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Intrahepatic congenital portosystemic shunts in dogs: short and long-term outcome of suture attenuation

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Structured Summary

Objectives: To report the short and long-term outcomes of one or two-staged suture attenuation for complete closure of intrahepatic congenital portosystemic shunts (IHCPSS) in dogs.

Methods: A retrospective cohort study of dogs surgically treated for IHCPSS between February 2000 and March 2015 was performed. Long-term follow-up was obtained by telephone conversations with the referring veterinary surgeon and / or the owner.

Results: Fifty-five dogs had suture attenuation of their IHCPSS. Ten dogs (18.2%) tolerated complete attenuation, whilst 45 dogs (81.8%) tolerated partial attenuation. Post-operative complications occurred in 24 dogs (43.6%), with six dogs (10.9%) dying. Repeat surgery was performed in 33/39 dogs (84.6%) that had partial attenuation and 27 of these (84.9%) ultimately achieved complete CPSS attenuation. One dog (3.0%) died following second surgery, resulting in an overall post-operative mortality of 7/55 (12.7%). Detailed follow-up was available for 22 dogs that were still alive at a median of 29 months' post-surgery (7.4-103.1) with a subjectively good quality of life. Fourteen out of 17 dogs (82.4%) with complete attenuation in one or two surgeries had an excellent outcome compared with 1/5 dogs (20%) with persistent shunting.

Clinical Significance: Staged suture ligation resulted in a good rate of complete attenuation and a reduced rate of persistent shunting compared with a single surgery. Repeat surgery was associated with a lower complications rate compared to first surgery. The proportion of dogs with an excellent outcome was greater for those that had complete attenuation in one or two surgeries compared to those with persistent shunting.

Keywords: Congenital portosystemic shunt; dog; outcome; surgery; intrahepatic

Introduction

Intrahepatic congenital portosystemic shunts (CPSS) are seen less commonly in dogs than their extrahepatic counterparts, making up approximately 25-33% of the total (Berent and Tobias 2009, Berent and Tobias 2012). For both types of CPSS surgical attenuation is recommended to restore normal portal blood flow and resolve clinical signs (Berent and Tobias 2009, Tivers *et al.* 2012, Greenhalgh *et al.* 2014, Tivers *et al.* 2017). However, intrahepatic CPSS (IHCPSS) can be challenging to manage surgically due to the location of the vessel within the liver parenchyma (Hunt *et al.* 1996, White *et al.* 1998, Berent and Tobias 2009). Surgical techniques for IHCPSS include suture ligation, ameroid constrictors, cellophane banding and hydraulic occluders (White *et al.* 1998, Hunt *et al.* 2004, Kummeling *et al.* 2004, Adin *et al.* 2006, Bright *et al.* 2006, Mehl *et al.* 2007). Intravascular techniques with hepatic inflow occlusion have been used to allow attenuation of some IHCPSS, which is technically demanding (Breznock *et al.* 1983, Hunt *et al.* 1996, White *et al.* 1998). Some studies have reported a high rate of complications (47-77%) and mortality (12.5-27.3%) with surgical attenuation of IHCPSS (Komtebedde *et al.* 1991, White *et al.* 1998, Papazoglou *et al.* 2002, Hunt *et al.* 2004). Hence, intravascular occlusion with interventional radiology has been recommended to reduce complications and mortality associated with traditional surgical techniques (Weisse *et al.* 2014). However, there is limited long-term follow-up information on dogs with IHCPSS and only one comparative study, making the evidence base for choosing one technique over another even more challenging (Mehl *et al.* 2007, Tivers 2017).

Only a minority of dogs (approximately 0-15.4%) can tolerate complete acute attenuation of their IHCPSS (Hottinger *et al.* 1995, White *et al.* 1998, Papazoglou *et al.*

2002, Kummeling *et al.* 2004). Dogs can be treated with partial attenuation but with this technique there remains a concern over residual shunting and the persistence or recurrence of clinical signs, which has been reported to be as high as 24.3-50% (Smith *et al.* 1995, White *et al.* 1998). Gradual attenuation devices such as ameroid constrictors and cellophane bands aim to achieve complete attenuation over a period of weeks (Hunt *et al.* 2004, Sereda and Adin 2005, Mehl *et al.* 2007). However, it is unclear how many dogs achieve complete attenuation and residual shunting may be present in a significant number of dogs (Mehl *et al.* 2007). Additionally, the technical challenge of placing a gradual attenuation device or material around an IHCPSS where the space around the shunt may be restricted can make placement impossible in some dogs. In dogs with IHCPSS or extrahepatic CPSS (EHCPSS) treated with partial suture ligation a second surgery has been described to attempt complete attenuation in a staged manner (Hottinger *et al.* 1995, White *et al.* 1998, Burton and White 2001, Lee *et al.* 2006). In three of these studies a proportion of dogs treated with partial attenuation had repeat surgery to attempt full ligation due to recurrence of clinical signs or persistently increased bile acids (Hottinger *et al.* 1995, White *et al.* 1998, Burton and White 2001). All 28 of the dogs treated with partial attenuation in one study (Lee *et al.* 2006) and 9/27 dogs treated with partial ligation in another study (Hottinger *et. al* 1995) had a scheduled repeat surgery, without recurrence of clinical signs. The potential advantage of this technique is that it will ensure complete attenuation of the shunt and therefore reduce the chances of persistent or recurrent clinical signs associated with on-going shunting. However, this technique has not been reported in detail, particularly the complications and outcomes after the second surgery.

Staged suture ligation has been the routine treatment of IHCPSS in dogs the authors' institution over the last 15 years. Subjectively this approach has been associated with a good short and long-term outcome. It was also our impression that the mortality rate had decreased with time, possibly associated with increased experience with surgical and anaesthetic management and the post-operative care. Historically dogs had been treated with non-steroidal anti-inflammatory drugs (NSAIDs) peri-operatively, to provide multi-modal analgesia. Subjectively the use of NSAIDs had been associated with mortality and their use had been discontinued.

