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Incidence and risk factors for neurological signs after attenuation of a single congenital portosystemic shunt in 50 cats

Rhiannon Strickland BVetMed¹  | Michael S. Tivers BVSc, PhD, DECVS²  |
Robert C. Fowkes BSc, PhD³ | Victoria J. Lipscomb MA, VetMB, DECVS¹

¹Department of Clinical Science and Services, Royal Veterinary College, University of London, London, United Kingdom

²Paragon Veterinary Referrals, Red Hall Crescent, Wakefield, United Kingdom

³Department of Comparative Biomedical Sciences, Royal Veterinary College, University of London, London, United Kingdom

Correspondence

Rhiannon Strickland, Department of Clinical Science and Services, Royal Veterinary College, University of London, London, United Kingdom.
Email: rstrickland@rvc.ac.uk

Abstract

Objective: To determine the incidence, outcome, and risk factors for postattenuation neurological signs (PANS) in cats treated for single congenital portosystemic shunts (CPSS).

Study design: Retrospective cohort study.

Animals: Cats (n = 50) with a single CPSS.

Methods: Medical records of cats treated by surgical attenuation of a single CPSS between 2003 and 2017 were reviewed for signalment, surgical technique, preoperative management and postoperative clinical outcomes. Binary logistic regression was performed to investigate risk factors for occurrence of PANS and seizures.

Results: Congenital portosystemic shunts in 50 cats included 40 extrahepatic and 10 intrahepatic shunts. Postattenuation neurological signs were recorded in 31 (62%) cats and graded as 1 in 10 cats, 2 in nine cats, and 3 in 12 cats. Postattenuation neurological signs included seizures in 11 cats. Five of 31 cats with PANS did not survive to discharge. No association was detected between PANS or seizures and the type of CPSS (intrahepatic or extrahepatic), degree of attenuation, age, or the use of perioperative levetiracetam or hepatic encephalopathy immediately preoperatively. Osmolality at a median 24 hours postoperatively was lower in cats with PANS ($P < .049$, Wald 3.867, odds ratio [Exp(B)] 0.855, CI 0.732-0.999).

Conclusion: Postattenuation neurological signs are common complications in cats treated for CPSS. Preoperative levetiracetam did not prevent the occurrence of PANS or seizures. The only risk factor for PANS detected was lower postoperative Osmolality in cats with PANS at 24 hours.

Preliminary results of this work were presented as an abstract at the British Small Animal Veterinary Association Congress; April 4-6, 2019; Birmingham, United Kingdom.

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Clinical significance: Postattenuation neurological signs including seizures occur frequently in cats undergoing surgical attenuation of a CPSS. Preoperative levetiracetam did not protect against the development of PANS.

1 | INTRODUCTION

Postattenuation neurological signs (PANS) are complications of the surgical management of congenital portosystemic shunts (CPSS) and are reported in up to 60% of cats.¹⁻⁴ Cats are more likely than dogs to develop PANS, and mortality rates for cats that develop this complication are between 4.1% and 22.2%.¹⁻⁵

Cats and dogs with CPSS may present with hepatic encephalopathy (HE).⁶ The pathogenesis of HE is not clear but may be related to a combination of factors, including ammonia, oxidative stress, inflammation, and false neurotransmitters.⁷⁻⁹ Neurological complications that develop after surgical attenuation of a CPSS are poorly understood, but they are distinct from preoperative signs of HE, with neurological signs seen despite complete shunt attenuation or normal serum ammonia in dogs.^{10,11} Signs of PANS vary substantially and may include ataxia, central blindness, and seizures. The unknown etiology prevents identification of at-risk cats and targeted treatment. The only known association in cats is less opacification of the intrahepatic portal vasculature on intraoperative mesenteric portovenography is positively associated with the development of PANS.³ In dogs, having signs of HE preoperatively and older age have been shown to be risk factors for PANS,¹² whereas, in cats, the presence of preoperative seizures, age of the cat, type of shunt, and the degree of attenuation did not appear to be associated with PANS.² There is limited information on the effect of prophylactic antiseizure medication in cats undergoing CPSS attenuation.¹³ In dogs, the authors of two recent large studies failed to find perioperative levetiracetam to be protective against the development of PANS or seizures,^{12,14} which is in contrast to an earlier report in which prophylactic levetiracetam was protective for development of seizures.¹⁵ Osmolality is affected by changes in natremia, which may be a factor implicated in the development of PANS.¹² Sodium balance may be altered by shunt attenuation, altered hepatic blood flow, and fluid therapy.¹⁶⁻¹⁸ Rapid fluctuations in osmolality increase risk of neurological complications and astrocyte swelling in experimental animals and in man.¹⁹⁻²¹

