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REVIEW

Treatment of intrahepatic congenital portosystemic shunts in dogs: a systematic review

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The aim of this study was to establish the evidence base for the treatment of intrahepatic congenital portosystemic shunts in dogs through a systematic review of the pertinent literature. Studies were filtered for evidence to answer the question "Which of the treatment options for intrahepatic CPSS in dogs offers the best short- and long-term outcome?" Studies were assigned a level of evidence based on a system published by the Oxford Centre for Evidence-Based Medicine. Thirty-two studies were included in the review. Twenty-six provided level 4 evidence and six provided level 5 evidence. There were no level 1, 2 or 3 studies. One study compared surgical treatment with medical management and one study compared suture ligation with ameroid constrictor placement. The remaining studies were case series describing the outcome for one treatment method alone. Methods and timings of assessments of short- and long-term outcomes were highly varied, making direct comparisons challenging. The evidence regarding the treatment of intrahepatic congenital portosystemic shunts in dogs is weak, with only two studies directly comparing treatments. There is a lack of evidence regarding short- and long-term outcomes on which to base clinical decisions.

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INTRODUCTION

A variety of treatments have been recommended for dogs with intrahepatic congenital portosystemic shunts (CPSS) (White *et al.* 1998, Hunt *et al.* 2004, Adin *et al.* 2006, Mehl *et al.* 2007, Berent & Tobias 2009, Weisse *et al.* 2014). Surgical intervention to acutely or gradually attenuate the abnormal vessel is recommended for most dogs (Berent & Tobias 2009, Greenhalgh *et al.* 2014). Improving or restoring normal portal blood flow typically resolves clinical signs and improves biochemical parameters (Breznock *et al.* 1983, White *et al.* 1998). However, incomplete treatment because of persistent shunting or the development of multiple acquired shunts can result in ongoing or recurrent clinical signs (White *et al.* 1998, Kummeling *et al.* 2004). Long-term medical management can also be used in animals if surgery is not available or is declined by the owner (Watson & Herrtage 1998, Greenhalgh *et al.* 2014).

For many years, surgical attenuation of intrahepatic CPSS was the recommended treatment, using suture ligation, an ameroid constrictor, a cellophane band or a hydraulic occluder (Komtebedde *et al.* 1991, White *et al.* 1998, Papazoglou *et al.* 2002, Hunt *et al.* 2004, Adin *et al.* 2006, Mehl *et al.* 2007). However, it is recognised that intrahepatic CPSS can be more challenging to treat surgically than extrahepatic CPSS due to the location of the abnormal vessel within the liver parenchyma. Different strategies have been used to access the CPSS for attenuation; the optimal method depends on the morphology of the CPSS. Extravascular surgery involves dissection of the CPSS itself, the draining hepatic vein or the portal vein branch supplying it. Reports have also described intravascular techniques to allow attenuation of some intrahepatic CPSS, which is technically more demanding

JSAP JOURNAL OF SMALL ANIMAL PRACTICE

(Breznock *et al.* 1983, Hunt *et al.* 1996, White *et al.* 1998). Concern over perioperative complications and mortality has prompted the development of a minimally invasive treatment for intrahepatic CPSS (Bussadori *et al.* 2008, Weisse *et al.* 2014). Endovascular coil embolisation with interventional radiology has been recommended to reduce complications and mortality associated with traditional surgical techniques (Weisse *et al.* 2014). Whilst many authorities recommend certain treatments, there is a lack of a consensus on which is best. Establishing the evidence base for the treatment of dogs with intrahepatic CPSS is very important to allow owners and veterinary surgeons to make informed decisions.

A previous review assessed the evidence base for the surgical treatment of extrahepatic CPSS in dogs (Tivers *et al.* 2012). Published studies on CPSS in dogs were graded on the level of evidence that they provided to answer this question. This previous review reported that the evidence base for the treatment of extrahepatic CPSS in dogs was weak, meaning that it was not possible to make firm recommendations.

We therefore undertook a systematic review of the current literature to determine the evidence base for the treatment of intrahepatic CPSS in dogs. The aim of the study was to assess the evidence base with a view to identify whether a single treatment could be recommended based on short- and long-term outcomes.

MATERIALS AND METHODS

The following question was formulated to establish the evidence base for the treatment of intrahepatic CPSS in dogs: "Which of the treatment options for intrahepatic CPSS in dogs offers the best short- and long-term outcome?" An online bibliographic search was performed in November 2016 for studies relating to the treatment of intrahepatic CPSS in dogs. The search utilised the PubMed (http://www.pubmed.gov/) and ISI Web of Science (http://wok.mimas.ac.uk/) databases. Databases were searched using the following terms: (portosystemic shunt OR portocaval shunt OR portovascular anomaly OR portosystemic communication OR intrahepatic vascular anomaly OR intrahepatic shunt) AND (dog OR canine OR canid) AND (treatment OR outcome OR mortality OR morbidity OR complications). Following this process, the databases were also searched using the following terms: [portosystemic shunt(s) OR portocaval shunt(s)] AND dog. This was to ensure that any studies not captured in the original, more specific search, were included.