The aim of the current study was to report the short and long-term outcomes of one or two staged suture attenuation to achieve complete closure of IHCPSS in a large cohort of dogs. An additional aim was to report any changes in mortality associated with, age at surgery, time-period of the study and the use of NSAIDs.

Materials and Methods

The medical records for dogs with IHCPSS treated surgically between February 2000 and March 2015 were retrospectively reviewed. Dogs were included in the study if they had been treated with a complete or partial suture ligation of their IHCPSS. Dogs treated via other surgical methods were excluded. During the study period a standard surgical protocol was routinely followed in all dogs treated with suture ligation, although anaesthetic and post-operative management was at the discretion of the individuals involved.

Dogs underwent laparotomy and intra-operative mesenteric portovenography (PVG) as previously described (Lee *et al.* 2006). The shunt was identified and the location that would provide the easiest access for ligation was determined, typically the shunt itself, the draining hepatic vein or the supplying portal vein branch. The vessel was dissected to allow two strands of 2m or 3m polypropylene (Prolene; Ethicon) or silk (Mersilk; Ethicon) suture material to be passed around it. A mesenteric vein was catheterised with a 20-24g over the needle catheter, which was used for portovenography and to measure portal venous pressure. Portovenography was performed using a mobile c-arm unit (Siremobil; Siemens) with a sterile cover. A bolus of 1ml/kg of iohexol contrast agent (Omnipaque 300; GE Healthcare Limited) was injected under fluoroscopic guidance, creating a series of portovenogram images. This allowed confirmation of portosystemic shunting and provided information on the morphology of the shunt and the intrahepatic portal vasculature. The vessel was temporarily completely attenuated using a Rummel tourniquet and the portovenogram was repeated, allowing confirmation of correct location of attenuation and reassessment of the intrahepatic portal vasculature. Dogs were treated with complete or partial suture attenuation with polypropylene or silk (Lee et al. 2006, Cariou *et al.* 2009a). The degree of attenuation

was based on subjective and objective assessment of intra-operative portal hypertension during temporary complete attenuation. Subjective assessment was performed by visual inspection of the intestines and pancreas during temporary complete attenuation for signs of portal hypertension, including bowel hypermotility, increased mesenteric arterial pulsations, pancreatic oedema and intestinal and pancreatic cyanosis (Mathews and Gofton 1988). If these signs were observed, then it was considered that the dog would not tolerate a complete attenuation. Portal blood pressure was measured before and during temporary complete attenuation of the vessel using a pressure transducer (Becton Dickinson UK Limited) and a multi-parameter monitor (S/5 Compact Monitor; GE Healthcare Limited) connected to the catheter in the mesenteric vein. The increase in portal pressure before and during temporary complete attenuation and the absolute portal pressure were used to determine whether complete attenuation could be performed (Bostwick and Twedt 1995, Breznock et al. 1983, Butler et al. 1990, Swalec and Smeak 1990, Swalec et al. 1991). Contraindications for complete attenuation were a post-attenuation portal pressure of >18mmHg (20cmH_2O), an increase in >8 mmHg (10cmH_2O) or a doubling of pre-attenuation portal pressure value. Additionally, a change in central venous pressure of >1mmHg or a change in arterial pressure of >5mmHg were considered contra-indications to complete attenuation.

Dogs treated with partial attenuation had a length of polypropylene suture left around the vessel to facilitate subsequent attenuation. A second surgery to attempt complete attenuation was recommended for all dogs that had partial attenuation, regardless of clinical response.

Descriptive data was recorded from the medical record as presented in the results. The cohort was separated into two groups, with the first group being the initial 50% of the

dogs that had surgery and the second group being the subsequent 50%. The subjective response to medical management pre-surgery and the subjective short-term response to surgery, as described in the medical record, was graded by the primary author as follows: good = resolution of clinical signs, moderate = improvement in clinical signs, poor = no improvement in clinical signs or relapse. Intra-operative complications were defined as an adverse surgical event that required intervention to correct. Post-operative complications were defined as an adverse event, occurring prior to hospital discharge. Complications were categorised into Neurological, Portal Hypertension, Gastrointestinal and Miscellaneous. Postoperative mortality was defined as those dogs that died or were euthanatized within 30 days of the surgery. This was further divided into those that died before or after hospital discharge.

Detailed follow-up was available for a proportion of the dogs as part of another study using a Health-Related Quality of Life (HRQOL) questionnaire (currently unpublished data). Follow-up was obtained for the remaining dogs by telephone calls to the referring veterinary surgeon and / or owner. For dogs that were alive at the time of follow-up outcome was graded by the primary author based on the information obtained from the owner via the HRQOL questionnaire and telephone call. The grading was based on a previous study (Mehl *et al.* 2007): excellent = resolution of clinical signs and no medical management / diet, fair = resolution of clinical signs with continued medical management / diet, poor = recurrent or persistent clinical signs, no response to surgery. Owners were also asked to subjectively rate their dog's quality of life.

Statistical analysis was performed using a statistical software package (PASW Statistics 21.0.0; Education SPSS (UK) Limited IBM, Woking, UK). Data was assessed graphically for normality. Median and range were reported for skewed data. Categorical data were reported as percentages.

Results

First surgery

Fifty-five dogs met the inclusion criteria. The first 28 dogs were in the first half of the study period (February 2001 to November 2006) and the subsequent 27 dogs were in the second half of the study period (December 2006 to March 2015). Three dogs were excluded as they were treated with placement of a cellophane band around their CPSS. No dogs were treated with an ameroid constrictor, hydraulic occluder or endovascular coil embolization. Signalment data and pre-surgical information is presented in Table 1.

Details of surgical variables are presented in Table 2. Fifty-four dogs were treated via an extravascular approach. The majority, including all left sided shunts, were ligated directly at their entry to the vena cava or via ligation of the draining hepatic vein. The remainder were treated via direct ligation of the shunt via dissection of the liver or via ligation of the portal vein branch supplying the shunt. One dog (central divisional CPSS) required an intravascular approach to shunt attenuation. Ten dogs (18.2%) tolerated a complete ligation and the remaining 45 dogs (81.8%) tolerated a partial ligation of their CPSS. Two dogs (3.6%) had an additional surgical procedure performed, one cystotomy and one gastric ulcer biopsy.

