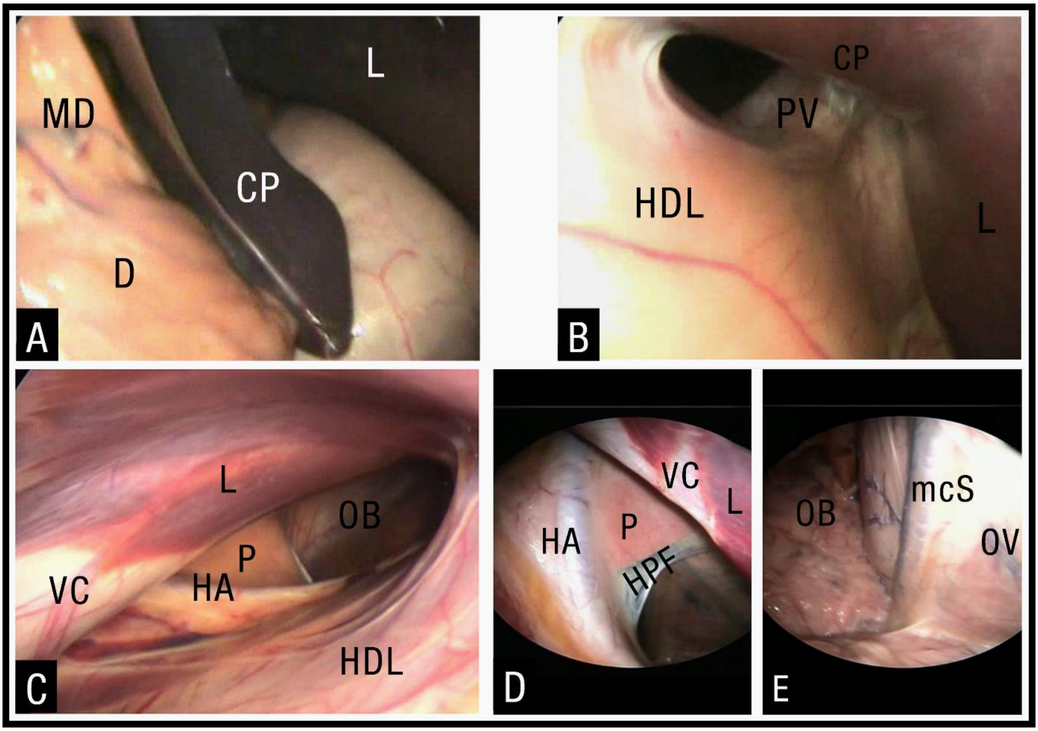

Figure 3: Right flank laparoscopic visualisation of the epiploic foramen, omental vestibule (OV) and omental bursa (OB).

A) Laparoscope directed cranially to visualise the caudate process (CP) of the liver (L)
B) Laparoscope passed between CP and mesoduodenum (MD) allows visualisation of the epiploic foramen at the base of the CP (image slightly tilted anticlockwise)
C) Laparoscope passed through the epiploic foramen allows visualisation of the 'funnel-like' omental vestibule leading to the caudal part of the omental bursa (image slightly tilted anticlockwise)
D) Detail of the hepatopancreatic fold (HPF) in the depth of the omental vestibule
E) Laparoscope passed through the orifice to the OB. Clockwise rotation gives a view within the OB; counter-clockwise rotation allows a view within the OV

D = duodenum; HA = hepatic artery; P = pancreas; VC = caudal vena cava; HDL = hepatoduodenal ligament; PV = portal vein; mcS = minor curvature of stomach with gastric vasculature

The hepatoduodenal ligament was continuous medially with the hepatogastric ligament which spans the space between the liver and the minor curvature of the stomach (Figure 2D). The funnel-like omental vestibule had two orifices: to the right the ovoid epiploic foramen which is the opening between the peritoneal cavity and the omental vestibule, and to the left a larger circular orifice which connects the omental vestibule with the caudal recess of the omental bursa (Figure 1). The latter orifice was much larger in diameter than the epiploic foramen, resulting in the funnel-like shape of the omental vestibule which was delineated ventrally by the minor curvature of the stomach and dorsally by the gastropancreatic and hepatopancreatic folds which contain the left gastric artery and the hepatic artery, respectively (Figure 1D). The gastropancreatic fold extended from the dorsal abdominal wall to the fundus of the stomach. The hepatopancreatic fold extended from the dorsal abdominal wall toward the pyloric region of the stomach (Figure 1D). Both folds were connected with each other dorsally. The hepatic artery was enclosed dorsally within the hepatopancreatic fold and then continued within the hepatoduodenal ligament, running parallel and to the left of the portal vein before entering the liver. The pancreas was situated ventrocaudal to the hepatoduodenal ligament, the hepatopancreatic and gastropancreatic folds. The portal vein perforated the pancreas as it courses craniolaterally and runs on the left side of the epiploic foramen before entering the liver. The dorsocranial delineation of the funnel-like omental vestibule was formed laterally by the base of the caudate process of the liver and medially by the caudal vena cava, which was more or less embedded in the liver. In all horses an extension of the omental vestibule was found dorsal to the caudal vena cava. This dorsal recess of the omental vestibule was situated on the dorsal and to left side of the caudal vena cava and was directly adjacent to the dorsal abdominal wall (Figure 1B, Figure 2). Cranially this dorsal recess was delineated by the right coronary ligament.

This study included 22 Warmblood horses, 4 Thoroughbreds, 3 ponies and 1 Standardbred. There were 2 stallions, 18 geldings and 10 mares. The age ranged from 9 weeks to 27 years with a mean of 12.4 ± 7.7 years. The body weight of the horses ranged from 140 to 700 kg with a mean of 498 ± 125 kg. The mean circumference of the epiploic foramen was 11.6 ± 2.6 cm (range 6.8-16.6 cm) (Table 1).

Table 1: Measurements of the epiploic foramen (EF) on the polyurethane casts in 30 horses.

Study number	Breed	Sex	Weight (kg)	Age (years)	Circumference EF (cm)	Length EF (cm)	Height EF (cm)
1	Warmblood	Mare	531	7.5	15.2	6.2	3.8
2	Thoroughbred	Gelding	502	10.7	16.6	7.0	4.0
3	Warmblood	Mare	675	13.4	15.3	6.2	2.0
4	Warmblood	Stallion	500	10.8	7.4	2.8	1.6
5	Warmblood	Gelding	555	18.0	15.2	6.0	3.2
6	Pony	Mare	350	3.8	11.5	4.8	2.0
7	Warmblood	Stallion	577	12.0	13.7	5.6	2.7
8	Thoroughbred	Mare	450	4.0	9.8	3.6	2.0
9	Warmblood	Mare	446	25.0	8.8	5.0	2.5
10	Warmblood	Gelding	660	11.0	10.5	4.7	3.0
11	Warmblood	Gelding	580	10.0	11.0	4.6	3.0
12	Warmblood	Gelding	474	27.0	13.5	5.5	3.2
13	Warmblood	Gelding	470	23.0	12.0	3.6	2.6
14	Warmblood	Mare	494	23.0	9.5	3.8	2.2
15	Pony	Mare	244	1.2	7.4	3.5	1.1
16	Warmblood	Gelding	385	1.2	8.8	3.2	1.2
17	Warmblood	Gelding	600	9.1	11.2	5.3	2.8
18	Warmblood	Gelding	510	3.0	10.5	4.6	2.6
19	Warmblood	Gelding	600	10.8	10.0	3.8	2.0
20	Warmblood	Gelding	700	10.4	10.8	3.6	1.0
21	Warmblood	Gelding	650	9.6	12.0	4.6	3.0
22	Thoroughbred	Mare	470	24.4	9.6	4.2	2.8
23	Warmblood	Gelding	578	17.2	11.8	5.2	2.8
24	Warmblood	Mare	140	0.2	6.8	2.6	1.0
25	Thoroughbred	Gelding	470	8.4	14.6	6.0	2.5
26	Warmblood	Gelding	523	20.3	11.0	4.2	2.6
27	Standardbred	Gelding	449	15.4	14.2	5.0	3.2
28	Warmblood	Mare	485	18.2	14.5	5.2	3.0
29	Warmblood	Gelding	592	14.7	11.4	4.0	1.6
30	Pony	Gelding	300	19.7	12.0	3.5	2.2

There was no significant difference in circumference of the epiploic foramen between the sexes. There was a significant positive correlation between the circumference of the epiploic foramen and body weight (Pearson r = 0.391; P = 0.033) (Figure 4) but no significant correlation with age (r = 0.301; P = 0.106). The mean length of the ovoid epiploic foramen measured 4.6 ± 1.1 cm (range 2.6-7.0 cm) and the mean height of the ovoid epiploic foramen measured 2.4 ± 0.8 cm (range 1.0-4.0 cm).

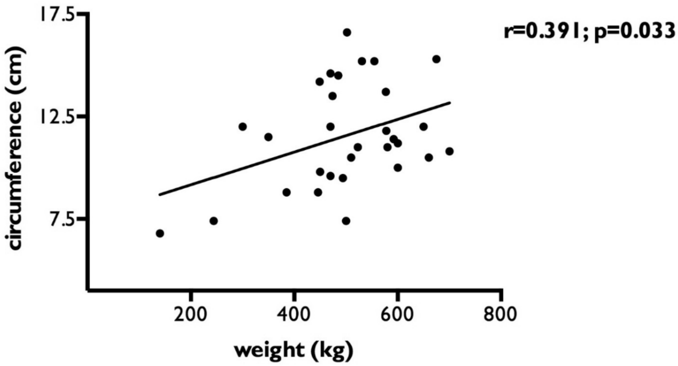

Figure 4: Correlation between the circumference of the epiploic foramen (cm) and body weight (kg).

Histological findings

At the level of the epiploic foramen, the hepatoduodenal ligament consisted of a central core of connective tissue, mainly composed of elastin fibres as demonstrated by markedly positive elastin staining on histology (Figure 5). Such a core was not found on histological sections of samples of the bursal part of the greater omentum and confirmed the ligamentous specialisation of this part of the lesser omentum.

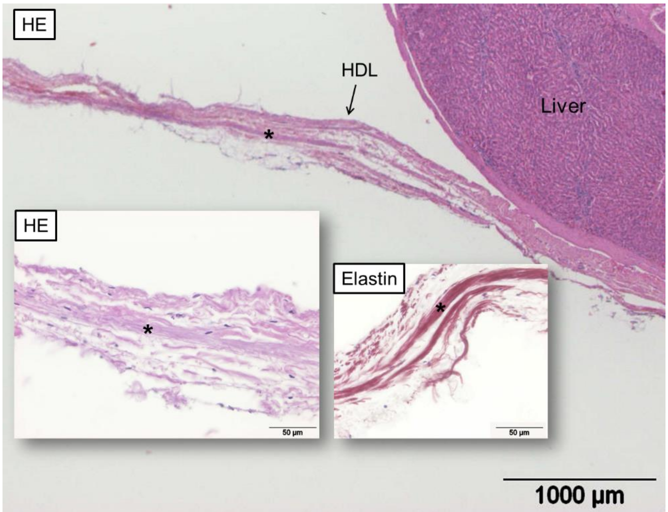

Figure 5: Histological sections of the hepatoduodenal ligament and its attachment to the liver with 2 detailed images (Haematoxylin-eosin (HE) staining and elastin staining). Note the central connective tissue core (asterisk) which stains positive for elastin fibres.

Laparoscopy

Laparoscopic images are represented in Figure 3. The laparoscope was directed cranially following the duodenum. After visualisation of the tip of the caudate process of the liver, the laparoscope was directed between the caudate process of the liver and the duodenum which is suspended at this level by the hepatoduodenal ligament. Care had to be taken not to pass the laparoscope cranial to the caudate process of the liver which is suspended by the hepatorenal ligament (Barone, 1997). This relatively broad ligament extended from the cranial pole of the right kidney to the caudate process of the liver and delineated a blind ending recess between the right lobe of the liver, the caudate process of the liver and the hepatorenal ligament which, if entered, might confuse the surgeon.

The epiploic foramen was visualised between the base of the caudate process and the hepatoduodenal ligament. The fold of the hepatoduodenal ligament which bordered the caudoventral side of the ellipsoid epiploic foramen was clearly visible (Figure 3B). Advancing the laparoscope into the epiploic foramen demonstrated the hepatoduodenal ligament as the ventral border of the lateral part of the omental vestibule (Figure 3C). At that location the portal vein was covered by the hepatoduodenal ligament precluding direct visualisation of the portal vein, although its contour was visible (Figure 3B). The caudal vena cava was encountered dorsally, midway within the omental vestibule, and was more or less embedded in hepatic tissue with quite some variation between animals. The part of the caudal vena cava that was not embedded in hepatic tissue lay directly within the omental vestibule. With the 30° angulated laparoscope it was not possible to visualise the dorsal recess above the caudal vena cava. Deeper inside the omental vestibule, the pulsating hepatic artery within the ventral hepatopancreatic fold was visible (Figure 3D). The pancreas was visible through this fold. This fold was seen as a very sharp border of the orifice between the omental vestibule and the caudal recess of the omental bursa. To visualise the omental bursa, the laparoscope was maximally introduced through the latter orifice and rotated clockwise. A counter-clockwise rotation allowed visualisation of the omental vestibule with the minor curvature of the stomach in between the two former views (Figure 3E).

Discussion

The different techniques used in the present study were complementary in fully defining the anatomy and relationships of the epiploic foramen and omental vestibule, as well as assisting in interpretation of the laparoscopic images.

Three vascular structures are immediately adjacent to the omental vestibule and were visualised during laparoscopy. The first one, the caudal vena cava, lies dorsally and is largely embedded in hepatic tissue. Variation in the amount of liver tissue that covered the ventral surface of the caudal vena cava was observed both during dissection and laparoscopy. The recess of the omental vestibule dorsal and to the left of the caudal vena cava has been previously described (Constantinescu and Schaller, 2012) and was large in all the casts. It could not be visualised laparoscopically with a 30° angulated laparoscope.

The second vascular structure is the hepatic artery which runs for part of its course within the hepatopancreatic fold and the hepatoduodenal ligament, ventral to the omental vestibule, originating from the coeliac artery. During laparoscopy, pulsation of this artery was observed. The coeliac artery trifurcates and gives origin to the left gastric artery, splenic artery and hepatic artery. The hepatic artery gives origin to the right gastric artery and finally bifurcates to become the gastroduodenal artery and the proper hepatic arterial branches (Barone, 1996). In man, this vascular anatomy is quite variable, which is of major interest for transplantation surgeons (Kim et al., 2012). Anatomical variations have also been previously described in horses (Barone, 1996).

The third vascular structure is the portal vein. This vein is covered by the hepatoduodenal ligament and its wall is not immediately adjacent to the omental vestibule nor can it be directly visualised during laparoscopy. Its course, ventral to the omental vestibule, is close to the omental vestibule and epiploic foramen, and the outline of the vein can be observed through the hepatoduodenal ligament. Consequently, attempts to manually stretch the epiploic foramen during equine colic surgery can lead to rupture of the portal vein (Vasey, 1988). Rupture of the portal vein or the caudal vena cava are known fatal complications during equine colic surgery (Vasey, 1988; Archer et al., 2004). Based on this anatomic study, rupture of the hepatic artery should also be considered as a differential diagnosis for fatal intra-operative haemorrhage during equine colic surgery.

In our dissections we demonstrated that the most relevant structure delineating the epiploic foramen and omental vestibule ventrally is the hepatoduodenal ligament which continues as the hepatogastric ligament. The caudoventral border of the epiploic foramen is delineated by a fold which protrudes from the hepatoduodenal ligament and not by the free border of the hepatoduodenal ligament as mentioned earlier (Nickel et al., 1973). The ventral aspect of the equine omental vestibule has been poorly defined so far in the literature. The *plica gastropancreaticoduodenalis* (Schmid, 1997), which has not been previously referenced in any anatomical works (Nickel et al., 1973; Sisson, 1975; Barone, 1997; Constantinescu and Schaller, 2012) and the gastropancreatic fold (Schmid et al., 1998; Freeman and Pearn, 2015) have been reported as ventral boundaries of the omental vestibule. The gastropancreatic fold, however, is defined as a fold of the wall of the omental bursa containing the left gastric vessels (Constantinescu and Schaller, 2012) and is therefore located at the opposite side of the stomach. This was confirmed in the present study by casting the coeliac artery with a liquid polymer in order to identify the left gastric artery and to demonstrate its location in the gastropancreatic fold. Similarly, the location of the hepatopancreatic fold was demonstrated by casting the coeliac artery and its various branches, including the hepatic artery, which we demonstrated to be included within this fold. The hepatopancreatic fold is defined as a fold of the wall of the omental bursa containing the hepatic artery. Together, the gastropancreatic and hepatopancreatic folds delineate the dorsal border of the orifice between the omental vestibule and the caudal recess of the omental bursa. This description is in agreement with the anatomical nomenclature and definitions (Constantinescu and Schaller, 2012).

Our polyurethane casting model in combination with the dissection of the specimens with casted coeliac artery and portal vein and the use of laparoscopic images clearly demonstrated the funnel-like shape of the omental vestibule which has two orifices: on the right the smaller ovoid epiploic foramen which is the orifice between the peritoneal cavity and the omental vestibule, and to the left a larger circular orifice which leads from the omental vestibule to the caudal recess of the omental bursa. We have demonstrated that the latter orifice was much larger in diameter than the epiploic foramen, resulting in the funnel-like shape of the omental vestibule. This larger orifice was delineated ventrally by the minor curvature of the stomach and dorsolaterally by the gastropancreatic and hepatopancreatic folds which contain the left gastric artery and the hepatic artery, respectively (Figure 1D).

The ovoid epiploic foramen has a mean length of 4.6 cm and a mean height of 2.4 cm. These dimensions are comparable with previously published data in which the “width” of the epiploic foramen was measured with a slide calliper on 51 cadavers (Schmid, 1997). However, since the slide calliper was blindly inserted in the epiploic foramen of recumbent cadavers and maximally opened, the measurements represent the maximal linear extension of the epiploic foramen, but they do not take into account the oval shape of the epiploic foramen *in situ*, which is needed for the development of an implant to close the epiploic foramen. In the current study, the cadavers were suspended in a natural standing position immediately after euthanasia to avoid distortion of the flexible structures in the region of interest. The epiploic foramen and omental vestibule were casted with a polyurethane prepolymer and the circumference, the height and the length of the epiploic foramen were measured on the cured casts. This approach for studying complex anatomical body cavities under circumstances comparable to the situation in the standing living animal generates a more comprehensive 3D understanding. However, we have to recognise that an overestimation of the measurements on our casts is possible due to dilatation by the pressurised foam.

Our data revealed some interesting findings. The circumference of the epiploic foramen of one horse (500 kg, Warmblood stallion, 2 years and 9 month old) was surprisingly small (7.4 cm). It was the same size as the epiploic foramen of a 14-month-old 244 kg pony mare and was only marginally larger than the epiploic foramen of a 9 week old 140 kg Warmblood filly (epiploic foramen circumference: 6.8 cm). The largest circumference of the epiploic foramen (16.6 cm) was measured in a 12-year-old Thoroughbred gelding of 502 kg. One of the horses studied was a 700 kg, 10-year-old Warmblood gelding that died due to atrial fibrillation and severe right heart dilatation. The outline of the dilated caudal vena cava on the cast was large, but this did not affect the shape of the epiploic foramen which is not directly bordered by this vein (epiploic foramen circumference: 10.8 cm). There was no significant correlation between the circumference of the epiploic foramen and age, and studies have also shown that increasing age does not predispose horses for EFE (Schmid, 1997; Schmid et al., 1998; Freeman and Schaeffer, 2001).

In our clinical experience, cases of EFE have small intestines passing from the left to the right through the epiploic foramen. After inverting the omental bursa, the intestines pass over the minor curvature of the stomach, proceed through the funnel-like omental vestibule and become entrapped at the level of the epiploic foramen which is the smaller and most rigid part of the opening. At some point in this process the greater omentum ruptures. It has been previously suggested that the difference in size of the 2 openings of the omental vestibule could explain the higher prevalence of left-to-right EFE (Schmid, 1997; Schmid et al., 1998; Freeman and Pearn, 2015).

The central connective tissue core within the hepatoduodenal ligament is probably responsible for the rigidity of the epiploic foramen walls and confirms the ligamentous specialisation of this omental structure. Its elastic nature could prevent it from rupturing during incarceration and/or surgical manipulation.
In the future, our novel anatomical and laparoscopic descriptions could contribute to the development of a safe preventive laparoscopic closure technique of the epiploic foramen.

Authors' declaration of interests

No competing interests have been declared.

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Manufacturers' addresses

[a]Sciencelab.com Inc., Houston, Texas

[b]Hygeco, Garges-les-Gonesse Cedex, France

[c]Polysciences Europe GmbH, Eppelheim, Germany

[d]Hubo België n.v., Wommelgem, Belgium

[e]Pfizer Animal Health n.v., Brussels, Belgium

[f]Sterop, Brussels, Belgium

[g]AstraZeneca n.v., Brussels, Belgium

[k]VMD n.v., Arendonk, Belgium

[l]Karl Storz GmbH, Tuttlingen, Germany

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CHAPTER 4

Development of a new laparoscopic Foramen Epiploicum Mesh Closure (FEMC) technique in horses

Adapted from:

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Abstract

Reasons for performing study: Epiploic foramen entrapment (EFE) is, based on the number of reports in the literature, a relatively important life-threatening cause of colic in horses that could be prevented by closing the epiploic foramen in horses at risk of developing EFE.

Objectives: To describe the laparoscopic Foramen Epiploicum Mesh Closure (FEMC) technique and its outcome.

Study design: Descriptive experimental study.

Methods: The epiploic foramen of 6 horses was closed with the novel FEMC technique. A diabolo-shaped constructed mesh was introduced in the omental vestibule through the epiploic foramen under laparoscopic visualisation in the standing sedated horse. Clinical and laboratory parameters were recorded during the post-operative period. Four weeks after the intervention repeat laparoscopy was performed in all horses. Three horses were subjected to euthanasia one, two and three months after the intervention, and were examined on necropsy and histopathology. The remaining 3 horses were followed clinically for 6 months.

Results: The 6 FEMC procedures were performed successfully in a median surgery time of 22 min (range 18-27 min). One horse was treated for large colon impaction in the immediate post-operative period. On repeat laparoscopy at 4 weeks all 6 epiploic foramina were closed and no undesired adhesions were identified. This was confirmed on gross and histopathologic examination of the 3 horses that were subjected to euthanasia. The 3 remaining horses were clinically normal in the 6 months post-operative observation period.

Conclusions: This FEMC technique provides a fast, simple, reliable and safe procedure to obliterate the epiploic foramen and may be useful in horses at risk for EFE.

Introduction

Small intestinal strangulating lesions including epiploic foramen entrapment (EFE) are serious life threatening conditions associated with high morbidity and mortality (Proudman et al., 2002a, 2002b, 2005), generating high expenses for surgery and post-operative management. In about 5% of surgically treated equine colic patients, colic signs are the result of intestinal EFE (Vachon and Fischer, 1995; Archer et al., 2004; Mair and Smith, 2005). For a EFE cohort that recovered following anaesthesia, the one-year post-operative survival rate of EFE was reported to be 50.6% and the two-year post-operative survival rate was 34.3% (Archer et al., 2011).

Several risk factors for EFE have been identified (Archer et al., 2008a, 2008b), the most important one being windsucking/crib-biting (Archer et al., 2008a). Epiploic foramen entrapment can be a recurrent condition (Vachon and Fischer, 1995; Archer et al., 2004; Freeman et al., 2014). The topographic and laparoscopic anatomy of the equine epiploic foramen and omental vestibule has been described in detail in Chapter 3 (van Bergen et al., 2015). In brief, the omental vestibule is a funnel-like structure with 2 openings: a smaller one on the right side of the median plane, which is the epiploic foramen, and a larger one on the left side, which is the opening from the omental vestibule to the caudal recess of the omental bursa. The epiploic foramen is delineated on its craniodorsal side by the base of the caudate lobe of the liver and on its caudoventral side by a secondary fold of the hepatoduodenal ligament which attaches to the cranial and the caudal aspect of the caudate lobe of the liver (van Bergen et al., 2015).

Recently a technique to close the epiploic foramen by means of 4 to 10 helical titanium coils placed in the liver and the gastropancreatic fold was described (Munsterman et al., 2014). In the current study we describe the laparoscopic Foramen Epiploicum Mesh Closure (FEMC) technique as a simplified and less invasive method to obliterate the epiploic foramen to prevent EFE in the standing sedated horse. We hypothesized that the FEMC technique is a fast and simple laparoscopic technique allowing complete closure of the epiploic foramen in all horses with minimal side effects.

Material and Methods

Animals

Six adult experimental horses (4 Warmbloods and 2 Thoroughbreds; 3 geldings and 3 mares) were used. Age was 4.2-23.4 years with a mean (± s.d.) of 11.7 ± 7.1 years, bodyweight (bwt) was 400-625 kg with a mean (± s.d.) of 520 ± 80 kg and the wither height was 1.54-1.69 m with a mean (± s.d.) of 1.64 ± 0.05 m. The horses had no history of abdominal disease or surgery. Pre-operative clinical examinations were normal. Blood samples were collected before surgery to determine baseline values for white blood cell count, plasma fibrinogen and serum bile acid concentrations, and serum activities of aspartate aminotransferase (AST), γ-glutamyl transferase (GGT), and amylase to monitor inflammatory, liver and pancreatic parameters during the study period.

Anaesthetic and perioperative protocols

Food but not water was withheld for 36 h prior to surgery. A 12 gauge catheter (Intraflon 2)[a] was placed in the left or right jugular vein. Ten million IU of sodium penicillin (Penicilline)[b] and 1.1 mg/kg bwt flunixin meglumine (Finadyne)[c] were administered intravenously (IV) shortly before surgery. During the procedure an intramuscular (IM) injection of 21000 IU/kg bwt benzylpenicillinum procainum (Peni-kel)[d] and a subcutaneous injection of 3480 IU antitetanus toxoid (antitetanus serum)[e] were given. Horses were sedated with 10 µg/kg bwt detomidine (Domosedan)[f] and 0.1 mg/kg bwt morphine (Morphine HC)[g] IV and sedation was maintained by constant rate infusion of 6 µg/kg bwt/h detomidine (Domosedan)[f]. Local analgesia was provided by infiltration of the right flank with 40 mL mepivacaine 2% (Scandicaine)[h] at the portal sites. The horse received 1.1 mg/kg bwt flunixin meglumine orally (Finadyne oral paste)[c] for 3 days following the laparoscopic procedure.

FEMC technique

(for more detailed explanation: see addendum "Clinical guidelines for laparoscopic FEMC" at the end of the Thesis)

Horses were restrained in stocks, the tail was bandaged, and the right abdominal flank was clipped from the epaxial musculature dorsally to the inguinal fold ventrally and from the *tuber coxae* caudally to the 12th intercostal space cranially. The surgical field was scrubbed with chlorhexidine digluconate and disinfected with 70% isopropyl alcohol. Before the start of the procedure the mesh was prepared. Two preformed oval shaped knitted polypropylene meshes (3DMax Mesh)[i] (10.8 x 16.0 cm), used for laparoscopic inguinal hernia repair in man, were used to prepare a diabolo-shaped implant to obliterate the epiploic foramen. The first mesh was grasped with a DeBakey tissue forceps on its smallest diameter as shown in Figure 1. The forceps was twisted 270° and subsequently withdrawn. Finally the rolled part of the mesh was retained and double folded on its longest diameter. The resultant pyramidal configuration was kept in place with a 2-0 polyglactin 910 (Vicryl)[j] horizontal mattress suture on the tip of the pyramid. The second mesh was prepared in the same manner and finally the tips of the 2 pyramids were secured together with an additional 2-0 polyglactin 910 (Vicryl)[j] horizontal mattress suture. The resultant diabolo configuration of the mesh was foldable, but after manipulation the original diabolo-shape was recovered (diameter: 10 cm, length: 10 cm). A 2.5 m long USP 2 polyamide wire (Supramid)[k] was passed through on one side of the implant which served as a security line to prevent loss of the implant into the abdomen or to retrieve a mesh placed too deeply into the omental vestibule.

The laparoscope portal was made midway between the last rib and the *tuber coxae* in the ventral half of the palpable crus of the internal oblique abdominal muscle to avoid interference between the laparoscope and the *tuber coxae* while directing the laparoscope cranially. A 1.5 cm stab incision was made through the skin and a 10 mm diameter, 20 cm long laparoscopic cannula[l] was introduced by means of a secured trocar[l]. A 58 cm 30° laparoscope[m] connected to a camera[n] was introduced through the cannula to ascertain its intra-abdominal position before carbon dioxide insufflation to 15 mmHg by means of an insufflator[m] was started. Subsequently the laparoscope was directed cranially between the caudate process of the liver and the mesoduodenum to inspect the epiploic foramen and omental vestibule as previously described (van Bergen et al., 2015). The single instrument portal was made 10 cm ventral to the laparoscopic portal. A 4 cm skin incision was performed followed by abdominal wall penetration with a secured trocar[l]. After removal of the secured trocar a stainless steel tube (applicator tube; length 68 cm, diameter 2 cm) slightly curved on its end (Figure 2A) with a blunt trocar in place was introduced through the instrument portal and directed into the epiploic foramen under laparoscopic guidance.

