Long-term serum bile acid concentrations in 51 dogs after complete extrahepatic congenital portosystemic shunt ligation

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OBJECTIVES: To report the long-term bile acid stimulation test results for dogs that have undergone complete suture ligation of a single congenital extrahepatic portosystemic shunt.

MATERIALS AND METHODS: Data were collected from the hospital records of all dogs that had undergone a complete suture ligation of a single congenital extrahepatic portosystemic shunt. Owners were invited to return to the referral centre or their local veterinarian for repeat serum bile acid measurement. Dogs diagnosed with idiopathic epilepsy and undergoing bile acid stimulation tests were used as a comparison population.

RESULTS: Fifty-one study dogs were included, with a mean follow-up time of 62 months. 48 dogs had no evidence of multiple acquired shunts and a significant reduction in the pre- and post-prandial serum bile acid concentrations at long-term follow-up compared with pre-operative measurements. Pre- and post-prandial serum bile acids were statistically significantly greater for dogs that had undergone a full ligation (with no evidence of multiple acquired shunts) at all time points compared to the control dogs (P<0.001 for all comparisons).

CLINICAL SIGNIFICANCE: The results suggest that in dogs treated with complete suture ligation mild increases in serum bile acids are not clinically relevant if there are no physical examination abnormalities, a normal body condition score and no relapse in clinical signs.

INTRODUCTION

A congenital portosystemic shunt (CPSS) is an abnormal vascular communication that diverts blood away from the portal circulation supplying the liver into the systemic circulation. The CPSS may be intra- (IHCPSS) or extra-hepatic (EHCPSS) and results in liver hypoplasia and hepatic insufficiency. Clinical signs commonly include poor body condition score and signs of hepatic encephalopathy (HE) (Centre & Magne 1990). CPSS are associated with a variety of hepatic histopathological abnormalities indicative of portal hypoperfusion, including biliary and arterial hyperplasia, portal vein hypoplasia and fibrosis (Cullen et al. 2006). Surgery to attenuate the shunting vessel, thus re-directing the hepatic portal blood flow to the liver, is the recommended treatment in most animals (Greenhalgh et al. 2014). The liver has a great capacity for regeneration via hyperplasia. Increased liver volume, suggestive of liver regeneration, postsurgery has been confirmed in a small number of dogs with IHCPSS and EHCPSS using contrast CT and MRI imaging (Stieger et al. 2007, Kummeling et al. 2010). Further studies have supported the concept that liver regeneration and angiogenesis are important
in the hepatic response to CPSS attenuation (Tivers et al. 2014a, 2014b, 2015).

A variety of surgical techniques can achieve acute or gradual CPSS attenuation at surgery, including suture ligation, cellophane band, amiodor constrictor or intravascular coils. Currently there is no convincing evidence to recommend one treatment over another (Tivers et al. 2012). Residual shunting after using a gradual attenuation device is to be expected within the first few months after surgery, although this should resolve as vessel closure progresses. If attenuation is incomplete after the use of a gradual occlusion technique then clinical signs can persist (Winkler et al. 2003). Similarly, if only partial ligation has been performed then, in some instances, clinical signs can persist due to continued flow through the CPSS. Recurrence of clinical signs can occur with any attenuation method (gradual occlusion, partial or complete ligation) and can be due to the development of multiple acquired shunts (MAS) or persistent shunting through an incompletely attenuated shunt. The incidence of MAS as a recorded complication varies depending on the study population and/or technique used. However, the development of MAS seems to be uncommon, with 3/29 dogs developing MAS after a partial suture ligation in one study (Burton & White 2001) and at least 2/15 partial ligations and 1/13 amiodor ring developing MAS in another study (Winkler et al. 2003). A further study into amiodor rings found 5/112 died or were euthanised due to MAS and another study found 3/16 to have MAS following cellophane band placement (Landon et al. 2008, Falls et al. 2013).

In dogs with complete suture ligation and no MAS, the long term clinical outcome is considered excellent (Lawrence et al. 1992, Bostwick et al. 1995, Hottinger et al. 1995, Smith et al. 1995, Hunt & Hughes 1999, Kummeling et al. 2004), but there is very limited information on whether this excellent clinical outcome is associated with a long-term return to normal biochemical and liver function (bile acid stimulation test) parameters.

Serum bile acids (SBAs) are commonly used as a diagnostic test for CPSS as well as to monitor response to surgery, due to the practical ease of performing the test and its high specificity and sensitivity (Ruland et al. 2010, Winkler et al. 2003).