Eight dogs (14.5%) suffered an intra-operative complication. All eight dogs tolerated partial attenuation only. Two dogs had an iatrogenic pneumothorax due to dissection of the shunt at the diaphragm. This was identified and treated during surgery. Two dogs had an apparent mild hypersensitivity reaction to pethidine, which was treated with a single intravenous dose of chlorpheniramine. Four dogs (7.3%) experienced intra-operative haemorrhage. Three of these dogs (two left and one right divisional)

experienced haemorrhage during dissection of the shunt. These dogs all required a blood transfusion but this complication did not prevent attenuation. The fourth dog (central divisional) experienced haemorrhage secondary to shunt dissection and the procedure was aborted without attenuation. This dog also required a blood transfusion. Partial attenuation was achieved at repeat surgery eight days later.

Twenty-four dogs (43.6%) had a post-operative complication, with four of these dogs suffering two complications each (Table 3). Six out of 10 dogs (60%) that could tolerate a complete ligation and 18 /45 dogs (40%) that were treated with a partial ligation experienced a post-operative complication. Post-operative complications affected 11/26 (42.3%) of dogs with a left divisional shunt, 4/15 (26.7%) of dogs with a right divisional shunt and 9/14 (64.3%) of dogs with a central divisional shunt.

Four dogs (7.3%) died in the immediate postoperative period (see Table 3 for details). Fifty-one dogs (92.7%) were discharged from the hospital. The median duration of hospitalisation was four days (range 2-13). Two dogs (3.6%) died in the immediate period following discharge from the hospital (see Table 3 for details). Overall six dogs (10.9%) died within 30 days of surgery. All six dogs had tolerated a partial attenuation only. Six out of 45 dogs (13.3%) treated with partial attenuation died post-operatively compared with 0/10 dogs (0%) that had complete attenuation. The median age of dogs that died during the post-operative period was 6.2 months (range 2.4-29.1 months) compared with a median of 18.7 months (range 4.3-38.2) for dogs that survived. Five out of 28 dogs (17.9%) that had their surgery in the first part of the study period died during the post-operative period compared with 1/27 dogs (3.7%) that had their surgery in the second part of the study period. Five out of 13 dogs (38.5%) that received

NSAIDs died during the post-operative period (up to 30 days) compared with 1/42 dogs (2.4%) that did not receive NSAIDs. All four dogs that died because of confirmed or suspected gastroduodenal haemorrhage received NSAIDs.

Second surgery

Overall 39/45 dogs that were treated with partial attenuation survived the post-operative period. Thirty-six out of the surviving 39 dogs (92.3%) were re-examined (see Table 4 for details). The other three dogs did not return for post-operative re-examination.

Thirty-three out of 39 dogs (84.6%) had a second surgery performed (see Table 5 for details). Three dogs were re-examined but the owners declined further surgery (two had a good response and one had a moderate response) and three did not return for post-operative re-examination.

Twenty-four dogs (72.7%) still had some blood flow through the CPSS on PVG but were able to tolerate complete attenuation, two dogs (6.1%) still had blood flow through the CPSS on PVG but were only able to tolerate further partial attenuation (one due to the presence of extensive adhesions preventing further dissection and one due to portal hypertension), three dogs (9.1%) had progressed to full attenuation with no blood flow through the CPSS on PVG and four dogs (12.1%) had developed multiple acquired shunts. The CPSS had been ligated with prolene alone in the three dogs that progressed to full attenuation. Overall, 27 dogs (81.8%) out of 33, achieved full attenuation of their CPSS in two surgeries. This is summarised in Figure 1.

Twenty-three dogs (69.7%) had another surgical procedure performed at the time of the second CPSS surgery, 15 ovariohysterectomy (OVH), six castration, one ovariectomy, and one entropion correction. Neutering was performed in all three of the

dogs that had progressed to full attenuation spontaneously and two of the dogs that had developed MAS.

There was one intra-operative complication (3.0%) where it was not possible to achieve full attenuation due to the presence of marked adhesions following the previous surgery, although further attenuation was possible. Seven dogs (21.2%) suffered a postoperative complication (Table 6). No dogs died or were euthanatized in the immediate post-operative period with all 33 dogs surviving to be discharged from the hospital. The median duration of hospitalisation was four days (range 1-7). One dog that had developed MAS and could not tolerate further attenuation started showing neurological signs five days after the surgery, following discharge from the hospital. The dog was euthanatized later that day by the referring veterinary surgeon. The overall post-operative mortality rate was 1/33 (3.0%).

Short-term post-operative re-examination

Eight out of 10 dogs (80%) that were treated with complete attenuation were re-examined in the short-term post-surgery (two by the referring vet) (see table 7 for details). One dog with a good outcome has MAS identified on follow-up portovenography.

Fourteen out of 32 dogs (43.8%) initially treated with partial attenuation and surviving their second shunt surgery, were re-examined in the short-term (three by the referring vet) (see table 8 for details). Two dogs had further attenuation of their shunt at a third surgery as follows. One dog with a moderate response to surgery had persistent shunting on portovenography and further partial attenuation was performed. Complete attenuation was subsequently achieved at an additional surgery. Another dog with a

good outcome had a very minimal amount of shunting on portovenography, performed at the same time as OVH, and this was treated with complete attenuation. In addition, one dog with a complete attenuation at their second surgery and a good response had MAS documented on a follow-up ultrasound scan.

Long-term Follow-up

Of the 48 dogs that survived surgery, 13 dogs (27.1%) were lost to long-term follow-up. Twenty-five out of 35 dogs (52.1%) were alive at a median follow-up of 33.5 months (range 7.4-103.1).

For three of these dogs, follow-up was limited to the fact that the dog was alive with a presumed good quality of life. Detailed information was available to grade outcome in 22 of these dogs (see table 9). One dog with an excellent outcome had mild visual impairment following post-operative blindness. One dog with a poor outcome was reported to drink a lot and tire easily. One dog with a poor outcome had experienced an episode of pyrexia of unknown origin and a separate episode of chronic diarrhoea. The dog was also considered to have some behavioural abnormalities. Neither dog with a poor outcome was on any medical management. The owners of all 22 dogs felt that their dogs subjectively had a good quality of life. Two of these dogs were documented to have died or been euthanased within two months of their follow-up, one due to gastric dilation and volvulus (GDV) and one due to suspected pulmonary neoplasia.