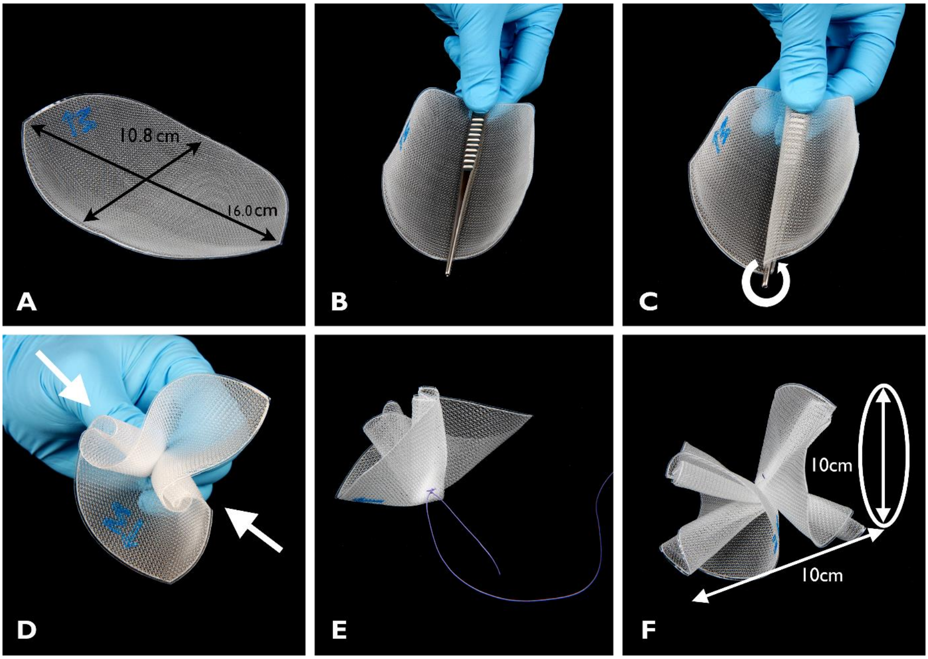

Figure 1: Preparation of the diabolo-shaped expandable mesh construct (diameter: 10 cm, length: 10 cm) with 2 preformed knitted polypropylene meshes (3DMax Mesh)[i] used for laparoscopic inguinal hernia repair in man.

A) Preformed knitted polypropylene mesh.
B) The mesh is grasped with a DeBakey tissue forceps on its smallest diameter.
C) The forceps is twisted 270° and subsequently withdrawn.
D) The mesh is folded on its longest diameter.
E) The resultant pyramidal configuration is secured with a 2-0 polyglactin 910 (Vicryl)[j] horizontal mattress suture on the tip of the pyramid.
F) A second mesh is prepared in the same manner and the tips of the 2 pyramids are secured together with an additional 2-0 polyglactin 910 (Vicryl)[j] horizontal mattress suture

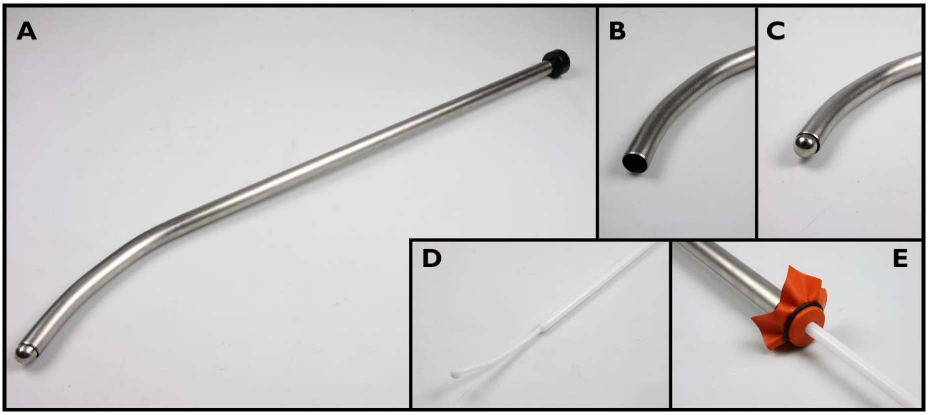

Figure 2: Custom-made instrumentation for the laparoscopic FEMC technique.

A) Stainless steel applicator tube (length 68 cm, outer diameter 2 cm) slightly curved on its end with a blunt trocar in place.
B) Detail of the tip of the applicator tube with the blunt trocar removed.
C) Detail of the tip of the applicator tube with the blunt trocar in place.
D) Tip of the flexible nylon pushing device.
E) Custom-made valve to prevent loss off intra-abdominal pressure

The applicator tube was manipulated by the surgeon while laparoscopic guidance was performed by the assistant (Figure 3A). Once the tube was introduced through the epiploic foramen within the omental vestibule, the blunt trocar was withdrawn and the diabolo-shaped implant was folded on its longitudinal axis and introduced in the applicator tube. A custom-made ring covered with a perforated piece of Eshmar bandage was placed on the end of the applicator tube to avoid loss of pressure and subsequent decreased visualization between the manipulations (Figure 2E). With a polyoxymethylene flexible pushing device (100 cm long; Figure 2D) the diabolo-shaped implant was pushed through the applicator tube. Under laparoscopic observation the implant was introduced into the omental vestibule (Figure 4C,D). Once the implant was almost completely out of the applicator tube, the applicator tube was withdrawn over the pushing device which kept the implant at its predetermined location (Figure 4E), leaving 1 cm of the implant protruding through the epiploic foramen into the abdominal cavity (Figure 4F). In this position the smallest middle part of the diabolo-shaped implant was located at the level of the portal vein (Figures 4D, 6). After a final verification of the correct position of the implant the security line was withdrawn keeping the pushing device in place against the mesh construct to avoid pulling the mesh out of the epiploic foramen. Finally the applicator tube with pushing device was removed from the abdomen. Portals were closed in 2 layers (subcutis and skin) with USP 2-0 polyglactin 910 (Vicryl)[j]. Time from first skin incision to first subcutaneous suture placement was recorded.

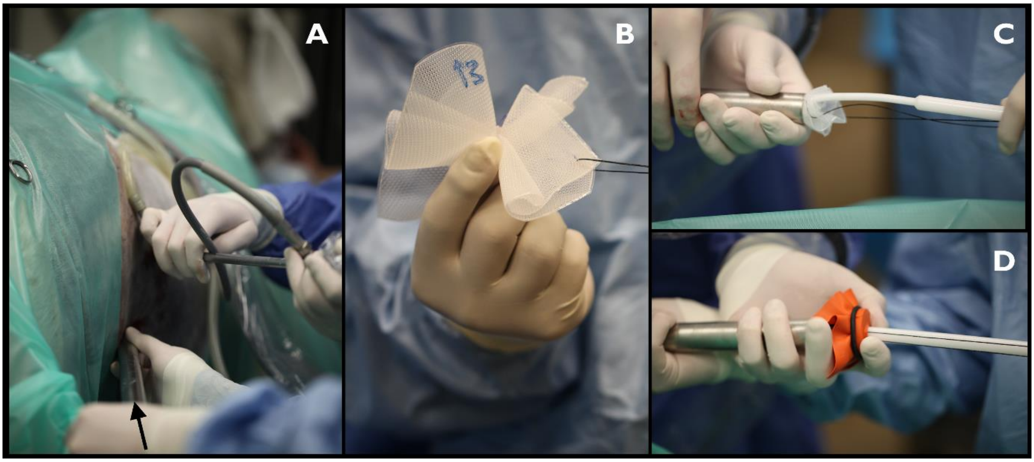

Figure 3: Laparoscopic FEMC technique.

A) Caudal view on the right abdomen. The surgeon manipulates the applicator tube (black arrow) through the epiploic foramen in the omental vestibule guided by an assistant manipulating the laparoscope.
B) The prepared diabolo-shaped mesh implant with the security line.
C) Once the applicator tube is introduced into the omental vestibule, the blunt trocar is withdrawn and the prepared diabolo-shaped mesh implant is folded and pushed through the applicator tube with the pushing device.
D) A custom-made valve is placed at the outer end of the applicator tube to prevent loss of abdominal pressure in between manipulations.

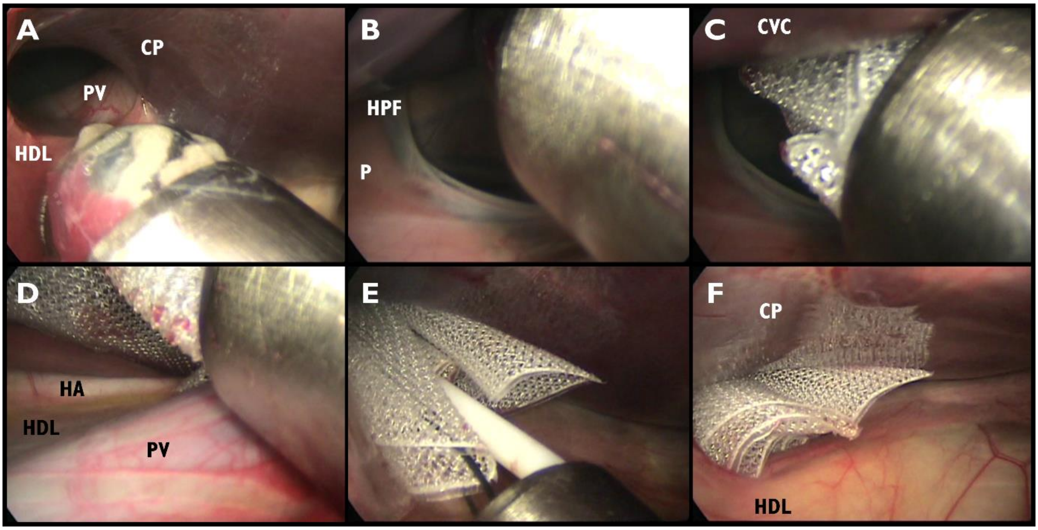

Figure 4: Laparoscopic images during the FEMC technique.

A) The applicator tube with blunt trocar (covered with fat from the abdominal penetration) before introduction through the epiploic foramen.
B) The applicator tube is introduced in the omental vestibule through the epiploic foramen. The blunt trocar has been removed.
C) The first part of the diabolo-shaped mesh is pushed through the applicator tube with the pushing device.
D) The applicator tube is withdrawn slightly over the pushing device to exteriorize the second half of the diabolo-shaped mesh.
E) The applicator tube is withdrawn over the pushing device (white) and the security line (black) out of the epiploic foramen.
F) Final inspection after removal of the applicator tube, the pushing device and the security line. The mesh protrudes approximately 1 cm out of the epiploic foramen in the abdominal cavity.

CP: caudate process of the liver, CVC: caudal vena cava, HA: hepatic artery, HDL: hepatoduodenal ligament, HPF: hepatopancreatic fold, P: pancreas, PV: portal vein.

Post-operative clinical and laboratory assessment

Horses were box rested for 1 month to allow mesh adherence to the surrounding tissues. Hand walking (3 times 10 min/day) was introduced in the third and fourth weeks. Horses were subjected to a daily clinical examination. White blood cell count, plasma fibrinogen and serum bile acid concentrations and serum activities of AST, GGT, and amylase activity were determined on days 1, 3, 5, 8 and 30 after surgery. Horses number 1, 3 and 5 were returned to pasture with daily observation from the second to the sixth month after the initial surgery.

Repeat laparoscopy

One month after the initial procedure all horses underwent repeat laparoscopic examination of the abdomen to determine the degree of obliteration of the epiploic foramen. Food but not water was withheld for 36 h. The same laparoscopic portal as described earlier was used and the abdominal cavity and epiploic foramen were inspected. Subsequently the portal was closed in 2 layers with USP 2-0 polyglactin 910 (Vicryl)[j] suture material.

Necropsy and histopathology

Horses were humanely subjected to euthanasia 1 month (horse 6), 2 months (horse 4) and 3 months (horse 2) after the FEMC procedure. Euthanasia was performed with 90 mg/kg bwt sodiumpentobarbital (Release)[o] IV after sedation with 10 µg/kg bwt detomidine (Domosedan)[f] + 0.1 mg/kg bwt morphine (Morphine HCL)[g] IV. Immediately after euthanasia the horses were positioned in left lateral recumbency and the right abdominal and thoracic wall was removed. On gross examination the degree of obliteration of the epiploic foramen was recorded from the right side and from the left side after opening the omental bursa. Particular attention was given to the detection of possible undesired adhesions to the right and left of the region of interest. Subsequently the epiploic foramen, including the surrounding organs (i.e. the liver, the pancreas, the stomach, the caudal vena cava, the portal vein and the hepatic artery) were removed from the carcasses and spread on a dissection table. Gross transverse sections at the level of the omental vestibule and epiploic foramen were obtained to document the degree of obliteration and to allow sampling of all the surrounding tissues for histopathologic examination. Tissue samples as close as possible to the surgical site were collected, including samples from the right lobe of the liver, the caudate lobe of the liver, the pancreas, the caudal vena cava, the portal vein and the hepatic artery, and submitted for routine histopathologic examination after fixation for 48 h in 10 % neutral buffered formalin. Additionally a complete section of the whole region including the mesh implant was fixed for 48 h in 10 % neutral buffered formalin. The pathologist was blinded to the study number to allow objective evaluation at the different post-operative times.

Results

FEMC technique

During the first procedure the portals were placed somewhat too far dorsally which caused interference between the laparoscope, the applicator tube and the *tuber coxae*. This problem was avoided in the subsequent procedures by using a more ventral portal. In our hands the procedure was considered easy to perform. All implants were correctly placed in the omental vestibule and epiploic foramen. After passage through the applicator tube the diabolo-shaped mesh construct expanded well and was in full contact with the surrounding tissues of the omental vestibule and epiploic foramen. No major intra-operative complications were encountered. The initial position of the mesh in the sixth horse was considered too deep into the omental vestibule in such a manner that the smallest part of the diabolo-shaped implant was located beyond the portal vein and consequently no part of the implant was protruding through, nor in contact with the epiploic foramen itself. The mesh was therefore withdrawn from the abdomen with the security line and was subsequently repositioned. The median surgery time was 22 min (range 18-27 min).

Post-operative clinical and laboratory assessment

No alterations in clinical parameters were recorded in the post-operative observation period except in horse 2 that developed a large colon impaction 24 h after food reintroduction that subsequently resolved with medical treatment. The surgical incisions healed well without complications. Horse 6 had very high baseline levels (day 0) of AST and GGT activity. These values diminished dramatically during the study period and were not taken into consideration. No value was beyond the laboratory reference interval at any time of the study in horses 1 to 5.

Horses 1, 3 and 5 displayed no complications during the 6 month post-operative observation period.

Repeat laparoscopy

On repeat laparoscopy, the epiploic foramen was completely obliterated in all horses (Figure 5). The hepatoduodenal ligament was attached to the caudate lobe of the liver by a firm adhesion in all 6 horses, which impeded passage through the epiploic foramen into the omental vestibule. No other adhesions in the abdominal cavity were detected on laparoscopic inspection.

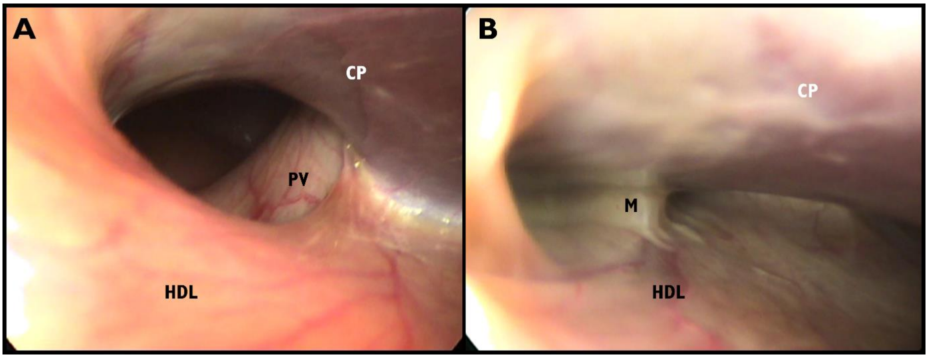

Figure 5: Laparoscopic view on the epiploic foramen of horse 3 before obliteration with the Foramen Epiploicum Mesh Closure (FEMC) technique (A) and 1 month after the obliteration with the FEMC technique (B).
CP: caudate process of the liver, PV: portal vein, HDL: hepatoduodenal ligament, M: mesh covered by fibrous tissue adhering the HDL to the CP.

Necropsy and histopathology

Gross evaluation of the abdomen revealed a consistent closure of the right and left side of the omental vestibule including the epiploic foramen in all 3 dissected horses (Figure 6). No undesired intra-abdominal adhesions were detected. Slight compression of liver tissue covering the caudal vena cava and small haemorrhage throughout the fibrotic area in the horse that was necropsied 1 month after surgery, but otherwise no significant pathology was found.

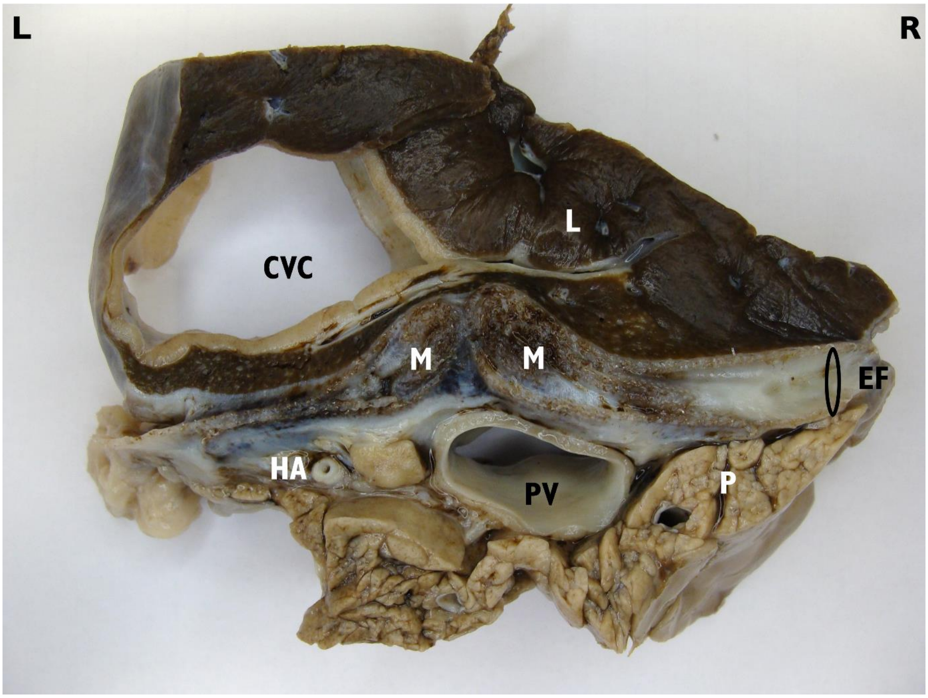

Figure 6: Caudo-cranial view on a cross-section through the omental vestibule and epiploic foramen (EF) 1 month after obliteration of the epiploic foramen and omental vestibule with the Foramen Epiploicum Mesh Closure technique. The tissues were fixed for 48 h in 10% neutral buffered formalin. Note the complete closure of the EF and omental vestibule by the diabolo-shaped mesh construct (M). Circle: entrance from the abdominal cavity into the omental vestibule through the EF.
CVC: caudal vena cava, HA: hepatic artery, L (black): left, L (white): liver, P: pancreas, PV: portal vein, R: right.

Histologically, the mesh was lost due to processing of the tissue. However, mesh-formed holes in the tissue clearly indicated where it was located. In all three horses the mesh was embedded in a fibrotic area, with a mixture of young, plump fibroblasts and more mature fibrocytes. Multiple small lymphocytic foci, and in horse 6 also multiple small haemorrhages, were dispersed throughout the fibrotic area. Neither the caudate process nor the right lobe of the liver showed remarkable changes in any horse, apart from some mild lipidosis, and in horse 6, moderate atrophy and compression of the liver lobules between the vena cava and the fibrotic area (Figure 7). This area of the liver of this horse also showed mild to moderate bile duct hyperplasia and mild to moderate lymphoplasmocytic infiltrations. In the pancreas, caudal vena cava, portal vein and hepatic artery, no histologic changes were seen in any of the horses.

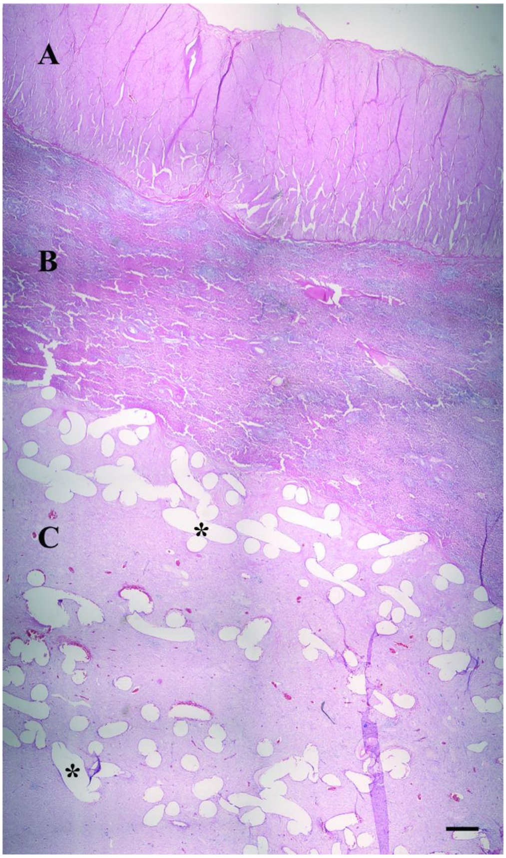

Figure 7: Haematoxylin and eosin staining of a section through the wall of the caudal vena cava (A), the liver (B) and the mesh-formed holes (*) surrounded by fibrosis (C) of horse 6. Compression of the liver lobuli located between the caudal vena cava and the fibrotic area is seen. The scale-bar represents 400 µm.

Discussion

In our hands, the novel FEMC technique allowed correct and rapid laparoscopic placement of a mesh in the epiploic foramen resulting in complete obliteration. Access to the epiploic foramen was gained by directing the laparoscope cranially between the mesoduodenum and the caudate process of the liver after full insufflation of the abdomen to 15 mmHg (van Bergen et al., 2015). To avoid interference from the camera with the *tuber coxae* it was important to create the portal relatively more ventral than most conventional laparoscopic techniques, at the level of the ventral half of the palpable crus of the internal oblique abdominal muscle.

An elective preventive surgery should be as safe as possible. For this reason we previously performed a thorough topographic and laparoscopic study to measure the dimensions of the epiploic foramen and to identify the exact position of the adjacent vasculature, including the caudal vena cava, the portal vein and the hepatic artery (van Bergen et al., 2015). The FEMC technique provided a safe method avoiding potential damage to the surrounding vasculature and/or organs and only 2 portals were used.

Some simple custom-made laparoscopic instruments (applicator tube, blunt trocar and polyoxymethylene flexible pushing device) are needed to perform the FEMC technique. The 2 cm diameter of the applicator tube was considered suitable to penetrate the abdominal wall, to pass the diabolo-shaped mesh implant and to pass through the epiploic foramen into the omental vestibule of which the mean circumference was previously determined to be 11.6 ± 2.6 cm (van Bergen et al., 2015). Introduction of the applicator tube through the epiploic foramen was easier to perform when manipulation of the laparoscope was performed by a second surgeon. The preformed knitted polypropylene meshes (3DMax Mesh)[i] used in this study are commercially available.

The diabolo-shaped mesh construct was in full contact with the tissues surrounding the funnel-like omental vestibule. One end of the diabolo protruded 1 cm out of the epiploic foramen into the abdominal cavity to ensure full contact with the epiploic foramen and to prevent the implant from gliding deeper into the omental vestibule or into the omental bursa. The expandable configuration of the implant and the funnel-like shape of the omental vestibule with the epiploic foramen as its narrowest point prevented the implant from moving out of the omental vestibule, through the epiploic foramen, into the abdominal cavity. The epiploic foramen was completely closed in all 6 horses on repeat laparoscopy 1 month after the mesh application. With the previously reported technique partial closure was observed in one horse where the gastropancreatic fold and right lobe of the pancreas were secured to the caudate process of the liver using 4 to 10 helical titanium coils (Munsterman et al., 2014). This incomplete closure was not observed in the current study and is unlikely to occur with the FEMC technique owing to the extensive contact of the implant with the surrounding structures. Contact between the mesh construct and the surrounding structures is likely to increase after release of intra-abdominal pressure at the end of the procedure, which collapses the virtual space in the omental vestibule and epiploic foramen. Horse 2 was a windsucking/crib-biting Thoroughbred, but this behaviour had no effect on the stability of the mesh construct and at repeat laparoscopy and at necroscopy the epiploic foramen was completely closed.

The concept of three-dimensional meshing without additional methods of fixation has gained popularity in human medicine in recent years. Fixation-free three-dimensional meshing induces ingrowth of viable and structured tissue instead of regressive fibrotic scarring causing pain, which is often encountered when fixed static implants are used (Amato et al., 2015). Clinical outcome using this meshing concept was considered excellent in human inguinal hernia repair (Bell and Price, 2003).

The median surgical time with the FEMC technique was 22 min (range 18-27 min) which is shorter compared to the previously reported technique (40.5 min (range 22-110 min)) (Munsterman et al., 2014). No post-operative complications related to the surgery occurred during the one month observation period of horse 6, the 2-month observation period of horse 4, and the 6-month observation period of horses 1, 3 and 5. Horse 2 was treated for large colon impaction in the immediate post-operative period but otherwise showed no clinical signs during its 3-month observation period.

Horse 6 had high base line AST and GGT activity without clinical signs of any disease. We decided to continue the experiment and to exclude the blood values from the final interpretation. The AST and GGT values from this horse decreased toward reference values during the study period. The exclusion of the blood values from horse 6 could be considered a limitation of our study. However, in the remaining 5 horses there were no laboratory abnormalities at any time of the study.

The complete funnel-like structure of the omental vestibule including the epiploic foramen was closed with nonreactive fibrous tissue. This is an advantage compared to the coil technique where only 1 tissue fold closed the epiploic foramen and where in 2 cases the tissue was fragile and could be digitally disrupted during *post-mortem* examination (Munsterman et al., 2014). Complete closure of the whole funnel-like omental vestibule obtained with the FEMC technique makes both left-to-right EFE and right-to-left EFE impossible. Left-to-right EFE is more prevalent (Archer et al., 2004) and this highlights the importance of closure of the large left entrance of the funnel-like omental vestibule.

Preventive closure of the epiploic foramen may be indicated for horses at risk for EFE and several risk factors have been identified (Archer et al., 2008a, 2008b), the most important being windsucking/crib-biting (Archer et al., 2008a). Closure of the epiploic foramen could also be performed to prevent recurrence of EFE, although recurrence after EFE is not very common (recurrence rate 1/53 (Vachon and Fischer, 1995), 2/71 (Archer et al., 2004) and 1/7 (Freeman et al., 2014)). Horses at risk that have undergone surgery for EFE might be candidates for preventive closure of the epiploic foramen. Preventive procedures are described for other specific types of colic, such as inguinal hernioplasty (Fischer et al., 1995; Mariën, 2001; Rossignol et al., 2007, 2014; Wilderjans et al., 2012) and nephrosplenic closure (Marien et al., 2001). Further research is needed to characterise specific risk factors for recurrence, but based on the current results we conclude that the FEMC technique provides a fast, simple, reliable and safe alternative to obliterate the epiploic foramen in horses at risk for EFE.

Authors' declaration of interests

No competing interests have been declared.

Ethical Animal Research

All procedures were approved and supervised by the Ethical Committee of Ghent University (EC2014/07).

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Manufactures' details

[a]Vygon nv, Brussels, Belgium

[b]Kela Pharma nv, Sint-Niklaas, Belgium

[c]Schering Plough Animal Health, Brussels, Belgium

[d]Kela Veterinaria, Sint-Niklaas, Belgium

[e]Intervet Belgium nv, Brussels, Belgium

[f]Pfizer Animal Health n.v., Brussels, Belgium

[g]Sterop, Brussels, Belgium

[h]AstraZeneca n.v., Brussels, Belgium

[i]Bard Davol Inc., Warwick RI, USA

[j]Johnson & Johnson Medical n.v., Diegem, Belgium

[k]SMI, St Vith, Belgium

[l]Dr Fritz GmbH, Tuttlingen, Germany

[m]Karl Storz GmbH, Tuttlingen, Germany

[n]Richard Wolf GmbH, Knittlingen, Germany

[o]Ecuphar n.v., Oostkamp, Belgium

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CHAPTER 5

Laparoscopic evaluation of the epiploic foramen after celiotomy for epiploic foramen entrapment in the horse

Adapted from:
van Bergen, T., Wiemer, P., Schauvliege, S., Paulussen, E., Ugahary, F., Martens, A., 2016. Laparoscopic evaluation of the epiploic foramen after celiotomy for epiploic foramen entrapment in the horse. Veterinary Surgery 45, 596–601.

Presented at:
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Abstract

Objectives: To evaluate the epiploic foramen laparoscopically in horses previously treated for epiploic foramen entrapment (EFE) and determine whether spontaneous epiploic foramen obliteration occurs.

Study design: Non-consecutive case series.

Animals: Seven horses.

Methods: The epiploic foramen was inspected by right flank laparoscopy between 35-71 days after successful surgical treatment for EFE. Data were collected on the presence of stereotypic behaviours, details about surgery for EFE (time from colic onset to surgery, site and length of entrapped intestine, direction of entrapment, compromise of the intestine, intestine resected), the time between surgery for EFE and laparoscopy, and the laparoscopic appearance of the epiploic foramen. If the epiploic foramen was open, a mesh was introduced to obliterate the epiploic foramen (Foramen Epiploic Mesh Closure [FEMC]). Clinical progress of the horses was followed by owner telephone interview at 1 and 4 months after laparoscopy, and a final interview between 135 and 282 days after laparoscopy. Owners were asked if specific post-operative complications had occurred and the level of exercise the horse was currently working at.

Results: At laparoscopy, 3/7 (43%) horses had complete closure of the epiploic foramen by dense fibrous tissue. The FEMC was performed in 4 horses without major complications. Post-operative colic episodes were recorded in 3 horses, all of which demonstrated windsucking/crib-biting behaviour.

Conclusions: Laparoscopic evaluation after celiotomy for EFE revealed spontaneous closure of the epiploic foramen in 3/7 EFE horses. This finding could explain the reported low recurrence rate after surgical treatment for EFE.