To our knowledge, there are no studies reporting long-term (>18 months post-operatively) SBAs in the veterinary literature for a large group of dogs after complete shunt ligation. Hunt & Hughes (1999) reported follow-up at a median of 13-5 months (range 2 weeks to >6 years) after partial or complete shunt ligation using a silk ligature, with 36 dogs having biochemistry and either a SBA sample or ammonia tolerance test (ATT) at the time of follow-up. 22% (8/36) of these were found to have abnormal ATT or post-prandial SBA and seven of these dogs experienced long-term problems related to persistent shunting, with 10 dogs in total experiencing relapse of clinical signs. All but one of these dogs did not undergo complete shunt ligation at surgery or imaging to investigate if they were still shunting at the time of follow-up. Therefore it is unknown whether the relapse in clinical signs was due to persistent shunting, the development of MAS or recanalisation of the originally ligated shunting vessel, all of which could have accounted for the increased ATT or SBA. A further study reported SBA values in 20 dogs at a mean time of 18-6 months (range 2-5 to 60) post-partial ligation (9 dogs) and complete ligation (11 dogs) of a CPSS. None of these dogs had normal pre-prandial SBA values at follow-up and only four had normal post-prandial SBAs (Lawrence et al. 1992).

There are reports that indicate improved biochemical and SBA parameters for dogs undergoing complete shunt ligation at various short-term time points (<one year; Burton & White 2001, Lee et al. 2006). However, there is a lack of long-term evidence on whether or not these improvements eventually normalise, stay the same or even deteriorate, and how this is related to long-term clinical outcome.

The main aim of this study was to investigate the long-term (>18 months) biochemical and bile acid stimulation test results for dogs that had undergone complete suture ligation of a single congenital extrahepatic portosystemic shunt (EHCPSS). Our null hypothesis was that there would be no difference in biochemistry and bile acid stimulation test results between dogs that had undergone complete suture ligation of a single congenital EHCPSS and control dogs free of liver disease. We hypothesised that these results would be normal at this length of time post-operatively for completely attenuated EHCPSS, without evidence of MAS, due to blood flow through the shunt being completely occluded and the substantial regenerative capacity of the liver following surgical correction. Additionally, we aimed to assess the long-term physical examination, body condition score and abdominal ultrasound findings for these dogs to accurately document their clinical outcome following complete shunt ligation.

**MATERIALS AND METHODS**

Institutional ethical approval was obtained for the study. Medical records were reviewed for all dogs that had undergone ligation of a single EHCPSS between January 2000 and February 2012. During the study period at our institution, complete attenuation with polypropylene (Prolene®) was performed on all dogs with CPSS if tolerated based on subjective and objective parameters (including measurement of intraoperative portal pressures, a portovenogram and subjective assessment of intestinal and pancreatic colour). In dogs that could only tolerate partial shunt ligation at the initial surgery, the shunt was attenuated as much as was deemed appropriate based on the above parameters and using a polypropylene ligature. A repeat surgery was recommended for all dogs, regardless of clinical response, approximately three months later with the aim of achieving complete shunt ligation in a second procedure. Those dogs that did not return for a second surgery were excluded from the study.

Data collected included signalment, body condition score (BCS), surgery date, anatomical description of the CPSS (at the time of first surgery for those that went on to have two surgeries) and whether a complete or partial ligation was achieved in one or two surgical procedures. Each dog's history was reviewed and serum bile acids, complete blood count and serum biochemistry from preoperatively (at the time of first surgery) and at short-term follow-up (three months postoperatively from when a complete attenuation had been achieved) performed at the referral centre were recorded.
Long-term (>18 month) follow-up data were collected by initially contacting referring veterinary surgeons to ascertain whether the animal was still alive and to obtain up to date client information and clinical histories. For those alive, owners were contacted by telephone, letter or email and invited to participate in the study.

Owners were instructed not to feed animals after 10 pm the night prior to the appointment. The same veterinary surgeon took a current history, including diet, medications and health problems since the last visit, and performed a physical examination and BCS. A blood sample was taken for pre-prandial serum bile acids (SBA) and biochemistry. Dogs were then fed and a blood sample for post-prandial SBA was taken two hours later. In the latter half of the study an abdominal ultrasound was performed by one of three board-certified radiologists. For owners unable to return to our hospital, biochemistry and bile acid stimulation tests were offered via the referring practice. As part of a related but separate study, health-related quality of life questionnaires were also completed by owners (Bristow et al. 2016).