Ten dogs (20.8%) were confirmed to have died or been euthanatized prior to follow-up. Three dogs died because of non-CPSS related causes including one haemoabdomen, one liver mass resection and one dogfight. Four dogs were euthanatized for CPSS or suspected CPSS related causes; two dogs due to on-going clinical signs, one dog due to aggression (presumed related to hepatic encephalopathy) and one dog due to liver

disease. The cause of death was unknown in three dogs. The time from surgery to death was available for four dogs with a median of 68.7 months (range 7.8-105.5).

Discussion

We have described the short and long-term outcome for 55 dogs with IHCPSS treated with suture ligation in one or two surgeries. IHCPSS are technically more challenging than EHCPSS due to the location of the CPSS within the liver parenchyma. Therefore, intra-operative complications are a major concern with haemorrhage reported in 6.7% to 33.1% of dogs in other studies (Komtebedde *et al.* 1991, Hunt *et al.* 1996, White *et al.* 1998). In the study reported here four dogs (7.3%) suffered haemorrhage during IHCPSS dissection at first surgery, none of which resulted in intra-operative mortality or ultimately precluded shunt attenuation. The overall rate of intra-operative complications at first surgery was 14.5%, which is similar to that reported for endovascular treatment, with major intra-operative complications in 3% and minor in 12% of dogs (Weisse *et al.* 2014). However, the differences in the procedures and therefore the type of complications seen make direct comparison difficult.

Previous studies have reported post-operative complication rates of 11.8-77% for suture ligation, 9.1-22.2% for ameroid constrictor placement and 54.5% for cellophane banding (Komtebedde *et al.* 1991, Hunt *et al.* 1996, Papazoglou *et al.* 2002, Hunt *et al.* 2004, Bright *et al.* 2006, Mehl *et al.* 2007). We found a post-operative complication rate at first surgery of 43.6%. Complications vary widely in type and severity and it is challenging to make direct comparisons between studies. The most common type of post-operative complication was categorized as Portal Hypertension / Gastrointestinal seen in 25.5% of dogs. These complications were grouped together as the underlying cause was not always clear. Four dogs (7.3%) suffered mild to moderate, self-limiting post-operative ascites. This finding is an expected sequel of acute CPSS attenuation and

therefore could be considered a routine occurrence rather than a complication (Berent and Tobias 2012). However, it was included for completeness.

The current study had a post-operative mortality rate at first surgery of 10.9%. This is comparable with previously reported rates of 5.9-22.6% for suture ligation, 0-9.1% for ameroid constrictor placement, 27.3% for cellophane bands and 0% for hydraulic occluder placement, particularly as many of these are relatively small studies (Komtebedde *et al.* 1991, Hunt *et al.* 1996, White *et al.* 1998, Papazoglou *et al.* 2002, Hunt *et al.* 2004, Adin *et al.* 2006, Bright *et al.* 2006, Mehl *et al.* 2007). However, these results are not as good as those reported for endovascular treatment of IHCPSS with a post-operative complication rate of 14% and a post-operative mortality rate of 5.3% (Weisse *et al.* 2014). Nevertheless, we should be cautious in making direct comparisons between studies due to wide variation in study design and clinical variables. Of the six dogs that died at first surgery, two had gastroduodenal ulceration confirmed at post-mortem, two had severe gastrointestinal haemorrhage suggestive of ulceration and two had suspected portal hypertension (one possibly related to a portal thrombus). Dogs with IHCPSS seem to be predisposed to gastrointestinal ulceration (Weisse *et al.* 2014). It is unclear whether the fatal post-operative complications seen in the current study relate to pre-existing GI ulceration, post-operative portal hypertension, the use of peri-operative NSAIDs earlier on in the cohort, or a combination of these factors.

Several studies have suggested that dogs with IHCPSS and EHCPSS treated with partial attenuation could benefit from repeat surgery to achieve complete attenuation (Hottinger *et al.* 1995, White *et al.* 1998, Burton and White 2001, Lee *et al.* 2006). In one study the outcome was improved for a proportion of IHCPSS dogs following an

additional procedure (White *et al.* 1998). The current study is the first to report a large cohort of IHCPSS dogs treated routinely in this manner. In common with previous reports, a minority of dogs (18.2%) could tolerate acute complete attenuation at first surgery. Repeat surgery was recommended in all dogs that survived a partial attenuation at first surgery, regardless of apparent response. Most of these dogs, 84.6%, had a second surgery and this was associated with a reduced rate of complications (21.2%) compared to the first surgery and mortality in one dog with MAS (3.0%). When both first and second surgeries are taken together this cohort of dogs had a mortality rate of 7/55 dogs (12.7%). Of the dogs that could not tolerate a complete attenuation at first surgery, repeat surgery allowed complete attenuation in 81.8%, including three dogs that had progressed to complete attenuation spontaneously. Overall, 77.1% of surviving dogs had complete attenuation of their shunt in one or two surgeries. Despite this, two of these dogs were subsequently identified to have persistent shunting and full attenuation was achieved at an additional surgery. In addition, two dogs were subsequently documented to have developed MAS on follow-up imaging. Overall, persistent shunting was demonstrated or suspected in 27.1% dogs (13/48). A limited number of dogs had follow-up imaging and therefore the exact rate of persistent shunting is unknown and may have been underestimated. However, this rate of persistent shunting compares well with a study of the use of ameroid constrictors in dogs with IHCPSS that identified persistent shunting on scintigraphy in 43% of dogs (Mehl *et al.* 2007). The true significance of persistent shunting is unclear. In EHCPSS dogs treated with ameroid constrictors those with a negative post-operative scintigraphy scans were >10 times more likely to experience a successful outcome (Falls *et al.* 2013). Intuitively dogs that achieve a complete attenuation without persistent shunting should have a better outcome, although this is unproven. Our data supports

the concept that repeat surgery markedly increases the proportion of dogs that achieve a complete attenuation and therefore reduces the proportion of dogs with persistent shunting compared with partial ligation alone and potentially the use of ameroid constrictors.