Introduction

Small intestinal strangulating lesions, including epiploic foramen entrapment (EFE), are life threatening conditions with a high morbidity and mortality (Proudman et al., 2002a, 2002b, 2005). Epiploic foramen entrapment is diagnosed in about 5% of horses undergoing surgery for colic (Vachon and Fischer, 1995; Archer et al., 2004; Mair and Smith, 2005). Several risk factors for EFE have been identified (Archer et al., 2008a, 2008b) with windsucking/crib-biting behaviour (odds ratio 67.3) having the strongest association (Archer et al., 2008a). The reported recurrence rates for EFE are low compared with other types of colic. Recurrence for EFE is reported as 2% (Vachon and Fischer, 1995), 3% (Archer et al., 2004) and 14% (Freeman et al., 2014) compared with nephrosplenic entrapment (up to 21%) (Röcken et al., 2005). Inguinal herniation is considered likely to re-occur and preventive measures such as castration or inguinal hernioplasty (Fischer et al., 1995; Mariën, 2001; Rossignol et al., 2007, 2014; Wilderjans et al., 2012) are recommended.
The omental vestibule is funnel shaped with 2 openings: a smaller one on the right side of the median plane, which is the epiploic foramen (Freeman and Pearn, 2015; van Bergen et al., 2015) and a larger one on the left side, which is the opening from the omental vestibule to the caudal recess of the omental bursa (van Bergen et al., 2015). It has been suggested that the funnel-like configuration could be the reason for the predominant left-to-right EFE occurrence (Freeman and Pearn, 2015; van Bergen et al., 2015). Increased intra-abdominal pressure during crib-biting (Albanese et al., 2013) has been hypothesised to be the reason for herniation through this structure in horses that crib (Freeman and Pearn, 2015), but this theory has not yet been proven/disproven.

Two standing laparoscopic techniques for closure of the epiploic foramen have been developed. The first technique used 4 to 10 helical titanium coils to obliterate the epiploic foramen tacking the gastropancreatic fold to the liver. The procedure resulted in complete closure of the epiploic foramen in 5/6 (83%) experimental horses and in a partial closure of the epiploic foramen in the sixth horse (Munsterman et al., 2014). A modified technique for closure of the epiploic foramen was later described: the Foramen Epiploicum Mesh Closure (FEMC), which obliterates the epiploic foramen using an expandable diabolo-shaped polypropylene mesh construct (van Bergen et al., 2016). Use of FEMC resulted in obliteration of the omental vestibule and epiploic foramen by formation of nonreactive fibrous tissue in 6/6 (100%) experimental horses (van Bergen et al., 2016).

It has been proposed that spontaneous closure of the epiploic foramen may occur after surgery for EFE (Archer et al., 2004). This proposal was based on the observation of organising fibrin in a horse euthanized 5 days after surgery to correct a strangulating EFE and the fact that recurrence only occurred in EFE that were non-strangulating. However, there is no further published evidence to support spontaneous closure of the epiploic foramen after surgery via a ventral midline celiotomy to correct EFE in the horse.

Laparoscopic examination of the epiploic foramen in 7 horses, that had previously undergone surgery via a ventral midline celiotomy to correct EFE, was performed in the present study whit the aim to determine whether spontaneous obliteration of the epiploic foramen occurs after EFE. The hypothesis was that spontaneous obliteration of the epiploic foramen occurs in a substantial amount of horses after EFE and that this spontaneous obliteration could explain the low recurrence rate of EFE, even in face of the reported strong risk factors for the condition.

Materials and Methods

All procedures were approved and supervised by the Ethical Committee of Ghent University (EC 2015/05).

All horses that survived to discharge after surgical correction of an EFE (with or without intestinal resection) between October 2014 and May 2015 were considered, of which 9 met the inclusion criteria. Their owners were contacted 1 month after the celiotomy to propose laparoscopic inspection of the epiploic foramen followed by application of FEMC if the epiploic foramen remained open (van Bergen et al., 2016). No costs were charged to the owners if the epiploic foramen was closed at the time of laparoscopy. Seven owners consented to the study.

Data collected prospectively at the time of celiotomy for EFE included signalment, presence of stereotypic behaviours, time from colic onset to surgery, surgeon identity, length of the entrapped intestine estimated after reduction, direction of the entrapment and involvement of the ileum. Bowel compromise after reduction was evaluated intra-operatively according to the revised Freeman grading system represented in Table 1.

Records were also obtained on whether or not a resection with a hand sutured end-to-end or hand sutured side-to-side anastomosis was performed.

Table 1: Bowel compromise based on intestinal injury according to the revised Freeman grading system (Freeman et al., 2014).

Grade I	By 15 min after correction of the lesion, the colour of the intestine is similar to healthy adjacent intestine, without any obvious constrictions at the point of strangulation, but with oedema and mild ecchymoses. Motility is spontaneous or induced by snapping a finger against the intestine.
Grade II	By 15 min after correction of the lesion, the intestine is similar in appearance to grade I, but darker pink to red, with more severe oedema and extensive ecchymoses. Mild constrictions (less than half the intestinal circumference) can be evident at points of strangulation. Motility is spontaneous or induced by snapping a finger against the intestine.
Grade III	By 15 min after correction of the lesion, the intestine is similar to grade II in all aspects, but differs by having one or more of the following: black strips or patches against a red background; and/or constrictions at points of strangulation that are half the intestinal circumference or less.
Grade IV	By 15 min after correction of the lesion, the intestine shows little or no improvement in colour and is dark red, purple or blue, with variable bowelwall thickness, ranging from normal to thick, and has little or no motility, even after snapping a finger against the intestine. Additional findings can include black striations and constrictions at points of strangulation that are half the intestinal circumference or less.
Grade V	Diffusely grey, black or green, amotile bowel, with or without a necrotic odour.

At least 1 month after the original colic surgery, the epiploic foramen was inspected via a right flank laparoscopy as was described in Chapter 3 (van Bergen et al., 2015). Food, but not water, was withheld for 36 h before laparoscopy. A 12 gauge catheter (Intraflon 2)[a] was placed in the left or right jugular vein. Twenty thousand IU/kg bwt of sodium penicillin (Penicilline)[b] and 1.1 mg/kg bwt flunixin meglumin (Finadyne)[c] were administered intravenously [IV] shortly before surgery. During the procedure an intramuscular [IM] injection of 21000 IU/kg bwt benzylpenicillin (Peni-kel)[d] and a subcutaneous injection of 3480 IU tetanus toxoid[e] were administered. Horses were sedated with 10 µg/kg bwt detomidine (Domosedan)[f] and 0.1 mg/kg bwt morphine (Morphine HCl)[g] IV. Sedation was maintained by constant rate infusion of detomidine (Domosedan)[f] starting at 6 µg/kg bwt/h and adjusted as required. Local analgesia was provided by infiltration of the right flank with 40 mL mepivacaine 2% (Scandicaine)[h] at the portal sites.

A 10 mm diameter, 20 cm long laparoscopic cannula[i] was introduced through a stab incision by means of a protected trocar[i] at the level of the right paralumbar fossa halfway between the last rib and the *tuber coxae* at the level of the ventral half of the palpable crus of the internal oblique abdominal muscle. Subsequently the protected trocar was replaced by a 58 cm 30° laparoscope[j]. The region of the epiploic foramen was thoroughly inspected as described previously in Chapter 3 (van Bergen et al., 2015). Any changes in anatomy, inflammation, presence of scar tissue, or spontaneous closure of the epiploic foramen were recorded.

If the epiploic foramen was open, FEMC was performed as described in Chapter 4 (van Bergen et al., 2016). Briefly, 2 preformed oval polypropylene meshes (3DMax Mesh)[k] (10.8 x 16.0 cm) were used to prepare a diabolo-shaped implant. A 2.5 m long USP 2 polyglycolic acid wire (Surgicryl)[l] was passed through on 1 side of the implant and served as a security line to prevent loss of the implant into the abdomen or to correct mesh placement into the omental vestibule. Subsequently, a stainless steel applicator tube (length 68 cm, diameter 2 cm), slightly curved on its end, with a blunt trocar in place, was introduced through a second flank portal, 10 cm ventrally from the laparoscopic portal, and was directed into the epiploic foramen under direct visualisation with the laparoscope. With a flexible pushing device (100 cm long) the implant was pushed through the applicator tube through the epiploic foramen into the omental vestibule. After final verification of the correct mesh position with the smallest part of the diabolo-shaped mesh construct at the level of the portal vein, the laparoscope and the applicator tube were withdrawn and the portals were closed in 2 layers (subcutaneous tissue and skin) with USP 2-0 polyglactin 910 (Vicryl)[m]. Horses undergoing laparoscopy alone received 1.1 mg/kg bwt flunixine meglumine orally (Finadyne oral paste)[c] for 1 day after laparoscopy and were returned immediately in their post-colic surgery rehabilitation program. Horses that underwent the FEMC procedure received 1.1 mg/kg flunixine meglumine orally (Finadyne oral paste)[c] for 3 days after laparoscopy and were box-rested for 2 weeks before returning to their post-colic surgery rehabilitation program.

Owners of the 7 horses were interviewed by telephone at 1 and 4 months after laparoscopy, and a final interview was performed between 135 and 282 days (mean 213, s.d. 63 days) following laparoscopic examination. Owners were questioned about post-operative complications, including systemic (fever, dullness, decreased appetite, colic) and local (suppuration, swelling of the incision) complications. The owners were also asked for the exercise level of the horse at the final interview.

Results

The 7 adult horses were 6 Warmbloods and 1 Appaloosa and included 5 geldings and 2 mares (Table 2).

The horses ranged in age from 3 years and 8 months to 14 years and 9 months (median of 5 years 7 months). The horses ranged in bodyweight from 500 to 644 kg (median of 580 kg). Four horses (57%) had a history of windsucking or crib-biting behaviour. Time between colic onset and surgery ranged from 3 to 10 hours with a mean ± s.d. of 5.6 ± 2.4 h. Four surgeons contributed to the management of the 7 horses. All EFE occurred from the left to the right through the epiploic foramen. Only the jejunum was involved in 3 horses (43%) and the ileum and jejunum were involved in 4 horses (57%). The compromise of the incarcerated intestines was graded I in 1 horse (14%), II in 3 horses (43%), III in 1 horse (14%) and IV in 2 horses (29%). Resection with hand sutured end-to-end anastomosis was performed in 2 cases (29%). Time from initial colic surgery to laparoscopy ranged from 35 to 71 days with a mean ± s.d. of 47 ± 14 days.

During laparoscopy, a roughened texture of the liver surface in the epiploic foramen region was noticed in 6/7 horses (86%). The epiploic foramen was completely closed with firm connective tissue in 3/7 cases (43%) (Figure 1). It was impossible to disrupt this connective tissue by manipulation with the laparoscope. The epiploic foramen was not closed in 4/7 horses (57%) although adhesions and inflammation were present within the omental vestibule of 2 horses (Figure 2).

Table 2: Characteristics of the 7 horses undergoing laparoscopy after surgery for Foramen Epiploicum Entrapment (EFE).
Y: years, M: months, m : meters, h: hours, EFE: epiploic foramen entrapment, FEMC: Foramen Epiploicum Mesh Closure

No.	Breed	Age	Sex Weight	Exercise	Behaviour	Colic to surgery	Entrapped intestine	Bowel (Freeman grade)[9]	Resection / anastomosis	Celiotomy to laparoscopy	Epiploic foramen at laparoscopy	FEMC	Follow-up after laparoscopy	Complications
1	Appaloosa	6Y 8M	Gelding 500 kg	Recreational use	Windsucking/crib-biting	7 hours	Jejunum 8m	II	none	41 days	Roughening at the level of caudate liver lobe. Inflammation and small adhesions in the epiploic foramen.	FEMC	282 days Two mild colic episodes, resolved without intervention. Return to previous exercise.	None reported
2	Warmblood	3Y 8M	Gelding 600 kg	Hippotherapy	none	3 hours	Jejunum 3m	II	none	48 days	Slight roughening at level of caudate liver lobe. Small adhesions at level of portal vein. Rent of greater omentum.	FEMC	280 days No colic episodes. Return to previous exercise.	Small hernia at celiotomy incision.
3	Warmblood	5Y 5M	Mare 580 kg	Dressage M level	Windsucking/crib-biting	4 hours	Jejunum-ileum 2m	IV	End-to-end anastomosis	35 days	Normal	FEMC	246 days Two colic episodes reported, 1 required medical intervention (tympany). Return to previous exercise.	None reported
4	Warmblood	7Y 5M	Mare 624 kg	Recreational use	none	6 hours	Jejunum length not recorded	I	none	71 days	Epiploic foramen closed. Slight roughening at the level of caudate liver lobe. Strong fibrous tissue, oedema at the level of the closed epiploic foramen.		240 days No colic episodes reported. Exercise at lower level.	None reported
5	Warmblood	5Y 7M	Gelding 560 kg	Jumping National	Windsucking/crib-biting	10 hours	Jejunum-ileum 1m	II	none	36 days	Epiploic foramen closed. Roughening at the level of caudate liver lobe and cecal serosa. Strong fibrous tissue, some oedema at level of closed epiploic foramen.		167 days No colic episodes. Return to previous exercise.	None reported
6	Warmblood	4Y 10M	Gelding 540 kg	Unbroken	Windsucking/crib-biting	4 hours	Jejunum-ileum 2m	IV	End-to-end anastomosis	60 days	Very slight roughening at level of caudate liver lobe. Rent in greater omentum.	FEMC	143 days One colic episode required medical intervention for (cecal tympany) Horse remains underweight (crib-biting). The horse is green broke.	None reported
7	Warmblood	14Y 9M	Gelding 644 kg	Recreation Dressage	none	5 hours	Jejunum-ileum 2m	III	none	35 days	Epiploic foramen closed. Strong fibrous tissue.		136 days No colic episodes. Return to previous exercise.	Facial nerve paresis after celiotomy, resolved spontaneously.

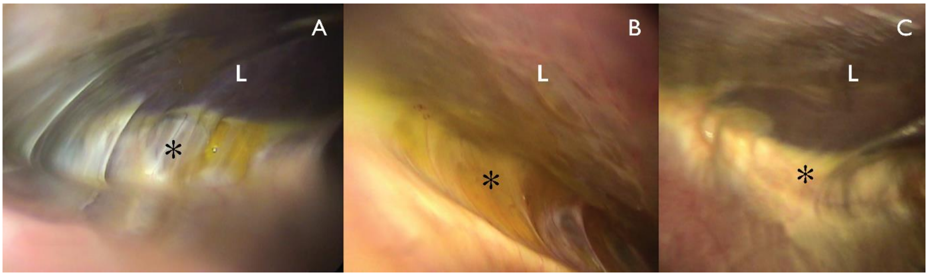

Figure 1: Laparoscopic images demonstrating the spontaneous closure of the epiploic foramen.
A) Horse 4
B) Horse 5
C) Horse 7
The firm fibrous adhesion is demonstrated with an asterisk. Notice the presence of oedema at the level of the fibrous adhesion in horse 4 (A) and horse 5 (B). L: liver.

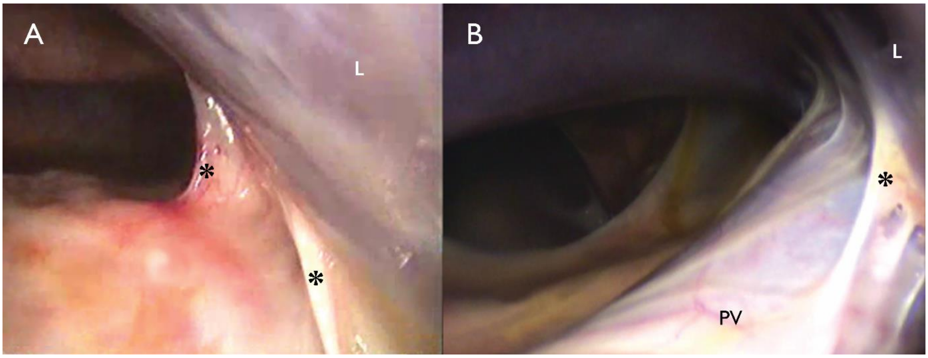

Figure 2: Laparoscopic images of the epiploic foramen showing adhesions (black asterisk). L: liver; PV: portal vein.
A) Horse 1
B) Horse 2

The FEMC procedure was performed in these 4 horses. In horse 2, the security line loosened too early, allowing the diabolo-shaped implant to slide into the omental bursa. A third portal was created between the 15th and 16th rib and the implant was successfully secured and withdrawn from the abdomen with a laparoscopic Babcock forceps[n] and was subsequently re-implanted without complications.

Follow-up after laparoscopy ranged from 135 to 282 days with a mean (±s.d.) of 213 ± 63 days. For 4 horses undergoing FEMC, follow-up ranged from 143 to 282 days with a mean (±s.d.) of 236 ± 69 days. One horse undergoing FEMC developed a small hernia at the ventral midline incision from the initial colic surgery that had no impact on its future athletic use. One horse with spontaneous epiploic foramen closure developed a mild facial nerve paresis after the initial colic surgery which had completely resolved at the final follow-up. Episodes of abdominal pain were reported in 3 horses undergoing FEMC, all of which demonstrated windsucking or crib-biting behaviour. In 2 of the 3 horses, one of these episodes needed medical intervention for tympany which was diagnosed by the referring veterinarian and treated with the combination of butylhyoscine and metamizol (Buscopan Compositum)[o]. Of the 7 horses, 5 returned to their previous level of exercise. Of the 2 remaining horses, 1 horse undergoing FEMC was unbroken at the time of colic surgery and 1 horse with spontaneous epiploic foramen closure was ridden less frequently than before surgery due to factors unrelated to the surgery.

Of the 2 horses invited but not included in the study, 1 was readmitted with recurrent EFE 239 days after the initial colic surgery. Repeat celiotomy revealed a left-to-right EFE involving 35 cm of the jejuno-ileal transition requiring resection with end-to-end anastomosis (grade IV). No follow-up was available for the second horse (Table 3).

Table 3: Characteristics of 2 horses undergoing surgery for epiploic foramen entrapment (EFE) that were not included in the study.
Y: years, M: months, m: meters

	Breed	Age	Sex, weight	Behaviour	Time from colic to surgery	Entrapped intestine/length	Freeman grade bowel compromise[9]	Resection / anastomosis	Outcome
1	Warmblood	5Y 9M	Gelding 405 kg	Windsucking /crib-biting	3.5 hours	Jejunum-ileum 0.1 m	Grade II	None	EFE recurrence 239 days after initial surgery for EFE. Incarceration of 35 cm of the jejuno-ileal transition; Resection and end-to-end anastomosis (Grade IV).
2	Warmblood	7Y 5M	Mare 511 kg	None	12 hours	Jejunum 4m	Grade II	None	No outcome available

Discussion

The findings of spontaneous epiploic foramen obliteration after EFE support a previously suggested hypothesis of spontaneous closure of the epiploic foramen, based on observation of organising fibrin in a horse euthanized 5 days after correction of a strangulating EFE (Archer et al., 2004). Although limited in number, the observation of spontaneous epiploic foramen closure after surgery for EFE in 3 out of 7 horses (43%) reported here indicates that the previous case report is not a single, spurious event. The closure of the epiploic foramen could explain the low recurrence of EFE, even in face of strong risk factors such as windsucking, crib-biting, history of colic in the previous 12 months, increased stabling and high height (Archer et al., 2008a, 2008b). While spontaneous closure of the epiploic foramen with fibrous tissue suggests that inflammation within the epiploic foramen subsequent to entrapment may have initiated the formation of the fibrous scar, adhesions could also have resulted from peritonitis secondary to bowel compromise, or surgical manipulation. The grading of bowel compromise for horses used in this study did not, however, appear to relate to spontaneous closure of the epiploic foramen.

This study included only 7 horses and gives preliminary insight into the frequency of spontaneous closure of the epiploic foramen. A multicentre study might identify factors contributing to the spontaneous closure of the epiploic foramen. The 7 horses in this report had a relatively short duration of clinical signs of colic and only 2 resections were performed. The frequency of spontaneous closure of the epiploic foramen may differ in a population of horses with more complex and longstanding entrapment.

Colic surgery requiring intestinal resection is a clean-contaminated procedure. A minimum of 1 month between colic surgery and laparoscopic FEMC was specified to avoid septic complications in face of mesh implantation. This interval also allowed time for the epiploic foramen to close spontaneously. Further investigation is warranted before manual mesh placement during the initial colic surgery could be advocated due to concerns about contamination. In addition, it is more difficult to place a mesh precisely without laparoscopic visualisation and the effect of recovery from general anaesthesia on retaining the mesh in place is unknown.

Colic episodes were reported in 3 of 4 horses undergoing FEMC, of which 2 required medical intervention for tympany. These 3 horses all had history of windsucking/crib-biting before surgery. Horses that display windsucking/crib-biting are more likely to develop colic compared to horses that do not display this form of stereotypic behaviour (Scantlebury et al., 2011) and these episodes may have been related to crib-biting rather than the FEMC procedure, although the latter cannot be excluded. Adhesion formation associated with intra-abdominal implantation of polypropylene mesh has been reported (Epstein and Parente, 2006) and could also occur with FEMC. However, this was not reported on laparoscopy or autopsy of the 6 experimental horses undergoing FEMC in Chapter 4 (van Bergen et al., 2016).

Laparoscopy is the most reliable method to assess the epiploic foramen after surgery for EFE. Offering laparoscopy to inspect the epiploic foramen at least 1 month after surgery for EFE might be prudent for horses that have risk factors for EFE such as windsucking or crib-biting. At the time of laparoscopy, the epiploic foramen can then be closed if spontaneous closure has not already occurred.

Disclosure Statement

The authors declare no conflict of interest related to this report.

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Manufactures' details

[a]Vygon nv, Brussels, Belgium

[b]Kela Pharma nv, Sint-Niklaas, Belgium

[c]Schering Plough Animal Health, Brussels, Belgium

[d]Kela Veterinaria, Sint-Niklaas, Belgium

[e]Intervet Belgium nv, Brussels, Belgium

[f]Pfizer Animal Health n.v., Brussels, Belgium

[g]Sterop, Brussels, Belgium

[h]AstraZeneca n.v., Brussels, Belgium

[i]Dr Fritz GmbH, Tuttlingen, Germany

[j]Karl Storz GmbH, Tuttlingen, Germany

[k]Bard Davol Inc., Warwick RI, USA

[l]SMI, St Vith, Belgium

[m]Johnson & Johnson Medical n.v., Diegem, Belgium

[n]Richard Wolf GmbH, Knittlingen, Germany

[o]Boehringer Ingelheim GmbH, Ingelheim, Germany

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CHAPTER 6

Foramen Epiploicum Mesh Closure (FEMC) through a ventral midline laparotomy in the horse

Adapted from:
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2017 ECVS Scientific Meeting, Edinburgh

Abstract

Background: Preventive laparoscopic closure of the epiploic foramen has previously been described, but methods for epiploic foramen closure during laparotomy for treatment of colic are lacking.

Objectives: To describe the Foramen Epiploicum Mesh Closure (FEMC) technique through a ventral midline laparotomy in horses under general anaesthesia and its outcome.

Study Design: Terminal surgical experiment and *in vivo* study.

Methods: In a pilot study a standard ventral midline laparotomy was performed under general anaesthesia in 10 experimental horses and a three-dimensional expandable diabolo-shaped mesh construct was manually introduced through the epiploic foramen into the omental vestibule. The laparotomy incision was routinely closed after which the horses were subjected to euthanasia. Subsequently the cadavers were extensively manipulated and finally mesh position was verified during necropsy. Thereafter, a ventral midline laparotomy, with simulation of abdominal manipulations during colic surgery was performed on 6 experimental horses. A three-dimensional expandable diabolo-shaped mesh with radiologic marker was introduced as in the pilot study. Clinical and laboratory parameters were recorded during the post-operative period. Four weeks after the intervention, abdominal radiography and laparoscopy were performed in all 6 horses.

Results: Insertion of all 16 diabolo-shaped mesh constructs during laparotomy was uneventful. The 10 mesh constructs of the pilot study were found to be positioned correctly at necropsy. No post-operative clinical or laboratory variable alterations were noticed in the other 6 horses, apart from a transient leucocytosis and an increase in serum amyloid A. Abdominal radiography at 4 weeks revealed consistent positioning of the mesh marker. Laparoscopy confirmed that all six epiploic foramina were closed, without intestinal adhesions.

Main limitations: Mesh insertion in clinical cases and during clean-contaminated surgery was not investigated.

Conclusion: The FEMC technique via laparotomy provides a fast, simple and reliable procedure to obliterate the epiploic foramen and may be useful during surgery for EFE to prevent recurrence of the disease, avoiding a subsequent laparoscopic procedure.

Introduction

Epiploic foramen entrapment (EFE) is a life threatening condition with a high morbidity and mortality (Proudman et al., 2002a, 2002b, 2005), which is encountered in about 5% of the surgically treated equine colic patients as is described in Chapter 1 of the present dissertation (Vachon and Fischer, 1995; Archer et al., 2004; Mair and Smith, 2005). The most important risk factor for the development of EFE is windsucking/crib-biting (odds ratio 67.3) (Archer et al., 2008a, 2008b) and recurrence rates of 2-14% have been reported in several case series (Vachon and Fischer, 1995; Archer et al., 2004; Freeman et al., 2014) and in one out of two cases in Chapter 5 (van Bergen et al., 2016b). Low recurrence rates despite strong risk factors may be explained by spontaneous closure of the epiploic foramen after EFE due to induced inflammation and subsequent serosal adhesions at the level of the epiploic foramen and omental vestibule. Such spontaneous closure of the epiploic foramen after surgical correction of EFE has been documented in Chapter 5 in three out of seven horses (van Bergen et al., 2016b). Unfortunately, a non-invasive diagnostic technique to determine whether spontaneous closure of the epiploic foramen has occurred after an EFE is currently unavailable. Laparoscopic inspection of the epiploic foramen subsequent to surgical correction of an EFE has therefore been proposed, followed by laparoscopic closure of the epiploic foramen if needed as was described in Chapter 5 (van Bergen et al., 2016b).

Two laparoscopic techniques for closure of the epiploic foramen have been described, both on the standing sedated horse. Using the first technique the epiploic foramen was closed with 4 to 10 helical titanium coils (Protack 5mm Fixation Device)[a], resulting in an obliteration of the epiploic foramen in five out of 6 experimental horses and in partial closure in the 6th horse (Munsterman et al., 2014). Subsequently, the Foramen Epiploicum Mesh Closure (FEMC) technique was described where the epiploic foramen is obliterated by means of an expandable three-dimensional diabolo-shaped polypropylene mesh construct (3D Max Mesh)[b] as described in Chapter 4 (van Bergen et al., 2016a). The diabolo-shaped mesh construct was held in place by its three-dimensional configuration and was not secured in place by additional means. It was demonstrated in Chapter 4 that with the laparoscopic FEMC technique, the entire funnel-shaped omental vestibule including the epiploic foramen was closed by nonreactive fibrous tissue in 6 out of 6 experimental horses (van Bergen et al., 2016a).

The previously reported epiploic foramen closure procedures necessitate a second surgical intervention subsequent to the initial colic surgery. A technique that can be performed during the initial laparotomy would avoid the need for a second surgery. An adaptation of the laparoscopic FEMC technique, whereby the mesh construct is inserted during the laparotomy, seems a logical way forward. Nevertheless, it has been mentioned in Chapter 5 that this adaptation raises some concerns including the lack of visibility and the unknown effect of recovery from general anaesthesia on the position of the mesh with its potential displacement from the epiploic foramen that warrants further investigation (van Bergen et al., 2016b).

The aim of the current study was, therefore, to develop a technique for insertion of a diabolo-shaped mesh construct in the epiploic foramen through a ventral midline laparotomy in horses. We hypothesised that this technique, performed in absence of a concurrent enterotomy or enterectomy, would be a fast and simple method for surgeons with detailed knowledge of the epiploic foramen anatomy (Chapter 3), allowing complete closure of the epiploic foramen without complications.

Materials and Methods

Pilot study

A standard ventral midline laparotomy was performed in 10 experimental horses under general anaesthesia. The horses were involved in a terminal small intestinal ischemia/reperfusion study. Horses without a history of previous abdominal surgery were selected. Median age was 4 years and 6 months (1 year and 5 months to 14 years), the median body weight was 537 kg (402 to 655 kg), and the study included six mares, two stallions and two geldings. Food but not water was withheld for 12 h prior to surgery. A 12 gauge catheter (Equicath)[c] was placed in the left or right jugular vein. Horses were sedated with 0.8-1.1 mg/kg bwt xylazine IV (Xylapan)[d]. Anaesthesia was induced with 2.2 mg/kg bwt ketamine IV (Narketan)[d] and 0.05 mg/kg bwt midazolam IV (Midazolam)[e]. After endotracheal intubation the horses were placed on a padded equine surgery table in dorsal recumbency and anaesthesia was maintained with isoflurane (Isofluran CP)[f] in a mixture of oxygen and medical air. After standard surgical preparation of the ventral abdomen, a 25 cm ventral midline incision was performed through the *linea alba*, starting 3 cm cranial to the umbilicus. Insertion of a three-dimensional expandable diabolo-shaped mesh construct into the omental vestibule through the epiploic foramen was performed concurrently with the ischemia/reperfusion procedure by two different surgeons (AR and TVB). The surgeon was positioned on the left side of the operating table facing the horses head and used the left hand to palpate the epiploic foramen. The number of fingers that could be introduced through the epiploic foramen was recorded as an estimation of the epiploic foramen dimension. A diabolo-shaped mesh construct was subsequently prepared as previously described for the laparoscopic FEMC technique (van Bergen et al., 2016a). In brief, two preformed oval shaped knitted polypropylene meshes (3DMax Mesh)[b] (10.8 x 16.0 cm), used for inguinal hernia repair in man, were used. The first mesh was grasped with a DeBakey tissue forceps at its smallest diameter. The forceps was twisted 270° and subsequently withdrawn. Next, the rolled part of the mesh was retained and double folded on its longest diameter. The resultant pyramidal configuration was kept in place with a USP 2-0 polyglactin 910 (Vicryl)[g] horizontal mattress suture at the apex of the pyramid. The second mesh was prepared in the same manner and finally the apices of the 2 pyramids were secured together with an additional USP 2-0 polyglactin 910 (Vicryl)[g] horizontal mattress suture, resulting in a diabolo-shaped mesh construct (van Bergen et al., 2016a). The diabolo-shaped mesh construct (diameter: 10 cm, length: 10 cm) is illustrated in Figure 1a.