Analysis was restricted to the English-language veterinary literature reporting information on the treatment of intrahepatic CPSS in dogs. The abstracts were reviewed for relevance to the question. Studies were excluded if they were experimental, described only acquired PSS or extrahepatic CPSS, were case reports or small case series (<five dogs) or did not provide any detail regarding outcome (*e.g.* studies describing diagnostic tests).

Studies meeting these criteria were reviewed by the primary author and were assigned a level of evidence based on the system published by the Oxford Centre for Evidence-Based Medicine (OCEBM Levels of Evidence Working Group 2017) (Table 1).

The following data were recorded from each study: the type of study described (*i.e.* case series, cohort study, *etc.*); the number of dogs included; the treatment used; the short-term mortality; and the long-term outcome, including duration of follow-up and method of assessment. It was anticipated that the type of outcomes reported, particularly for long-term outcomes, would vary between studies. Therefore, the method of outcome assessment, the timing and the result were also recorded.

RESULTS

Thirty-two studies were identified as providing relevant information for answering the question (Table 2). Twenty-six were classified as level 4, and the remaining six were classified as level 5. There were no level 1, 2 or 3 studies.

Direct comparison of different treatments

Three studies were identified that compared the outcome of two different treatments (Mehl *et al.* 2007, Greenhalgh *et al.* 2010, Greenhalgh *et al.* 2014). Two of these studies described a prospective comparison of medical and surgical management in the same cohort of dogs, so the more recent paper was chosen to represent this data set (Greenhalgh *et al.* 2010, Greenhalgh *et al.* 2014). This was a prospective cohort study that directly compared the short- and long-term outcomes for 27 dogs treated with medical management and 97 dogs treated with surgical attenuation (Greenhalgh *et al.* 2014). The study included 110 dogs with extrahepatic CPSS and 14 dogs with intrahepatic CPSS. Eight of the intrahepatic CPSS dogs had surgery and six were treated medically. Long-term follow-up was conducted using owner questionnaires and telephone calls with owners and the referring veterinary surgeons. Of 27 dogs treated medically, 24 (89%) died or were euthanased during the follow-up period. The median survival time was 836 days.

Table 1. Taken from Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence (OCEBM Levels of Evidence Working Group 2017)

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
Does this intervention help? (treatment benefits)	Systematic review of randomised trials or *n*-of-1 trials	Randomised trial or observational study with dramatic effect	Non-randomised controlled cohort/ follow-up study†	Case series, case–control studies or historically controlled studies†	Mechanism-based reasoning

*Level may be graded down based on study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies or because the absolute effect size is very small. Level may be graded up if there is a large or very large effect size.
†As always, a systematic review is generally better than an individual study.

Table 2. Summary of studies providing evidence for the treatment of intrahepatic CPSS in dogs

Level of evidence	Type of study	Papers included
Level 4	Non-randomised prospective cohort study	• Greenhalgh *et al.* (2010) *Journal of the American Veterinary Medical Association* • Greenhalgh *et al.* (2014) *Journal of the American Veterinary Medical Association*
	Non-randomised retrospective cohort study	• Mehl *et al.* (2007) *Veterinary Surgery*
	Case series – describing outcome for one treatment method with no control group	• Breznock *et al.* (1983) *Journal of the American Veterinary Medical Association* • Komtebedde *et al.* (1991) *Veterinary Surgery* • Bostwick & Twedt (1995) *Journal of the American Veterinary Medical Association* • Smith *et al.* (1995) *Journal of Small Animal Practice* • Hunt *et al.* (1996) *Veterinary Surgery* • Watson & Herrtage (1998) *Journal of Small Animal Practice* • White *et al.* (1998) *Veterinary Record* • Kyles *et al.* (2001) *Veterinary Surgery* • Papazoglou *et al.* (2002) *Veterinary Surgery* • Winkler *et al.* (2003) *Journal of the American Animal Hospital Association* • Hunt *et al.* (2004) *Veterinary Surgery* • Kummeling *et al.* (2004) *Veterinary Surgery* • Kyles *et al.* (2004) *Veterinary Surgery* • Adin *et al.* (2006) *Journal of the American Veterinary Medical Association* • Bright *et al.* (2006) *Veterinary Surgery* • Kummeling *et al.* (2006) *Journal of Veterinary Internal Medicine* • Bussadori *et al.* (2008) *The Veterinary Journal* • Parker *et al.* (2008) *Journal of the American Veterinary Medical Association* • Schneider *et al.* (2009) *Veterinary Radiology and Ultrasound* • Weisse *et al.* (2014) *Journal of the American Veterinary Medical Association* • Knapp *et al.* (2015) *Research in Veterinary Science*
Level 5	Case series – not providing good information on outcome	• Swalec & Smeak (1990) *Veterinary Surgery* • Meyer *et al.* (1999) *Veterinary Record* • Tisdall *et al.* (2000) *Journal of Small Animal Practice* • Wolschrijn *et al.* (2000) *Veterinary Quarterly* • Szatmari *et al.* (2003) *Journal of Veterinary Internal Medicine* • Lee *et al.* (2006) *Journal of the American Veterinary Medical Association* • Lee *et al.* (2011) *Journal of the American Veterinary Medical Association* • Kummeling *et al.* (2012) *The Veterinary Journal*