The current study focused on the short-term outcome of suture ligation of IHCPSS. However, long-term follow-up was available for some dogs with IHCPSS as part of another study validating a HRQOL questionnaire in a large group of dogs with EHCPSS and IHCPSS and follow-up was also obtained for dogs that were not part of that study (unpublished data). Several studies have reported the long-term follow up of dogs treated for IHCPSS, typically assessing outcome by simple owner assessment, although the wide variations in the precise definition of a successful outcome, the data reported and the follow-up times makes direct comparison challenging. In a large study of endovascular occlusion 19% of dogs had a poor outcome with continued or worsening clinical signs despite medical management or surgical related death at a median of 32 months post-treatment (Weisse *et al.* 2014). In two studies of ameroid constrictor placement a poor outcome, with euthanasia due to persistence or recurrent clinical signs was reported in 12.5-30% of dogs at an average of 28.5-38.3 months post-surgery (Bright *et al.* 2006, Mehl *et al.* 2007). In three studies of suture ligation 0-16.3% of dogs had a poor outcome with recurrent or persistent signs and / or shunting at an average of 18-50 months post-surgery (White *et al.* 1998, Kummeling *et al.* 2004, Mehl *et al.* 2007). We assessed the long-term outcome of 22 dogs alive at a median time of 29 months post-operatively. Twenty of these 22 dogs (90.9%) had an excellent or fair outcome with a poor outcome in two dogs (9.1%). Additionally, a further three dogs had an apparently good outcome but without sufficient detail to categorise this further. This

overall outcome is very good and compares favourably with other techniques, although detailed follow-up was only available for 45.8% of the dogs in our study. Overall, 14/17 dogs (82.4%) that had complete attenuation of their shunt had an excellent outcome in comparison with 1/5 dogs (20%) that had documented or suspected persistent shunting. Although, the number of dogs with persistent shunting is small this data does suggest that dogs with complete attenuation and no persistent shunting are more likely to have an excellent long term outcome. This would support our recommendation for follow-up surgery in dogs with persistent shunting.

We explored the possible association between age, study period and use of NSAIDs with mortality following first surgery. Due to the small number of dogs and the retrospective nature of the study it was not considered appropriate to statistically analyse the data. Future, prospective studies may want to explore these factors in more detail. Interestingly, dogs that died during the postoperative period were younger than those that survived. It is not clear why that may be the case. As most of the dogs died due to complications related to GI bleeding or portal hypertension it is not clear why this would be. It is possible that older dogs are more at risk for GI bleeding but this remains unproven. The mortality rate was greater in the first part of the study period. This apparent improvement could have related to greater experience in determining the degree of attenuation and thus a reduced risk of portal hypertension. This could also have been associated with general improvements in the anaesthetic and postoperative management of these dogs over time, although the study did not look at these aspects specifically. Mortality at first surgery seemed to be associated with the use of NSAIDs. All four of the dogs that died because of confirmed or suspected gastroduodenal ulceration had received NSAIDs post-operatively. NSAIDs are a risk factor for

gastrointestinal ulceration due to their effect on prostaglandin synthesis and gastric mucosal integrity (Stanton and Bright 1989, Cariou *et al.* 2009b). As previously mentioned dogs with IHCPSS seem to be predisposed to gastrointestinal ulceration (Weisse *et al.* 2014). Therefore, the use of NSAIDs in these dogs may have contributed to these complications. There were no complications or mortality related to gastrointestinal haemorrhage at second surgery, despite the use of NSAIDs. The authors believe that this is because all dogs undergoing repeat surgery had previously had a partial shunt ligation and therefore their portal blood flow and hence liver function should have been improved. This presumably makes them less vulnerable to surgical complications, particularly those that could have been precipitated by NSAID use. The authors no longer use NSAIDs in dogs with IHCPSS or EHCPSS.

The current study has several limitations, primarily due to its retrospective nature. Dogs were all operated on at a single centre and over a long period of time. Importantly, a proportion of dogs (27.1%) were lost to long-term follow-up. Determining the long-term outcome of dogs treated for IHCPSS is challenging, partly due to the lack of a 'gold standard' assessment method. A more comprehensive follow-up with owner assessment of quality of life, dynamic bile acids and imaging studies to detect persistent shunting, in all dogs, would have strengthened the findings of our study. A prospective study looking at the long-term outcome of dogs surgically treated for IHCPSS would allow firmer conclusions to be drawn.

This study demonstrates that complete suture attenuation of IHCPSS in one or two surgeries is associated in a good long-term outcome. For dogs that could not tolerate a complete ligation at first surgery, repeat surgery was associated with a lower rate of