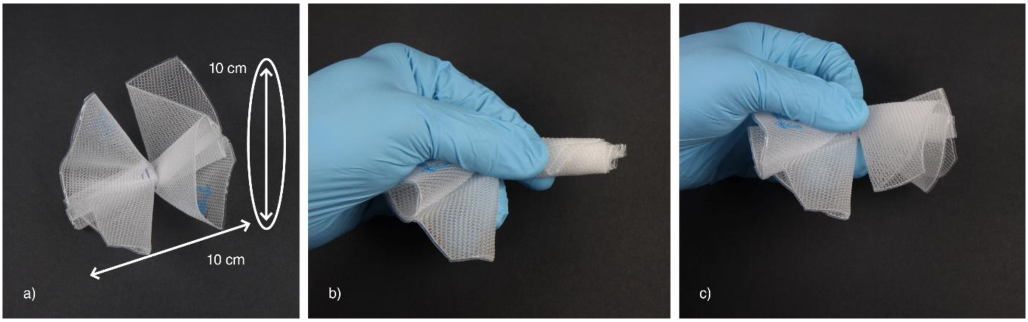

Figure 1:

A) Prepared expandable three-dimensional diabolo-shaped mesh construct made from 2 preformed knitted polypropylene meshes (3DMax Mesh)[b] used for laparoscopic inguinal hernia repair in man (van Bergen et al., 2016a).
B) One half of the diabolo-shaped mesh construct is rolled on itself and secured between the index finger and thumb of the surgeon's left hand, to allow introduction of the mesh construct into the omental vestibule through the epiploic foramen.
C) Once the index finger and thumb of the surgeon's left hand are released, the expandable three-dimensional diabolo-shaped mesh construct recovers its original shape.

After preparation, the mesh construct was manipulated with the surgeon's left hand and introduced through the epiploic foramen into the omental vestibule. To do so, one half of the construct was rolled on itself and secured between thumb and index finger as demonstrated in Figure 1b. Standing on the left side of the recumbent horse facing the horses head, the surgeon manipulated the mesh construct with its his/her hand through the epiploic foramen into the omental vestibule on the right side of the abdomen, between the caudate process of the liver and the hepatoduodenal ligament. About 1 cm of the mesh construct was left protruding out of the epiploic foramen into the abdominal cavity. Once the index finger and thumb of the surgeon's left hand were released, the expandable three-dimensional diabolo-shaped mesh construct recovered its original shape as demonstrated in Figure 1c.

After completion of the ischemia/reperfusion procedure, the laparotomy incision was closed with a continuous USP 6 polyglactin 910 (Vicryl)[h] suture pattern in the *linea alba*, USP 1 polyglactin 910 (Vicryl)[h] in the subcutaneous tissues and USP 0 polyglyconate (Maxon)[i] in the skin. The horses were not recovered from general anaesthesia. Euthanasia was induced by lethal injection of 70 mg/kg bwt pentobarbital IV (Euthadorm 400)[j]. Time from mesh placement to euthanasia was recorded.

Subsequently, the 10 cadavers were used for a neck CT study. The cadavers were hoisted from the surgery table and transported to the CT facility where they were manipulated on the CT table. At completion of the CT study, the cadavers were hoisted on a truck and transported for 5 km to a dissection facility. The next day the cadavers were dissected for student demonstration. After removal of the intestines, the caudal part of the body was removed to achieve better visualisation of the cranial abdominal organs. Subsequently the pancreas was removed to visualise the hepatoduodenal ligament through which the exact position of the mesh construct could be determined. The relative position of the mesh construct to the portal vein was recorded.

Main study

An exploratory laparotomy was performed on six experimental geldings without a history of previous abdominal surgery. The median age was 11 years and 5 months (6 years and 2 months to 16 years and 5 months), the median bodyweight (bwt) was 583 kg (520 to 727 kg) and the median withers height was 1.62 m (1.57 to 1.74 m). None of the horses had a history of windsucking/crib-biting behaviour. Food but not water was withheld for 12 h prior to surgery. A 12 gauge catheter (Intraflon)[k] was placed in the left or right jugular vein. Pre-operatively 6.6 mg/kg bwt gentamicin IV (Genta-Equine)[l], 22000 IU/kg bwt sodium penicillin IV (Penicilline)[m] and 1.1 mg/kg bwt flunixin meglumine IV (Finadyne)[n] were administered. Horses were sedated with 10 µg/kg bwt detomidine IV (Domosedan)[o] and 0.1 mg/kg bwt morphine IV (Morphine Hcl)[p]. Anaesthesia was induced with 2.2 mg/kg bwt ketamine IV (Ketamidor)[q] and 0.06 mg/kg bwt midazolam IV (Dormicum)[r]. After endotracheal intubation the horses were placed on a padded equine surgery table in dorsal recumbency and anaesthesia was maintained with isoflurane (Isoflo)[o] in a mixture of oxygen and medical air. Three different surgeons were involved in the mesh application procedure (TVB, PW and AM). After standard surgical preparation of the ventral abdomen, a 25 cm ventral midline incision was performed followed by a standard abdominal exploration. The number of fingers that could be introduced through the epiploic foramen was recorded as an estimation of the epiploic foramen dimension. A diabolo-shaped mesh construct was prepared and a 4 hole 2.4 Locking Compression Plate (LCP; length 32 mm, thickness 1.7 mm)[s] was sutured to the middle of the diabolo-shaped mesh construct to serve as a radiologic marker. The mesh construct was introduced into the omental vestibule through the epiploic foramen and then the abdominal incision was closed, as described above. The incision was protected with an adhesive sterile stent bandage. The horses were recovered from anaesthesia with head and tail rope assistance. Surgery and recovery duration were recorded and the recovery quality was scored by a board certified anaesthesiologist (Score 1 to 5 with score 1 defined as “standing in 1 attempt, no or light ataxia” and score 5 as “very bad recovery with substantial risk for trauma”). Post-operatively, the horses were treated with 6.6 mg/kg bwt gentamicin (Genta-Equine)[l] IV q24h, 22000 IU/kg bwt sodium penicillin (Penicilline)[m] IV q8h and 1.1 mg/kg bwt flunixin meglumine (Finadyne)[n] IV q12h for 3 days. Horses were examined daily for one month after surgery including alertness, appetite, rectal temperature, heart rate, respiratory rate, abdominal auscultation, colic signs and faecal output. White blood cell count, plasma fibrinogen and serum amyloid A (SAA) concentrations, serum bile acid concentrations and serum activities of aspartate aminotransferase (AST), ɣ-glutamyltransferase (GGT) and amylase activity were measured on Days 1, 3, 5, 8 and 30 after surgery. One month post-operatively, a left-to-right lateral radiograph of the craniodorsal abdomen with a grid applied (Canon CXDI-801C Wireless Digital Radiography System)[t] using 85 kV and 80mAs was obtained to determine the position of the mesh. Right flank standing laparoscopy was then performed as described in Chapter 3, 4 and 5 to determine the degree of obliteration of the epiploic foramen and to inspect for undesired abdominal adhesions.

To analyse the response of the different laboratory data over time, a Friedman test was used, followed by Dunn's test with correction for multiple comparisons. Significance was set at $P < 0.05$. Normally distributed laboratory variables are reported as mean ± standard deviation (s.d.), whereas non-normally distributed variables are reported as median (range).

Results

Pilot study

The dimension of the epiploic foramen was estimated in 8 horses. A median of 2.5 (1.5 to 3.5) fingers could be introduced corresponding to a median circumference of 11 (7 to 12) cm measured on the fingers of a "7.5 gloved" surgeon. In general, introduction of the diabolo-shaped mesh construct through the epiploic foramen into the omental vestibule was considered to be easy. Mesh insertion was considered more difficult in horses with a smaller epiploic foramen. Time between mesh insertion and euthanasia varied between 123 and 222 minutes (mean 198 minutes). On autopsy, all diabolo-shaped mesh implants were in the correct position leaving about 1 cm of the mesh construct protruding out of the omental vestibule through the epiploic foramen into the abdominal cavity. The narrowest part of the diabolo-shaped mesh construct was located at the level of the portal vein in all 10 carcasses, as was described in Chapter 4 for the original laparoscopic FEMC technique (van Bergen et al., 2016a). In horses 3 and 6, a small section of the deeper part of the diabolo-shaped mesh construct was partially folded back onto itself. The position of the deepest part of the diabolo-shaped mesh construct could not be evaluated in horses 5 and 8 due to inadequate student dissection.

Main study

Abdominal exploration, mesh application and recovery from anaesthesia were un-eventful except for a serosal rent that occurred in the ascending colon as a result of manipulation in one horse. The serosal rent was sutured. Median surgical time was

47.5 (29 to 67) minutes. Median recovery time was 21 (17 to 50) minutes. Median overall recovery quality was scored 1.5 (1 to 3).

The estimated median dimension of the epiploic foramen was 3 (2 to 4) fingers corresponding to a median circumference of 12 (8 to 16) cm measured on the fingers of a “7.5 gloved” surgeon.

Post-operatively, clinical and laboratory variables were within normal limits except for an increase in WBC between day 0 (5.60±0.78 cells/μL) and day 8 (10.50±1.54 cells/μL; $P < 0.001$), and an increase in SAA between day 0 (0.20 μg/mL (0.20-1.40)) and day 3 (1105.65 μg/mL (967.60-1134.00); $P < 0.001$) and between day 0 and day 5 (926.70 μg/mL (632.40-976.20); $P = 0.006$). Both WBC and SAA returned to baseline levels by day 30. Abdominal radiography at 4 weeks confirmed that the mesh was in the craniodorsal part of the abdomen, superimposed over the outline of the liver, in all horses (Figure 2). Laparoscopic evaluation demonstrated that all epiploic foramina were closed with strong nonreactive fibrous tissue. There were no major undesired abdominal adhesions (Figure 3). In one horse the caudate process of the liver was adhered to the right liver lobe (Figure 4).

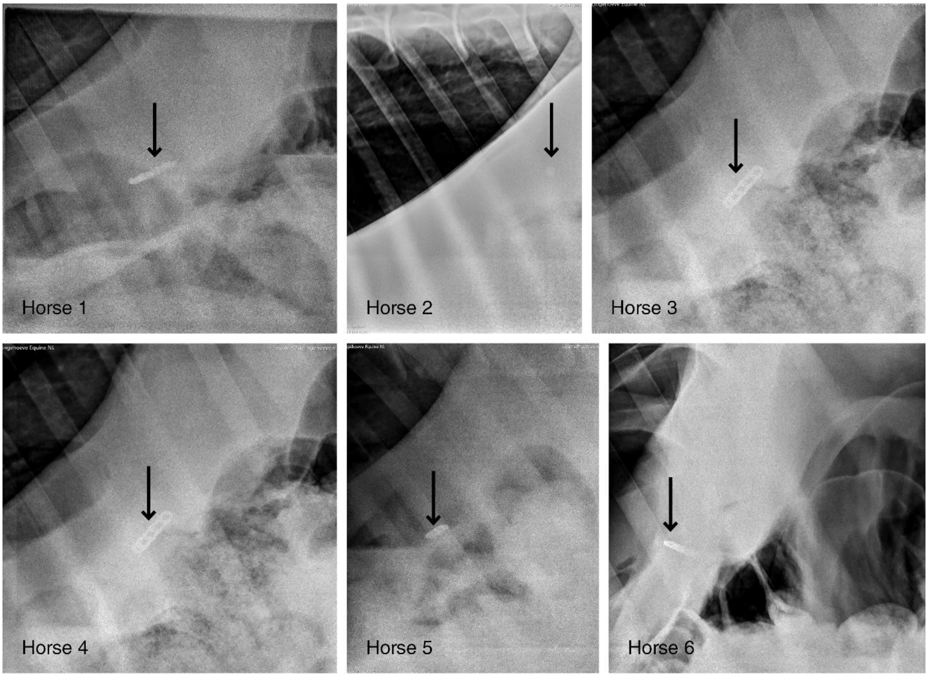

Figure 2: Abdominal radiography in the six experimental horses 1 month after mesh placement in the epiploic foramen via laparotomy with a 4 hole LCP plate as radiologic marker (Canon CXDI-801C Wireless Digital Radiography System)[t]. A grid was applied and radiographs were taken using 85 kV and 80mAs. The radiologic marker is consistently located in the craniodorsal aspect of the abdomen, over the outline of the liver (cranial is to the left).

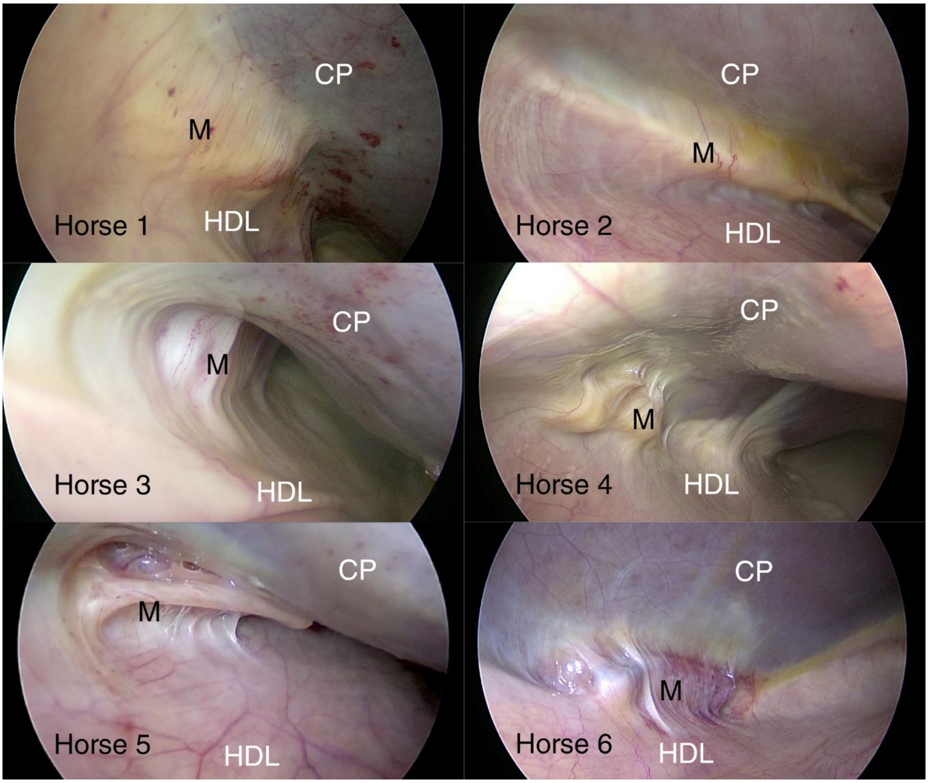

Figure 3: Laparoscopic images of the epiploic foramen 1 month after mesh placement via laparotomy into the epiploic foramen in the six experimental horses from the main study, demonstrating consistent mesh-induced epiploic foramen closure with dense fibrous tissue (M) between the base of the caudate process of the liver (CP) and the hepatoduodenal ligament (HDL) .

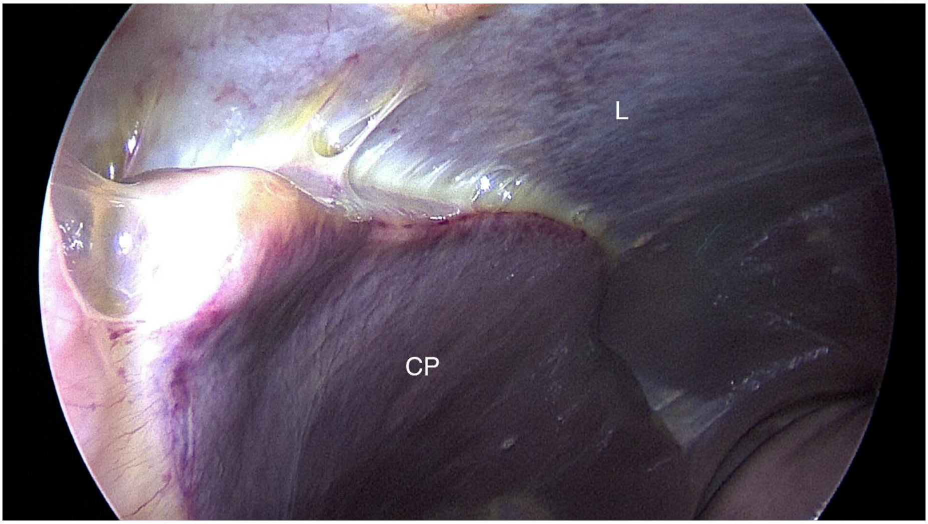

Figure 4: At follow-up laparoscopy 1 month after mesh placement via laparotomy into the epiploic foramen the caudate process (CP) of the liver was adhered to the right lobe of the liver (L) in one horse (horse number 6, clinically normal) .

Discussion

This study showed that the diabolo-shaped mesh construct as used for the laparoscopic FEMC procedure can also be introduced into its correct position during a standard midline laparotomy approach. Epiploic foramen closure with dense fibrous tissue was confirmed in all horses 30 days after placement. The technique was considered to be fast and easy to perform. No post-operative complications related to mesh application occurred in any of the horses that were recovered from general anaesthesia. The observed transient WBC and SAA responses are likely due to the abdominal surgery and not specifically to the FEMC procedure and have been previously reported (Jacobsen et al., 2009).

Mesh introduction during the pilot study was considered slightly more difficult in horses with a smaller epiploic foramen. The two horses in which a small section of the deeper part of the diabolo-shaped mesh construct was partially folded back onto itself were horses with a smaller epiploic foramen. The authors do not expect any clinical consequences from a small section of the deeper part of the diabolo-shaped mesh construct being folded back onto itself; however it should be noted that this prognosis is based upon experience from a small number of horses with a short follow-up. Introduction of the diabolo-shaped mesh construct in the horses that were recovered from anaesthesia and had comparable epiploic foramen dimensions was uneventful and resulted in complete closure of the epiploic foramen with dense fibrous tissue after 1 month. In the earlier anatomic study (Chapter3, van Bergen et al., 2015), the mean circumference of the epiploic foramen in 30 normal horses was 11.6 ± 2.6 cm which is comparable to the estimated median circumference of the epiploic foramen of 11 cm in the pilot study and 12 cm in the main study of the present investigation.

At follow-up laparoscopy, no undesired abdominal adhesions were noticed apart from an adhesion between the caudate process of the liver and the right liver lobe in one horse. None of the horses in the present study, including the horse with the adhered caudate process of the liver, suffered from any complications and the adhesion of the caudate process of the liver to the right liver lobe appeared to be clinically insignificant. Hypothetically, post-operative adhesions between the mesh and the intestines could have been a cause of post-operative colic episodes. None of the horses in the present study demonstrated post-operative colic signs nor did the horses in the previous laparoscopic FEMC investigation as found in Chapter 4 (van Bergen et al., 2016a).

Radiologic and laparoscopic confirmation of positioning of the mesh construct 1 month following the FEMC procedure via laparotomy enabled us to confirm correct and consistent mesh placement and closure of the epiploic foramen. This avoided the need for horses to be subjected to euthanasia. The individual contributions of the mesh and the plate to the formation of dense fibrous tissue in the epiploic foramen and omental vestibule were not investigated. However, the laparoscopic appearance of the dense fibrous adhesion between the base of the caudate process of the liver and the hepatoduodenal ligament at follow-up laparoscopy 1 month after mesh application was comparable to the previously published appearance at laparoscopy 1 month after laparoscopic mesh application without a plate as represented in Chapter 4 (van Bergen et al., 2016a). The formation of the dense fibrous tissue between the base of the caudate process of the liver and the hepatoduodenal ligament has to be contributed largely to the diabolo-shaped mesh construct as the plate is biologically relatively inert.

The current study confirms the stability of the diabolo-shaped mesh construct into the epiploic foramen and omental vestibule even after extensive manipulation of the horses after euthanasia and after recovery from general anaesthesia which gives additional support to the FEMC technique. In a previous study reported in Chapter 4, the FEMC technique was performed laparoscopically on standing sedated horses and no implant migration was noticed (van Bergen et al., 2016a). In that study horses were box-rested for 1 month after the laparoscopic FEMC procedure to allow the mesh construct to adhere to the surrounding tissues (van Bergen et al., 2016a). Monitoring of these horses ranged from 1 to 6 months during which they were hand walked (3 times 10 min/day; hand walking was introduced in the third and fourth weeks) and underwent pasture turn out (introduced during the second month) (van Bergen et al., 2016a). Based on the stable mesh position encountered in the present study, this resting period after laparoscopic FEMC could possibly be reduced. Reduction of the rest period after FEMC might be the subject of further investigations.

Foramen Epiploicum Mesh Closure during the initial EFE colic surgery has been discouraged in Chapter 5 due to concerns regarding imprecise mesh placement, migration of the mesh during anaesthetic recovery and the implant acting as a septic focus (van Bergen et al., 2016b). Subclinical or clinically evident septic peritonitis may develop in horses suffering from systemic inflammatory response syndrome, in horses where necrotic bowel has been removed from the epiploic foramen or in horses that underwent bowel resection and enterotomy. This could be a potential concern regarding the mesh becoming a septic focus. However, an enterotomy or enterectomy is not necessarily performed in all EFE colic surgery cases. Moreover, recent data in human patients confirmed that the presence of intestinal ischemia or necrosis and thus the necessity to perform intestinal resection cannot be considered a contraindication for prosthetic polypropylene mesh repair during emergency management of acutely incarcerated and/or strangulated groin hernias (Bessa et al., 2015). Great care to avoid spillage of intestinal contents into the surgical field and appropriate use of prophylactic antimicrobials were considered important in this situation (Bessa et al., 2015).

Foramen Epiploicum Mesh Closure during the initial EFE colic surgery could avoid the need for a second (laparoscopic) procedure. The technique is fast and simple in the hands of surgeons with detailed knowledge of the epiploic foramen anatomy as described in Chapter 3. Complete closure of the omental vestibule and epiploic foramen may be accomplished without complications in a clean colic surgery. A clinical prospective multicentre study should be performed to assess safety of the laparotomic FEMC technique during initial colic surgery in a clinical setting.

Authors' declaration of interests

The autors have declared no competing interests.

Ethical considerations

Procedures in the pilot study were approved by the Niedersächsisches Landesamt für Verbraucherschutz und Lebensmittelsicherheit (33.12-42502-04-15/1834) and all procedures in the main study were approved and supervised by the Ethical Committee of the Ghent University (EC 2016/58).

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Manufactures' details

[a]Covidien, Norwalk, CT, USA

[b]Bard Davol Inc., Warwick, RI, USA

[c]Braun, Tuttlingen, Germany

[d]Vetoquinol GmbH, Ravensburg, Germany

[e]Ratiopharm GmbH, Ulm, Germany

[f]CP-Pharma, Burgdorf, Germany

[g]Johnson and Johnson medical nv, Diegem, Belgium

[h]Johnson and Johnson GmbH, Neuss, Germany

[i]Covidien GmbH, Neustadt, Germany

[j]CP-Pharma, Burgdorf, Germany

[k]Vygon nv, Brussels, Belgium

[l]Franklin Pharmaceuticals Limited, Meath Co Meath, Ireland

[m]Kela Pharma nv, Sint-Niklaas, Belgium

[n]Schering Plough Animal Health, Brussels, Belgium

[o]Zoetis Belux, Zaventem, Belgium

[p]Sterop, Brussels, Belgium

[q]Ecuphar, Oostkamp, Belgium

[r]Roche, Brussel, Belgium

[s]DePuy Synthes, Diegem, Belgium

[t]Canon Inc., Tokyo, Japan

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CHAPTER 7

Horses undergoing surgery for epiploic foramen entrapment: retrospective study of 145 cases on the European continent (2008-2016)

Adapted from submitted article:
van Bergen T., Haspeslagh M., Wiemer P., Swagemakers M., van Loon G, Martens A., 2018. Horses undergoing surgery for epiploic foramen entrapment: retrospective study of 145 cases on the European continent (2008-2016). Veterinary Surgery, *re-submitted after major revisions*

Presented at:
Journées annuelles AVEF 2017, Paris

Abstract

Objectives: To document perioperative variables, survival to and after discharge, and variables associated with survival of horses with epiploic foramen entrapment (EFE).
Study Design: Retrospective study.
Animals: Horses undergoing surgery for EFE (n=145).
Methods: Pre-, peri- and post-operative data of horses that underwent exploratory laparotomy for EFE were obtained. Post-operative process was assessed by follow-up telephone calls with the owner/carer. Factors associated with post-operative reflux (POR), re-laparotomy, hospital discharge, colic after hospital discharge and on survival after discharge were assessed.
Results: The 145 surgeries were performed on 142 horses (recurrence in 3%). Warmblood horses represented 123 of the 145 operated horses (85%). Windsucking/crib-biting was confirmed in 42 out of 70 horses (60%). In 145/145 cases (100%) intestines were entrapped from left-to-right. Ileal involvement was recorded in 107/145 cases (74%). Uncontrollable intra-operative haemorrhage was encountered during 8/145 surgeries (6%). One hundred and seven out of 145 horses (74%) recovered from surgery. Seventy horses amongst all the horses undergoing surgery survived to discharge (48%). Survival to discharge of the 107 horses recovering from surgery was 65% (70/107), so 37 from the 107 (35%) recovered horses died prior to discharge. Median survival of the 70 discharged horses was 1529 days. Resection performed predisposed horses for POR and horses undergoing jejunoileostomy were more prone to POR development compared to horses undergoing jejunojejunostomy. Horses that developed POR were less likely to be discharged and horses that underwent resection had shorter life expectations after hospital discharge.
Conclusions and clinical significance: High morbidity and mortality associated with EFE colic surgery were demonstrated. Beside moderate results, the condition recurred in at least 3% of the survivors.

Introduction

Epiploic foramen entrapment (EFE) is a life threatening condition which is encountered in about 5% of surgically treated equine colic patients (Vachon and Fischer, 1995; Archer et al., 2004; Mair and Smith, 2005). Windsucking/crib-biting has been identified as an important factor (OR 67.3, 95% CI 15.3-296.5) related to the development of EFE in an international matched case-control study (Archer et al., 2008). Pre-operative diagnosis of EFE is more specific compared to other strangulating lesions and is based on the ultrasonographic detection of thick walled distended intestinal loops at the level of the right cranial abdomen in areas imaged to assess the duodenum and liver (Freeman, 2002; Scharner et al., 2002).

Epiploic foramen entrapment has been associated with a high morbidity and mortality (Proudman et al., 2002a, 2002b, 2005). Horses with EFE were more than 4 times as likely to have re-laparotomy because of unfavourable post-operative progression compared to horses with other types of colic (Proudman et al., 2002b). Survival to hospital discharge of horses that left the recovery box alive after EFE colic surgery ranged between 79 and 85% in previous studies (Vachon and Fischer, 1995; Archer et al., 2004, 2011). In 1 study 95% hospital discharge was reported (20/21 cases) (Freeman and Schaeffer, 2005). Long-term survival is difficult to compare between studies due to different definitions (Vachon and Fischer, 1995; Archer et al., 2004, 2011).

Increased pre-operative Packed Cell Volume (PCV), increased length of small intestine resected and post-operative ileus (POI) have been associated with increased likelihood of mortality in EFE cases (Archer et al., 2011).

Recurrence of EFE has been reported in several case series (1/53 (2%) (Vachon and Fischer, 1995), 2/71 (3%) (Archer et al., 2004) and 1/7 (14%) (Freeman et al., 2014). Low recurrence rates despite strong risk factors may be explained by spontaneous closure of the epiploic foramen after EFE due to induced inflammation and subsequent serosal adhesions at the level of the epiploic foramen and omental vestibule. Such spontaneous closure of the epiploic foramen after surgical correction of EFE has been described in Chapter 5 in 3 out of 7 horses (43%) (van Bergen et al., 2016b) and is supported by more recent multicentre data revealing spontaneous closure in 9/28 cases (32%) (unpublished data). Standing preventive laparoscopic epiploic foramen closure techniques have been described (Munsterman et al., 2014; Chapter 4; van Bergen et al., 2016a) and performed on clinical cases in Chapter 5 (van Bergen et al., 2016b).

The existing epidemiologic studies on survival after surgery for EFE have been performed in the United Kingdom and North America and were mainly conducted in Thoroughbred dominated populations. Our clinical impression was that outcome for EFE in our mainly Warmblood population was inferior to results reported in these United Kingdom and North American studies. Recent data from a large European horse population, including a large amount of Warmblood horses, regarding EFE survival, recurrence, and factors influencing outcome, are lacking. Thoroughbred horses are light horses kept in different management conditions compared to Warmblood horses, potentially influencing outcome of procedures under general anaesthesia. Retrospective analysis of outcome after general anaesthesia revealed more favourable results for a large private practice in North Amerika mainly treating Thoroughbred horses (Bidwel et al., 2007) compared to published outcome of general anaesthesia of a mixed breed population (Johnston et al., 2002). Population-specific evidence-based information from a large patient group could help surgeons to inform owners and referring veterinarians correctly on surgery for EFE and possible subsequent preventive epiploic foramen closure. The aim of the present study is therefore to report the percentage of discharged horses and their median survival after hospital discharge in a large population of horses that underwent surgery for EFE in an equine referral institution on the European continent and to determine factors influencing outcome.