Of 97 dogs treated surgically, 21 (22%) died or were euthanased during the follow-up period. This included five dogs (5·2%) that died in the perioperative period (≤seven days after surgery), including one dog that died following a second surgery. Seven dogs (7·2%) in the surgery group were lost to follow-up. It was not possible to estimate median survival for the surgically treated dogs due to the large number that were still alive at follow-up. The survival rate for surgically treated dogs was statistically significantly greater than that of those managed medically. There was no significant effect of shunt type (extrahepatic *versus* intrahepatic) on survival. The frequency of ongoing clinical signs was statistically significantly better for surgically treated dogs (completed questionnaires from 46/75 dogs alive) compared with medically treated dogs (completed questionnaires from 6/9 dogs alive) four to seven years after study entry.

There was a single retrospective study comparing the outcomes for dogs with left divisional intrahepatic CPSS treated with suture ligation and ameroid constrictors (Mehl *et al.* 2007). This study reported the short- and long-term outcomes for 17 dogs treated with partial ligation, and 11 dogs treated with ameroid constrictors. Two dogs in the partial ligation group (11·8%) and one dog in the ameroid constrictor group (9·1%) suffered postoperative complications. Overall, one dog died in the partial ligation group (5·9%) due to severe coagulopathy and one dog died in the ameroid constrictor group (9·1%) due to postoperative seizures. There was not a significant difference in the surgical morbidity or mortality between the two techniques. A proportion of the dogs had portal scintigraphy performed at 6 to 10 weeks postsurgery. Persistent shunting was identified in seven of eight dogs in the partial ligation group (87·5%) and in three of seven dogs in the ameroid constrictor group (42·9%). There was not a statistically significant difference in the proportion of dogs with persistent shunting on scintigraphy between the two groups. Long-term clinical outcome was assessed *via* a telephone questionnaire with the owner or referring veterinary surgeon. An excellent outcome was defined as "dogs that were free of any clinical signs and not on any special dietary requirements or medications", a good outcome included "dogs that were perceived to be clinically normal according to the owners, and were maintained on low protein diets, medical therapy or both" and a poor outcome included "dogs that showed no improvement after surgery and remained symptomatic for a PSS or had worsening clinical signs" (Mehl *et al.* 2007). Outcomes were obtained for 13 dogs in the partial ligation group at a median of 50 months (range 6 to 122) after surgery and for 10 dogs in the ameroid constrictor group at a median of 28·5 months (range 14 to 54) after surgery. In the partial ligation group, outcomes were excellent in 12 of 13 (92%) and good in 1 of 13 (8%) animals. The dog with a good outcome had persistent flow through the shunt. A second surgery was performed and complete attenuation was achieved, resulting in an excellent outcome for this dog. In the ameroid constrictor group, the outcome was excellent in 2 of 10 (20%), good in 5 of 10 (50%) and poor in 3 of 10 (30%).

The three dogs with a poor outcome had all been euthanased due to signs of hepatic insufficiency at 14, 19 and 27 months after surgery. The long-term outcome, in terms of grade, was significantly better in dogs treated with suture ligation compared with ameroid constrictors.

Case series reporting the outcome for one treatment

There were 21 studies that were case series reporting either short-term or long-term outcomes, or both, for a single treatment for intrahepatic CPSS in dogs. Two of these were prospective studies and the remainder were retrospective. Sixteen studies described various types of surgical treatment, and these are summarised in Table 3. Four studies described endovascular coil embolisation, and these are summarised in Table 4. One study described medical management, and this is summarised in Table 5.

An additional eight studies were identified that were level 5 evidence (Table 2). Whilst they contained some information on outcomes, this was either insufficient to justify their inclusion or it was not possible to differentiate the outcome data for dogs with intrahepatic CPSS from those with extrahepatic CPSS. A summary of short- and long-term outcomes for different surgical procedures (including endovascular coil embolisation) is presented in Table 6. For suture ligation and endovascular coil embolisation, this included the larger studies only.