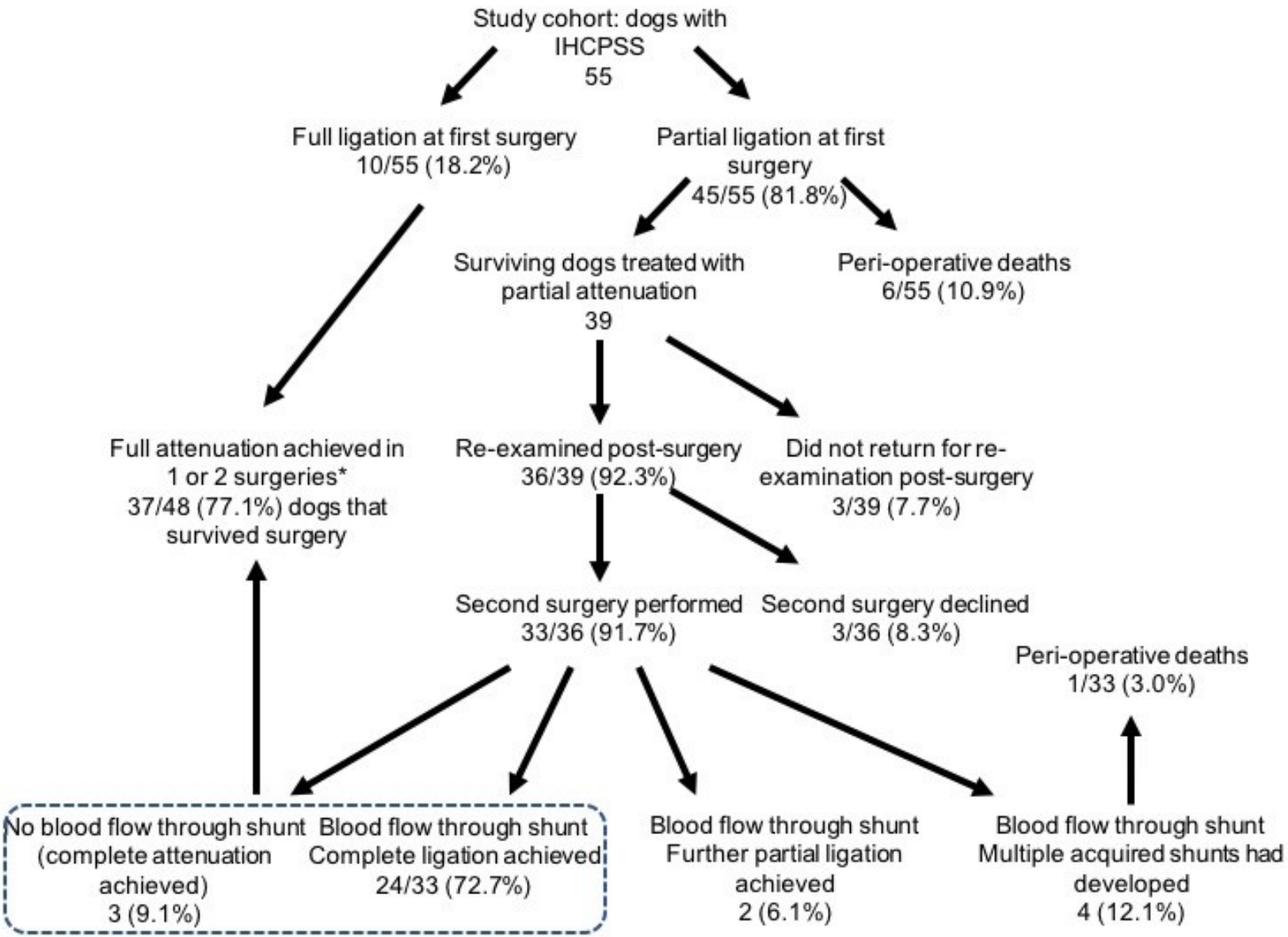
complications and a good rate of complete attenuation. The long-term outcome was excellent in a high proportion (82.4%) of dogs that had complete attenuation in one or two surgeries, compared to those with persistent shunting where a minority (20%) had an excellent outcome. Further work is needed to clarify the exact significance of persistent shunting on long-term outcome and quality of life.

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.

Figure Legends

Figure 1: Flow diagram showing the short-term follow-up and second surgery in dogs initially treated with partial ligation of an intrahepatic congenital portosystemic shunt (IHCPSS). * Despite complete ligation of their CPSS, two dogs were subsequently identified to have persistent flow through their CPSS. Both dogs had full attenuation achieved in an additional surgery. In addition, multiple acquired shunts were subsequently identified on imaging in two dogs.


Study cohort: dogs with IHCPSS
55
Full ligation at first surgery
10/55 (18.2%)
Partial ligation at first surgery
45/55 (81.8%)
Surviving dogs treated with partial attenuation
39
Peri-operative deaths
6/55 (10.9%)
Full attenuation achieved in 1 or 2 surgeries*
37/48 (77.1%) dogs that survived surgery
Re-examined post-surgery
36/39 (92.3%)
Did not return for re-examination post-surgery
3/39 (7.7%)
Second surgery performed
33/36 (91.7%)
Second surgery declined
3/36 (8.3%)
Peri-operative deaths
1/33 (3.0%)
No blood flow through shunt (complete attenuation achieved)
3 (9.1%)
Blood flow through shunt Complete ligation achieved
24/33 (72.7%)
Blood flow through shunt Further partial ligation achieved
2 (6.1%)
Blood flow through shunt Multiple acquired shunts had developed
4 (12.1%)

Sex	Male entire 21 (38.2%)	Male neutered 7 (12.7%)	Female entire 25 (45.5%)	Female neutered 2 (3.6%)
Age	Median 7.1 months (range 2.4-38.2)			
Weight	Median 17.3kg (range 3.1-50.0)			
Breed	Labrador			15
	Crossbreed, Golden Retriever			5 per breed
	Border Collie, Border Terrier, Cavalier King Charles Spaniel, German Shepherd Dog, Samoyed, Staffordshire Bull terrier			2 per breed
	Basset Hound, Beagle, British Bulldog, Cocker Spaniel, Flat Coat Retriever, Grand Basset Griffon Vendeen, Great Dane, Hovawort, Irish Water Spaniel, Irish Wolfhound, Labradoodle, Lurcher, Newfoundland, Old English Sheepdog, Pyrenean Mastiff, Rhodesian Ridgeback, St. Bernard, Weimaraner			1 per breed
Duration of clinical signs prior to surgery	Median 49 days (range 12-289)			
Medical management prior to surgery (all dogs)	Prescription diet 47 (85.5%)	Antibiotics 51 (92.7%)	Lactulose 54 (98.2%)	
Duration of medical management	Median 25 days (range 6-289)			
Improvement following medical management	Good 36 (65.5%)	Moderate 17 (30.9%)	Poor 2 (3.6%)	
Pre-prandial bile acids / μmo/l	Measured in 46 Median 89.5 (range 3.4-614.2)			
Postprandial bile acids / μmo/l	Measured in 45 Median 207.7 (range 19.7-668.0)			

Table 1: Signalment data and pre-surgical information for 55 dogs undergoing suture ligation for the treatment of an intrahepatic congenital portosystemic shunt (IHCPSS)

Intrahepatic CPSS morphology	Left division 26 (47.3%)	Central division 14 (25.4%)	Right division 15 (27.3%)
Degree of attenuation tolerated	Partial ligation 45 (81.8%)	Complete ligation 10 (18.2%)	
Suture material used	Polypropylene 53 (96.4%)	Silk 1 (1.8%)	Silk and polypropylene 1 (1.8%)
NSAIDs given intra or postoperatively	No 42 (76.4%)	Yes 13 (23.6%)	

Table 2: Details of surgical variables for 55 dogs undergoing suture ligation for the treatment of an intrahepatic congenital portosystemic shunt (IHCPSS).