The objective of this study was to determine the incidence, outcome, and risk factors for PANS, including seizures, after attenuation of single CPSS in cats. We hypothesized that age, the presence of HE preoperatively,

and postoperative osmolality would be risk factors for the development of PANS and seizures. We also hypothesized that prophylactic administration of levetiracetam would not prevent or reduce the incidence of PANS, including seizures after surgery.

2 | MATERIALS AND METHODS

2.1 | Case selection

Case records of cats that had surgical attenuation of a single CPSS at our hospital between 2003 and 2017 were reviewed. Cases were excluded when medical records were incomplete. A mesenteric portovenogram was performed to confirm diagnosis of CPSS in all cats.³

2.2 | Data collection

Details retrieved were body weight at the time of surgery, signalment, details of HE prior to surgery (Table 1), and details of medical treatment and response to that treatment. A “good” response was assigned to cats with no remaining clinical signs, a “moderate” response was assigned to cats with some improvement but clinical signs of HE still present, and a “poor” response was assigned to cats with little or no clinical improvement.²³ Additional details retrieved included serum albumin preoperatively and postoperatively, plasma ammonia preoperatively and postoperatively, and perioperative levetiracetam administration. Perioperative details included shunt morphology; method and degree of attenuation; postoperative serum osmolality; the nature and timing of

TABLE 1 Grading system for HE in cats

HE grade	Clinical signs
1	Normal, absence of abnormal clinical signs
2	Hypersalivation, lethargy, apathy, minimal disorientation, subtle personality change, inappropriate behavior
3	Blindness, severe ataxia, somnolence but responds to verbal stimuli, circling, head pressing
4	Coma, stupor, repeated seizures

Note: Adapted from Proot et al.²²

Abbreviation: HE, hepatic encephalopathy.

complications related to PANS; and whether the cat survived to discharge, died, or was euthanized.

Electrolytes, urea, and glucose were measured by using a blood gas analyzer. Serum osmolality was calculated by the blood gas analyzer by using the formula: $\text{osmolality(mOsm/kg)} = 1.86[\text{Na}^+] + (\text{glucose}/18) + (\text{blood urea nitrogen}/2.8) + 9$.

The same blood gas, electrolyte, and metabolite analyzer was used for each sample from individual cats, but two analyzers were used over the study period (from 2003-2011: Stat Profile Critical Care Xpress; Nova Biomedical, Cheshire, United Kingdom; after 2011: Stat Profile pHox Ultra; Nova Biomedical, Waltham, Massachusetts). Albumin was measured with an ILab 600 clinical chemistry analyzer (Instrumentation Laboratory, Werfen, Warrington, United Kingdom). Ammonia was measured with a Stasar III spectrophotometer (Gilford Instrument Laboratories, Oberlin, Ohio) or a Jenway 6310 spectrophotometer (Bibby Scientific Limited, Staffordshire, United Kingdom). Samples were ideally measured patient side; those that were not were transported on ice to an onsite laboratory.

Signs of HE were graded, according to clinical notes, before the initiation of medical management and immediately preoperatively (Table 1). Any neurological signs noted after surgery and before discharge were classified as PANS and graded mild, moderate, or severe (Table 2). Grades were assigned retrospectively on the basis of notes on the kennel sheets. Congenital portosystemic shunt attenuation was performed according to previously published surgical protocol; anesthetic procedures were decided by the anesthetist.² Visual assessment of the

pancreas and intestines for signs of portal hypertension alongside measurement of portal pressure via catheterization of a mesenteric vein was used to determine whether complete or partial attenuation was performed.^{2,3,23} Complete attenuation was not performed when, after temporary occlusion, the portal pressure doubled, was over 18 mm Hg, there was a change in central venous pressure of >1 mm Hg, or there was a change in direct arterial pressure of >5 mm Hg. Complete ligation was not performed regardless of the portal pressure measurement when any visual changes such as hypermotility or congestion of the intestine or discoloration of the pancreas were observed. Complete attenuation was achieved by acute suture ligation; partial attenuation was achieved by suture ligation or placement of a thin film band partially tightened around the shunt.