DISCUSSION

This systematic review of the literature regarding the treatment of intrahepatic CPSS in dogs reveals that the evidence base for recommending any one type of treatment is very weak. When attempting to determine the most effective treatment or intervention for a given disease or condition, the decision should ideally be based on the most reliable evidence available. There are several systems available that can be used to rank evidence (Howick *et al.* 2017). A previous review of the evidence base for the treatment of extrahepatic CPSS in dogs used a modification of an existing grading system (Tivers *et al.* 2012). This system was published by the Oxford Centre for Evidence-Based Medicine but has subsequently been revised (OCEBM Levels of Evidence Working Group 2017). The revised version was designed so that the structure reflects clinical decision-making and is simpler, refraining from making definitive recommendations (Howick *et al.* 2017). Importantly, unlike other systems, it is suitable for use when no systematic reviews are available (Howick *et al.* 2017). The current review used the revised version as we believed that these modifications made it more suitable for application to the veterinary literature.

It is generally accepted that systematic reviews of randomised controlled trials (RCTs) provide the most reliable evidence. Unfortunately, RCTs are very uncommon in veterinary literature. Perhaps unsurprisingly, the current review did not identify any level 1, 2 or 3 studies reporting the outcome for dogs with intrahepatic CPSS. Most studies were level 4 case series describing the outcome of a single treatment. Therefore, the evidence available to make decisions on which treatment to use is very limited. Several studies were level 5, providing minimal evidence to answer the question. These studies either did not provide any useful information regarding outcome or provided combined outcome data for intrahepatic and extrahepatic CPSS, and it was not possible to separate these out. This is not intended as a criticism of these studies, rather that they did not provide good evidence for the question asked in the current review.

We did not attempt to categorise the level 4 studies further, although Table 2 does show the types of study represented. There was one prospective cohort study that compared the outcomes of surgical treatment with those of medical treatment (Greenhalgh *et al.* 2014). The results of this study strongly support the use of surgical treatment over medical management for most dogs. However, it should be recognised that although this study was prospective, it was not randomised, and there may have been significant selection bias affecting the distribution of dogs into the two treatment groups. In addition, the study included dogs treated with a variety of techniques, and it is therefore difficult to determine the effect of a given surgery. Importantly, the study included dogs with both intrahepatic CPSS and extrahepatic CPSS, and it was not possible to separate the data for the two groups in detail (although morphology did not appear to influence survival). There was also a relatively small number of dogs with intrahepatic CPSS, with eight treated surgically and six managed medically.

A single study retrospectively compared dogs treated with partial suture ligation with those treated with ameroid constrictor placement (Mehl *et al.* 2007). This study found that there was no difference in perioperative complications and mortality but that the long-term outcome was significantly better for those dogs treated with suture ligation. This study had good long-term follow-up, but there were relatively small numbers of dogs in both groups (17 suture ligation and 11 ameroid constrictor). It is noteworthy that this report only described dogs with one type of intrahepatic CPSS (left divisional). It is therefore unclear if these results can be extrapolated to other morphologies of intrahepatic CPSS.

The remaining studies were case series describing the outcome for one type of treatment only, including surgical techniques, endovascular coil embolisation and medical management (summarised in Tables 3–5). However, several studies reported more than one surgical technique, which makes drawing firm conclusions on individual treatments difficult. Some studies described dogs that had suture ligation, intravascular attenuation with or without placement of mattress sutures or hemoclips (Breznock *et al.* 1983, Komtebedde *et al.* 1991, White *et al.* 1998). It is arguable that these can be considered one group because they are techniques providing acute attenuation, and the choice is dictated largely by the morphology of the shunt. However, it is well recognised that intravascular techniques are more complex and technically demanding, and their use in some case series and not in others may have skewed the results. Two other studies report dogs treated with a variety of techniques, including

Table 3. Summary of articles reporting short-term (perioperative mortality) and/or long-term outcome of surgical treatment of intrahepatic congenital portosystemic shunts (CPSS) in dogs