Complication classification	Number of dogs with complications (%)	Signalment	Shunt morphology	Degree of attenuation	Complication details	Mortality
Neurological	5 /55 (9.1%)	Male entire, 11.8-month-old, Cavalier King Charles Spaniel	Central	Partial	Several seizures post-operatively – treated with phenobarbitone and potassium bromide.	0
		Female entire, 7.4-month-old, Old English Sheepdog	Left	Complete	Altered mentation and ataxia – treated with phenobarbitone.*	
		Male entire, 7.1-month-old, Grand Basset Griffon Vendeen	Left	Partial	Mild facial twitching – treated with levetiracetam.	
		Male neutered, 29.1-month-old, Beagle	Central	Complete	Suffered a seizure post-operatively (although had seizure prior to surgery) – treated with phenobarbitone and continued levetiracetam.	
		Female entire, 10.1-month-old, Labrador	Central	Complete	Ataxia, depression and blindness – treated with phenobarbitone.	
Portal Hypertension / Gastrointestinal	14/55 (25.5%)	Male entire, 4.3-month-old, Flat Coat Retriever	Left	Partial	Severe haematomesis, melena, hypovolaemic shock – exploratory laparotomy, no obvious portal hypertension – **died**. Post-mortem - severe gastrointestinal haemorrhage.	6
		Male neutered, 38.2-month-old, Border Collie	Right	Partial	Acute hypotension and hypovolaemic shock – exploratory laparotomy, perforated gastric ulcer, further gastric ulceration and septic peritonitis – **euthanasia**. No post-mortem.	
		Male entire, 14.4-month-old, Labrador	Central	Partial	Regurgitation followed by two serious episodes of gastrointestinal haemorrhage – **euthanasia**. Post mortem showed duodenal ulceration.	
		Male entire, 9.2-month-old, Pyrenean Mastiff	Central	Partial	Hypoproteinaemic with ascites and pleural effusion, suspected portal hypertension. Respiratory crisis, suspect pulmonary thromboembolus – **euthanasia**. No post-mortem.	
		Male entire, 5.4-month-old, Labrador	Central	Partial	Mild, self-limiting ascites.‡	
		Male entire, 15.4-month-old, Labrador	Left	Complete	Mild, self-limiting ascites.	

		Female entire, 6.4-month-old, Labrador	Left	Partial	Mild, self-limiting ascites.	
		Female entire, 3.4-month-old, Labrador	Left	Partial	Moderate, self-limiting ascites.	
		Female entire, 7.4-month-old, Old English Sheepdog	Left	Complete	Regurgitation – treated with omeprazole.*	
		Female entire, 2.7-month-old, St. Bernard	Left	Complete	Vomiting.†	
		Male Entire, 5.4-month-old, Labrador	Central	Partial	Vomiting.‡	
		Male neutered, 17.8-month-old, Labrador	Central	Partial	Vomiting.	
		Female entire, 12-month-old, Bassett Hound	Left	Partial	Vomiting.	
		Male neutered, 23-month-old, Irish Wolfhound	Left	Partial	Discharged without complications, however developed haematomesis and melena the following day – supportive treatment – **died**. No post-mortem.	
		Female neutered, 24.8-month-old, Labrador	Left	Partial	Discharged without complication, however developed vomiting and lethargy the following day. Re-examination confirmed hypovolaemic shock and ascites – portal thrombus suspected – **euthanasia**. No post-mortem.	
Miscellaneous	7/55 (12.7%)	Female entire, 9.8-month-old, German Shepherd Dog	Central	Partial	Hypotensive post-operatively – treated with two units of plasma	0
		Male entire, 4.4-month-old, Border Terrier	Central	Complete	Mild anaemia post-operatively – received blood transfusion	
		Female entire, 2.7-month-old, St. Bernard	Left	Complete	Wound infection – treated with antibiotics.†	
		Female entire, 4.5-month-old, Great Dane	Right	Partial	Septic arthritis of elbow – treated with antibiotics and drainage.	
		Female entire, 3.9-month-old, Golden Retriever	Right	Partial	Septic arthritis of stifle – treated with antibiotics.	
		Male neutered, 18-month-old, Rhodesian Ridgeback	Right	Partial	Immune mediated polyarthritis – responded well to analgesia.¶	

		Male neutered, 18-month-old, Rhodesian Ridgeback	Right	Partial	Ventricular premature complexes seen for 24 hours.¶	
		Male entire, 7.1-month-old, Border Collie	Left	Partial	Ventricular tachycardia post-operatively.	

Table 3: Table showing the details of post-operative complications in 55 dogs undergoing initial suture ligation for the treatment of an intrahepatic congenital portosystemic shunt (IHCPSS).

*¶†‡ Dogs suffered two complications post-operatively.

Time between surgery and re-examination	Median 102 days (range 48-358)		
Improvement following surgery	Good 25 (69.4%)	Moderate 10 (27.8%)	Poor 1 (2.8%)
Medical management at re-examination (31/36 dogs – 86.1%)	Prescription diet 30 (83.3%)	Antibiotics 17(47.2%)	Lactulose 23 (63.9%)
Pre-prandial bile acids / μmo/l	Measured in 26 Median 57.6 (range 0.4-291.9)		
Postprandial bile acids / μmo/l	Measured in 27 Median 172.1 (range 2.7-549.0)		

Table 4: Re-examination information for 36/39 dogs initially treated with partial suture ligation for the treatment of an intrahepatic congenital portosystemic shunt (IHCPSS).