Materials and Methods

Case selection

Records of the equine clinic of Ghent University were searched to identify horses that underwent surgery for EFE between April 2008 and December 2016. All horses that underwent surgery for EFE during this period, whether they survived the surgery or not, were included.

Medical records review

Data collected included breed, age (months), sex, weight (kg), duration of colic before surgery (h) and whether the horse had a history of crib-biting/windsucking behaviour. Specific pre-operative data included heart rate (beats per minute (BPM)), respiratory rate (RR) (respirations per minute (RPM)), packed cell volume (PCV) (%), blood lactate (mmol/L) and abdominal lactate (mmol/L). Surgical reports were reviewed to identify the surgeon involved, the direction of small intestinal entrapment, ileal involvement, estimated length of the entrapment (cm), whether an intestinal resection was performed or not, length of resected small intestine (cm), type of anastomosis performed, whether the horse was euthanized during surgery, displayed intra-operative haemorrhage, duration of surgery (min) (from incision to final closure) and general anaesthesia (min) and whether the horse survived the recovery from anaesthesia or not. Post-operative events were reviewed and the occurrence of post-operative reflux (POR) (defined as >2 L reflux obtained through a nasogastric tube on at least 1 occasion (Archer et al., 2011)), number of days of POR, whether re-laparotomy was performed during the hospitalization period, number of days of hospitalization, and successful hospital discharge were recorded.

Telephone interview

Owners of horses that were discharged from the hospital were contacted for long-term follow-up and were asked if the horse was still alive, if the horse had suffered from 1 or more significant colic episodes after discharge, necessitating medical intervention, and, in case of mortality, if it was related to a colic episode.

Cases were recorded as recurrent EFE cases only if the diagnosis of recurrence was made during surgery in our hospital to avoid overestimation of recurrence due to owner misinterpretation of colic events.

Statistical analysis

Data were explored with commercially available software (Excel 2016)[a] for descriptive analysis, and subsequently analysed with a statistical program (SPSS, version 23)[b] to explore potential associations between relevant selected variables and outcome. Significance for all tests was set at $P \leq 0.05$.

The effects of selected independent variables on POR occurrence, on re-laparotomy during the surgery for EFE hospitalization period, on successful hospital discharge and on recurrence of colic after hospital discharge were assessed. First, univariable logistic regressions were performed to estimate the general effect of the independent variables on each dependent variable. For continuous independent variables, the linearity of the relationship between the independent variable and the log odds of the model was assessed by examining scatter plots and by performing a Box-Tidwell procedure. Independent variables yielding an effect with $P \leq 0.20$ were then considered for inclusion in a multivariable logistic regression model. First, potential correlations between the independent variables were assessed using the Pearson's correlation coefficient, with values >0.6 indicating significant correlation. When correlation was present, only the variable with the most significant effect was used in the multivariable analysis. Variables with >30% missing data were excluded from analysis. The multivariable models were then further refined by stepwise elimination of variables with a significance of $P > 0.05$, until only independent variables with a significance of $P \leq 0.05$ remained in the model. At each elimination step, the model fit (assessed by a Hosmer-Lemeshow test) and how the elimination influenced the effect of other independent variables were evaluated. When an elimination decreased the model fit or drastically changed the effect of the remaining independent variables, the eliminated variable was forced back in the model, even when the effect was not significant. The variables remaining in the final model were then considered to have a significant effect on the respective dependent variable.

Survival time of discharged horses was measured as a continuous variable starting at the moment horses left the recovery box alive and ending the day of confirmed colic-related death or censoring (horses still alive at the end of follow-up). Survival analysis was performed to estimate which of the selected independent variables significantly influenced colic related mortality, counting from the day the horses left the recovery box alive. The effect of independent variables on survival was first tested using a univariable Cox-regression analysis. For continuous independent variables, the linearity of the relationship with survival time was evaluated by calculating the martingale residuals and plotting them against the independent variable. For categorical variables, the assumption of proportional hazards was evaluated by examining cumulative hazard plots. Variables yielding an effect with a significance of

$P \leq 0.20$ were then considered for a multivariable Cox-regression analysis. First, potential collinearity was assessed by calculating the Pearson's correlation coefficients, with values of >0.6 indicating significant correlation. If there was correlation, only the variable with the most significant effect was included in the multivariable model. The model was then further refined by stepwise elimination of the variable with the least significant effect, until only significant variables ($P \leq 0.05$) remained.

Results

Included horses

During the study period of 8.75 years, 6473 horses were admitted with colic signs to the equine referral hospital of Ghent University. Two-thousand and four of these horses underwent colic surgery and in 145 (7.2%) of these cases, colic was due to EFE. Ten different surgeons were involved during the study period with a mixed level of experience inherent to a training institution. One hundred and twenty-three (85%) surgeries were performed on Warmblood horses. There were 36 mares (25%), 18 stallions (13%) and 88 geldings (62%). Information about windsucking/crib-biting was obtained for 70 horses. In 42 of these 70 horses (60%) this stereotypic behaviour was confirmed.

Surgical data

Pre-, intra- and post-operative continuous variables are summarized in Table 1.

Table 1: Continuous variables of the horses that underwent surgery for EFE.

Variable	Number of horses	Median	Range
Age (months)	145	97	12-279
Weight (kg)	145	535	239-777
Duration colic signs (h)	143	6.83	0.50-29.00
Heart rate (beats/min)	141	60	24-128
Respiration rate (respirations/min)	105	28	16-120
Packed cell volume (%)	144	38	26-62
Base excess (mEq/L)	144	2.8	-12.5-23.5
Blood lactate (mmol/L)	33	3.3	0.0-18.9
Peritoneal fluid lactate (mmol/L)	46	4.6	0.0-18.0
Length involved intestine (cm)	139	200	5-2000
Length resected intestine (cm)	51	400	50-1500
Duration anaesthesia (min)	145	125	45-335
Duration surgery (min)	145	95	20-300
Hospitalization (days)	70	10	6-52

In all of the 145 cases (100%) the intestines were entrapped though the epiploic foramen from left-to-right. The ileum was involved in 107 cases (74%). Thirty-seven horses (26%) were euthanized during surgery for EFE. In 8 cases (6%) euthanasia was due to uncontrollable intra-operative haemorrhage at the level of the epiploic foramen after intestinal reduction. Seventeen horses (12%) were euthanized because of technical restrictions due to involvement of a very large portion of the ileum and 12 horses (8%) due to owners being unwilling to allow intestinal resection for financial or prognostic reasons. After reduction of the intestines, small intestinal decompression without resection was performed in 57 out of the 108 horses that were not euthanized during surgery (53%). A resection was performed in 51 surgeries (47%). End-to-end jejunoileostomy was performed in 24 of those cases (47%), end-to-end jejunojejunostomy was performed in 21 cases (41%), and 6 cases underwent side-to-side jejunocaecostomy (12%). One additional horse undergoing jejunojejunostomy was euthanized during recovery because of severe femoral nerve paralysis, resulting in a final number of 107 (74%) horses that survived recovery.

Immediate post-operative period

Horses undergoing jejunoileostomy, jejunojejunostomy or jejunocaecostomy developed POR in 19/24 (79%), 8/20 (40%) and 3/6 (50%) of cases respectively, while horses that only underwent small intestinal decompression developed POR in 11/56 (20%) of cases.

Seventy horses survived to discharge, which represents 48% from the 145 EFE surgeries and 65% from the 107 recoveries. During the post-operative hospitalization period, 10 horses (7%) underwent re-laparotomy because of POR and ongoing colic signs. Obstruction at the level of the anastomosis was found in 3 out of these 10 cases (30%), of which 2 were resolved by massage and 1 by performing a side-to-side jejunocaecostomy bypass. In 3 cases (30%) a resection was necessary that was not performed during the initial surgery for EFE, in 2 cases (20%) problems were associated with adhesions which were broken down during re-laparotomy, in 1 horse (10%) small intestine passed through a mesenteric defect at the level of the anastomosis, and 1 horse (10%) developed EFE recurrence 1 day after the initial surgery for EFE. All horses recovered from this second intervention but only 2 of these horses (20%) survived to discharge (1 with adhesions and 1 with a resection performed during the second surgery for EFE). In total, 37 horses did not survive the post-operative hospitalization period. Death or euthanasia was the result of ongoing POR in 26 cases (70%), of endotoxaemia in 4 cases (11%), of peritonitis in 3 cases (8%), of laminitis (due to endotoxaemia/SIRS) in 2 cases (5%), of pelvic trauma in 1 case (3%) and of eventration after re-laparotomy for EFE recurrence in 1 case (3%).

Detailed results for the univariable and multivariable effects of potential explanatory independent variables on POR occurrence, on re-laparotomy during the surgery for EFE hospitalization period and on non-survival to hospital discharge are summarized in Table 2, 3 and 4.

Table 2: Univariable and multivariable associations between potential explanatory variables and post-operative reflux (POR). Horses available for analysis: 107. The odds ratios (OR) represent the effect of the specific variable in relation to POR with an OR between 0 and 1 as protective factor and an OR > 1 determining a risk-factor for POR.

	Univariable analysis					Multivariable analysis		
Variable	**Number available**	**Missing data (%)**	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Continuous variables								
Age (years)	107	0	1.001	0.10-1.01	0.73			
Weight (kg)	107	0	1.002	0.10-1.01	0.48			
Duration colic signs (min)	105	2	1.02	0.94-1.11	0.59			
Heart rate (beats/min)	106	1	1.03	1.00-1.05	0.03*,§			
Respiratory rate (respirations/min)	79	26	0.97	0.94-1.01	0.11§			
Packed cell volume (%)	106	1	1.14	1.06-1.22	<0.01*,§	1.13	1.04-1.23	0.01*
Base excess (mEq/L)	106	1	0.99	0.91-1.08	0.78			
Blood lactate (mmol/L)	18	83						
Peritoneal fluid lactate (mmol/L)	32	70	;					
Duration anaesthesia (min)	107	0	1.02	1.01-1.03	0.00*,§			
Length involved intestine (cm)	101	6	1.00	1.00-1.00	0.14§			
Length resection (cm)	50	0	1.00	1.00-1.00	0.28			
Categorical variables								
Breed	107	0						
Warmblood	91		Ref					
Others	16		0.88	0.31-2.74	0.37			
Sex	107	0						
Mare	25		1.51	0.60-3.80	0.38	1.21	0.40-3.65	0.74
Stallion	15		0.10	0.1-0.80	0.03*,§	0.07	0.01-0.63	0.02*
Gelding	67		Ref			Ref		
Ileum involved	107	0						
NO	25		Ref					
YES	82		0.96	0.39-2.40	0.93			
Resection	107	0						
NO	57		Ref			Ref		
YES	50		5.63	2.40-13.19	<0.01*,§	4.81	1.86-12.45	<0.01*
Type anastomosis	50	0						
End-to-end jejunoileostomy	24		Ref			Ref		
End-to-end jejunojejunostomy	20		0.18	0.05-0.66	0.01*,§	0.13	0.03-0.62	0.01*
Side-to-side jejunocaecostomy	6		0.26	0.40-1.72	0.16§	0.20	0.02-2.32	0.20

*: P value ≤ 0.05 is considered significant; §: P value ≤ 0.2 selected for the multivariable binary logistic regression model; Ref: referent

Table 3: Univariable and multivariable associations between potential explanatory variables and re-laparotomy during the post epiploic foramen entrapment (EFE) surgery hospitalization period. Horses available for analysis: 107. The odds ratios (OR) represent the effect of the specific variable in relation to re-laparotomy with an OR between 0 and 1 as protective factor and an OR > 1 determining a risk-factor for re-laparotomy during the post-surgery for EFE hospitalization period. This analysis is underpowered, as there were only 10 horses that underwent re-laparotomy.

	Univariable analysis					Multivariable analysis		
Variable	**Number available**	**Missing data (%)**	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Continuous variables								
Duration colic signs (min)	105	2	0.82	0.64-1.04	0.096§	0.82	0.64-1.06	0.13
Heart rate (beats/min)	106	1	1.03	0.99-1.07	0.13§	1.02	0.99-1.06	0.24
Respiratory rate (respirations/min)	79	26	1.04	0.99-1.09	0.14			
Packed cell volume (%)	106	1	1.03	0.93-1.13	0.58			
Base excess (mEq/L)	106	1	1.07	0.90-1.26	0.44			
Blood lactate (mmol/L)	18	83						
Peritoneal fluid lactate (mmol/L)	32	70						
Duration anaesthesia (min)	107	0	1.01	1.00-1.02	0.17§	1.01	0.99-1.02	0.35
Length involved intestine (cm)	101	6	1.00	1.00-1.00	0.85			
Length resected intestine (cm)	39	24	1.00	0.99-1.01	0.85			
Post-operative reflux (days)	107	0	1.09	0.86-1.38	0.47			
Categorical variables								
Resection	107	0						
NO	56		Ref					
YES	51		1.80	0.48-6.81	0.38			
Type anastomosis	50	0						
End-to-end jejunoileostomy	24		Ref					
End-to-end jejunojejunostomy	20		0.26	0.027-2.57	0.25			
Side-to-side jejunocaecostomy	6		1.00	0.091-11.028	1.00			
Post-operative reflux	107	0						
NO	66		Ref					
YES	41		2.54	0.67-9.62	0.17§			

§: P value ≤ 0.2 selected for the multivariable binary logistic regression model; Ref: referent

Table 4: Univariable and multivariable associations between potential explanatory variables and non-survival to hospital discharge. Horses available for analysis: 145.The odds ratios (OR) represent the effect of the specific variable in relation to hospital discharge with an OR between 0 and 1 as protective factor and an OR > 1 determining a risk-factor for death during hospitalization.

	Univariable analysis					Multivariable analysis		
Variable	**Number available**	**Missing data (%)**	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Continuous variables								
Age (years)	145	0	1.00	0.10-1.01	0.65			
Weight (kg)	145	0	1.00	0.10-1.01	0.21			
Duration colic signs (min)	143	1	0.97	0.89-1.04	0.37			
Heart rate (beats/min)	141	3	1.05	1.03-1.08	<0.01*,§	1.07	1.00-1.15	0.04*
Respiratory rate (respirations/min)	105	28	1.00	0.98-1.03	0.77			
Packed cell volume (%)	144	1	1.06	1.01-1.11	0.02§	0.80	0.68-0.95	0.01*
Base excess (mEq/L)	144	1	0.99	0.92-1.06	0.68			
Blood lactate (mmol/L)	33	77						
Peritoneal fluid lactate (mmol/L)	46	68						
Duration anaesthesia (min)	145	0	0.10	0.99-1.00	0.30			
Length involved intestine (cm)	141	3	1.00	1.00-1.00	<0.01*,§			
Length resection (cm)	51	0	1.00	0.10-1.00	0.80			
Categorical variables								
Recurrence EFE	145	0						
NO	141	0	Ref					
YES	4	0	2.86	0.29-28.31	0.37			
Ileum involved	141	3						
NO	34		Ref					
YES	107		1.19	0.55-2.58	0.66			
Resection	108	0						
NO	57		Ref					
YES	51		3.25	1.42-7.44	<0.01*,§			
Type anastomosis	51	0						
End-to-end jejunoileostomy	24		Ref			Ref		
End-to-end jejunojejunostomy	21		0.30	0.09-1.02	0.06§	0.13	0.00-4.78	0.26
Side-to-side jejunocaecostomy	6		0.60	0.10-3.63	0.58	0.08	0.00-3.36	0.19
Post-operative reflux	107	0						
NO	66		Ref			Ref		
YES	41		20.71	7.39-58.09	<0.01*,§	129.83	9.03-1866.70	<0.01*
Surgeon, nr cases	145	0						
Surgeon 1, 16			0.38	0.08-1.69	0.20			
Surgeon 2, 19			0.84	0.20-3.63	0.84			
Surgeon 3 , 6			0.83	0.16-9.54	0.83			
Surgeon 4¥, 6			-	-	-			
Surgeon 5, 8			1.04	0.17-6.40	0.97			
Surgeon 6, 17			0.56	0.13-2.41	0.43			
Surgeon 7, 32			0.63	0.17-2.33	0.48			
Surgeon 8, 13			0.73	0.15-3.47	0.69			
Surgeon 9, 15			0.23	0.05-1.12	0.07			
Surgeon 10, 14			Ref					

*: P value ≤ 0.05 is considered significant; §: P value ≤ 0.2 selected for the multivariable binary logistic regression model; ¥: Surgeon 4 has been removed from the analysis because all horses were euthanized during anaesthesia for reasons unrelated to the surgeon; Ref: referent

After multivariable analysis PCV, being a stallion, resection and an end-to-end jejunojejunostomy proved to have a significant effect on POR. The risk of POR development increased with an increasing pre-operative PCV (mean ± s.d. PCV horses without POR 36 ± 6%, mean ± s.d. PCV horses with POR 41 ± 7%). Stallions had significant less chance to develop POR. Horses with a resection performed had significantly more chance to develop POR and horses that had a jejunojejunostomy performed had significantly less chance to develop POR compared to horses whit a jejunoileostomy performed.

Multivariable analysis for the effects on re-laparotomy during the surgery for EFE hospitalization period yielded no significant effects.

After multivariable analysis, POR, pre-operative heart rate and pre-operative PCV proved to have a significant effect on successful hospital discharge. Horses with POR had significantly less chance to be discharged from the hospital. The risk of death before discharge from the hospital significantly increased with an increasing pre-operative heart rate (mean ± s.d. heart rate discharged horses 54 ± 15 BPM, mean ± s.d. heart rate not discharged horses 70 ± 21 BPM) and significantly decreased with an increasing pre-operative PCV (mean ± s.d. PCV discharged horses 40 ± 8%, mean ± s.d. PCV not discharged horses 37 ± 7%).

Post-hospital discharge events

Owners from 63/70 discharged horses could be reached (90%). One owner confirmed that the horse was still alive but was unwilling to provide further information resulting in 62/70 horses (89%) being available for analysis of post-discharge events.

After discharge, 19 horses (30%) had at least 1 colic episode. Nine horses (13%) died because of colic, of which 5 horses (7%) had a specific diagnosis (3 intestinal strangulation due to intra-abdominal adhesions (4%) and 2 recurrent EFE (3%)), and 4 horses (6%) died without specific colic diagnosis. Four horses (6%) died because of reasons unrelated to colic.

Detailed results for the univariable and multivariable effects of potential explanatory independent variables on occurrence of colic after hospital discharge are shown in Table 5.

Table 5: Univariable and multivariable associations between potential explanatory variables and occurrence of colic after hospital discharge. Horses available for analysis: 70. The odds ratio (OR) represent the effect of the specific variable in relation to the occurrence of colic after hospital discharge with an OR between 0 and 1 as protective factor and an OR > 1 determining a risk-factor for occurrence of colic after hospital discharge.

	Univariable analysis					Multivariable analysis		
Variable	**Number available**	**Missing data (%)**	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Continuous variables								
Age (years)	62	11	1.00	1.00-1.01	0.49			
Weight (kg)	62	11	1.00	1.00-1.01	0.41			
Duration colic signs (min)	61	13	1.05	0.95-1.16	0.37			
Heart rate (beats/min)	62	11	1.02	0.98-1.06	0.39			
Respiratory rate (respirations/min)	44	37						
Packed cell volume (%)	62	11	0.96	0.88-1.05	0.41			
Base excess (mEq/L)	62	11	1.08	0.94-1.24	0.31			
Blood lactate (mmol/L)	11	84						
Peritoneal fluid lactate (mmol/L)	18	74						
Length involved intestine (cm)	58	17	1.00	1.00-1.00	0.68			
Duration anaesthesia (min)	62	11	1.01	0.99-1.02	0.40			
Duration hospitalization (days)	62	11	1.05	0.98-1.11	0.15§	1.08	1.01-1.15	0.03*
Categorical variables								
Breed	62	11						
Warmblood	52		Ref					
Others	10		1.06	0.24-4.64	0.94			
Sex	62	11						
Mare	12		0.18	0.021-1.58	0.12§			
Stallion	14		1.11	0.31-4.05	0.87			
Gelding	36		Ref					
Ileum involved	62	11						
NO	15		Ref					
YES	47		0.77	0.22-2.67	0.67			
Resection performed	62	11						
NO	40		Ref					
YES	22		1.71	0.56-5.28	0.35			
Post-operative reflux	62	11						
NO	52		Ref					
YES	10		0.56	0.11-2.95	0.50			
Windsucking/crib-biting	54	23						
NO	29		Ref					
YES	25		1.49	0.43-5.22	0.53			

*: P value ≤ 0.05 is considered significant; §: P value ≤ 0.2 selected for the multivariable binary logistic regression model; Ref: referent

Multivariable analysis demonstrated a significant effect of the length of hospitalisation on the occurrence of colic after hospital discharge. The risk for colic after hospital discharge increased significantly with an increasing hospitalisation time (mean ± s.d. hospitalisation time horses without colic after hospital discharge 11 ± 7 days, mean ± s.d. hospitalisation time horses with colic after hospital discharge 15 ± 11 days). Survival information was missing for 7 horses. Survival for all 138 EFE surgeries for which survival data were available, including horses that underwent intra-operative euthanasia and horses that were not discharged, ranged from 0 to 3193 days with a median of 9 days. Survival of the 107 horses recovered from anaesthesia ranged from 1 to 3193 days with a median of 2187 days. Survival of the 63 horses that were discharged from the hospital and for which survival data were available ranged from 17 to 3193 days with a median of 1529 days.

Detailed results for univariable and multivariable Cox-regression analyses between potential explanatory variables and cumulative probability of survival of discharged horses are shown in Table 6.

After multivariable analysis, pre-operative PCV and whether a resection was performed proved to have a significant effect on survival after discharge. The cumulative probability of survival was significantly higher in horses with a higher pre-operative PCV (mean ± s.d. PCV in deceased horses was 34±7%, mean ± s.d. PCV in horses alive was 38±7), and lower in horses in which a resection was performed.

Epiploic foramen entrapment recurrences

Recurrence of EFE was confirmed during 4 EFE surgeries; the initial surgery of one of these horses was performed before start of data collection, so within the described timeframe, 3 horses underwent 2 EFE surgeries, which represents 3% from the recovered horses. The time between 2 EFE surgeries in the 4 recurrent cases ranged from 1 day to 3 years 10 months and 10 days with a median of 2 years 3 months and 4 days. One of these 4 horses survived to discharge following the second surgery.

Table 6: Univariable and multivariable associations between potential explanatory variables and cumulative probability of survival of horses discharge from the hospital (univariable and multivariable Cox regression analysis). Horses available for analysis: 70. The hazard ratios (HR) represent the effects of the specific variables in relation to the cumulative probability of survival after hospital discharge with a HR between 0 and 1 as protective factor and a HR > 1 determining a risk-factor for the cumulative probability of survival after hospital discharge. Censored horses: non-colic related death and horses still alive at the end of their specific follow-up period.

	Univariable analysis						Multivariable analysis		
Variable	**Number available**	**Missing data (%)**	**Number censored (%)**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
Continuous variables									
Age (months)	63	10%	54 (85.7%)	1.00	0.99-1.01	0.68			
Weight (kg)	63	10%	54 (85.7%)	1.00	0.99-1.00	0.46			
Duration colic signs (min)	62	11%	53 (85.5%)	0.90	0.72-1.12	0.35			
Heart rate (BPM)	63	10%	54 (85.7%)	1.03	0.99-1.08	0.18§			
Respiratory rate	42	40%	34 (81.0%)						
Packed cell volume (%)	63	10%	54 (85.7%)	0.91	0.81-1.03	0.13§	0.85	0.73-0.99	0.04*
Base excess (mEq/L)	63	10%	54 (85.7%)	1.06	0.90-1.25	0.49			
Blood lactate (mmol/L)	7	90%							
Peritoneal fluid lactate (mmol/L)	19	73%							
Duration anaesthesia (min)	63	10%	54 (85.7%)	1.00	0.99-1.01	0.66			
Length involved intestine (cm)	59	16%	50 (84.9%)	1.00	0.10-1.00	0.85			
Length resection (cm)	23	0%	18 (78.3%)	1.00	1.00-1.00	0.77			
Categorical variables									
Breed	63	10%	54 (85.7%)						
Warmblood	53			Ref					
Other breeds	10			1.34	0.27-6.56	0.72			
Sex	63	10%	54 (85.7%)						
Mare	13			0.50	0.06-4.12	0.52			
Stallion	14			0.43	0.05-3.53	0.43			
Gelding	36			Ref					
Ileum involved	63	10%	54 (85.7%)						
NO	15			Ref					
YES	48			0.61	0.12-3.10	0.55			
Resection	63	10%	54 (85.7%)						
NO	40			Ref			Ref		
YES	23			2.65	0.70-10.06	0.15§	5.28	1.13-24.67	0.03*
Type anastomosis	23	0%	18 (78.3%)						
End-to-end jejunoileostomy	9			Ref					
End-to-end jejunojejunostomy	12			0.69	0.10-5.02	0.72			
Side-to-side jejunocaecostomy	2			1.47	0.12-17.39	0.76			

*: P value ≤ 0.05 is considered significant; §: P value ≤ 0.2 selected for the multivariable Cox-regression model, Ref: referent

Discussion

In the present study data were obtained from the largest study population in regard of EFE to date in a single equine referral clinic during an 8.75 year period. The population consisted mainly of European Warmblood horses (85%), which is a population that, to the best of our knowledge, has not been reported in a large case series in the published literature before. High morbidity and mortality associated with EFE colic surgery were demonstrated as 26% of the horses underwent intra-operative euthanasia and 35% of recovered horses died prior to hospital discharge. Furthermore, beside these moderate results, the condition recurred in at least 3% of the survivors. In a retrospective case control study windsucking/crib-biting was significantly associated with surgery for EFE cases (49%) compared to the whole colic surgery population (Archer et al., 2004). In our case series this stereotypic behaviour was confirmed in an even higher percentage (60%). Prevention of stereotypic behaviours could be based upon housing and management conditions which allow tactile contact with other horses, daily free movement in paddock or pasture, as well as the provision of high amounts of roughage but little or no concentrates (Bachmann et al., 2003).

The recently reported funnel-like shape of the equine epiploic foramen (Freeman and Pearn, 2015; van Bergen et al., 2015) is considered to be the main cause of predominant left-to-right EFE occurrence (Freeman and Pearn, 2015; van Bergen et al., 2015). This is confirmed in our case series where all 145 entrapments were from left-to-right and agrees with recent EFE case series where 97-100% of entrapments occurred from the left to the right through the epiploic foramen (Vachon and Fischer, 1995; Archer et al., 2004). Only older case series reported predominant right-to-left EFE (Turner et al., 1984; Vasey, 1988).

The overall survival until hospital discharge of all horses undergoing surgery for EFE in our study was 48%. Sixty-five percent of horses that left the recovery box alive after surgery for EFE survived to discharge, indicating that 35% of the recovered horses died during the hospitalization period. Our reported discharge percentages are substantially lower compared to the previously reported 79 to 85% hospital discharge for horses that left the recovery box alive and compared to the 66 to 69% discharge when all horses undergoing EFE colic surgery were considered (Vachon and Fischer, 1995; Archer et al., 2004, 2011). In the present study the median survival of the 63 discharged horses from which survival data were available was 1529 days which is substantially longer compared to the 700 days reported by Archer and co-workers (Archer et al., 2004). In our study the median survival time of all EFE cases undergoing surgery was only 9 days compared to 397 days in the prospective study from Archer (Archer et al., 2011). The low median survival of the whole surgery population in our case series is primarily due to the high number of horses that were euthanized during surgery (26%) compared to the previously cited study (15%) (Archer et al., 2011) or compared to the study of Vachon (13%) (Vachon and Fischer, 1995). Taking the decision of intra-operative euthanasia is a complex and multifactorial process that renders comparison between intra-operative euthanasia percentages inappropriate. Uncontrollable intra-operative haemorrhage leading to intra-operative euthanasia can occur due to rupture of the portal vein, caudal vena cava or hepatic artery (van Bergen et al., 2015). This can be caused by difficult repositioning, a small epiploic foramen, oedematous small intestine or a lack of surgical skills. Such haemorrhage occurred in 6% of the EFE surgeries reported in the present case series which is in line with previously reported numbers ranging from 1.6 to 12% (Vasey, 1988; Livesey et al., 1991; Vachon and Fischer, 1995; Archer et al., 2004, 2011; Steenhaut et al., 2004).