Article	Number of dogs	Surgical technique	Perioperative mortality	Follow-up period	Follow-up and long-term outcome
Breznock *et al.* (1983) *Journal of the American Veterinary Medical Association*	12	9 – suture ligation 3 – intravascular attenuation	3/12 (25%)	See adjacent long-term outcome section	All dogs had repeat biochemistry and ammonia tolerance testing at 2 to 10 months postsurgery and showed markedly improved hepatic function. Two dogs were euthanased due to unrelated disease at six to eight months and 10 months. Seven dogs were clinically normal six months to three years after surgery with biochemical improvements consistent with improved hepatic function.
Komtebedde *et al.* (1991) *Veterinary Surgery*	13	11 – suture ligation 2 – hemoclips	3/13 (23·1%)	12 to 46 months	Follow-up via telephone interview with owner. All 10 dogs doing well and all owners considered their dog to be behaving normally. However, one dog had occasional focal seizure activity and one dog had infrequent periods of mild depression.
Bostwick & Twedt (1995) *Journal of the American Veterinary Medical Association**	15	Suture ligation	2/15 (13·3%)	See adjacent long-term outcome section	Follow-up via direct contact with owner or veterinary surgeon. Of the 13 surgically treated dogs, three dogs died of related disease at 1, 2 and 14 months after surgery. Ten dogs were alive or died of unrelated causes at a mean of 38 months postsurgery (standard deviation ±29). Two dogs had repeat surgery to achieve complete ligation of their shunt.
Smith *et al.* (1995) *Journal of Small Animal Practice**	11	Suture ligation	Not reported	Median 36 months (range 3 to 84)	Follow-up with owner questionnaire. Five dogs had recurrence of clinical signs at <3 to 24 months of age, and two of these dogs were euthanased at 3 and 12 months of age. Owners considered their dog's quality of life after surgery to be excellent or good in nine dogs and poor in two.
Hunt *et al.* (1996) *Veterinary Surgery*	9	Intravascular attenuation	2/9 (22·2%) Including one dog euthanased due to portal vein hypoplasia	See adjacent long-term outcome section	Follow-up with owner and repeated clinical examination and biochemical testing in 5/7 dogs. Four dogs normal at 6, 20, 21 and 26 months after surgery (although one on restricted protein diet). Two re-examined and ammonia tolerance testing normal. Three dogs suffered recurrent signs at two weeks, six months and 12 months after surgery. Revision surgery performed to increase attenuation in all three, although one dog required further revision surgery. All significantly improved or considered normal.
White *et al.* (1998) *Veterinary Record*	45	37 – suture ligation 8 – intravascular attenuation	8/45 (17·8%)	Mean 16 months (range 1 to 66)	Short-term follow-up at 1-month after surgery with re-examination, biochemical testing (bile acids), ultrasound +/− scintigraphy. Long-term follow-up via telephone contact with owner. Follow-up was available for all 37 surviving dogs; 28 (75·7%) became clinically normal and required no medication or diet (in seven scintigraphy at one to six months after surgery showed no shunting). Nine dogs showed persistent or recurrent clinical signs or their laboratory data were consistent with continued shunting. Three of these dogs were euthanased at the owners' request. Repeat surgery was performed in six dogs, with three of these being euthanased due to failure to ligate the shunt, and in the other three, the shunt was successfully completely attenuated. These three dogs became clinically normal with no long-term biochemical abnormalities.

Table 3 (Continued)

Article	Number of dogs	Surgical technique	Perioperative mortality	Follow-up period	Follow-up and long-term outcome
Kyles *et al.* (2001) *Veterinary Surgery*	10	Portocaval venograft and ameroid constrictor	1/10 (10%)	See adjacent long-term outcome section	8/9 dogs were re-examined at 8 to 10 weeks after surgery. Six dogs normal with excellent outcome and two dogs had good outcome (one dog was not re-examined as owner considered it normal). There was no shunting on scintigraphy in three dogs and continued shunting in five dogs. Four of the dogs with persistent shunting on scintigraphy were re-examined at 16 to 52 weeks. All four had continued shunting documented on scintigraphy, and this was confirmed to be due to multiple acquired shunts. At final re-check examination in eight dogs and one dog via telephone conversation at 8 to 52 weeks after surgery, the clinical outcome was considered to be excellent, with no dogs receiving medical treatment or special diet.
Papazoglou *et al.* (2002) *Veterinary Surgery*	32	20 – suture ligation 6 – mattress sutures 2 – unknown 1 – ameroid constrictor 1 – intravascular attenuation 1 – portocaval venograft and partial ligation	4/32 (12·5%)	Median 82 days (range 6 to 1746)	Long-term survival determined from clinical records or telephone contact with owner; 50% survival time was 35·68 months. One-year and Two-year probabilities of survival were 60% and 55%, respectively. Overall, 13 dogs (40·6%) died of related causes and one dog died of unrelated causes. Ten dogs were lost to follow-up after a median of 66 days (range 7·8 to 1137·3).
Winkler *et al.* (2003) *Journal of the American Animal Hospital Association*	5	Suture ligation	1/5 (20%)	See adjacent long-term outcome section	One dog had persistent shunting on ultrasound at six weeks after surgery and mild increases in bile acids. No clinical signs on medical management at four years after surgery. One dog was suspected to have portal hypertension on ultrasound at four months after surgery and mild increases in bile acids. No clinical signs. One dog was lethargic and had increased bile acids at seven months after surgery. No further attenuation possible at repeat surgery. No clinical signs on medical management at 11 months. One dog lost to follow-up.
Hunt *et al.* (2004) *Veterinary Surgery*	11	Cellophane band	3/11 (27·3%)	2·25 months (range 2 to 6) –includes extrahepatic dogs	Postoperative evaluation of liver function performed in 7/8 surviving dogs. Hepatic function normal in 5/7 dogs (71·4%). Four dogs had abnormal liver function testing suggestive of persistent shunting. One of these dogs had ascites 10 days after surgery, suggestive of portal hypertension, and repeat surgery in one dog revealed multiple acquired shunts.
Kummeling *et al.* (2004) *Veterinary Surgery*	31	Suture ligation	7/31 (22·6%) Includes several dogs euthanased due to portal vein hypoplasia	Median 1·6 years (range 1 to 5·6) – includes extrahepatic dogs	Follow-up with telephone interview for 24 surviving dogs. No long-term mortality. Three dogs (12·5%) had clinical signs suggestive of recurrent or persistent shunting. Two of these dogs had normal ammonia and bile acids, and one of these dogs had increased bile acids, an abnormal ammonia tolerance test and persistent shunting was identified on scintigraphy.
Kyles *et al.* (2004) *Veterinary Surgery*	7	Portocaval venograft and ameroid constrictor	0	Median 82 days (range 20 to 990)	Follow-up information from repeat examination or telephone contact with the owner. Six dogs died or were euthanased with clinical signs consistent with portal hypertension (median survival 82 days). One dog was clinically normal at 33 months after surgery with negative scintigraphy at 4 weeks.