2.3 | Data analysis

Statistical analysis was performed in SPSS Statistics 23.0.0 (SPSS UK Limited IBM, Woking, United Kingdom). Data were assessed graphically for normality. Median and range are reported for nonnormally distributed variables, and mean and SD are reported for normally distributed variables. Categorical data are reported as percentages.

Initial screening was performed with univariable binary logistic regression by using each potential predictor variable to identify possible risk factors for PANS including seizures and seizures as a separate outcome for use in a multivariable model. Selected variables had previously been associated with outcome or were related to the study hypotheses. The variables included were the type of shunt, complete vs partial attenuation, preoperative albumin, preoperative ammonia, age, the duration of clinical signs preoperatively, whether HE was present before medical management, how HE was managed, the response to treatment, and whether HE was present immediately preoperatively. Serum osmolality was recorded at three time points postoperatively, as dictated by the timing of sampling in the clinical records. These values were three separate variables and included in the univariable binary logistic regression.

Variables with $P \leq .10$ in the univariable analysis were used in multivariable logistic regression. Variables were sequentially entered into the logistic regression model and retained when $P \leq .05$.

TABLE 2 Grading system for PANS in cats undergoing surgical management of a single CPSS

Grade	Clinical signs
1: Mild	Subtle depression or behavior change, mild tremors or twitching; self-resolves or responds immediately to AED administration
2: Moderate	Marked depression or behavior change, whole body tremors or twitching, \pm reduced response to visual stimuli; requires one or more IV AED and ongoing increases in drugs with regular monitoring/ICU support to control PANS
3: Severe	Progressive, severe depression/coma, nystagmus, complete blindness, seizures, requires maximum intervention with two or more AED \pm propofol and/or other drugs with continuous monitoring/ICU support

Note: Adapted from the grading system used in dogs with PANS by Strickland et al.¹²

Abbreviations: AED, antiepileptic drug; CPSS, congenital portosystemic shunt; ICU, intensive care unit; PANS, post attenuation neurological signs.

3 | RESULTS

Fifty cats with a single CPSS were found, and all were included in the study. Fourteen cats were male entire, 20

TABLE 3 Clinical findings and outcomes of 31 cats with PANS after surgical treatment of a single CPSS

Case	PANS grade	Onset PANS, h	Neurological Signs	Perioperative levetiracetam	Survival to discharge
1	1	5	Mild twitching, resolved without treatment	No	Yes
2	1	8	Mild twitching and obtundation, resolved with phenobarbitone treatment	No	Yes
3	1	20	Mild twitching and obtundation, resolved with phenobarbitone treatment	No	Yes
4	1	5	Mild twitching, resolved with phenobarbitone treatment	No	Yes
5	1	3	Mild tremor, partially resolved with phenobarbitone treatment	No	Yes
6	1	3	Mild twitching, partially resolved with diazepam and phenobarbitone	No	Yes
7	1	72	Mild twitching, complete response to phenobarbitone	Yes	Yes
8	1	29	Tremors, resolved with phenobarbitone	No	Yes
9	1	28	Twitching, complete response to phenobarbitone	No	Yes
10	1	48	Mild depression and twitching, complete response to phenobarbitone	Yes	Yes
11	2	40	Ataxia, complete response to phenobarbitone	No	Yes
12	2	49	Tremors and blindness, partial response to phenobarbitone	No	Yes
13	2	0	Ataxic and blindness, complete response to phenobarbitone	No	Yes
14	2	48	Twitching, partial response to phenobarbitone	No	Yes
15	2	3	Twitching, hyperesthesia and bilateral mydriasis, partial response to treatment with phenobarbitone	No	Yes
16	2	36	Tremoring, complete response to phenobarbitone	Yes	Yes
17	2	96	Tremors, blindness 96 h, partial improvement with phenobarbitone	Yes	Yes
18	2	72	Ataxic and obtunded, complete response to phenobarbitone	Yes	Yes
19	2	6	Circling, obtunded, head pressing with absent menace response, partial improvement with phenobarbitone	No	Yes
20	3	0	Partial seizure activity, partial response to phenobarbitone and levetiracetam	No	Yes
21	3	40	Seizures and blindness, partial response to phenobarbitone	No	Yes
22	3	60	Seizures, complete response to diazepam and phenobarbitone	No	Yes
23	3	24	Seizures and blindness, partial response to diazepam and phenobarbitone	No	Yes
24	3	12	Ataxia, extensor rigidity and seizure, partial response to phenobarbitone and levetiracetam	No	Yes
25	3	8	Seizures, partial response to levetiracetam	No	Yes
26	3	12	Tremors, seizures and blindness, partial response to diazepam, phenobarbitone and propofol CRI.	No	Yes
27	3	48	Seizures, poor response to diazepam and phenobarbitone	No	No
28	3	9	Tremors, seizures and blindness, poor response to phenobarbitone and midazolam	Yes	No