Discussion of the effect of PVC on the occurrence of POR, on hospital discharge and on survival, of heart rate on hospital discharge and of duration of hospitalization on colic after hospital discharge, is questionable because the respectively corresponding odds ratios or hazard ratios are of questionable clinical importance. Analysis on intestinal resection, jejunoileostomy compared to jejunojejunostomy and the occurrence of POR on the other hand generated odds ratios or hazard ratios that merits further attention. Horses with POR after surgery were less likely to be discharged from the hospital, which is in line with previous results on surgery for EFE (Archer et al., 2011). Horses undergoing resection, and more specific end-to-end jejunoileostomy, were considerably more prone to POR development compared to horses undergoing jejunojejunostomy without ileal involvement in the present study. An association between small intestinal resection for various small intestinal lesions and post-operative ileus (POI) was previously demonstrated in our hospital (Torfs et al., 2009). Ileal involvement in the majority of EFE cases (74%) could contribute to the high morbidity and mortality in EFE. However, we were not able to demonstrate a significant effect of ileal involvement within the described EFE population. Ileal involvement in about 2/3 of the cases has been reported in a rather consistent way in the literature: 10/15 cases (66.7%) (Vasey, 1988), 12/19 cases (63.2%) (Engelbert et al., 1993), 37/53 cases (69.8%) (Vachon and Fischer, 1995) and 47/71 cases (66.2%) (Archer et al., 2004). High hospital discharge percentages (20/21 horses (95%) discharged) were obtained in a case series with 81% ileal involvement where a large number of horses was treated by jejunocaecostomy instead of jejunoileostomy, suggesting that the avoidance of jejunoileostomy could improve results (Freeman and Schaeffer, 2005). However, no significant benefit from jejunocaecostomy compared to jejunoileostomy in regard of POR development could be proved in our study, but only 6 jejunocaecostomies were performed. The disparity in wall thickness between the jejunum and ileum and considerable cuff formation that can result from an inverting suture pattern in the thicker ileal wall could be responsible for problematic short-term outcomes with end-to-end jejonoileostomy (Stewart et al., 2014). More horses undergoing jejunoileostomy underwent repeat laparotomy during the hospitalisation period compared to horses that underwent jejunojejunostomy or jejunocaecostomy in a population of horses that recovered from general anaesthesia following resection and anastomosis for treatment of a small intestinal obstruction (Stewart et al., 2014). However, there was no difference in short-term outcome between groups, whereas horses with a jejunocaecostomy were more likely to have long-term complications with colic (Stewart et al., 2014). On the other hand, no greater risk for morbidity or mortality was found for end-to-end jejunoileostomy than for end-to-end jejonojejonostomy in another study comparing 30 cases of strangulated small intestine treated by jejunoileostomy and 70 cases by jejunojejunostomy (Rendle et al., 2005). After survival analysis in a prospective, nonrandomised, observational study, morbidity and mortality were significantly higher in a group of horses treated by side-to-side jejunocaecostomy (178 horses) compared to a group treated by end-to-end jejunojejunostomy (184 horses) (Proudman et al., 2007). However, end-to-end jejunoileostomy was not conducted at all in this study-population (Proudman et al., 2007). Retrospective analysis of 74 horses that recovered from anaesthesia after small intestinal surgery demonstrated that POI was more likely to occur after a jejunocaecostomy than after other procedures, and POI did not develop after a jejunojejunostomy (Freeman et al., 2000). From these 74 horses, 47 underwent resection and anastomosis with 23 horses that underwent an end-to-end anastomosis and 25 a jejunocaecostomy. Short-term survival was poorest in horses that had a jejunocaecostomy, but long-term survival was less affected by the anastomosis used (Freeman et al., 2000). Survival after hospital discharge was affected by the presence of a resection in the present study. However, no effect of any specific anastomosis technique could be demonstrated on survival after hospital discharge, but side-to-side jejunocaecostomy was only preformed in 6 cases. Stallions seemed to be less prone to POR development in the present case series, but the number of stallions was small and the prognostic value of this finding should probably not be overestimated.

In an earlier study reporting about 53 EFE cases, 12/44 (27%) recovered horses underwent re-laparotomy, mainly due to POR (Vachon and Fischer, 1995). Survival after re-laparotomy was 50% (6/12) and a mechanical factor (adhesion, impaction, stricture) at the anastomotic side was the most common cause of re-laparotomy (Vachon and Fischer, 1995). Ten percent of 300 horses that underwent surgical treatment of all kinds of colic needed re-laparotomy (Mair and Smith, 2005). Short- and long-term survival were 50 and 22% respectively. Nearly 40% of horses surviving re-laparotomy developed episodes of acute colic that necessitated further surgery (Mair and Smith, 2005). Another study amongst horses that underwent colic surgery for various reasons reported hospital discharge of 53% after re-laparotomy due to persistent colic and 37% after re-laparotomy for POR (Findley et al., 2016). In our study which included only EFE horses, re-laparotomy was conducted in 10/107 (9%) surgeries and hospital discharge after re-laparotomy was achieved in 2/10 horses (20%). The majority of the undischarged horses from the present case series were suffering from POR (70%). Specific causes for this POR were found and solved in all horses that underwent re-laparotomy. Nevertheless, only 2 out of 10 horses that underwent re-laparotomy survived to discharge. The cause of POR is probably multifactorial, with functional ileus as only one component, while many other factors related to the surgery probably contribute individually or more collectively to the problem (Freeman, 2017). Twenty-two horses underwent re-laparotomy for POR or post-operative colic after an initial jejunojejunostomy (Bauck et al., 2017). From the 11 horses with initial jejunojejunostomy, 9 required resection of the original anastomosis due to anastomotic complications. In 8 horses without resection, second surgery included resection (4) or decompression (4). All recovered horses (19) were discharged from the hospital (Bauck et al, 2017). These results, together with the findings at re-laparotomy in the present study, illustrates that mechanical problems can contribute to POR in a large amount of cases often catalogued as POI and that the POI problematic should not be restricted to functional disturbance of the intestinal motility (Salem et al., 2016).

A more proactive approach with more frequent and earlier re-laparotomy in horses suffering POR, compared to the approach used in our study, might be beneficial. However, recent data from another study demonstrated that only 24% of horses were still alive 6 months post-surgery after repeat laparotomy performed on 95 horses (Dunkel et al. 2015). Incisional infections occurred in 68.4% (26/38) of horses that survived to hospital discharge, and 31.6% (12/38) developed incisional hernias or dehiscence (Dunkel et al. 2015). This results indicate that the overall prognosis for re-laparotomy is guarded.

Recurrence of EFE was reported in 3% of the cases and was in line with previously reported recurrence rates ranging from 2% to 14% (Vachon and Fischer, 1995; Archer et al., 2004; Freeman et al., 2014). Recurrence of EFE in the present study was probably underestimated due to the stringent classification of this event taking place (diagnosis of recurrent EFE made on our surgery table). Horses that do not have spontaneous epiploic foramen closure after surgery for EFE are likely to be at a substantially higher risk to develop EFE recurrence as spontaneous closure of the epiploic foramen has been reported in 43% of horses undergoing laparoscopic inspection after surgery for EFE (van Bergen et al., 2016b). Standing right flank control laparoscopy with subsequent mesh closure (van Bergen et al., 2016a) about 1 month after the initial colic surgery has been proposed (van Bergen et al., 2016b). Alternatively, mesh closure could be performed during the initial EFE colic surgery (van Bergen et al., 2017). These approaches could be of particular interest for windsucking/crib-biting horses (van Bergen et al., 2016b) that are known to be at increased risk of EFE.

The moment of death after discharge was not directly recorded during this study, but was gathered from telephone interviews. As a consequence, the outcome variable “time to death” was biased by the best guess the owner could provide (recall bias). Other limitations of the study consisted of missing data in the clinical files, which is somewhat inherent to retrospective studies. The re-laparotomy analysis is underpowered, as there were only 10 horses that underwent re-laparotomy.

Retrospective analysis of a large dataset of horses undergoing surgery for EFE in the present study demonstrated high morbidity and mortality, as 26% of the horses were euthanized during surgery and 35% of recovered horses died prior to hospital discharge. Resection performed predisposed horses for POR and horses undergoing jejunoileostomy were more prone to POR development compared to horses undergoing jejunojejunostomy. Horses that developed POR were less likely to be discharged from the hospital and horses that underwent a resection had shorter life expectations after hospital discharge compared to horses without resection. Post-operative reflux in a high percentage of cases could have contributed to the disappointing outcome after surgery. A combination of good intestinal anastomosis technique, more frequent re-laparotomy and prevention of recurrences of EFE might be beneficial to improve results presented in the present case series.

Disclosure Statement

The authors declare no conflict of interest.

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Manufactures' details

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CHAPTER 8

General Discussion

Horses admitted for emergency treatment to a referral hospital are often presented with signs of colic due to acute gastrointestinal disease (Southwood et al., 2009). Between 2008 and 2017, 6473 horses were admitted with acute colic at the Ghent University Equine Referral Hospital. Two-thousand and four (31%) emergency laparotomies were performed within this population. In 145 (7.2%) of the horses that underwent laparotomy, the clinical signs were provoked by intestinal epiploic foramen entrapment (EFE), which is higher than the 5% reported in literature (Vachon and Fischer, 1995; Archer et al., 2004; Mair and Smith, 2005). Horses that undergo surgery for EFE carry a worse prognosis for post-operative survival compared to other surgical colic cases (Proudman et al., 2002a, 2002b).

Despite the importance of this severe form of colic in horses with high mortality despite surgical intervention, there remains a considerable gap in knowledge about this specific type of colic amongst equine practitioners and equine surgeons. Further research will help to explore new ways in which the outcome for this type of colic could be improved. Discrepancies exist in literature about the anatomic description of the epiploic foramen in horses and knowledge is lacking about the specific surgical anatomic landmarks and 3D-configuration of the epiploic foramen and omental vestibule which are needed for the development and description of novel surgical techniques in the region. Knowledge is also lacking about the pathophysiology of EFE and the reasons for the more frequent occurrence of this disease in horses compared to other mammalian species including man. Spontaneous or preventive surgical closure after EFE has been sporadically reported in human medicine (Erskine, 1967a, 1967b; Osvaldt et al., 2008; Garg et al., 2016). Despite several large case series of EFE in horses, there has been very limited discussion about prevention of EFE recurrence apart from a single study on surgical epiploic foramen closure in experimental horses which resulted in an inconsistent outcome (Munsterman et al., 2014). The latter investigation was published during the course of the present study.

The findings that were presented throughout this thesis will be discussed in 3 sections. The first section discusses the anatomy of the equine epiploic foramen, which is the base for surgery and subsequent surgical scientific communication. Next, a section is dedicated to the pathophysiology of equine EFE and, finally, the surgical technique and surgical prevention are discussed in the section “Toward a better outcome in EFE colic surgery”.

Anatomy of the equine epiploic foramen

Recent increased availability of minimally invasive surgical techniques has resulted in renewed anatomical interest amongst surgeons. Minimally invasive surgery is conducted under video-endoscopic control *in situ*, providing a different view on anatomic structures compared to classic drawings in anatomic reference works. Available anatomic drawings are basically produced after anatomical dissection on a dissection table and the relative 3D anatomical *in situ* arrangement of foldable structures is often lost. Structures such as the epiploic foramen were only palpated and never visualized *in situ* in standing animals by equine surgeons before the availability of laparoscopy.

In addition to this, dissimilar description of the exact anatomy of the equine epiploic foramen persists throughout literature. Structures surrounding the epiploic foramen and omental vestibule in horses are arranged in a specific funnel-like configuration as described in Chapter 3 (Freeman and Pearn, 2015; van Bergen et al., 2015). This funnel-shape results from the presence of a second ring to the left of the epiploic foramen between the omental vestibule and the caudal recess of the omental bursa, and has confused equine clinicians searching for names for this additional structure. However, tracing back to the accepted interspecies anatomical definitions, all structures surrounding the epiploic foramen could be identified in our study (Chapter 3) without contradictions against the generally accepted anatomical definitions (van Bergen et al., 2015). All structures could also be correlated to the visualized structures during laparoscopy (van Bergen et al., 2015). Dimensions of the equine epiploic foramen were obtained, which allowed us to design a correctly fitting mesh-construct and applicator instruments as described in Chapter 4 (van Bergen et al., 2016a).

A recent publication identified the gastropancreatic fold as the caudoventral boundary of the epiploic foramen (Freeman and Pearn, 2015). This described contribution of the gastropancreatic fold was in agreement with one veterinary anatomy book (Sisson, 1975) but disagreed with all other major veterinary (Nickel et al., 1973; Barone, 1997, 2001) and human (Putz and Pabst, 1994) anatomical reference works. The interspecies definition of the gastropancreatic fold in the Illustrated Veterinary Anatomical Nomenclature edited by Constantinescu and Schaller is given as "*a fold of the wall of the omental bursa containing the left gastric vessels*" (Constantinescu and

Schaller, 2012) and it is therefore highly unlikely that the gastropancreatic fold itself really borders the epiploic foramen caudoventrally, as the epiploic foramen is located to the right side of the stomach. The hepatopancreatic fold, defined as "*a fold in the wall of the omental bursa containing the hepatic artery*" (Constantinescu and Schaller, 2012) has been neglected in recent literature. Barone described that the dorsal arch of the opening between the omental vestibule and the caudal recess of the omental bursa is formed by the fusion between the gastropancreatic fold to the left and the hepatopancreatic fold to the right (Barone, 2001). The pancreas lies caudoventral to and in contact with the hepatoduodenal ligament and hepatopancreatic fold and its left lobe runs further to the left covering the arch formed by the fusion of the hepatopancreatic and gastropancretic folds as shown in Figure 1 of Chapter 3 (van Bergen et al., 2015). Contact with the left pancreatic lobe explains the name of the gastropancreatic fold. Nevertheless, this fold is localized to the left side of the stomach and contributes to the formation of the omental vestibule, but not to the formation of the epiploic foramen itself, as the latter is bordered craniodorsally by the base of the caudate process of the liver and caudoventrally by a secondary fold within the hepatoduodenal ligament as shown in Figure 1 Chapter 3 (van Bergen et al., 2015). Our description of the specific contribution of the hepatoduodenal ligament, the hepatogastric ligament and the gastropancreatic and hepatopancreatic folds to the formation of the epiploic foramen and omental vestibule are in line with the anatomic definitions from the Illustrated Veterinary Anatomical Nomenclature (Constantinescu and Schaller, 2012). In the latter reference work, the structures named in the "*Nomina Anatomica Veterinaria*" (World Association of Veterinary Anatomists, 2017) are depicted and defined. The arrangement of the content adheres strictly to that of the *Nomina Anatomica Veterinaria* and focuses on the gross anatomical structures of the cat, dog, pig, ox, sheep, goat, and horse. The Illustrated Veterinary Anatomical Nomenclature is edited by the renowned anatomists G.M. Constantinescu and O. Schaller with contributions of R.E. Habel, A. Hillebrand, W.O. Sack, P. Simoens and N.R. de Vos, all of them prominent contributors to veterinary anatomical nomenclature. Intellectual correctness obliges clinicians publishing about anatomy to test their hypothesis to the *Nomina Anatomica Veterinaria* and the definitions of the anatomic names from this list given in the Illustrated Veterinary Anatomical Nomenclature. Failure to do so will lead to misinterpretation, poor communication and problematic scientific claims.

In the human literature reports about Winslow foramen herniation and related anatomical descriptions are limited. However, the anatomy and surgical approach to the region is described in detail in regard to hepatic lobectomy procedures for cancer treatment (Netter, 1967) and for hepatic transplantation surgery (Kim et al., 2012). The hepatoduodenal ligament and the relative position of the portal vein, hepatic artery, common bile duct and the numerous anatomic variations of the hepatic artery have been documented over many years in human surgical reference work (Netter, 1967). In addition to the above-mentioned highly undesirable misuse of anatomic nomenclature in recent veterinary literature, there is no justifiable reason to diverge in the equine surgical literature from nomenclature used in the human surgical literature.

The potential implications of the presence of the hepatic artery adjacent to the epiploic foramen have not been mentioned in the equine clinical literature as this vascular structure has up to now been totally neglected. The anatomic and laparoscopic knowledge of this structure provided in Chapter 3 might be important for surgeons as damage to this artery during intestinal reduction during EFE colic surgery or during laparoscopic epiploic foramen closure could have devastating consequences for the patient. Previous work of the French veterinary anatomist Barone mentioned the presence of anatomic variation of the equine hepatic artery (Barone, 1996) comparable to reports in humans (Netter, 1967; Song et al., 2010; Kim et al., 2012). During laparoscopic examination of the epiploic foramen we were not able to document the bile duct and we did not focus on this structure during our dissections at the level of the hepatoduodenal ligament. This could be interpreted as a limitation of our anatomical study and an opportunity for further research. Pressure on the bile duct during EFE could obliterate the duct which might have impact on pre-operative bile acid and bilirubin concentrations and on serum activities of γ-glutamyl transferase (GGT), allowing more specific pre-operative diagnosis of EFE.

Pathophysiology of equine EFE

In human medicine Winslow foramen hernias are very uncommon and intestinal entrapment occurs in the vast majority of cases from right-to-left, thus from the abdominal cavity through the epiploic foramen into the omental bursa (Erskine, 1967a). This is in contrast to equine colic patients, where EFE represents 5% (and even 7.8% at our institution) of surgically treated horses (Vachon and Fischer, 1995; Archer et al., 2004; Mair and Smith, 2005) and where the entrapment occurs in the vast majority of cases (97-100%) from the left to the right through the epiploic foramen (Vachon and Fischer, 1995; Archer et al., 2004; Steenhaut et al., 2004). Older publications reported a predominant right-to-left entrapment of intestines through the epiploic foramen (Turner et al., 1984; Vasey, 1988). However, based on the more recent and larger case series and our own cases presented in Chapter 7, this historically reported predominant right-to-left intestinal entrapment has to be interpreted with care and is probably inaccurate. Confusion about left and right on the horse in dorsal recumbency could have been at the origin of these inaccurate right-to-left reports in the past. The high prevalence of EFE in horses and the almost exclusive left-to-right entrapment of intestines through the epiploic foramen both contrast with human medicine, suggesting some specific anatomical or physiological features influencing the occurrence of this disease in horses.

Specific anatomical features of the equine epiploic foramen

In contrast to other mammalian species, where the epiploic foramen is more a ring-like structure, the epiploic foramen in horses, together with the omental vestibule, is a funnel-like structure (Freeman and Pearn, 2015) as demonstrated in Chapter 3 (van Bergen et al., 2015). This funnel-structure in horses is the result of the specific arrangement of the hepatoduodenal and hepatogastric ligaments and the gastropancreatic and hepatopancreatic folds resulting in a smaller opening, i.e. the epiploic foramen, to the right and a larger opening, dorsally bordered by the fused gastropancreatic and hepatopancreatic folds and ventrally by the minor curvature of the stomach to the left (Chapter 3) (van Bergen et al., 2015). The latter large opening forms the connection between the omental vestibule and the caudal recess of the omental bursa (van Bergen et al., 2015). The described funnel acts as a trap that allows intestines to enter the wide opening of the omental vestibule, and then move through it from the left to the right toward the smaller epiploic foramen, where the intestines become entrapped (Freeman and Pearn, 2015). *In situ,* the larger opening to the left lies more ventrally compared to the dorsal localization of the epiploic foramen (Chapter 3, Figure 1C). It lies in close proximity to the natural localization of the majority of the small intestine and the only structure separating the small intestine from the large opening of the omental vestibule is the greater omentum, which encloses the omental bursa. When intestines enter the funnel of the omental vestibule, the greater omentum inverts into the omental vestibule and ruptures at some point in this process due to the pressure exerted by the intestines. The fragile nature of the greater omentum, which is typically observed in horses, implies that the greater omentum is not able to withhold intestines from entering the omental vestibule and epiploic foramen from the left to the right. During laparoscopic inspection of the epiploic foramen 1 month after surgery for EFE we could document a large defect in the greater omentum in 2 cases supporting this theory (case 2 and 6, Chapter 5) (van Bergen et al., 2016b). In a previous case series conducted at our institution the duodenum was included in the entrapment only in one single case amongst 47 cases, that had EFE from the right to the left (Steenhaut et al., 2004). The duodenum is the only part of the small intestine that is localized under normal circumstances in the right dorsocranial quadrant of the abdomen, near to the epiploic foramen which might explain this observation of right-to-left entrapment of the duodenum through the epiploic foramen. A similar case has previously been observed by one of the promotors of the present dissertation (unpublished data).

Specific physiologic features of equine EFE

Crib-biting/windsucking behaviour has been associated with EFE by Archer *et al.* (OR 67.3, 95% CI15.3–296.5) (Archer et al., 2008a). Crib-biting/windsucking is a specific stereotypic behaviour, during which horses contract the strap muscles of the ventral throat and draw air into the cranial oesophagus with or without grasping a horizontal fixed object with their incisor teeth (Waters et al., 2002; Albright et al., 2009). Crib-biting or windsucking was confirmed in 60% of the horses that underwent surgery for EFE in our case series (Chapter 7). This is substantially higher than the reported occurrence of crib-biting/windsucking in the general horse population, which is reported to be between 4.4 and 6.8% (Albright et al., 2009; Malamed et al., 2010).

Horses displaying crib-biting/windsucking behaviour are also known to be at increased risk for recurrent colic problems other than EFE (Scantlebury et al., 2011). Crib-biting/windsucking was significantly associated with colic, but was not associated with any specific category or severity of colic over another (Malamed et al., 2010). However, no specific relation between crib-biting/windsucking and EFE was evaluated due to the small sample size of horses diagnosed with EFE (Malamed et al., 2010). Hillyer and co-workers identified a significant association between crib-biting/windsucking behaviour and simple colonic obstipation/distension (forwards stepwise model OR

89.46, 95% CI 8.98-890.69 - backwards elimination model OR 203.90, 95% CI 10.55-3941.42) (Hillyer et al., 2002). Longer total gut transit times without alterations in the orocaecal transit times were demonstrated in 4 crib-biting horses compared to 4 normal horses (McGreevy et al., 2001). This could explain the increased occurrence of colonic-related colic episodes in crib-biting/windsucking horses.

Albanese and co-workers were able to demonstrate an increased intra-abdominal pressure during and after a crib-biting episode (Albanese et al., 2013). It has been suggested that increased intra-abdominal pressure could expand the omental vestibule and force small intestines into it (Freeman and Pearn, 2015), with the funnel-like omental vestibule acting as a trap, advancing the intestines toward the epiploic foramen where they become entrapped. However, simple and uniform intra-abdominal pressure increase is unlikely to result in intestinal displacement. More complex phenomena as for example different intra-abdominal pressure between the caudal-cranial and ventral-dorsal abdomen could result in displacement, but these theories were not investigated in the present study. Rhythmic movement of the abdominal wall, diaphragm and liver during windsucking/crib-biting might be involved in EFE development. Historically windsucking/crib-biting has been associated with aerophagia (Frauenfelder, 1981) and in consequence intestinal gas accumulation might be involved in small intestinal displacements in windsucking/crib-biting horses. However, meticulous observation of crib-biting horses by means of fluoroscopy and endoscopy revealed that the large majority of accumulated air at the level of the cranial oesophagus during crib-biting was released through the nasopharynx and only very little amounts of air moved caudally toward the stomach (McGreevy et al., 1995). The latter observation may also explain why cases of tympanic colic are not seen more frequently in crib-biting horses (McGreevy et al., 1995).

Windsucking/crib-biting behaviour, although present in the majority of EFE cases, was absent in several horses that developed the disease, indicating that there are likely to be other factors involved in the development of EFE. Therefore, it is possible that the combination of the funnel-like shape of the equine epiploic foramen, rhythmic movement of the abdominal wall, diaphragm and liver, and possible occurrence of pressure differences throughout the abdomen during windsucking/crib-biting may be involved in EFE development in horses and warrants further investigation.

Recurrence of EFE in horses

Recurrence of a disease that can only be cured by surgical intervention and with a poor prognosis for survival despite surgery as is the case for EFE, is not a desirable situation. Reported EFE recurrence rates amongst horses that survived colic surgery for EFE range between 2 and 14% (Vachon and Fischer, 1995; Archer et al., 2004; Freeman et al., 2014) and was 3% in our case series (Chapter 7). The recurrences reported in Chapter 7 are probably an underestimation due to the stringent definition of recurrent EFE cases used in our study, only classifying cases as recurrent if the diagnosis of recurrence was made in our own clinic at laparotomy. However, in light of the strong predilection for EFE in crib-biting/windsucking horses (OR 67.3, 95% CI15.3–296.5) (Archer et al., 2008a), recurrence between 2 and 14% can be interpreted as rather low. In Chapter 5 we have demonstrated spontaneous closure of the epiploic foramen after EFE due to induced inflammation and subsequent serosal adhesions at the level of the epiploic foramen and omental vestibule induced by mechanical serosal damage during incarceration and during manipulations while reducing the entrapped intestine. Such spontaneous closure of the epiploic foramen after surgical correction of EFE was encountered in 3 out of 7 horses (43%) (van Bergen et al., 2016b) and is supported by more recent multicentre data revealing spontaneous closure in 9/28 cases (32%) (unpublished data). It is difficult to predict if the natural process of inflammation with subsequent adhesion formation can be relied upon to obliterate the epiploic foramen after EFE and subsequently to prevent EFE recurrence in individual cases. Future investigations could focus on ultrasonographic technique to detect spontaneous closure of the epiploic foramen after EFE, although challenges have to be recognized due to the difficult ultrasonographic interpretation of “closure” of a virtual space and due to potential obliteration of the ultrasound-beam by gas filled intestine.

Toward a better outcome in EFE colic surgery

Surgical technique

A retrospective study reviewing records of 300 horses undergoing colic surgery identified small intestinal and caecal lesions as carrying a worse prognosis for survival compared to other surgically treated colic patients (Mair and Smith, 2005). The presence of ischemic/strangulating lesions was also correlated with a lower survival rate compared to simple obstructions (Mair and Smith, 2005). Small intestine is involved in almost all equine EFE cases, apart from a few colonic or caecal entrapments reported in literature (Foerner et al., 1993; Steenhaut et al., 1993; Segura et al., 1999; Grzeskowiak et al., 2017). The ileum was involved in 63-81% of reported EFE cases (Vasey, 1988; Engelbert et al., 1993; Vachon and Fischer, 1995; Archer et al., 2004; Freeman and Schaeffer, 2005). Repositioning of the entrapped intestine can be challenging. The equine epiploic foramen is a rigid structure due to the reinforcement of the hepatoduodenal ligament with a central connective tissue core composed of elastin fibres as demonstrated in Chapter 3 (van Bergen et al., 2015). The epiploic foramen often causes acute vascular constriction resulting in a combination of oedema, swelling and accumulation of luminal content at the level of the strangulated part of the intestine, rendering its reduction through the epiploic foramen difficult. Very often surgeons have to use both hands to reduce EFE, one hand to pull carefully and the other to push in the same direction. Massaging luminal content from the strangulated intestine into the non-strangulated part, possibly after pulling an additional part of non-strangulated intestine into the entrapment, can facilitate reduction (Vachon and Fischer, 1995) by avoiding reduction of the thickened intestinal wall at the same time with its distended luminal content. In the very rare case where reduction is not possible by means of the above described techniques, strangulated intestine can be emptied through an enterotomy or transection (Freeman, 1997). Intestine can then be reduced after suture closure of the enterotomy or transection (Freeman, 1997). Care should be taken to perform all manoeuvres in the horizontal plane to avoid portal vein (Freeman, 1997; van Bergen et al., 2015) or hepatic artery (van Bergen et al., 2015) damage when pulling upwards into the abdominal wall incision leading to fatal intra-operative haemorrhage. Very recently, digital enlargement of the caudal part of the epiploic foramen to facilitate intestinal reduction by separating its caudal edge has been reported (Smith and Freeman, 2017). Anatomical knowledge permitted the authors to identify the caudal part of the epiploic foramen as the only relatively safe location to perform digital enlargement. Fatal intra-operative haemorrhage was not encountered in the 6 experimental horses that were used during the development of the technique, nor in a clinical patient. The authors however, did not take the hepatic artery into consideration. The hepatic artery runs to the left of the portal vein, and lies further away from the epiploic foramen itself compared to the portal vein. In consequence, the hepatic artery should be less prone to damage compared to the portal vein while separating the caudal epiploic foramen edge. Separation at the cranial corner of the epiploic foramen should also in my opinion be avoided by all means, as this is the location where the portal vein penetrates the liver.

Horses undergoing surgery for EFE were treated by repositioning of the intestines from the epiploic foramen and small intestinal decompression without resection only in 1/11 (9%) (Turner et al., 1984), 1/8 (13%) (Vasey, 1988), 3/16 (19%) (Engelbert et al., 1993), 7/46 (15%) (Vachon and Fischer, 1995) and 6/58 (10%) (Archer et al., 2004) of cases reported in literature. Thirty-five of 79 (44%) of the cases reported in the previous study conducted at our institution were treated without resection (Steenhaut et al., 2004) and in our cases presented in Chapter 7 resection was not performed in 57/107 (53%). The more conservative approach toward intestinal resection at our institution has not led to improved rates of survival to hospital discharge. The opposite is even true: the overall survival to hospital discharge of all horses undergoing surgery for EFE was 49% (Steenhaut et al., 2004) and 48% in the more recent case series reported in Chapter 7 compared to 66 to 69% in comparable case series in which resection was not performed in only 10-15% of cases (Vachon and Fischer, 1995; Archer et al., 2004, 2011). If the ileum needs to be resected, end-to-end jejunoileostomy can be performed when the strangulated ileum is limited to its most oral extent. Where a large part of the ileum is involved (more aboral involvement) this is not always technically possible. Indeed, the dorsal localization of the ileocaecal junction often impedes end-to-end anastomotic techniques during conventional ventral midline laparotomy in horses. Alternatively, the ileum can be transected, followed by an end-to-side or side-to-side jejunocaecostomy. Historically, jejunocaecostomy has been associated with a poor prognosis, independent of whether an end-to-side or side-to-side anastomosis between the jejunum and caecum was performed (Kersjes et al., 1988). The mortality rate was higher in horses that required side-to-side jejunocaecal anastomosis as was the occurrence of post-operative colic, compared to horses that underwent an end-to-end jejunojejunal anastomosis (Proudman et al., 2007). A recent study of 258 cases of small intestinal strangulating lesions identified resection-anastomosis in general, and jejunocaecostomy specifically, as factors correlated with non-survival to hospital discharge (Espinosa et al., 2017). Another study including 112 cases that underwent small intestinal resection did not identify significant differences in hospital discharge percentages between jejunojejunostomy, jejunoileostomy or jejunocaecostomy, although jejunoileostomy was associated with increased repeat celiotomy during hospitalization, while horses that underwent jejunocaecostomy had more colic episodes and a shorter post-discharge survival (Stewart et al., 2014).

The high percentage of ileal involvement and the frequent need for intestinal resection in EFE cases might be an explanation for the worse prognosis for post-operative survival that has been reported for EFE compared to other colic cases (Proudman et al., 2002a, 2002b). However, a worse prognosis for post-operative survival could not be demonstrated when comparing ileal involvement or intestinal resection within a group containing only EFE horses although this study is limited by low power to detect a difference due to relative small numbers (Chapter 7). Furthermore, complications at the level of the epiploic foramen itself, such as uncontrollable intra-operative haemorrhage encountered in 3-12% (Vasey, 1988; Livesey et al., 1991; Vachon and Fischer, 1995; Archer et al., 2004; Steenhaut et al., 2004) or hepatic ischemic necrosis (Davis et al., 1992), might contribute to an additional decrease in overall survival of horses suffering from EFE.