Blood samples were sent to Idexx Laboratories for serum bile acid concentration and biochemical analysis. The laboratory’s reference intervals for serum bile acid concentration are 0-1 to 5·0 μmol/L and 0·1 to 10·0 μmol/L for pre- and post-prandial samples, respectively. Albumin, alanine transaminase (ALT) and alkaline phosphate (ALP) were analysed from the biochemical results. The laboratory’s reference intervals for these are albumin 25 to 40 g/L, ALT 5 to 60 U/L and ALP≤130 U/L.

A control population of “normal” dogs undergoing bile acid stimulation tests and taken from a previous unrelated study performed at our institution were used for comparison. The control samples were obtained as part of the diagnostic investigation for idiopathic epilepsy in accordance with tier 2 of the international veterinary epilepsy task force consensus (De Risio et al. 2015).

Statistical analysis was performed using a commercially available software package (SPSS IBM Statistics version 20). Categorical data were reported as percentages and compared with Chi-square or Fisher’s exact tests. Continuous data were assessed for normality using the Shapiro-Wilk Test and histograms. Median and 25th to 75th percentiles were reported for skewed data and mean±SD were reported for normally distributed data. Normally distributed continuous data were analysed using an independent samples t-test and skewed data were analysed with a Mann-Whitney U test for independent samples or Wilcoxon signed rank test for related-samples. Significance was set at P<0·05.

**RESULTS**

One hundred and forty-five dogs met the inclusion criteria. Of these 94 (66-2%) were still alive at a mean±SD follow-up time of 177±75 months. Sixteen dogs (11-3%) had died of an unrelated cause at a mean time of 194 months postoperatively (SD 71). Two (1-4%) had died of causes related to CPSS, 13 and 201 months postoperatively. Six (4-2%) dogs died of an unknown cause at a mean time of 212 months postoperatively, (SD 124). Twenty-five (17-6%) dogs were lost to follow-up at a mean time of 263 months postoperatively (SD 75).

Fifty-one dogs participated in the study with three of these having their follow-up blood tests performed by their local veterinary practice. The mean±SD follow-up time for these cases was 62±27·4 months from time of complete shunt ligation.

At first surgery, 49% (n=25) of dogs had a full attenuation, and 51% (n=26) had a partial attenuation. Of the 27 dogs that had a second surgical attenuation, 26 tolerated a full attenuation, and one dog had developed MAS but had no apparent further shunting through the original CPSS on portovenography.

A variety of breeds were represented with miniature schnauzers (15-4%) and cross breeds (13-5%) being the most common, (Table 1). Sex and neutering status are presented in Table 2. The median age at first surgery was 11·9 months (5-8 to 19·5).

### Physical examination

None of the dogs examined (n=48), had physical examination findings potentially associated with a CPSS. Twelve dogs had abnormalities including periodontal disease (n=3), ocular discharge (n=2), lipoma (n=2) and one each of: cyst on neck, bilateral luxating patellae, pyoderma, brachycephalic obstructive airway syndrome and grade II/VI heart murmur. The median body condition score was 5/10 (range 4 to 6/10). Preoperative body condition score was only available for three dogs and therefore no comparison was made. No owners reported a relapse in clinical signs since surgery.

### Complete attenuation dogs, n=48

#### Bile acid stimulation test results

The median preoperative pre- and post-prandial SBA were 99·5 (62·3 to 124·8) and 245 umol/L, (147·7 to 351·2) respectively (results available for 45 dogs).

| Table 1. Breeds of study population (without MAS) |
|-----------------|-----------------|-----------------|
| Breed           | Number | %    |
| Bichon frise    | 3      | 5·8  |
| Cocker spaniel  | 4      | 7·7  |
| Cross breed     | 7      | 13·5 |
| Jack Russell terrier | 4 | 7·7  |
| Lhasa apso      | 2      | 3·8  |
| Miniature dachshund | 1  | 1·9  |
| Miniature schnauzer | 8  | 15·4 |
| Norfolk terrier | 2      | 3·8  |
| Pug             | 4      | 7·7  |
| Samoyed         | 1      | 1·9  |
| Shih-tzu        | 5      | 9·6  |
| Springer spaniel| 1      | 1·9  |
| West Highland white terrier | 6  | 11·5 |
| Yorkshire terrier | 4   | 7·7  |

| Table 2. Sex and neuter status of study population (without MAS) |
|-----------------|-----------------|-----------------|
| Sex             | Number | %    |
| Female entire   | 16     | 30·8 |
| Female neutered | 7      | 13·5 |
| Male entire     | 14     | 28·8 |
| Male neutered   | 15     | 28·8 |
At short-term follow-up (mean 12 months, SD 15), they were a median of 7.0 (1.28 to 19.65) and 21.6 μmol/L (14.9 to 47), respectively, (results available for 22 dogs).