TABLE 3 (Continued)

Case	PANS grade	Onset PANS, h	Neurological Signs	Perioperative levetiracetam	Survival to discharge
29	3	5	Twitching progressed to seizures, poor response to diazepam, midazolam and propofol	No	No
30	3	36	Ataxic and seizures, partial response to phenobarbitone and levetiracetam	No	No
31	3	40	Tremors, obtunded, no improvement with phenobarbitone, euthanized	Yes	No

Abbreviations: CPSS, congenital portosystemic shunt; CRI, constant rate infusion; PANS, post attenuation neurological signs.

TABLE 4 Clinical variables of cats with or without PANS after attenuation of a single CPSS

General variables	PANS, n = 31 cats	No PANS, n = 19 cats	P value
Type of shunt, n (%)	Extrahepatic 26 (83.9) Intrahepatic 5 (16.1)	Extrahepatic 14 (73.7) Intrahepatic 5 (26.3)	.386
Degree of attenuation, n (%)	Complete 9 (29) Partial 22 (71)	Complete 2 (10.5) Partial 17 (89.5)	.141
Preoperative albumin, mean (SD), g/L	30.94 (2.27) 28 cats	29.21 (4.50) 17 cats	.100
Preoperative ammonia, median (range), $\mu\text{mol/L}$	396.5 (140-782) 22 cats	292.5 (115-485) 12 cats	.078
Age, median (range), y	0.75 (0.33-8.64)	0.77 (0.24-5.86)	.886
HE present prior to medical management, n (%)	Yes 31 (100)	Yes 19 (100)	...
Duration of clinical signs presurgery, median (range), d	80 (1-626) 31 cats	73 (28-591) 18 cats	.909
Duration of medical management presurgery, median (range), d	26 (5-120) 27 cats	29 (6-587) 19 cats	.375
Response to medical management, n (%)	Good 12 (41.4) Moderate/poor 17 (58.6)	Good 10 (52.6) Moderate/poor 9 (47.4)	.445
Signs of HE immediately presurgery, n (%)	No 12 (38.7) Yes 19 (61.3)	No 10 (52.6) Yes 9 (47.4)	.338
Prophylactic levetiracetam, n (%)	Yes 7 (22.6) No 24 (77.4)	Yes 6 (31.6) No 13 (68.4)	.483
Osm at postoperative time point 1, mean (SD)	15 cats 296.8 (6)	8 cats 292.8 (6.7)	.164
Osm at postoperative time point 2, mean (SD)	15 cats 295.0 (4.9)	9 cats 292.2 (12.0)	.421
Osm at postoperative time point 3, mean (SD)	18 cats 287.9 (7.3)	6 cats 296.3 (8.6)	.049

Abbreviations:; CPSS, congenital portosystemic shunt; HE, hepatic encephalopathy; Osm, osmolality; PANS, post attenuation neurological signs.

cats were male neutered, four cats were female entire, and 12 cats were female neutered. The median age of cats at the time of surgery was 0.76 years (range, 0.24-8.64). The median weight of cats was 2.85 kg (range, 1.20-5.45).