However, several factors, such as intestinal reduction from the epiploic foramen or anastomosis technique, are likely to be amenable for improvement by meticulous surgical technique. Knowledge of topographic anatomy might help surgeons to perform atraumatic intestinal reduction from the epiploic foramen avoiding complications associated with severe haemorrhage (Chapter 3). Nighty-five percent discharge amongst recovered horses, of which the ileum was involved in 81% of cases, was achieved under supervision of the renowned colic surgeon Prof. Freeman (Freeman and Schaeffer, 2005). Eight out of 21 horses (38%) underwent intestinal reduction followed by small intestinal decompression alone, while resection followed by jejunocaecosotomy was performed in 9/13 (69%) cases, jejunoileostomy in 2/13 (15%) cases and jejunojejunostomy in 2/13 (15%) cases. These results are excellent despite the high percentage of jejunocaecostomies that had to be performed, which is considered a more difficult technique that is more prone to failure compared to jejunojejunostomy or jejunoileostomy. These outcomes set the bar high for colic surgeons throughout the world at least suggesting that there is room for improvement.

The cause of post-operative reflux (POR) is probably multifactorial, with functional ileus as only one component, while many other factors related to the surgery probably contribute individually or more collectively to the problem (Freeman, 2017). Specific causes of horses refluxing in the post-operative period were found in all horses that underwent re-laparotomy presented in Chapter 7. An impaction was present at the level of the anastomosis in 3 cases, a resection was necessary that was not performed during the initial surgery for EFE due to intestinal devitalisation that occurred following the initial surgery in 3 cases, problems were due to adhesions in 2 cases, small intestines passed through a mesenteric defect at the level of the anastomosis in 1 horse, and 1 horse developed EFE recurrence 1 day after the initial surgery for EFE. Most of these problems are best treated surgically, or could have been avoided by a meticulous surgical technique. Post-operative reflux was significantly associated with non-survival to hospital discharge (Chapter 7). One could suppose that comparable problems might have occurred in the group of undischarged horses suffering from POR that had no repeat laparotomy performed. A recent study analysed results of 22 repeat laparotomies due to POR or post-operative colic after surgical treatment of jejunal strangulation (Bauck et al., 2017). This publication adds interesting information to this discussion, giving additional support for the high prevalence of mechanical (surgical) problems in refluxing horses and further suggests the beneficial effect of repeat laparotomy in cases of POR after small intestinal surgery (Bauck et al., 2017). Nine out of 11 horses that underwent jejunojejunostomy during the initial colic surgery required resection of the initial anastomosis due to anastomotic complications. In 8 horses without resection during the initial colic surgery, second surgery included resection in 4 horses and decompression in the other 4 horses. Three of the 22 horses underwent euthanasia during the second surgery. Finally, all of the 19 recovered horses were discharged after repeat laparotomy (Bauck et al., 2017) in contrast to the results presented in Chapter 7 where only 2/10 (20%) of the horses that underwent re-laparotomy survived to discharge. As suggested by Salem and co-authors in a recent review article it is more prudent to use the more generic term “POR” for horses refluxing after colic surgery and to assign the diagnosis of POI as an additional variable/outcome measure where other causes of POR can be excluded after re-laparotomy or necropsy (Selam et al., 2016). Delicate surgical complications (e.g. too small anastomotic lumen, intestinal rotation at or close to the anastomosis, mesenteric shortening or rotation, secondary intestinal displacement) can be missed by pathologists at necropsy, leaving re-laparotomy as the only reliable tool for real functional POI diagnosis in equine colic surgery (Freeman, 2008). Recently Prof. Freeman stated the following hypothesis:

“The awareness of the importance of physical factors in the anastomosis and the sensitivity of the horse small intestine to them should redirect our efforts to preventing these problems at the surgery table rather than relying solely on post-operative medication. As with any post-operative complication, the surgeon should be the first held accountable for post-operative reflux, and not the horse. If we continue with heavy emphasis on post-operative medical management instead of surgical prevention, we will deny horses an approach that might actually work.” (Freeman, 2017). Bearing this quote in mind surgeons can question themselves about their own results. High costs of colic surgery and the major impact on welfare make this area of equine surgery particularly suited for “clinical governance” and “clinical audit” as is performed since years in human medicine (Mair, 2009). “Clinical governance” is the term used to describe a systematic approach to maintaining and improving the quality of patient care within a health system and is composed of 6 different elements: education/training, clinical audit, clinical effectiveness, research/development, openness and risk management. The absence of readily available standards in many areas of veterinary clinical work makes it difficult to undertake effective clinical audit. An international database of equine colic surgery could be a first step in this direction allowing quality measurement and identification of surgical error on an individual base at hospital or clinician level and potentially this database could serve as a quality comparing tool for the public as is the case in human medicine (Mair, 2009).

Resection performed and more specifically end-to-end jejunoileostomy was significantly associated with POR in our cases (Chapter 7). Until yet, the approach toward POR was mainly focused on post-operative medical treatment in our hospital as the diagnosis of POI was to easily established when POR appeared. The modest support that was provided in favour of the prophylactic use of Lidocaine for POI prevention (Malone et al., 2006; Torfs et al., 2009) was recently countered (Salem et al., 2016). There is need for a well-designed, multicentre prospective randomized controlled trial to assess the effectiveness of lidocaine and other medical treatments in regard of their potential prophylactic and curative effect on POI/POR, before continuing these very expensive treatments in a standard way.

Focus should be directed towards meticulous surgical technique. Small intestinal colic surgery should be categorized in the group of “major and complex surgeries”. Results are influenced by multiple critical steps. Undoubtedly, every surgeon would benefit from the opportunity to identify and correct surgical problems during re-laparotomy in case of POR. This would allow identifying personal critical control points, and opportunities for further optimization.

Preventive epiploic foramen closure

Reflections were made about preventive strategies in light of the severity of the disease and the well-defined risk factors (Archer et al., 2008b). Some of the identified factors associated with EFE, such as withers height or individual's response to a stimulus causing fright are difficult or impossible to alter. Others, such as crib-biting/windsucking, can be prevented physically or surgically (Baia et al., 2014) and by doing so, might hypothetically reduce the risk of EFE development, provided that an exclusive and causal relationship exists. Apart from the hypothetical nature of this indirect relationship, major welfare issues have to be recognised with this physical means of stereotypic behaviour prevention. Easier measures are to avoid sudden increase in duration of stabling, not feeding horses in the same group at the same time and providing mineral or salt lick, again, if the relationship between this factors and the occurrence of EFE is assumed to be causal (Archer et al., 2008b).

Closure of the Winslow foramen with sutures to prevent recurrence of foramen of Winslow herniation at the end of the laparotomy procedure (Osvaldt et al., 2008) or even laparoscopically (Garg et al., 2016) has been sporadically performed in humans. In these cases closure was performed despite the absence of reported recurrence of Winslow foramen herniation in humans. The latter laparoscopic procedure was done by "*suturing the peritoneum adjacent to the "portal triad" down to the retroperitoneum just lateral to the inferior vena cava with silk sutures*" (Garg et al., 2016). The equine epiploic foramen is not accessible for suture closure during ventral midline exploratory laparotomy, due to the large volume of the equine abdomen and the dorsal localization of the epiploic foramen. Visualization of the epiploic foramen is indeed impossible during ventral midline laparotomy in dorsal recumbency. Laparoscopic access to the equine epiploic foramen via the right flank on the standing sedated horse has been described in Chapter 3 (van Bergen et al., 2015) and, based on this experience and knowledge of surrounding anatomical structures, it was judged that laparoscopic suture closure would be impractical due to difficult accessibility and might lead to morbidity in case of accidental damaging of important structures as for example the portal vein. Nevertheless, interest in the development of a safe surgical technique that could prevent EFE persisted, as surgical techniques for prevention of other types of colic had been developed and performed successfully on clinical patients (Fischer et al., 1995; Mariën, 2001; Marien et al., 2001; Epstein and Parente, 2006; Rossignol et al., 2007, 2014; Wilderjans et al., 2012).

During the course of our study, colleagues from Auburn University (Alabama, USA) described a technique to close the epiploic foramen during a right flank standing laparoscopy by means of 4 to 10 helical titanium coils placed between the gastropancreatic fold and the caudate lobe of the liver in 6 experimental horses (Munsterman et al., 2014). However, it is unlikely that the used fold was really the gastropancreatic fold, as this fold contains the left gastric vessels, and the epiploic foramen is situated at the right side of the stomach (Constantinescu and Schaller, 2012). According to the provided pictures in their publication (Munsterman et al., 2014), it was the hepatopancreatic fold that was tacked to the caudate lobe of the liver. The described technique resulted in epiploic foramen closure with a thin fragile tissue fold in 5/6 of these experimental horses and in partial closure in the sixth horse (Munsterman et al., 2014). Although not reported by those authors, vascular damage by coil penetration is a real possibility as visualization of the hepatic artery cannot clearly be achieved in every horse and is largely dependent on the amount of fat surrounding this vessel. Vascular coil penetration would have deleterious effects for the patient. This concern, together with the inconsistent closure results, stimulated us in the continued development of an alternative technique.

After gathering the 3D insights and dimensions of the epiploic foramen (Chapter 3) we developed a 3D mesh-construct that could be introduced into the omental vestibule through the epiploic foramen and that would stay in place without additional methods of fixation thanks to its 3D configuration.

For the development of our mesh-closure technique we were inspired and helped by the general human surgeon Dr Ugahary, who has a special interest in the field of prosthetic abdominal hernia repair. He developed the open minimally invasive grid-iron technique (non-laparoscopic) for preperitoneal (retroperitoneal) groin hernia mesh repair in man, that bears his name. Using the Ugahary-technique, a 10 x 15 cm polypropylene mesh is rolled on a long-legged forceps, is introduced in the dissected preperitoneal space through a small incision, after which the mesh is unfurled using narrow long retractors and positioned to nicely cover the myopectineal orifice (Ugahary and Simmermacher, 1998; Simmermacher et al., 2000; Ugahary, 2004; Ugahary et al., 2010). The used mesh had to be soft, pliable and elastic with some plastic memory since the mesh had to be smoothly rolled up and unfurled to conform to the abdominal wall (Ugahary, 2004). Rectangular monofilament polypropylene (Prolene)[a] meshes were used. The intra-abdominal pressure and raw maze of this type of meshes which gives them a rough structure, kept the meshes in place without need for further fixation (Ugahary, 2004). The attractive concept of fixation-free mesh obliteration was further explored in light of our project in Chapter 4. By means of two 3DMax[b] preformed knitted polypropylene meshes we were able to construct a 3D diabolo-shaped mesh construct that fitted in the equine epiploic foramen with the smallest part of the diabolo at the level of the portal vein (van Bergen et al., 2016a). The 3DMax[b] mesh was specially developed for laparoscopic preperitoneal groin hernia repair in man. Additional advantages of the 3DMax[b] mesh for use in the diabolo-shaped mesh construct, compared to the traditional polypropylene mesh (Prolene)[a], are its curved shape together with its sealed edge giving the mesh additional 3D memory which help the mesh-construct recover its original shape after application through a custom-made 2 cm diameter applicator tube. The diabolo-shape of the mesh construct, together with the raw maze of the polypropylene structure, prevented migration of the mesh construct either to the left or the right. Feasibility, safety and effectiveness of the laparoscopic Foramen Epiploicum Mesh Closure (FEMC) technique were demonstrated both on experimental horses in Chapter 4 (van Bergen et al., 2016a) and clinical patients in Chapter 5 (van Bergen et al., 2016b).

Different groups of synthetic mesh material are typically used in hernia repair: polypropylene, polytetrafluoroethylene and polyester (Bilsel and Abci, 2012). Polypropylene is flexible, strong, easily cut, readily integrated by surrounding tissues and resists infection. The monofilament nature provides large pores facilitating fibrovascular ingrowth, infection resistance and improved compliance (Bilsel and Abci, 2012). Lightweight polypropylene meshes that have thinner filaments and larger pores are more flexible and allow increased soft tissue ingrowth (Brown and Finch, 2010). Polytetrafluoroethylene does not incorporate into tissues, becomes encapsulated and is microporous, which allows bacterial passage but prevents macrophage passage and therefore cannot clear infection (Bilsel and Abci, 2012). However, polytetrafluoroethylene is inert and results in little inflammation, which allows it to be placed directly on viscera (Bilsel and Abci, 2012). Polyester can be fashioned into very strong fibres suitable to be woven into prosthetic meshes (Bilsel and Abci, 2012). A variety of composite meshes have been proposed, combining materials promoting good tissue incorporation with materials avoiding intestinal serosal adhesion to the mesh (Brown and Finch, 2010; Bilsel and Abci, 2012; Ramakrishna and Lakshman, 2013). These composite meshes were developed for use in laparoscopic intraperitoneal hernia repair techniques in humans where no peritoneal mesh coverage is performed. They provide good tissue incorporation while avoiding intestinal adhesions to the mesh (Ramakrishna and Lakshman, 2013). However, these composite meshes are 15 to 20 times more expensive compared to classic polypropylene meshes (Ramakrishna and Lakshman, 2013). Indian human medicine researchers questioned whether polypropylene meshes could also be acceptable for intraperitoneal placement without peritoneal coverage, as a large number of their patients could benefit from laparoscopic hernia repair, but couldn’t afford the expensive composite meshes (Ramakrishna and Lakshman, 2013). After meta-analysis of the available literature they concluded that there is no published evidence available to disapprove intraperitoneal polypropylene meshes due to increased likelihood for adhesion formation in ventral hernia repair in human clinical patients (Ramakrishna and Lakshman, 2013).

In the FEMC technique in horses, polypropylene meshes were applied in a rather atypical intraperitoneal localization compared to laparoscopic ventral hernia repair in man where intestines are in full contact with the applied mesh. The vast majority of the diabolo-shaped mesh construct is surrounded by the tissues forming the omental vestibule and epiploic foramen. To the left there is the greater omentum, forming the omental bursa, which impedes direct contact between the mesh and intestines. The only place where intestines could theoretically become adhered to the mesh construct is at the right side, where about 1 cm of the mesh construct protrudes through the epiploic foramen into the abdominal cavity. However, in the normal standing horse, no small intestine than the duodenum are normally found at the level of the right dorso-cranial quadrant of the abdomen, where the epiploic foramen is localized. The duodenum hangs ventral to the epiploic foramen, but no adhesions between the protruding mesh and duodenum were noticed in the 6 experimental horses in which the mesh was inserted laparoscopically in Chapter 4 (van Bergen et al., 2016a), nor in the 6 experimental horses in which the mesh was inserted manually via ventral midline laparotomy under general anaesthesia in Chapter 6 (van Bergen et al., 2017). It has to be recognised though that these were all healthy experimental horses without concurrent abdominal pathology. The potential risk of adhesion formation between the polypropylene mesh construct and intestines, which was not encountered during our studies nor confirmed to be a relevant problem after meta-analysis of the available human literature (Ramakrishna and Lakshman, 2013), does not outweigh the advantages of this construct: it is strong, flexible, readily integrated, infection resistant and relatively inexpensive.

The concept of 3D meshing without additional methods of fixation has gained popularity in human medicine in recent years. Fixation-free 3D meshing induces ingrowth of viable and structured tissue instead of regressive fibrotic scarring causing pain, which is often encountered when fixed static implants are used (Amato et al., 2015). Clinical outcome using the 3DMax[b] mesh without additional fixation was considered excellent in human pre-peritoneal inguinal hernia repair (Bell and Price, 2003).

Since its development, the laparoscopic FEMC technique in horses has been used as a routine procedure after EFE colic surgery to prevent recurrence of this disease in several referral equine hospitals throughout Europe. In first instance (Chapter 5) we had discouraged manual application of the diabolo-shaped mesh construct at the time of EFE colic surgery due to concerns of the lack of visual control during mesh application, potential mesh migration during recovery from general anaesthesia and the risk of septic complications in horses undergoing clean-contaminated colic surgery including enterotomy or enterectomy (van Bergen et al., 2016b). However, direct FEMC during initial EFE colic surgery would avoid the need for a second laparoscopic procedure to prevent EFE recurrences. In Chapter 6 we have demonstrated that the lack of visual control does not impede correct mesh positioning and that mesh migration does not seem to occur during recovery (van Bergen et al., 2017).

Recent outcomes in 3 clinical patients in our clinic provided us encouraging data on the potential low risk of septic complications when applying the mesh construct during clean-contaminated procedures.

A first case to be discussed in regard of the risk for septic complications was a 9 year old Warmblood gelding that underwent EFE colic surgery without small intestinal resection. The horse had an uneventful recovery. The horse underwent laparoscopic FEMC 2 months after the initial colic surgery. During trocar placement the caecum was accidentally punctured which resulted in slight abdominal contamination. After laparoscopic suture placement at the puncture site, we decided to continue the procedure and introduce the diabolo-shaped mesh construct in the epiploic foramen. Post-operatively, the horse was treated IV with 6.6 mg/kg bwt gentamicin (Genta-Equine)[c] IV q24h and 22000 IU/kg bwt sodium penicillin (Penicilline)[d] IV q8h daily for 10 days post laparoscopy. On day 10 post-laparoscopy abdominocentesis cultured positive for *Paenibacillus amylolyticus*, which is a facultative anaerobic, endospore-forming bacterium. Driven by concerns about septic complications at the level of the mesh in the epiploic foramen, we continued the IV antibiotic therapy for an additional 4 days. In absence of any clinical signs consistent with septic peritonitis, we decided to send the horse home 3 weeks after surgery. Seven months after the laparoscopic FEMC procedure the horse is doing well. This patient provided us with some evidence that mesh implantation at the level of the epiploic foramen during clean-contaminated surgery does not appear to result in apparent septic complications related to the implant. Recent data from human patients confirmed that the presence of intestinal ischemia or necrosis and thus the necessity to perform intestinal resection is not necessarily a contraindication for prosthetic polypropylene mesh repair during emergency management of acutely incarcerated and/or strangulated groin hernias (Bessa et al., 2015). Great care to avoid spillage of intestinal contents into the surgical field and appropriate use of prophylactic antimicrobials were considered important in this situation (Bessa et al., 2015). With this in mind, we have recently applied the diabolo-shaped mesh in the epiploic foramen during clean-contaminated EFE colic surgeries in 2 additional horses. The first of those 2 horses was a 12 year old Warmblood gelding that underwent a resection of 5 m necrotic small intestine (Freeman grade IV) (Freeman et al., 2014) followed by an end-to-end jejunoileostomy. Foramen Epiploicum Mesh Closure as described in Chapter 6 (van Bergen et al., 2017) was accomplished at the end of the procedure after benzylpenicillinum procainum (Peni-kel)[d] impregnation of the mesh construct. Before abdominal closure 22000 IU/kg bwt benzylpenicillinum procainum (Penikel)[d] was introduced into the abdomen. The second of those 2 horses was a 9 year old Warmblood gelding in which 5 m of ileum-jejunum was repositioned from the epiploic foramen. It was decided that the small intestine was healthy enough to be left in place without intestinal resection (Freeman grade I-II) (Freeman et al., 2014), but the ascending colon was impacted and needed to be lavaged through an enterotomy at the level of the pelvic flexure. At completion of these procedures and after gentamicin (Genta-Equine)[c] impregnation of the diabolo-shaped mesh construct, FEMC was performed as described in Chapter 6 (van Bergen et al., 2017). No additional antibiotics were administered into the abdomen. Both horses had 6.6 mg/kg bwt gentamicin IV (Genta-Equine)[c], 22000 IU/kg bwt sodium penicillin IV (Penicilline)[d] and 1.1 mg/kg bwt flunixin meglumine IV (Finadyne)[e] administered pre-operatively. Post-operatively, both horses were treated with 6.6 mg/kg bwt gentamicin (Genta-Equine)[c] IV q24h, 22000 IU/kg bwt sodium penicillin (Penicilline)[d] IV q8h and 1.1 mg/kg bwt flunixin meglumine (Finadyne)[e] IV q12h for 5 days. The horses recovered uneventfully to discharge and are doing well at home with a follow up of 5 and 2 months respectively.

Although very limited in number, these 3 clinical cases are encouraging for the future. Moreover, not all EFE colic surgeries require an enterotomy or enterectomy and could, in absence of these procedures, be considered as “clean” procedures without any restriction for mesh application. A multicentre trial should be performed to document patient outcome for mesh application during initial EFE colic surgery. If FEMC during EFE colic surgery is considered inappropriate, the epiploic foramen can be closed during a subsequent laparoscopic procedure. In addition, preventive laparoscopic FEMC could also be considered in horses displaying risk-factors for EFE such as crib-biting/windsucking.

Conclusion

Overall, the clinical outcome in EFE colic surgery is disappointing and little improvement is made over the past decades. Improved knowledge of the 3D configuration of the equine epiploic foramen and its surrounding structures might assist in performing more careful surgical technique in this area and to a better understanding of the occurrence of EFE in horses. This study demonstrates that spontaneous closure of the epiploic foramen occurs in some horses following EFE and may be the reason for the less frequent recurrence compared to some other forms of colic. The availability of a safe thoroughly validated laparoscopic technique for epiploic foramen obliteration should stimulate equine surgeons to consider advising clients about preventive laparoscopic epiploic foramen closure for windsucking/crib-biting horses which are known to be at increased risk of EFE development. Laparoscopic FEMC or FEMC during the initial EFE colic surgery could also contribute to a better outcome for surgery for EFE, by preventing recurrence in horses without spontaneous obliteration of the epiploic foramen after EFE colic surgery.

Manufactures' details

[a]Johnson & Johnson Medical NV, Diegem, Belgium
[b]Bard Davol Inc., Warwick RI, USA
[c]Franklin Pharmaceuticals Limited, Meath Co Meath, Ireland
[d]Kela Pharma nv, Sint-Niklaas, Belgium
[e]Schering Plough Animal Health, Brussels, Belgium

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Summary

Colic is an important disease in horses and is the primary reason for emergency consultation in referral hospitals. In contrast to human medicine where foramen of Winslow herniation is very uncommon, “epiploic foramen entrapment or EFE”, as the condition is named in the equine veterinary literature, is an important cause of surgical colic in horses. This surgical emergency condition, in which intestines are entrapped at the level of the epiploic foramen, is associated with high morbidity and mortality. Little is known about the reason for the high occurrence of EFE in horses, compared to other mammalian species including man, despite the identification of several risk factors in horses developing EFE. The most important of these risk factors is the crib-biting/windsucking stereotypic behaviour. Equine practitioners and equine surgeons are often unaware of the precise topographic anatomy of the equine epiploic foramen and its three-dimensional (3D) configuration, which is an impediment for the progression that is needed for better, faster and less traumatic abdominal interventions during equine EFE colic surgery and for the development of surgical techniques that could obliterate the epiploic foramen to prevent EFE (recurrences).

In **Chapter 1** an overview of the published literature concerning EFE in horses is provided. Much larger case series are reported compared to human medicine, where the condition is rather exceptional. High morbidity and mortality are confirmed in equine literature and improvement in the disappointing outcome is scarce throughout recent papers. Incarcerated viscera consist almost always of small intestine with entrapment from the left to the right through the epiploic foramen in horses, in contrast to humans where it is the caecum or the large intestine in the majority of cases that herniates from the right to the left through the epiploic foramen (Winslow foramen). The ileum is involved in at least 2/3 of EFE cases in horses. Recurrence of the disease has been reported in 2 to 14% of cases that survived an EFE colic surgery.

After defining the aims of the study in **Chapter 2**, the topographic, 3D and laparoscopic anatomy of the equine epiploic foramen is explored in **Chapter 3**. The defining structures of the epiploic foramen and omental vestibule are the hepatoduodenal ligament, the hepatogastric ligament and the gastropancreatic and hepatopancreatic folds. The combination of the omental vestibule and the epiploic foramen forms a funnel, with a large opening to the left that is delineated by the minor curvature of the stomach ventrally and the fused gastropancreatic and hepatopancreatic folds dorsally, and a smaller opening to the right, which is the epiploic foramen itself. The epiploic

foramen is bordered craniodorsally by the base of the caudate process of the liver and caudoventrally by the hepatoduodenal ligament that has a secondary fold at the level of the epiploic foramen before it merges with the mesoduodenum. The hepatic artery for part of its course is incorporated in the hepatoduodenal ligament. The caudal vena cava runs dorsal to the omental vestibule, to the left of the epiploic foramen, and is to some extent embedded in liver tissue. Ventral to the omental vestibule, the portal vein penetrates the pancreas via the pancreatic ring *(anulus pancreatis)*, and before entering the liver, lies superficial to the hepatoduodenal ligament. It courses in between the epiploic foramen that is situated to the right of the portal vein and the hepatic artery that is situated to the left of the portal vein. All these structures are clearly visible during right flank standing laparoscopy. The mean circumference of the epiploic foramen is 11.6 ± 2.6 cm and its circumference is positively correlated with body weight but is unrelated to age or sex.

In **Chapter 4** the novel laparoscopic Foramen Epiploicum Mesh Closure (FEMC) technique is described. The epiploic foramen was closed by means of a 3D fixation-free application of a diabolo-shaped mesh construct through the epiploic foramen into the omental vestibule. The smallest part of the diabolo-shaped mesh construct was placed at the level of the portal vein. It was demonstrated that the laparoscopic FEMC technique is a fast, simple, reliable and safe procedure to obliterate the epiploic foramen in horses.

While performing the laparoscopic FEMC technique on the first clinical patients, it was documented that in 3 out of 7 cases (43%) the epiploic foramen obliterated spontaneously after EFE colic surgery due to serosal inflammation at the level of the epiploic foramen and the omental vestibule. These findings are reported in **Chapter 5**. Spontaneous obliteration of the epiploic foramen after EFE colic surgery in some cases could explain that, despite persistent strong risk factors for the condition, recurrence occurs only in 2 to 14% of the cases. Spontaneous obliteration is supported by more recent multicentre data revealing spontaneous closure in 9/28 cases (32%) (unpublished data).

Laparoscopic FEMC necessitates a second surgical intervention subsequent to the initial colic surgery. A closure or obliteration technique that can be performed during the initial laparotomy would avoid the need for a second surgery. An adaptation of the laparoscopic FEMC technique, during which the mesh construct is inserted during the laparotomy, seems a logical way forward. Nevertheless, this adaptation raises some concerns including the lack of visibility and the unknown effect of recovery from general anaesthesia on the position of the mesh with a possible risk of displacement from the epiploic foramen. In **Chapter 6** it is demonstrated that the FEMC technique via laparotomy provides a fast, simple and reliable procedure to obliterate the epiploic foramen and may be useful during surgery for EFE to prevent recurrence of the disease, avoiding a subsequent laparoscopic procedure. Lack of visual control and recovery from general anaesthesia had no influence on the final outcome. However, mesh application during clean-contaminated surgery, as is sometimes the case during colic surgery, was not investigated.

The available literature has been compared with the cases reported in a retrospective study of 145 EFE colic surgeries during the past 8 years in **Chapter 7**. Warmblood horses represented 85% of all cases. Surgery for EFE was associated with high morbidity and mortality. Survival to discharge of all horses undergoing surgery was 48%. Survival to discharge of all horses recovering from surgery was 65%, so 35% of recovered horses died prior to discharge. Resection performed predisposed horses for post-operative reflux (POR) and horses undergoing jejunoileostomy were more prone to POR development compared to horses undergoing jejunojejunostomy. Horses with an increased pre-operative heart rate and that developed POR were less likely to be discharged from the hospital. Prolonged hospitalisation predisposed horses for colic episodes after hospital discharge and horses that underwent a resection had shorter life expectations after hospital discharge compared to horses without resection. Post-operative reflux in a high percentage of cases could have contributed to the disappointing outcome after surgery. Recurrence of the condition occurred in 3% of the horses that survived the surgery for EFE.

The importance of the specific anatomic configuration of the omental vestibule and epiploic foramen on the occurrence of EFE in horses is discussed in **Chapter 8**. Several pathways for EFE outcome improvement are explored in this chapter. The importance of meticulous surgical technique during small intestinal colic surgery in general, and for EFE colic surgery in particular are discussed. Preventive closure of the epiploic foramen can have an additional positive effect to the efforts that have to be conducted to improve surgical outcomes.

Clinical guidelines for the laparoscopic FEMC techniques are provided in an **Addendum** at the end of the thesis.

Samenvatting

Koliek is de belangrijkste oorzaak voor spoedconsultaties in doorverwijsklinieken bij paarden. In tegenstelling tot de situatie bij de mens, waar interne hernia's door het foramen van Winslow zeer zeldzaam zijn, zijn incarceraties door het *foramen epiploicum* bij paarden een belangrijke oorzaak voor koliek en deze dienen chirurgisch behandeld te worden. Deze chirurgische spoedindicatie gaat gepaard met een hoge morbiditeit en mortaliteit. Ondanks de identificatie van specifieke risicofactoren voor het ontstaan van deze aandoening bij het paard, is er weinig bekend over het ontstaan van en de hoge prevalentie van deze aandoening bij paarden in vergelijking met andere zoogdieren inclusief de mens. De belangrijkste risicofactor geassocieerd met het ontwikkelen van een *foramen epiploicum* incarceratie bij paarden is de aanwezigheid van het stereotiep gedrag van kribbebijten of luchtzuigen. Paardendierenartsen en chirurgen zijn vaak slecht op de hoogte van de precieze topografische anatomie en de drie-dimensionele (3D) configuratie van het *foramen epiploicum* bij het paard. Dit vormt een hindernis voor de noodzakelijke progressie in het ontwikkelen van betere, snellere en minder traumatische chirurgische technieken voor *foramen epiploicum* incarceraties en voor het ontwikkelen van technieken om het *foramen epiploicum* preventief te sluiten om incarceraties (of recidieven) te voorkomen.