At long-term follow-up (mean±SD 158±832.7 months) they were a median of 14.5 μmol/L (1.52 to 29.5) and 38.9 μmol/L (17.1 to 52.5), respectively, (n=48 dogs).

Preoperatively, 98% of pre- and 100% of post-prandial bile acids were above the laboratory reference range. At short-term follow-up these numbers were 64-7 and 86.3% for pre and post-prandial, respectively.

There was a significant reduction in the pre and post-prandial serum bile acid concentrations at both short (P ≤ 0.01 and 0.01, respectively) and long-term follow up, (P≤0.01 and 0.01, respectively, Figs 1 and 2), compared to the preoperative values. There was no significant difference in pre- or post-prandial serum bile acid concentrations between short- and long-term follow-up (P=0.09 and 0.06, respectively, Figs 1 and 2).

**CBC and biochemistry results**

At long-term follow-up, two dogs were hypoalbuminaemic (15.8 and 27.9 g/L) and seven dogs had increased ALT at a median of 179.3 U/L. No other abnormalities were detected.

There was a significant difference in the PCV between pre-surgical and short-term values, increasing from a mean of 40.4% (range 38.4 to 50.6%) pre-surgical to 48.2% (45.7-50.3%) at short term, (P=0.016). There was insufficient data available to assess PCV at long-term follow-up. There was a significant decrease in ALP values between pre-surgical and three-month post-surgical samples (P=0.004) and between pre-surgical to long-term (P≤0.001), but no difference between short- and long-term follow-up (P=0.45).

There was a significant decrease in ALT values between pre-surgical and three-month post-surgical samples (P=0.002) and between pre-surgical and long-term follow-up samples (P<0.001). However the ALT did increase significantly between three-month post-surgical and long-term follow-up samples (P=0.04).

There was a significant increase in urea, creatinine and albumin values between pre-surgical and short-term samples (P≤0.001 for all) and for all values between preoperatively and long-term (P≤0.001 for all). There was no significant difference in urea or creatinine values between three-month post-surgical and long-term follow-up samples (P=0.45 and 0.91, respectively), but there was a significant increase in albumin values from three-month post-surgical to long-term follow-up samples (P=0.017).

**Abdominal ultrasound results**

Overall 27 dogs underwent abdominal ultrasound at median follow-up of 1406 days (range 598 to 2917), 25 of which were in the complete attenuation group. These 25 dogs had no evidence of persistent shunting or MAS. Two dogs had evidence of urolithiasis and one of these dogs had a subjectively small liver.

Four of 48 dogs had a post-prandial bile acid at long-term follow-up >100 μmol/L. Of these four dogs, three had an abdominal ultrasound performed; in one dog no evidence of liver abnormalities, MAS or persistent shunting was seen but there were cystoliths. A second dog had situs inversus and a full abdominal ultrasound could not be performed, but there was a subjectively small liver and cystoliths. A third case had some turbulence associated with the shunt ligation site, as had been apparent on a previous postoperative ultrasound, but this dog had undergone an exploratory laparotomy and portovenogram during which no evidence of persistent shunting or MAS were seen. The final case
was not able to come back to our referral centre for an abdominal ultrasound due to owner restrictions.

At short-term follow-up, excluding the two cases described above in which an abdominal ultrasound was not or could not be performed, the pre-prandial 95th percentile was 49.2 umol/L and post-prandial 90.6 umol/L. At long-term follow-up these values were 93.9 and 119 umol/L, respectively.

**MAS dogs (n=3)**

Three dogs were diagnosed with MAS. One dog was diagnosed at the time of second surgery, where the previous macroscopic shunt had closed despite being partially attenuated with a polypropylene ligature. The remaining two dogs were found to have MAS on abdominal ultrasound when re-examined for this study, following full shunt attenuation. This population consisted of two cocker spaniels (one male castrated and one female spayed (age 4.8 and 9.8 years, respectively), and one male castrated bichon frise, age 3.6 years.

