JAVMA

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Long-term outcome and quality of life of dogs that developed neurologic signs after surgical treatment of a congenital portosystemic shunt: 50 cases (2005–2020)

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https://doi.org/10.2460/javma.20.11.0606

OBJECTIVE
To determine survival time and quality of life of dogs that developed postattenuation neurologic signs (PANS) after surgical treatment of a single congenital portosystemic shunt and survived at least 30 days and identify whether neurologic signs present at the time of discharge would resolve or reoccur.

ANIMALS
50 client-owned dogs.

PROCEDURES
Medical records were retrospectively reviewed, and follow-up data relating to neurologic signs and seizure activity were obtained. Owners were asked to complete a questionnaire related to the presence of neurologic signs, including seizures, and their dog's quality of life.

RESULTS
Thirty of the 50 (60%) dogs had postattenuation seizures with or without other nonseizure neurologic signs, and 20 (40%) had neurologic signs other than seizures. Neurologic signs had fully resolved by the time of discharge in 24 (48%) dogs. Signs resolved in 18 of the remaining 26 (69%) dogs that still had PANS other than seizures at the time of discharge. Seizures reoccurred in 15 of the 30 dogs that had postattenuation seizures. Twenty-seven of 33 (82%) owners graded their dog's long-term (> 30 days after surgery) quality-of-life as high. Forty-five (90%) dogs survived > 6 months. Most (29/43 [67%]) neurologic signs (other than seizures) present at the time of hospital discharge resolved.

CLINICAL RELEVANCE
Findings highlighted that survival times of > 6 months and a high QOL can be achieved in most dogs with PANS that survive at least 30 days. Most neurologic signs other than seizures resolved within 1 month postoperatively. Half of the dogs with postattenuation seizures had a reoccurrence.

Postattenuation seizures (PAS) are a potentially life-threatening neurologic complication that can develop after surgical treatment of congenital portosystemic shunts (PSSs) in dogs.[1–25] Postattenuation seizures most commonly occur within 7 days postoperatively and are typically unrelated to hypoglycemia, electrolyte disturbances, or hyperammonemia.[6,8,9,17–19,22,23] Investigators in 5 retrospective studies[16,18,19,22,25] reported an incidence of 3.2% to 8.1%, with a short-term (≤ 30 days after surgery) survival rate of 0.0% to 58.3%. Although some studies[1–4,6,9,12,13–18,21–23] describe only dogs affected by seizures, Strickland et al[19] recently described a 3-tier grading system that included all postattenuation

neurologic signs (PANS), ranging from subtle depression, tremors, and twitching to seizure activity and coma. In that study,[19] PANS reportedly occurred in 11.1% of dogs and were associated with a survival-to-discharge rate of 82.1%.

With the exception of a small number of case reports and small mostly retrospective case series, limited information is available regarding long-term survival and neurologic outcomes of dogs that experience PANS and survive at least 30 days after surgery.[2,3,5,7,8,9,13,15,17,19] On the basis of previous reports, reoccurrence of seizure activity and persistence of other PANS is common.[2,3,5,6,8,9,17] However, owing to the overall small number of reported cases and inconsistent follow-up times, it is difficult to provide owners of dogs with PANS meaningful prognostic information regarding survival time or information on whether PANS will reoccur or resolve and the potential timing of resolution.

Therefore, the objectives of the study reported here were to determine survival time and quality of life (QOL) of dogs surviving at least 30 days after development of PANS and investigate whether PANS present at the time of discharge would resolve or reoccur. We hypothesized that most dogs would survive > 6 months, most owners would report a high QOL at long-term follow-up, most dogs that developed PAS would experience seizure reoccurrence, and most PANS other than seizures present at the time of discharge would resolve.

Materials and Methods

Inclusion and exclusion criteria

Electronic medical records at 9 veterinary institutions were retrospectively reviewed to identify client-owned dogs that underwent complete or partial surgical attenuation of a single congenital extrahepatic or intrahepatic PSS between January 1, 2005, and February 29, 2020. Medical records of these dogs were searched for development of PANS within 7 days postoperatively,[22,23] and details of dogs that survived at least 30 days after surgery were extracted into a spreadsheet (Excel; Microsoft Corp). Exclusion criteria included dogs that were known to have developed multiple acquired shunts postoperatively, dogs with concurrent neurologic disorders (eg, meningitis), and dogs whose owner could not be contacted and for which the referring veterinarian or contributing surgeon could not provide the necessary follow-up information. Although we excluded dogs that were known to have developed multiple acquired shunts, not all dogs underwent evaluation for the presence of multiple acquired shunts, and thus, some affected dogs may have been included. Short-term survival was defined as ≤ 30 days postoperatively, whereas long-term survival was defined as > 30 days postoperatively. Ethical approval for the study was granted by the Human Research Ethics Committee at University College Dublin (LS-E-18-183-Mullins).