Table 3 (Continued)

Article	Number of dogs	Surgical technique	Perioperative mortality	Follow-up period	Follow-up and long-term outcome
Adin *et al.* (2006) *Journal of the American Veterinary Medical Association*	10	Hydraulic occluder	0	See adjacent long-term outcome section	Ten dogs re-examined at 10 weeks after surgery. Postprandial bile acids within reference range in 6/10 dogs. Scintigraphy showed persistent shunting in 5/10 dogs. Long-term follow-up in all dogs at 12 months with re-examination (6) or telephone contact with the veterinary surgeon (4). One dog was lost to follow-up six months after surgery, and one dog died of an unrelated cause at four months after surgery. Both dogs had postprandial bile acids within the reference range at last follow-up. In the remaining dogs, 5/8 had postprandial bile acids within the reference range at 12 months after surgery. All eight dogs were clinically normal at a median of 22 months (range 13 to 28).
Bright *et al.* (2006) *Veterinary Surgery*	9	Ameroid constrictor	0	Mean 38·3 months (range 12 to 67 months)	Long-term follow-up was obtained by telephone contact with the owners. One dog died suddenly at 16 months after surgery of an unknown cause. The remaining eight dogs were all considered by their owners to have an excellent quality of life although one still had intermittent signs of hepatic encephalopathy. Additional follow-up was conducted eight months after the initial contact. The dog that had displayed intermittent signs of hepatic encephalopathy had deteriorated and was euthanased 23 months after surgery. No further complications were noted in the other seven dogs.
Kummeling *et al.* (2006) *Journal of Veterinary Internal Medicine*	13	Suture ligation	2/13 (15·4%)	–	–
Parker *et al.* (2008) *Journal of the American Veterinary Medical Association*	25	9 – suture ligation 6 – cellophane band 5 – cellophane band and suture 3 – mattress sutures 1 – ameroid constrictor 1 – extrahepatic graft	1/25 (4%)	Median 35·7 months (range 0 to 86·6)	Long-term outcome determined by review of clinical record or telephone contact with the veterinary surgeon or owner. Nine dogs alive at follow-up of median 51·7 months (range 15·6 to 74·5). Two dogs died of unrelated causes at 71 and 87 months after surgery. Four dogs lost to follow-up at a median of 8 months after surgery (range 0·06 to 46 months). Nine died of shunt-related causes at a median of 7·9 months (range 1·4 to 28 months). Median survival 45·7 months (range 0 to 86·6).

*Included a small number of dogs that were managed medically.

both acute and gradual attenuation methods, and this makes the interpretation of these results difficult (Papazoglou *et al.* 2002, Parker *et al.* 2008).

Overall, the studies identified in this review provide a considerable amount of information, but it is difficult to directly compare them due to the wide variation in the way that outcome has been measured and reported. Short-term outcomes can be considered easier to quantify, particularly in terms of morbidity and mortality. However, studies vary in the type of complications that are reported and the time frame in terms of intra-, peri- and post-operative periods. We did not record complication rates for most studies due to this variability. Mortality is a better-defined variable, although the time frame for peri- or postoperative mortality can range from the duration of hospitalisation to 30 days after surgery. Some small studies report a mortality rate of 0%, but this is likely to reflect the number of dogs included rather than the absolute success of the procedure. A summary of the short-term outcome according to surgical procedure is presented in Table 6. This is particularly limited by the small numbers of dogs treated with ameroid constrictors and cellophane bands, making direct comparison from this table challenging. Surgical attenuation of intrahepatic CPSS has been associated with a relatively high rate of perioperative complications and mortality. Two studies, which are commonly referenced, were not included in Table 6, one because of relatively small numbers (Komtebedde *et al.* 1991) and one due to the inclusion of several different surgical techniques (Papazoglou *et al.* 2002). These studies reported complication rates of 77% and 47%, respectively, which were greater than those included in Table 6. These studies also reported a mortality rate of 23·1% and 12·5%, respectively, both within