Two dogs had a preoperative pre-prandial SBA value available (125.4 and 165 umol/L). All dogs had a pre-operative post-prandial sample (90, 307.3 and 338.9 umol/L). At short-term follow-up (n=3), pre-prandial SBAs were 1.4, 10.7 and 17.3 umol/L and post-prandial SBAs were 23.4, 92 and 133 umol/L. At long-term follow-up, (mean 124 months, SD 47.8), the pre-prandial SBAs were 50.6, 102.4 and 199.2 umol/L and post-prandial 98.4, 147.3 and 224.7 umol/L. All dogs had SBAs above the reference interval pre-operatively and at long-term follow-up. The number of dogs in this group was too small to perform statistical comparisons.

On biochemical analysis one dog had increased ALT activity (66.2 U/L). No other abnormalities were detected. The three dogs with MAS were all receiving a restricted protein diet and one was receiving lactulose. No owners reported a relapse in clinical signs or other abnormalities and the only abnormality detected on physical examination was ventral pyoderma in one dog.

**Control dogs (n=36)**

Median age of the control dogs was 19 months (range 6 to 165 months). Breeds are shown in Table 3. The median pre-prandial SBAs for control dogs were 0.9 umol/L (25th to 75th percentiles 0.5 to 1.5) and post-prandial 3.5 umol/L (25th to 75th percentiles 1.8 to 5.3). Pre- and post-prandial SBAs were statistically significantly greater for dogs that had undergone a full attenuation with no evidence of MAS at all time points compared to the control dogs (P<0.001 for all comparisons).

### DISCUSSION

The clinical outcome of all dogs available for long-term follow-up following complete CPSS ligation surgery was excellent based on the body condition score and lack of physical examination abnormalities. However, our null hypothesis that the SBA of dogs following complete surgical ligation of a CPSS would have returned to normal at long-term follow-up was rejected. There was a statistically significant decrease in pre- and post-prandial SBA at long-term follow-up compared to pre-operatively, but 65 and 83% of pre- and post-prandial SBA, respectively, were still above the laboratory reference interval at a mean follow-up of 62 months. This is an interesting finding and the reason(s) for it are unclear. Abdominal ultrasound was performed in the latter half of the study (once extra funding became available to do this) to evaluate dogs for possible development of MAS that were not causing clinical signs as a reason for increased SBA. Only two dogs (out of 27) were detected with MAS on abdominal ultrasound at long-term follow-up. However, the dog with the greatest post-prandial SBA value (215 umol/L) was unable to return for an abdominal ultrasound, and the dog with the second greatest value was not able to have a full ultrasound performed due to her situs inversus. Interestingly, this dog did have a subjectively small liver and cystoliths and therefore it would be reasonable to suspect either development of MAS or persistent shunting. Nevertheless, this dog had a full suture ligation, making the latter possibility unlikely. The sensitivity and specificity of abdominal ultrasound for the detection of MAS has not been studied extensively although in one study one of six cases of MAS were detected by AUS compared to four of five with computed tomography angiography (CTA), (Kim et al. 2013). CTA would have been a more sensitive and specific method of detecting MAS but is more expensive and requires sedation. Regardless, the incidence of MAS detected in this study is comparable with many other studies that report rates of MAS between 10 and 18% (Burton & White 2001, Winkler et al. 2003, Landon et al. 2008). Most importantly, the rate of MAS in this study (3-5%) is simply far too low to be solely responsible for the 56 and 79% persistently elevated pre- and post-prandial SBA at long-term follow-up, even if the imaging methods for detecting MAS are not 100% sensitive. Additional support for MAS not being a major cause of the increased SBAs in our population of dogs was provided by the three dogs that were known to already have MAS; none of these dogs with MAS had a post-prandial SBA <98 umol/L. Overall, our study showed that long-term, pre-prandial values above 94 umol/L and post-prandial above 119 umol/L.

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**Table 3. Breeds of control population**

| Breed                  | Number |
|------------------------|--------|
| Boxers                 | 6      |
| Labrador Retrievers    | 4      |
| Border Collies         | 3      |
| Weimaraners            | 3      |
| German Shepherd Dogs   | 2      |
| German Pointers        | 2      |
| Cross Breeds           | 2      |
| Bichon Frise           | 1      |
| Jack Russell Terrier   | 1      |
| Golden Retriever       | 1      |
| Shih-Tzu               | 1      |
| Welsh Springer Spaniel | 1      |
| Rottweiler             | 1      |
| Mastiff                | 1      |
| Dogue de Bordeaux      | 1      |
| Doberman               | 1      |
| Italian Spinoni        | 1      |
| Staffordshire Bull Terrier | 1  |
| Scottish Terrier       | 1      |
| Beagle                 | 1      |
| Dalmation              | 1      |
give a 95% chance of being abnormal, i.e. further investigation of likely residual shunting is warranted.