All cats exhibited HE at presentation. The median duration of clinical signs of HE prior to surgery was 80 days (range, 1-626) in 49 cats (in one cat the duration

was unknown). Hepatic encephalopathy grade prior to medical management was 2 in 24 cats, 3 in 14 cats, and 4 in 12 cats. Forty-nine of 50 cats had medical management (including at least one of dietary modification, lactulose, or antibiotics) prior to surgery. The median duration of medical management prior to surgery was 29 days (available for 46 cats; range, 5-587). A good response to medical

management occurred in 22 of 46 cats, 18 of 46 cats had a moderate response, and eight of 46 cats had a poor response (one cat did not have a response recorded and one did not have medical management). Hepatic encephalopathy grade after medical management was 1 in 22 cats, 2 in 22 cats, 3 in three cats, and 4 in two cats. The cat that did not undergo medical management had HE grade 2 at the time of surgery.

Thirteen cats received prophylactic levetiracetam prior to surgery, and 37 cats did not. Levetiracetam was administered at 20 mg/kg orally three times daily for at least 24 hours preoperatively and 5 days postoperatively. Cats may have received levetiracetam for longer if it had been prescribed by the referring veterinarian.

Forty of fifty cats had an extrahepatic CPSS, and 10 cats had an intrahepatic CPSS. At surgery, 11 (22%) cats could tolerate complete attenuation, and 39 (80%) cats were able to tolerate only partial attenuation (35 with Prolene suture [Ethicon, Cornelia, Georgia] and four with a thin film band).

Preoperative serum albumin was measured in 45 (90%) cats, with a mean of 30.28 g/L (SD \pm 3.35; reference range, 49-71 g/L). Preoperative plasma ammonia was measured in 34 (58.1%) cats, with a median of 329 μ mol/L (range, 115-792; reference range, 0-70 μ mol/L). Four cats had postoperative plasma ammonia measured; two of the measurements were within normal limits of 16 and 22 μ mol/L, and these cats developed PANS grade 2 and 3, respectively. One cat had a measurement of 134 μ mol/L and developed PANS grade 3, and one cat had a postoperative plasma ammonia of 258 μ mol/L and did not develop PANS.

Thirty-one (62%) cats had PANS at the time of discharge, with the remaining 19 cats (38%) not displaying any postoperative neurological complications. Median time from anesthetic recovery to onset of PANS was 24 hours (0-96). Severity of PANS was grade 1 in ten (32%) cats, grade 2 in nine (29%) cats, and grade 3 in 12 (38.7%) cats. Eleven (22%) cats had postoperative seizures, all grade 3. Among the 31 cats that had PANS, five (16.1%)

TABLE 5 Clinical variables of cats with or without seizures after attenuation of a single CPSS

General variables	Seizures, n = 11 cats	No seizures, n = 39 cats	P value
Type of shunt, n (%)	Extrahepatic 8 (72.7) Intrahepatic 3 (27.3)	Extrahepatic 32 (82.1) Intrahepatic 7 (17.9)	.498
Degree of attenuation, n (%)	Complete 3 (27.3) Partial 8 (72.7)	Complete 8 (20.5) Partial 31 (79.5)	.634
Preoperative albumin, mean (SD), g/L	30.38 (1.99) 10 cats	30.26 (3.67) 35 cats	.918
Preoperative ammonia, median (range), μ mol/L	317.0 (140-506) 6 cats	329.0 (115-792) 28 cats	.527
Age, median (range), y	0.75 (0.33-8.64)	0.76 (0.24-5.86)	.165
HE present prior to medical management, n (%)	Yes 11 (100)	Yes 39 (100)	...
Duration of clinical signs presurgery, median (range), d	88 (13-365) 11 cats	73.5 (1-626) 38 cats	.944
Duration of medical management presurgery, median (range), d	21 (5-120) 9 cats	29 (6-587) 37 cats	.601
Response to medical management, n (%)	Good 2 (20) Moderate/poor 8 (80)	Good 20 (52.6) Moderate/poor 18 (47.4)	.081
Signs of HE immediately presurgery, n (%)	No 3 (27.3) Yes 8 (72.7)	No 19 (48.7) Yes 20 (51.3)	.215
Prophylactic levetiracetam, n (%)	Yes 1 (9.1) No 10 (90.9)	Yes 12 (30.8) No 27 (69.2)	.177
Osm at postoperative time point 1, mean (SD)	7 cats 295.4 (7.1)	16 cats 295.5 (SD 6.3)	.978
Osm at postoperative time point 2, mean (SD)	8 cats 295.5 (3.6)	16 cats 293.2 (SD 9.7)	.514
Osm at postoperative time point 3, mean (SD)	11 cats 286.4 (7.7)	13 cats 293.1 (SD 7.9)	.067