Table 4. Summary of articles reporting short-term (perioperative mortality) and/or long-term outcome of treatment with endovascular coil embolisation of intrahepatic congenital portosystemic shunts (CPSS) in dogs

Article	Number of dogs	Surgical technique	Perioperative mortality	Follow-up period	Long-term outcome
Bussadori *et al.* (2008) *Veterinary Journal*	5	Endovascular coil	0	See adjacent long-term outcome section	Follow-up consisted of ultrasound examinations until closure of shunt was documented and haematological analysis was repeated. All dogs normal at follow-up with no clinical signs. Complete closure of the shunt was documented with ultrasound at one to two months postsurgery. One dog died of other reasons seven months after surgery. Three dogs had normal haematological findings and one dog abnormal haematological findings at two years after surgery.
Schneider *et al.* (2009) *Veterinary Radiology & Ultrasound*	7	Endovascular coil (step-wise procedure with stent placed first and then coils placed in subsequent procedures)	2/7 (28·6%)	See adjacent long-term outcome section	Four dogs had embolisation of the hepatic vein draining the shunt. They were re-examined at 2·5, 5·2, 6·8 and 20·9 months after surgery. One dog had complete occlusion of the shunt on portovenography and was considered to be normal by the owner. Three dogs had developed secondary intrahepatic collaterals on portovenography. These dogs had ongoing clinical signs and biochemical evidence of reduced liver function. One dog with a left divisional shunt had concurrent primary intrahepatic collaterals draining into the vena cava. This dog and the three with secondary intrahepatic collaterals were treated with embolisation of the shunt or portal vein branch. Follow-up of these dogs was performed at 2·1, 3·5, 4·6 and 4·7 months following repeat coil placement. Three had complete occlusion on portovenography and one had a small amount of residual shunting. In all dogs, haematology and biochemistry were normal, but there were mild increases in dynamic bile acids, although ammonia and ammonia tolerance testing were normal in three dogs.
Weisse *et al.*(2014) *Journal of the American Veterinary Medical Association*	100	95 – Endovascular coil 5 – No treatment due to excessive portal pressures	5/95 (5·3%)	See adjacent long-term outcome section	Long-term follow-up obtained by repeat examination or telephone contact with the veterinary surgeon or owner. Two dogs lost to follow-up at 118 and 127 days following the procedure. For the remaining 98 dogs, follow-up time was a median of 962 days (0 to 3411 days); 39 dogs were dead at follow-up, and 59 were alive. Of the dogs that were dead, 17% were confirmed to be dead due to their shunt or the procedure, 25% were suspected to have died due to their shunt or the procedure, 28% were considered unlikely to have died due to their shunt or the procedure, and 31% were confirmed to have died due to unrelated reasons. A total of 88 dogs were re-examined for recurrence of clinical signs; 59/88 (67%) had no clinical signs, and 29/88 (33%) ultimately developed one or more signs of persistent or recurrent shunting. Five dogs had repeat coil placement that resolved the signs. The owners of the remaining 24 dogs declined repeat coil placement and, the dogs either improved or ultimately deteriorated. Outcome was considered excellent in 66% dogs, fair in 15% and poor in 19%. The median survival time was 2204 days (range 0 to 3411).
Knapp *et al.* (2015) *Research in Veterinary Science*	8	Endovascular embolization	0	See adjacent long-term outcome section	Dogs had repeat blood testing at three and six months following coil placement, and long-term follow-up was conducted via telephone contact with the veterinary surgeon or owner. Six dogs had a single procedure and showed an excellent postoperative outcome at three months follow-up with no residual flow, significant improvement in biochemical and haematological assessment and absence of clinical signs without medical management. Two dogs had persistent flow through the shunt and required an additional procedure at six months.

Table 5. Summary of articles reporting the long-term outcome of medical treatment of intrahepatic congenital portosystemic shunts (CPSS) in dogs

Article	Number of dogs	Treatment	Perioperative mortality	Follow-up period	Long-term outcome
Watson & Herrtage (1998) *Journal of Small Animal Practice*	17	Medical management	N/A	See adjacent long-term outcome section	Follow-up was obtained by examining the clinical records and by telephone contact with the owners. Of 17 dogs, 11 were euthanased at a mean of 10·2 months (SD ±9·5) from diagnosis; 5 of 17 were alive at the time of follow-up at a mean of 45·7 months (SD ±5·9) from diagnosis. One dog was lost to follow-up.