In **Hoofdstuk 1** wordt er een overzicht van de gepubliceerde literatuur in verband met *foramen epiploicum* incarceraties bij paarden gegeven. Er werden bij het paard veel grotere klinische reeksen gerapporteerd in vergelijking met de sporadisch gerapporteerde gevallen bij de mens. De hoge morbiditeit en mortaliteit worden bevestigd in de literatuur en uit recente publicaties blijkt dat er slechts weinig vooruitgang geboekt werd. In tegenstelling tot de mens waar voornamelijk het caecum en dikke darm van rechts naar links door het *foramen epiploicum* (foramen van Winslow) herniëren, is het bij het paard bijna altijd de dunne darm die van links naar rechts door het *foramen epiploicum* vast komt te zitten. Het *ileum* is betrokken bij minstens 2/3 van de gevallen. Recidief van de aandoening werd gerapporteerd bij 2 tot 14% van de gevallen die een operatie voor *foramen epiploicum* incarceratie overleefden.

Na het oplijsten van de doelstellingen van deze studie in **Hoofdstuk 2,** worden de topografische, de drie-dimensionele en de laparoscopische anatomie van het *foramen epiploicum* bij het paard in **Hoofdstuk 3** beschreven. Het *ligamentum* *hepatoduodenale* en *hepatogastricum* en de *plica gastropancreatica* en *hepatopancreatica* zijn bepalend voor de vorm van het *vestibulum omentale* en het *foramen epiploicum.* De combinatie van het *vestibulum omentale* en het *foramen epiploicum* vormt een trechter met links een grote opening, omsloten door de *curvatura minor* van de maag ventraal en de samenvloeiende *plica gastropancreatica* en *plica hepatopancreatica* dorsaal, en rechts een kleinere opening, die het *foramen epiploicum* zelf is. Het *foramen epiploicum* wordt craniodorsaal begrensd door de basis van de *processus caudatus* van de lever en caudoventraal door het *ligamentum hepatoduodenale* dat een secundaire plooi heeft ter hoogte van het *foramen epiploicum* en vervolgens samenvloeit met het *mesoduodenum*. Voor een gedeelte van zijn verloop loopt de *arteria hepatica* in het *ligamentum hepatoduodenale*. De *vena cava caudalis* loopt dorsaal van het *vestibulum omentale*, links van het *foramen epiploicum*, en is in mindere of meerdere mate in leverweefsel ingebed. De *vena portae* perforeert de pancreas ventraal van het *vestibulum omentale* en komt oppervlakkig te liggen ter hoogte van het *ligamentum hepatoduodenale* voordat ze de lever binnen dringt. De *vena portae* loopt tussen het *foramen epiploicum*, dat zich rechts van de *vena portae* bevindt, en de *arteria hepatica* die links van de *vena portae* gesitueerd is. Al deze structuren zijn laparoscopisch duidelijk identificeerbaar. Het *foramen epiploicum* heeft een gemiddelde omtrek van 11.6 ± 2.6 cm en deze omtrek is positief gecorreleerd met lichaamsgewicht, maar niet met leeftijd of geslacht.

In **Hoofdstuk 4** wordt de nieuwe Foramen Epiploicum Mesh Closure (FEMC) techniek beschreven. Het *foramen epiploicum* werd gesloten met behulp van een 3D diabolo-vormige netconstructie die door het *foramen epiploicum* in het *vestibulum omentale* werd aangebracht zonder bijkomende fixatie. Het smalste gedeelte van de diabolo-vormige constructie werd ter hoogte van de *vena portae* gepositioneerd. Er werd aangetoond dat de laparoscopische FEMC techniek een snelle, eenvoudige, betrouwbare en veilige procedure is om het *foramen epiploicum* bij het paard te sluiten.

Terwijl de laparoscopische FEMC techniek op de eerste patiënten werd toegepast, kon gedocumenteerd worden dat in 3 van de 7 (43%) gevallen het *foramen epiploicum* spontaan sluit na een koliek operatie voor *foramen epiploicum* incarceratie, en dit door toedoen van serosale ontsteking ter hoogte van het *foramen epiploicum* en het *vestibulum omentale*. Deze bevindingen worden gerapporteerd in **Hoofdstuk 5**. Spontaan sluiten van het *foramen epiploicum* na *foramen epiploicum* incarceratie zou een mogelijke uitleg kunnen zijn voor het relatief lage percentage recidieven (slechts 2 tot 14%), ondanks de blijvende aanwezigheid van duidelijke risicofactoren. Spontaan sluiten van het *foramen epiploicum* wordt verder bevestigd door recentere data uit verschillende centra waarbij dit voorkwam in 9 van de 28 gevallen (ongepubliceerde data).

Voor de laparoscopische FEMC is er een tweede chirurgische interventie noodzakelijk na de initiële koliek chirurgie. Een sluitingstechniek die kan uitgevoerd worden tijdens de initiële koliekoperatie zou een tweede operatie overbodig maken. Een aanpassing van de laparoscopische FEMC techniek waarbij de netconstructie aangebracht wordt tijdens de laparotomie leek een logische stap vooruit. Desalniettemin waren er een aantal bezorgdheden in verband met deze aanpassing, waaronder het gebrek aan visuele controle bij het plaatsen van het net en de mogelijke verplaatsing ervan uit het *foramen epiploicum* tijdens de recovery uit algemene anesthesie. In **Hoofdstuk 6** tonen we aan dat de FEMC techniek via de laparotomie-incisie een snelle, eenvoudige en betrouwbare procedure is om het *foramen epiploicum* te sluiten en dat deze techniek kan toegepast worden tijdens *foramen epiploicum* incarceratie-operaties om recidieven te voorkomen en zodoende een bijkomende laparoscopische procedure te vermijden. Het gebrek aan visuele controle en de recovery uit algemene anesthesie waren van geen tel voor het finale resultaat. Het aanbrengen van het netje tijdens een "schoon-gecontamineerde procedure", zoals soms bij koliekoperaties het geval is, werd echter niet onderzocht.

In **Hoofdstuk 7** werden de resultaten van een retrospectieve studie van 145 *foramen epiploicum* koliekoperaties over een periode van 8 jaar vergeleken met de beschikbare literatuur. De studiepopulatie bestond voor 85% uit Warmbloedpaarden. Koliekchirurgie voor *foramen epiploicum* incarceraties was geassocieerd met een hoge morbiditeit en mortaliteit. Het overlevingspercentage tot op het moment van ontslag uit de kliniek van alle geopereerde paarden bedroeg 48%. Het overlevingspercentage tot op het moment van ontslag uit de kliniek van alle paarden die wakker werden na de operatie bedroeg 65%, dus 35% van de paarden die wakker werden na de operatie stierven voor ze uit de kliniek ontslagen werden. Paarden waarbij een darmresectie werd uitgevoerd hadden meer kans om postoperatieve reflux (POR) te ontwikkelen en deze predispositie was meer uitgesproken bij paarden die een jejunoileostomie ondergingen vergeleken met paarden die een jejunojejunostomie ondergingen.

Paarden met een verhoogde preoperatieve hartslag en paarden die POR ontwikkelden hadden minder kans om de kliniek levend te verlaten. Paarden die gedurende langere tijd gehospitaliseerd waren hadden meer kans om koliek te ontwikkelen nadat ze de kliniek verlaten hadden en paarden die een darmresectie ondergingen hadden een kortere levensverwachting vergeleken met paarden die geen darmresectie ondergingen. Het veelvuldig voorkomen van POR kan hebben bijgedragen tot de tegenvallende resultaten. Drie procent van de paarden die een *foramen epiploicum* koliekoperatie overleefden ontwikkelden een recidief.

Het belang van de specifieke configuratie van het *vestibulum omentale* en het *foramen epiploicum* voor het voorkomen van *foramen epiploicum* incarceraties bij paarden wordt besproken in de algemene discussie (**Hoofdstuk 8**). Verschillende mogelijkheden om de uitkomst bij *foramen epiploicum* incarceraties te verbeteren worden geëxploreerd in dit hoofdstuk. Het belang van een nauwkeurige chirurgische techniek bij dunne darm koliekchirurgie in het algemeen en bij *foramen epiploicum* incarceraties in het bijzonder wordt benadrukt. Het preventief sluiten van het *foramen epiploicum* kan een bijkomend positief effect toevoegen aan de inspanningen die noodzakelijk zijn om de resultaten te verbeteren.

Finaal werd aan het einde van de thesis een klinische handleiding toegevoegd met praktische richtlijnen voor het uitvoeren van de FEMC techniek **(Addendum)**.

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Curriculum Vitae

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Previous positions:

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Surgery Internship………..…………………………..……………………….**2011 - 2012**
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Master Veterinary Medicine - magna cum laude ………………………… **2002 - 2005**
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Antwerp University

SCIENTIFIC CAREER

Theses

PhD thesis

"Closure of the Epiploic Foramen in the horse: an anatomical and clinical study."
Promotor: Prof. Dr. A. Martens and Drs. P Wiemer.

Master thesis

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Scientific activities

Articles in international peer-reviewed scientific journals

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van Bergen T., Martens A., 2016. Meest courante fracturen bij het paard: een update (Most prevalent equine fractures: an update). Lecture for the Institute of Continuing Education (IPV)

van Bergen T., Pint E., Martens A., 2015. Wond behandeling en het plaatsen van spalken en gipsen (Wound treatment and the application of splints and casts). Lecture for the Institute of Continuing Education (IPV)

van Bergen T., van Loon G., Martens A., 2015. “First Aid” bij het paard (First Aid in horses). Lecture for the Institute of Continuing Education (IPV)

Scientific Awards

Honourable Mention 2015 ECVS Resident Award Best Large Animal Presentation. 24th Annual Scientific Meeting of the European College of Veterinary Surgeons (ECVS), 2-4 July, Berlin, Germany.

Winner 2013 ECVS Resident Award Best Large Animal Presentation. 22th Annual Scientific Meeting of the European College of Veterinary Surgeons (ECVS), 4-6 July, Rome, Italy.

ADDENDUM

Clinical guidelines for laparoscopic FEMC

Instuments needed

- 10 mm, 58 cm 30° angled laparoscope
- 10 mm diameter, 20 cm long trocar-cannula unit (the “protected-trocar” from the trocar-cannula unit can also be used to “pre-perforate” the abdomen before introduction of the applicator tube)
- 68 cm long, 2 cm diameter applicator tube with corresponding trocar
- 100 cm long flexible pushing device
- Valve for the applicator tube to prevent loss of abdominal pressure in between manipulations
- 2 x 3DMax Meshes (10.8x16.0 cm) Bard Davol Inc, Warwick RI, USA
- 2-0 polyglactin 910 (Vicryl) with needle
- Security line: 2.5 m long USP 2 polyglycolic acid wire (or other polyfilament)

FEMC technique

- Right flank standing laparoscopic procedure
- The procedure is easiest to perform with 3 persons scrubbed-in (1 surgeon and 2 assistants), but it is possible to do it with 2.
- Stocks: it is important to have enough space at the right caudal end of the stocks to allow the instruments to be directed cranially. The entire right caudal part of the stocks needs to be included in the draping.
- Prepare the diabolo-shaped mesh construct before starting the surgery as demonstrated in the figures below. Use toothless forceps to avoid damage to the mesh.
- When the prepared mesh construct is not implanted due to spontaneous closure it can be re-sterilised without problems by means of gas or plasma-sterilization.
- Introduction of the (58 cm long, 30° angled) laparoscope: to avoid interference from the camera with the *tuber coxae* it was important to create the portal relatively more ventral than most conventional laparoscopic techniques, at the level of the ventral half of the palpable crus of the internal oblique abdominal muscle

- After introduction of the laparoscope wait for full insufflation of the abdomen (12-15 mmHg).
- Direct the laparoscope between the caecum and the abdominal wall and advance the laparoscope cranially between the duodenum and the caudate lobe of the liver until the epiploic foramen is visualised.
- Redraw the laparoscope into its initial position
- The instrument portal for the applicator tube is made about 10 cm ventral to the laparoscopic portal. A 4 cm skin incision is created. The musculature is divided bluntly and the abdomen penetrated by means of a protected trocar or a mayo scissor which is subsequently removed. The applicator tube with its blunt trocar in place is introduced into the abdomen and directed cranially between the duodenum on the left and the caudate process of the liver on the right through the epiploic foramen into the omental vestibule under laparoscopic visualisation. The manipulation is easiest when the surgeon manipulates the tube and an assistant the laparoscope.
- Once in place remove the blunt trocar and introduce the mesh construct in its longitudinal axis.
- *Recently we abandoned the use of a valve. No problems were encountered and manipulations are simplified without the valve.*
- Push the mesh through the tube until it gently exits the end of the applicator tube (visualised laparoscopically). The correct position of the mesh is ascertained by pushing with the applicator tube while keeping tension (sometimes pulling) on the security line. The best way to do this is by withdrawing the applicator tube over the pushing device. The smallest part of the mesh construct has to be positioned at the level of the portal vein leaving 0.5 to 1 cm of the mesh protruding through the epiploic foramen into the abdomen.
- It is of outmost importance that the assistant keeps a nice overview of the region with the laparoscope while the surgeon performs these manipulations.
- When the mesh is correctly positioned the security line has to be withdrawn. It is important to keep the pushing device in place against the mesh construct to avoid pulling the mesh out of the epiploic foramen while withdrawing the security line. *We have recently switched to a polyfilament security line while*

we encountered some difficulties pulling out a monofilament security line. Avoid twisting the security line when pushing the mesh construct through the applicator tube to avoid difficulties during security line withdrawal.

- A third portal can be created dorsally between the 15th and 16th rib to secure and withdraw the diabolo-shaped implant with a laparoscopic Babcock forceps from the omental bursa in the very rare case the security line loosens too early, allowing the diabolo-shaped implant to slide to the left into the omental bursa (this complication was encountered in 1 case by the author).

Preparation of the diabolo-shaped expandable mesh construct (diameter: 10 cm, length: 10 cm) with 2 preformed knitted polypropylene meshes (3DMax Mesh).

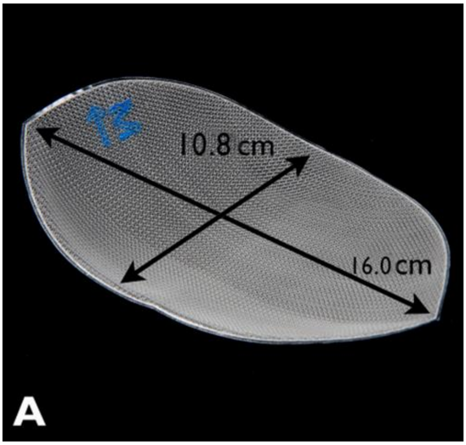

Figure 1A: Preformed knitted polypropylene mesh (3DMax Meshes (10.8x16.0 cm) Bard Davol Inc, Warwick RI, USA.

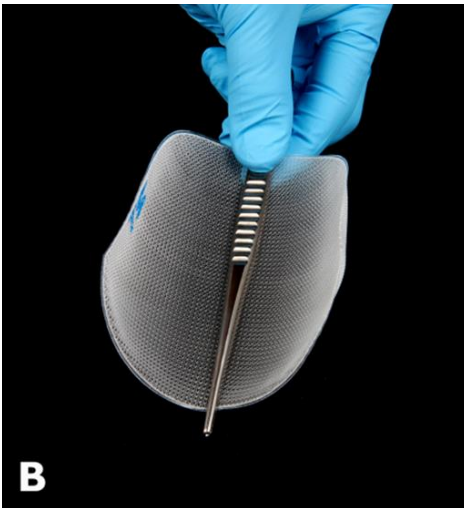

Figure 1B: The mesh is grasped with a DeBakey tissue forceps on its smallest diameter.

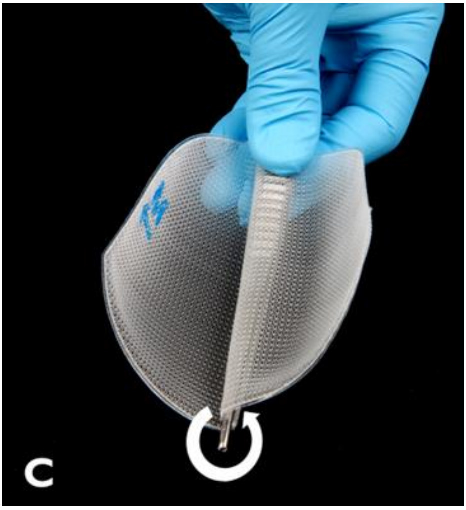

Figure 1C: The forceps is twisted 270° and subsequently withdrawn while holding the folded part in position.

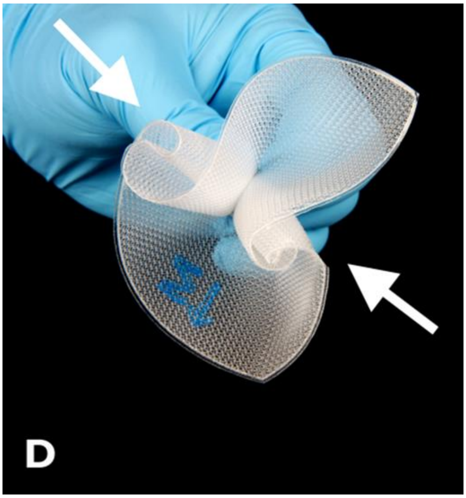

Figure 1D: The mesh is subsequently folded on its longest diameter.

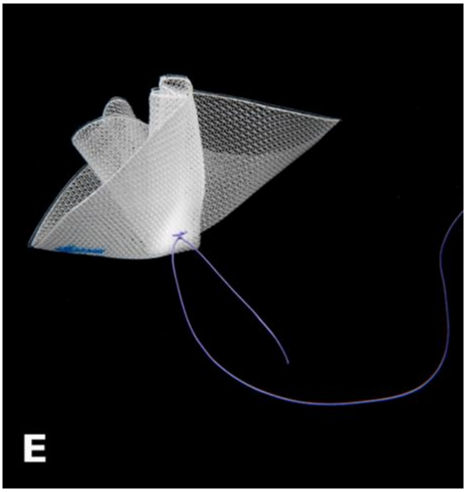

Figure 1E: The resultant pyramidal configuration is secured with a 2-0 polyglactin 910 (Vicryl) horizontal mattress suture on the tip of the pyramid.

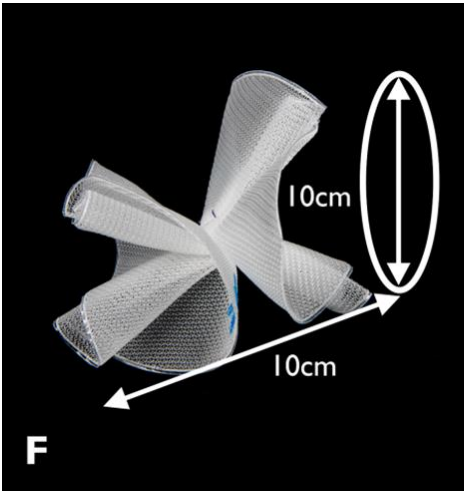

Figure 1F: A second mesh is prepared in the same manner and the tips of the 2 pyramids are secured together with an additional 2-0 polyglactin 910 (Vicryl) horizontal mattress suture.

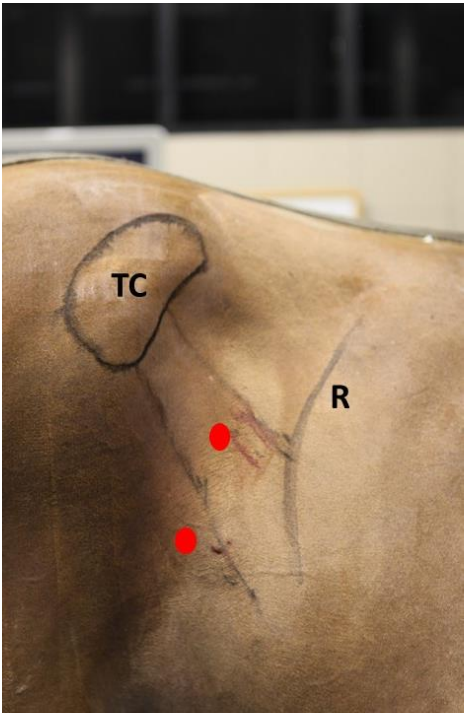

Figure 2: View of the right flank of a standing horse. The *tuber coxae (TC),* the last rib (R) and in between the crus of the internal oblique abdominal muscle are highlighted on the skin. The red dots indicate the location for the laparoscope portal (dorsal) and for the applicator tube introduction (ventral). (Caudal is to the left and cranial to the right).

Right flank laparoscopic visualisation of the epiploic foramen, omental vestibule and omental bursa (OB).

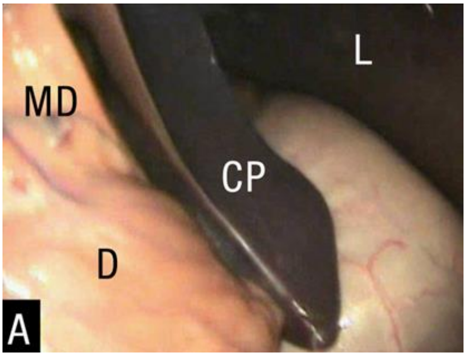

Figure 3A: Laparoscope directed cranially to visualise the caudate process (CP) of the liver (L), the duodenum (D) and medoduodenum (MD). To visualise the epiploic foramen the laparoscope has to be advanced between the CP and the MD/D.

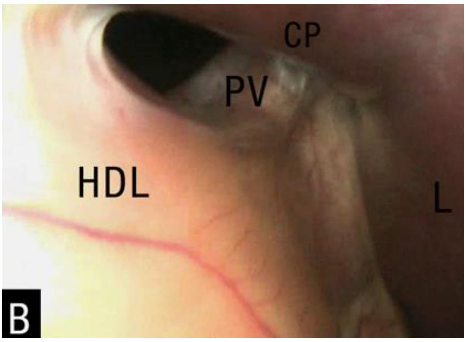

Figure 3B: Laparoscope passed between the caudate process (CP) of the liver (L) and mesoduodenum allows visualisation of the epiploic foramen at the base of the CP. (HDL: hepatoduodenal ligament, PV: portal vein)

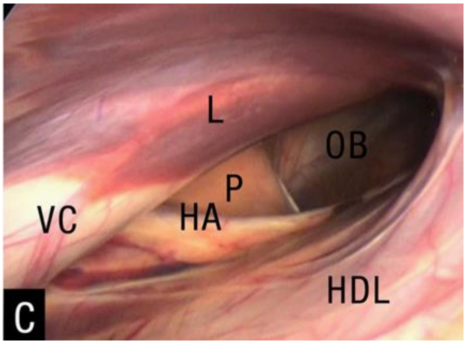

Figure 3C (image slightly tilted anticlockwise): Laparoscope passed through the epiploic foramen from right-to-left allows visualisation of the omental vestibule leading to the caudal part of the omental bursa (OB). (VC: caudal vena cava, HA: hepatic artery, P: pancreas (covered by the hepatopancreatic fold))

Instrument manipulations.

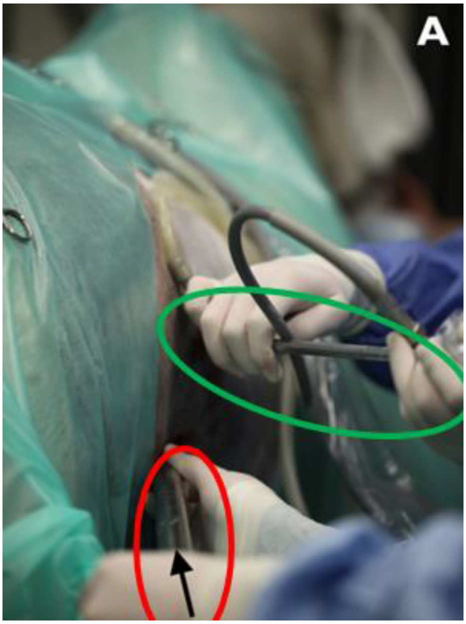

Figure 4A: Caudal view on the right abdomen of a standing sedated horse. The surgeon manipulates the applicator tube (black arrow) through the epiploic foramen from right-to-left in the omental vestibule guided by an assistant manipulating the laparoscope. During the rest of the procedure, the assistant holding the scope keeps the end of the applicator tube continuously into the visual field and checks that it remains in place in the epiploic foramen.

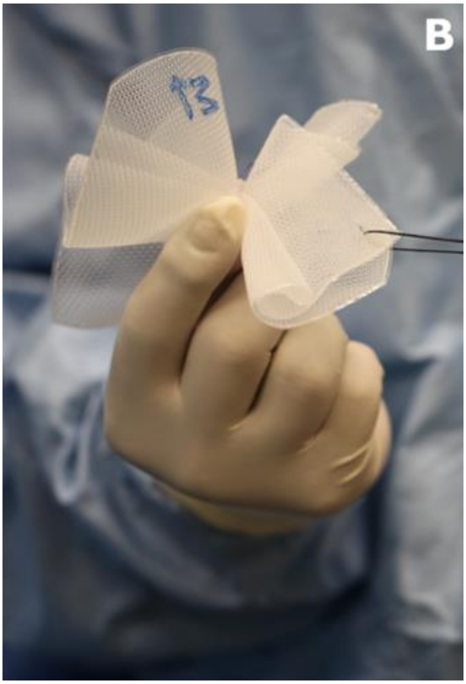

Figure 4B: The prepared diabolo-shaped mesh implant with the security line in place.

Figure 4C: The blunt trocar is withdrawn and the prepared diabolo-shaped mesh implant is folded and pushed through the applicator tube with the pushing device.

Figure 4D: A custom-made valve is placed at the outer end of the applicator tube to prevent loss of abdominal pressure in between manipulations. Recently we have performed the procedure without this valve. No problems were encountered and without the valve manipulations were simplified.

Laparoscopic images of the mesh introduction.

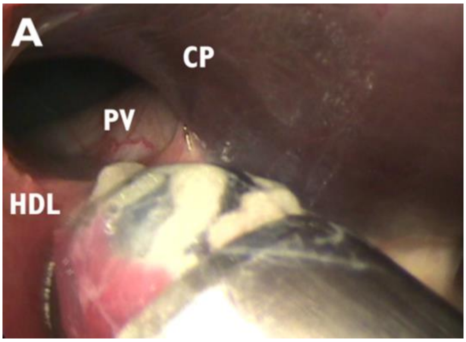

Figure 5A: The applicator tube with blunt trocar (covered with fat from the abdominal penetration) before introduction through the epiploic foramen. (HDL: hepatoduodenal ligament, PV: portal vein, CP: caudate process of the liver)

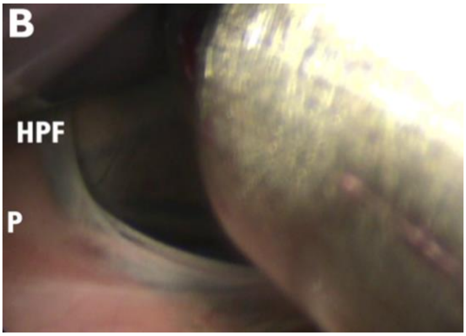

Figure 5B: The applicator tube introduced in the omental vestibule through the epiploic foramen. The blunt trocar has been removed. (HPF: hepatopancreatic fold, P: pancreas)

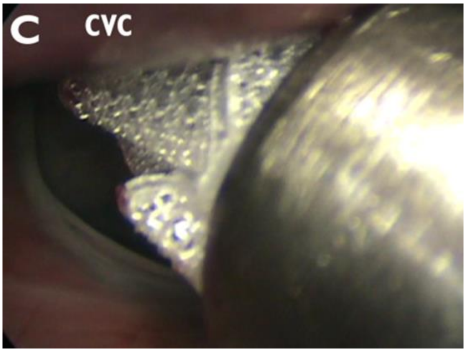

Figure 5C: The first part of the diabolo-shaped mesh is pushed through the applicator tube with the pushing device. (CVC: caudal vena cava)

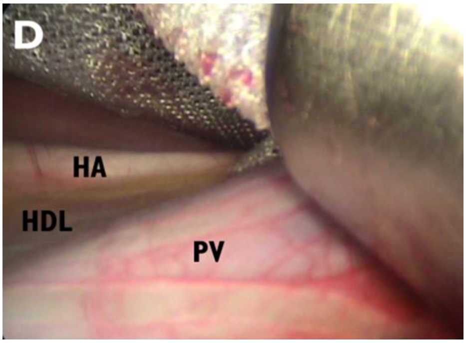

Figure 5D: The applicator tube is withdrawn slightly over the pushing device to exteriorize the second half of the diabolo-shaped mesh. (HDL: hepatoduodenal ligament, PV: portal vein, HA: hepatic artery)

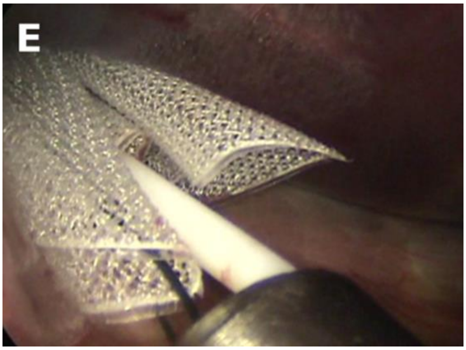

Figure 5E: The applicator tube is withdrawn out of the epiploic foramen over the pushing device (white) and the security line (black).

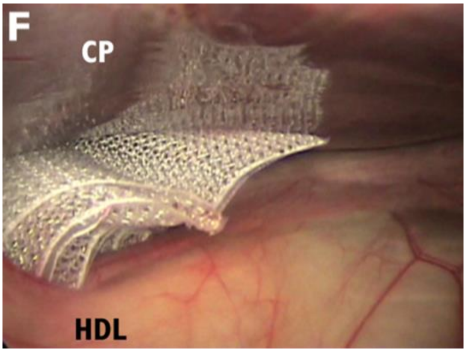

Figure 5F: Final inspection after removal of the applicator tube, the pushing device and the security line. The mesh protrudes approximately 0.5 to 1 cm out of the epiploic foramen in the abdominal cavity. (CP: caudate process of the liver, HDL: hepatoduodenal ligament)