Data collection

Data retrieved from the medical records of dogs that met the inclusion criteria consisted of breed; age; sex, neuter status, and weight at the time of surgery; preattenuation neurologic signs; shunt morphology (extrahepatic [portocaval, portoazygos, or portophrenic] or intrahepatic [left-, central-, or right-divisional]); date of surgery; method of shunt attenuation (thin-film banding, ameroid constrictor, or suture ligation); degree of acute intraoperative shunt attenuation (complete, partial, or none); details of pre- and postoperative (before and after development of PANS) medical management (antimicrobials, lactulose, and antiseizure medications); type and timing (in hours postoperatively or converted to hours if recorded in days) of PANS development; treatment of PANS; and date of last examination at the contributing and referring veterinary institutions. At last follow-up, dogs were recorded as alive, lost to follow-up, or dead. If a dog had died, the cause of death was recorded as related or unrelated to PANS or unknown. For dogs that underwent > 1 shunt attenuation procedure, details related to the surgery after which PANS occurred were recorded (ie, the surgery after which PANS occurred was classified as the reference surgery). In dogs in which PANS occurred after > 1 attenuation procedure, details related to the first surgery were recorded (ie, the first surgery was classified as the reference surgery).

Long-term neurologic outcome

Details concerning whether PANS were still present or had resolved at the time of hospital discharge were obtained from the in-hospital medical records of contributing veterinary institutions. Information regarding whether PANS that were present at hospital discharge persisted or resolved, PAS experienced as part of PANS reoccurred, and affected dogs developed new neurologic signs not observed as part of the original PANS was obtained from medical records at the contributing and referring veterinary institutions as well as via telephone conversations or email correspondence with owners.

Owner questionnaire

Owners of dogs were contacted by the contributing surgeons via telephone or email and asked whether they would be willing to participate in a follow-up questionnaire, which included an 11-point assessment of the dog's QOL preoperatively and at the time of follow-up. Quality of life was scored on a scale from 0 (worst imaginable) to 10 (best imaginable). A modification of a previously published questionnaire[24,26] was used **(Supplementary Appendix)**. If an owner could not be contacted, the referring veterinarian was contacted and asked to provide information on the date the dog was last recorded alive or date of death, cause of death (if applicable), details of ongoing antiseizure medication at the time the dog was last recorded alive or dead, and, on the basis of information recorded in the medical record within the 6 months prior to the last time the dog was recorded alive or dead, whether any neurologic signs were

present. If the referring veterinary institution had not reexamined the dog long-term, whatever information was available was obtained from the medical record of the contributing veterinary institution.

Statistical analysis

Continuous variables were tested with the Shapiro-Wilk test to determine whether they were normally distributed. Normally distributed continuous data are presented as mean and SD; nonnormally distributed continuous data are presented as median and range. Categorical variables are reported as frequency and percentages. Survival time was defined as the time in days from the date of surgery to the date the dog was last recorded alive or the date of death. Statistical analyses were performed with commercially available software (SPSS statistics version 24; IBM Corp).

Results

Fifty-six dogs met the study inclusion criteria. However, 3 dogs were excluded because multiple acquired shunts were identified by means of scintigraphy (n = 2) or CT angiography (1) ≤ 3 months postoperatively, 2 dogs were excluded because of concurrent idiopathic epilepsy (1) or meningitis of unknown origin (1), and 1 dog was excluded because the owner could not be contacted and neither the referring veterinarian nor contributing surgeon could provide the necessary follow-up information. The remaining 50 dogs were included in the study.

Dogs included Yorkshire Terriers (n = 9), Bichon Frises (7), mixed-breed dogs (6), Pugs (5), Miniature Schnauzers (4), Jack Russell Terriers (3), Shih Tzus (3), and others (13). There were 17 (34%) spayed females, 15 (30%) sexually intact females, 10 (20%) sexually intact males, 7 (14%) neutered males, and 1 (2%) female of unspecified neuter status. Median age was 21.5 months (range, 3 to 145 months). Median weight was 5.8 kg (range, 1.4 to 30.1 kg).