Time interval between surgeries	Median 103 days (range 48-358)			
Sex distribution at second surgery	Male entire 10 (30.3%)	Male neutered 3 (9.1%)	Female entire 20 (60.6%)	Female neutered (0%)
Age at second surgery	Median 9.5 months (range 6.4-26.4)			
Weight at second surgery	Median 20.7kg (range 5.1-45.7)			
Breeds represented at second surgery	Labrador			10
	Crossbreed, Golden Retriever			5
	Golden Retriever			3
	German Shepherd Dog, Staffordshire Bull terrier			2 per breed
	Basset Hound, Border Terrier, British Bulldog, Cavalier King Charles Spaniel, Cocker Spaniel, Grand Basset Griffon Vendeen, Great Dane, Hovawort, Irish Water Spaniel, Labradoodle, Rhodesian Ridgeback			1 per breed
Intrahepatic CPSS morphology at second surgery	Left division 16 (48.5%)	Central division 6 (18.2%)	Right division 11 (33.3%)	
Degree of attenuation tolerated	Complete ligation 25 (75.8%)	Partial ligation 2 (6.1%)	Progressed to full attenuation (no flow on portovenography) 3 (9.1%)	Multiple acquired shunts had developed 3 (9.1%)
NSAIDs given intra or postoperatively	No 23 (69.7%)		Yes 10 (30.3%)	

Table 5: Further information for 33 dogs undergoing a second surgery following initial partial suture ligation for the treatment of an intrahepatic congenital portosystemic shunt (IHCPSS).

Complication Classification	Number of dogs with complications (%)	Signalment	Shunt morphology	Degree of attenuation	Complication Details	Mortality
Neurological	2 (6.1%)	Male entire, 6.5-month-old, Labrador	Left	Multiple acquired shunts had developed	Several seizures postoperatively – treated with phenobarbitone.	1
		Female entire, 13.9-month-old, German Shepherd dog	Central	Multiple acquired shunts had developed	Discharged without complications. However, developed neurological signs later that day Re-examined by referring veterinary surgeon – **euthanasia.**	
Miscellaneous	6 (18.2%)	Male neutered, 12.4-month-old, Labrador	Left	Complete	Urinary tract infection– responded well to antibiotics.	0
		Female entire, 10.9-month-old, Cavalier King Charles Spaniel	Left	Complete	Diarrhoea.	
		Female entire, 15.8-month-old, British Bulldog	Central	Progressed to full attenuation (no flow on portovenography)	Pyrexia and neutrophilic abdominal effusion, presumed post-operative peritonitis – treated successfully with antibiotics.	
		Female entire, 10.9-month-old, crossbreed	Right	Complete	Haemorrhage from ovarian pedicle following ovariohysterectomy – blood transfusion, exploratory laparotomy and re-ligation.	
		Female entire, 11.6-month-old, Labrador	Left	Partial (complete ligation prevented by adhesions)	Mild bleeding from abdominal wound – resolved with supportive treatment.	
		Male entire, 7.1-month-old, Grand Basset Griffon Vendeen	Left	Complete	Mild scrotal swelling after castration.	

Table 6: Table showing the details of post-operative complications in 33 dogs undergoing repeat surgery for the attenuation of an intrahepatic congenital portosystemic shunt IHCPSS.

Time between surgery and re-examination	Median 121.5 days (range 78-388)		
Improvement following surgery	Good 6 (75.0%)	Moderate 1 (12.5%)	Poor 1 (12.5%)
Pre-prandial bile acids / μmo/l	Measured in 5 Median 14.9 (range 1.2-274.0)		
Postprandial bile acids / μmo/l	Measured in 5 Median 22.3 (range 1.7-503.1)		

Table 7: Re-examination information for 8/10 dogs (80%) initially treated with complete suture ligation for the treatment of an intrahepatic congenital portosystemic shunt (IHCPSS).

Time between surgery and re-examination	Median 105.5 days (range 32-180)		
Improvement following surgery	Good 11 (78.6%)	Moderate 3 (21.4%)	Poor 0 (0%)
Pre-prandial bile acids / μmo/l	Measured in 11 Median 40.6 (range 2.1-237.1)		
Postprandial bile acids / μmo/l	Measured in 9 Median 183.3 (range 3.3-378.0)		

Table 8: Re-examination information following second surgery for 14/32 dogs (43.8%) initially treated with partial suture ligation for the treatment of an intrahepatic congenital portosystemic shunt (IHCPSS).

Time between surgery and follow-up	Median 29 months (range 7.4-103.1)				
Overall outcome	Excellent 15 (68.2%)		Fair 5 (22.7%)		Poor 2 (9.1%)
Surgical treatment and overall outcome	Complete ligation at 1st surgery 4 (18.2%) Excellent - 4 Fair - 0 Poor - 0	Partial ligation at 1st surgery and no repeat surgery 2 (9.1%) Excellent - 0 Fair - 2 Poor - 0	Complete ligation in two procedures 12 (54.5%) Excellent - 9 Fair - 2 Poor - 1	Progressed to complete attenuation following partial ligation 1 (4.5%) Excellent - 1 Fair - 0 Poor - 0	Development of multiple acquired shunts documented* 3 (13.6%) Excellent - 1 Fair - 1 Poor - 1
Overall outcome based on surgical outcome	Complete attenuation of shunt (in one or two surgeries) 17 (77.3%) Excellent - 14 (82.4%) Fair – 2 (11.7%) Poor – 1 (5.9%)		Documented or presumed persistent shunting due to incomplete attenuation or multiple acquired shunts 5 (22.7%) Excellent – 1 (20%) Fair – 3 (60%) Poor – 1 (20%)		
Pre-prandial bile acids / μmo/l	Measured in 9 Median 11.5 (range 0.7-257.4)				
Postprandial bile acids / μmo/l	Measured in 9 Median 130.5 (range 2.3-381.8)				

Table 9: Long-term follow-up information for 22 dogs surgically treated for an intrahepatic congenital portosystemic shunt (IHCPSS) that were alive at the time of the study.

*Two documented on portovenography at repeat surgery following partial ligation and one documented on ultrasound following complete ligation in two procedures.

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