Abbreviations:; CPSS, congenital portosystemic shunt; HE, hepatic encephalopathy; Osm, osmolality.

cats did not survive to hospital discharge. All five of the cats that died had severe grade 3 PANS, four of these five cats had seizures. Among the five cats that died or were euthanized because of PANS, two cats had received preoperative levetiracetam. Postattenuation neurological signs were treated symptomatically, and phenobarbitone was typically the first line antiseizure medication. Additional medications including levetiracetam, diazepam or midazolam, and propofol were administered when neurological signs continued to progress (Table 3).

Six (12%) cats did not survive to discharge; five of these six cats (10% of study population, 83% of cats that did not survive) died or were euthanized for reasons related to PANS (Table 3). The other cat had a postoperative hemoabdomen due to a complication from a liver biopsy and was euthanized after a poor recovery from a second exploratory laparotomy.

Osmolality was calculated at three time points postoperatively. The median time interval from surgery to first sampling was 1 hour (range, 0-6), from surgery to second sample 8.5 hours (range, 6-17), and from surgery to third sample 24 hours (range, 15-72). Osmolality was calculated at first sampling in 23 cats with a mean (SD) of 295.4 (6.4), at second sampling in 24 cats with a mean (SD) of 294 (8.1), and at third sampling in 24 cats with a mean (SD) of 290 (8.3).

3.1 | Univariable analysis

The results of the univariable binary logistic regression for possible risk factors of PANS and seizures are presented in Tables 4 and 5, respectively. Osmolality at time point 3 was a risk factor for PANS ($P < .049$, Wald 3.867, odds ratio [Exp(B)] 0.855, CI 0.732-0.999).

3.2 | Multivariable analysis

It was not possible to create a multivariable model for PANS or seizures.

4 | DISCUSSION

In this study, cats frequently developed PANS as the major cause of mortality. At 24 hours postoperatively, cats with PANS had lower serum osmolality compared with cats that didn't develop PANS. The administration of perioperative levetiracetam did not seem to be protective for the development of PANS, and neither age nor the presence of HE preoperatively were associated with the development of PANS.

Cats frequently develop PANS, with 62% affected in this study, similarly to previous reports.¹⁻³ Overall mortality in this study was 10%, which is in line with other studies; PANS accounted for most of the mortality in this study.¹⁻³ However, cats with PANS can make a good recovery,² with only 16% of cats with PANS not surviving to discharge in this study, a rate similar to that reported in dogs.¹² All cats with grade 1 or 2 PANS survived with appropriate treatment, whereas five cats with PANS grade 3 died or were euthanized despite appropriate treatment, providing evidence that severity of PANS is a concern with regard to survival.

To the best of our knowledge, postoperative electrolyte disturbances have not been analyzed previously in relation to the development of PANS or seizures in cats. Changes in osmolality are associated with HE in man,^{9,24} and imbalance may be associated with HE in cats. In the current study, lower osmolality at a median of 24 hours postoperatively was a risk factor for cats developing PANS compared with cats that did not develop PANS. Osmolality was also calculated at 1 hour and 8.5 hours postsurgery, and the values at these times were not different between cats with PANS or seizures alone and unaffected cats. In a publication by the same authors, osmolality was a risk factor in univariable analysis for PANS and seizures in dogs; however, in contrast to the findings of the current study, osmolality was higher in dogs with PANS or seizures.¹² This may represent a species difference or reflect that fact that it is the alteration in osmolality that is important rather than a specific increase or decrease, or it may be a type II error due to the low numbers of cats for which these data were available. It should be noted that osmolality was calculated and not measured in this study, so this may not be a true reflection of the osmolality in these cats. It is also important to recognize that alterations in sodium and, therefore, osmolality have been reported as a result of lactulose treatment, which most cats in this study received preoperatively and postoperatively.²⁵ Osmolality would ideally have been calculated preoperatively and at set timepoints through recovery to allow for assessment of trends for each cat and whether a change in osmolality could be related to the timing of PANS. The median onset of PANS was 24 hours, and it is tempting to relate this to the difference in osmolality at 24 hours, but it is important to note that osmolality was available in only 24 cats at this timepoint, and the range of time to onset of PANS is large (0-96 hours). Additional data are required to explore this hypothesis and draw conclusions about the role of osmolality changes in relation to development of PANS in cats (and dogs).