Continued shunting through the original CPSS is another possibility for persistently increased SBA if the shunt has not been completely attenuated (by a ligature, cellophane band or ameroid constrictor). However, the dogs in this study had documented complete shunt ligation at surgery eliminating residual shunting as a cause for elevated SBA seen in this population of dogs.

We therefore conclude that there must be another cause for the long-term increased SBAs seen in the majority of dogs undergoing complete EHCPSS ligation in this study, and assume that subclinical liver abnormalities persist after the CPSS is ligated and normal hepatic portal flow resumes. Aetiologies for this persistent liver dysfunction include concurrent microvascular dysplasia/primary portal vein hypoplasia (PVH) and/or a failure of the liver to recover normal function after correction of the abnormal blood flow through the CPSS. PVH has been reported as a separate entity in dogs and it has also been suggested that it can occur concurrently with a macroscopic shunt (Schermerhorn et al. 1996, Allen et al. 1999, Christiansen et al. 2000). Our data suggest that there is a spectrum of varying degrees of concurrent congenital microvascular dysplasia that results in a high proportion of dogs with a CPSS failing to have normal SBAs after surgical correction of the single congenital macroscopic shunt. A similar suggestion was made in a previous study where the authors suggested that it may be possible for some dogs with EHCPSS to have microscopic shunting as well as a macroscopic shunt, resulting in failure of SBAs to normalise following successful surgical ligation (O’Leary et al. 2014). It would be very difficult to provide evidence for this theory because the histopathological hepatic findings associated with PVH are indistinguishable from those seen in dogs with a macroscopic CPSS and all of the dogs in our study had an excellent long-term clinical outcome. We therefore conclude that whatever the exact aetiology of the liver pathology causing persistent, mildly (<50 umol/L) increased SBAs in dogs with complete CPSS ligation but without MAS (median pre prandial 14·5 and post prandial 39·5 umol/L), it is of minimal clinical significance with regards to long-term outcome and does not require further imaging investigations, medical therapy or special diet. This is further supported by findings in a concurrent study performed at our hospital, assessing long-term quality of life following surgical attenuation of an EHCPSS or IHCPSS (Bristow et al. 2016). Additionally, the 95% confidence intervals calculated in the current study suggest that dogs with pre-prandial and post-prandial values approximately higher than 94 and 119 umol/L, respectively, do warrant further investigation of likely persistent shunting. Interestingly, people with liver disease can suffer from minimal hepatic encephalopathy (Shawcross et al. 2007) and although they do not show obvious signs of HE they do have significant abnormalities in neurophysiological performance and on psychometric testing which may be something too subtle for us to detect in dogs.

We will continue to recommend a repeat SBA stimulation test at short-term follow-up post-operatively so that if the bile acids are moderately or markedly increased an abdominal ultrasound examination or other imaging can be performed to assess for residual shunting or MAS. However, because there was no significant difference between the SBA at short-term and long-term follow-up, repeat SBA testing seems unnecessary in the long term providing the dog remains free of clinical signs.

The main limitation of our study is the small number of dogs with MAS, allowing no statistical comparison between groups. We suspect that if a greater number of dogs had been included with MAS, a statistically significant difference would have been found in both pre- and post-prandial bile acids at long-term follow-up. However, the limited numbers also reflects the low number of dogs that develop MAS following full ligation with a polypropylene suture.

Of further note, the few papers in the veterinary literature that do include results of long-term follow-up SBAs have either no reference interval reported making it hard to make comparisons between papers on the percentage of dogs with abnormal results, or variable reference intervals from 5·3 to 9·9 umol/L up to <40umol/L (Lawrence et al. 1992, Hunt & Hughes 1999, Burton & White 2001, O’Leary et al. 2014, Winkler et al. 2003).

To conclude, SBAs do not normalise in the majority of dogs surgically corrected for their EHCPSS although they become mildly rather than moderately or severely increased in the vast majority of dogs. Given the excellent clinical outcome of all dogs in this study, long-term mildly increased SBA is not a major concern if present in combination with no physical examination abnormalities, a normal body condition score and no relapse in clinical signs.

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Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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