Table 6. Reported postoperative complications and perioperative mortality for different surgical treatments for intrahepatic congenital portosystemic shunts in dogs

Technique	Number of dogs	Postoperative complications	Perioperative mortality	Excellent/ good outcome	Persistent shunting	Average follow-up
Suture ligation (White *et al.* 1998, Kummeling *et al.* 2004, Mehl *et al.* 2007)	17 to 45	11·8 to 22·6%*	5·9 to 22·6%	75·7 to 100%†	87·5%‡	16 to 50 months
Ameroid constrictor (Bright *et al.* 2006, Mehl *et al.* 2007)	9 to 11	9·1 to 22·2%	0 to 9·1%	70 to 87·5%	42·9%§	28·5 to 38·3 months
Cellophane band (Hunt *et al.* 2004)	11	54·5%	27·3%	71·4%¶	–	2·25 months
Coil embolisation (Weisse *et al.* 2014)	95	18·9%**	5·3%	81%	–	32·1 months

*Only one of these studies specifically reports the number of dogs affected with postoperative complications. We have used the mortality rate as a surrogate for postoperative complications, but it is likely that there were a greater proportion of dogs affected.
†In study with 75·7% excellent/good outcomes, repeat surgery resulted in an increase to 83·8% excellent/good outcome.
‡Persistent shunting in the short term (6 to 10 weeks) and all dogs treated with partial attenuation.
§Persistent shunting on scintigraphy in the short term (6 to 10 weeks).
¶Clinical outcome not given but 71% normal liver function on biochemical testing.
**Twenty-one complications in 16 dogs following 111 treatments.

the range reported in Table 6. Endovascular coil embolisation is recommended as a minimally invasive treatment for intrahepatic CPSS to reduce the morbidity and mortality associated with open surgery. A large study of 95 dogs treated with endovascular coil embolisation reported a postoperative complication rate of 18·9% and a mortality of 5·3%. The complication rate for this group of dogs is somewhat unclear as both intraoperative and postoperative complications are reported separately, and complications are reported for 111 procedures, including repeat procedures in several dogs and five animals that did not have coils placed because of suspected portal hypertension.

The long-term outcome of intrahepatic CPSS treatment is more challenging to assess than the short-term outcome. A variety of outcome measures have been used, including clinical assessment, owner assessment, serum bile acids or ammonia tolerance testing, ultrasound and scintigraphy (White *et al.* 1998, Hunt *et al.* 2004, Kummeling *et al.* 2004, Adin *et al.* 2006, Mehl *et al.* 2007, Weisse *et al.* 2014). However, it is unclear which of these represent the most appropriate or reliable assessment. Table 6 also summarises the long-term outcomes of the different treatments, showing that all have relatively similar results. The wide variation in both the method of long-term follow-up and the definition of an "excellent" or "good" outcome makes direct comparison of the different techniques challenging. If we consider a poor outcome, then we can summarise the data as follows. For dogs treated with suture ligation, 0% to 16·2% of dogs had a poor outcome with recurrent or persistent signs with or without shunting at an average of 16 to 50 months after surgery (including those that had repeat surgery) (White *et al.* 1998, Kummeling *et al.* 2004, Mehl *et al.* 2007). For dogs treated with ameroid constrictors, 12·5% to 30% had a poor outcome, with euthanasia, due to persistence or recurrent clinical signs at an average of 28·5 to 38·3 months after surgery (Bright *et al.* 2006, Mehl *et al.* 2007). This is compared to coil embolisation for which 19% of dogs had a poor outcome with continued or worsening clinical signs, despite medical management, or surgical-related death at a median of 32·1 months after treatment (Weisse *et al.* 2014). Similarly, it should be recognised that this information is based on a small number of dogs treated with ameroid constrictors and a single study, albeit with a large number of dogs, treated by coil embolisation.

This review highlights the relative lack of information on long-term outcomes for intrahepatic CPSS treatment. Further information is needed to determine which treatment provides the best long-term outcome. Currently, the ideal end point for CPSS occlusion is unclear. It is unknown whether the aim of surgery should be to achieve full attenuation in every animal or whether some degree of persistent shunting is acceptable. This should be addressed so that the most appropriate treatment can be recommended to achieve a good long-term outcome. Further comparative clinical studies are essential to determine the precise pros and cons of different treatment options. Importantly, we need studies that compare both the short-term morbidity and mortality and the long-term outcome in terms of quality of life. Ideally, studies would compare different types of surgical attenuation with each other and coil embolisation based on random allocation. However, different shunt morphology may also influence the results

of different surgical techniques, and therefore, it may be sensible to compare treatments for each broad shunt morphology. There is a need for studies to include larger numbers of dogs to increase their reliability. This may be best achieved through collaboration between several centres.

There are other factors besides risk of morbidity and mortality that will influence decision-making, which were not assessed as part of the current review. These include the availability of equipment and expertise, financial considerations and client and surgeon preference. Importantly, there may be factors relating to the individual dog—particularly the morphology of the CPSS—that may influence choice of treatment. As knowledge about the morphology of intrahepatic CPSS increases through use of CT scanning, it may be that we can identify some animals that would benefit specifically from surgical treatment and some specifically from endovascular coil embolisation, although this is currently speculative.

There are still many unanswered questions regarding the management of dogs with intrahepatic CPSS. Large randomised prospective studies are needed to compare treatments to determine the ones associated with the best outcome. Further investigation is also needed to develop consistent and validated outcome measures.

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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