In 2012, our institution began perioperative administration of levetiracetam for dogs and cats undergoing CPSS surgery as result of a study by Fryer et al¹⁵ in which

perioperative administration of levetiracetam was shown to reduce postoperative seizure activity in dogs. Therefore, in the study reported here, there were two groups of cats undergoing CPSS surgery that could be compared, those that had surgery prior to or during 2012 that did not receive levetiracetam and those after 2012 that did receive levetiracetam.

Similarly to recent findings in dogs, we did not find a protective effect for administration of perioperative levetiracetam.^{12,14} The lack of protective effect of an anti-seizure medication was also the case in a study in which neurological complications occurred in a large proportion of cats despite 83% of cats having received perioperative phenobarbitone.¹³ These findings underscore the requirement for additional research in this area.

In contrast to dogs,¹² age has not been shown to be related to complications in cats with CPSS and, age at the time of treatment was not related to PANS or seizure activity in this study. This may reflect a true lack of association or result from a small sample. Cats were only slightly younger at the time of surgery (0.76 years; range, 0.24-8.74) compared with dogs in a previous study from the same institution (0.87 years; range, 0.2-11.98), so the difference in findings with regard to age cannot be attributed to varying ages at presentation.¹²

Hepatic encephalopathy has a marked effect on the central nervous system; it seems logical that cats that have HE immediately prior to attenuation could be more likely to develop PANS, and this has been shown in dogs.¹² The lack of association in this population could be the result of the fact that all cats had HE (grade 2 or above) at initial presentation, so any alterations as a result of HE may be common to the entire study population in varying degrees, even after a period of medical management. In comparison, the presenting clinical signs of dogs with CPSS are more varied, and fewer dogs present with HE.¹²

This study has significant limitations, many of which are inherent to its retrospective design. The sample size and data collected could not be controlled, so there were small subgroups for many variables, including the number of cats receiving prophylactic levetiracetam and cats with a postoperative ammonia measurement. Although the study included 50 cats, this is still a relatively small sample that could have resulted in a type II statistical error. Although a preexisting grading scale was used for analysis of complications and behavioral changes, analysis was reliant on observations made at the time, often by owners, and is open to interpretation. Timing of postoperative electrolyte analysis was not standardized. The differentiation of HE from the development of PANS is difficult, particularly in cats affected by HE at the time of surgery. In the future, larger prospective studies including clearly defined critical care, anesthetic, and surgical

protocols (especially if multiple institutions are involved to acquire appropriate numbers of cats) would significantly enhance the power and quality of the data that could be captured regarding identification of additional risk factors for PANS and seizures in cats after CPSS surgical attenuation.

In conclusion, this report documents the high incidence of PANS and associated mortality in cats undergoing CPSS attenuation. The administration of perioperative levetiracetam was not found protective against the development of PANS or seizures. The only risk factor identified in this population consisted of lower postoperative osmolality in cats with PANS at a single timepoint postoperatively.

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CONFLICT OF INTEREST

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

AUTHOR CONTRIBUTIONS

Strickland R, BVetMed: Contributed to the conception and design of the work and the acquisition, analysis, and interpretation of data in addition to drafting the article and approving it for publication; Tivers M, BVSc, PhD, DECVS: Contributed to the conception and design of the work and analysis and interpretation of data in addition to revising the article and approving it for publication; Fowkes R, BSc, PhD: Contributed to the conception of the work and interpretation of data in addition to revising the article and approving it for publication; Lipscomb V, MA, VetMB, DECVS: Contributed to the conception and design of the work and interpretation of data in addition to revising the article and approving it for publication.

ORCID

Rhiannon Strickland  <https://orcid.org/0000-0003-3705-1154>

Michael S. Tivers  <https://orcid.org/0000-0001-7047-9334>

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