Preoperative neurologic signs

Preoperative neurologic signs were recorded in 43 (86%) dogs. Fourteen of these 43 (33%) dogs had a history of preoperative seizures; all 14 dogs with preoperative seizures had a congenital extrahepatic PSS. The most common preoperative neurologic signs included lethargy, dullness, abnormal mentation, or signs of depression (n = 27 [63%]); head pressing (12 [28%]); hypersalivation (10 [23%]); ataxia (9 [21%]); circling (8 [19%]); abnormal behavior or aggressiveness (7 [16%]); disorientation (7 [16%]); pacing or wandering (6 [14%]); blindness or partial blindness (6 [14%]); tremors or twitching (5 [12%]); paresis or weakness (5 [12%]); and shaking (3 [7%]).

Shunt morphology

Forty-seven (94%) dogs had a congenital extrahepatic PSS (portocaval [n = 32], portoazygos [14], or unknown [1]). The remaining 3 (6%) dogs had a congenital intrahepatic PSS (left-divisional [n = 2] or right-divisional [1]).

Preoperative medical management

Forty-seven (94%) dogs received lactulose for ≥ 1 week prior to surgery, and 43 (86%) received antimicrobial treatment for ≥ 1 week prior to surgery. Nineteen (38%) dogs received antiseizure medication, which included levetiracetam alone in 17 of the 19 (89%) dogs, levetiracetam combined with potassium bromide in 1 (5%) dog, and levetiracetam in combination with phenobarbital and potassium bromide in 1 (5%) dog. Perioperative antiseizure medication was administered as part of the treatment for preoperative seizures, in an effort to prevent PANS, or both.

Method and degree of acute intraoperative shunt attenuation

Shunts were attenuated by means of suture ligation in 24 (48%) dogs, with complete ligation in 20 and partial ligation in 4; thin-film banding in 14 (28%) dogs, with partial attenuation in 11 and no attenuation in 3; and ameroid constrictor placement in 12 (24%) dogs, with no acute attenuation in any of the 12. Overall, 20 (40%) dogs underwent complete acute attenuation, 15 (30%) underwent partial acute attenuation, and 15 (30%) underwent no acute intraoperative attenuation. Three dogs that underwent partial attenuation by means of suture ligation (n = 2) or thin-film banding (1) underwent a second attenuation procedure 91, 110, and 371 days after the first surgery. One of these dogs developed PANS only after the first surgery, whereas the other 2 experienced PANS after both surgical procedures. At the time of the second attenuation procedure, 2 of the 3 shunts were fully attenuated by means of suture ligation and the remaining shunt was further partially attenuated by means of suture ligation. One additional dog had undergone surgical attenuation of a congenital extrahepatic PSS elsewhere 210 days previously; however, details of this procedure were not available. The shunt was attenuated by means of thin-film banding at the contributing institution, and the dog developed PANS.

Postoperative medical management prior to development of PANS

Prior to the development of PANS, 40 (80%) dogs received lactulose postoperatively (6 did not receive lactulose, and for 4, whether lactulose was administered was not recorded) and 39 (78%) received antimicrobials (7 did not receive antimicrobials, and for 4, whether antimicrobials were administered was not recorded). Twenty-two (44%) dogs received antiseizure medication (27 did not receive antiseizure medication, and for 1, whether antiseizure medication was administered was not recorded), which consisted of levetiracetam alone in 20 dogs, levetiracetam combined with potassium bromide in 1 dog, and levetiracetam in combination with phenobarbital and potassium bromide in 1 dog.

Timing and type of PANS

Information regarding timing of the onset of PANS in relation to surgery was available for 46

(92%) dogs, unknown in 2 dogs, and recorded as < 24 hours postoperatively in 1 dog and between 156 and 168 hours postoperatively in another dog. Neurologic signs were identified a median of 48 hours (range, 6 to 120 hours) postoperatively. Thirty (60%) dogs were recorded as having PAS with or without other nonseizure neurologic signs. Of these dogs, 17 had generalized seizures with or without focal seizures, and 12 had focal seizures alone; seizure type was not recorded in the remaining dog. Eleven of the 30 (37%) dogs with PAS had a history of preoperative seizure activity. The remaining 20 (40%) dogs with PANS had neurologic signs other than seizures.

Additional neurologic signs recorded in the 17 dogs that had generalized PAS with or without focal seizures included blindness or impaired vision (n = 7), ataxia (5), tremors (4), head pressing (3), nonambulatory tetraparesis (2), disorientation (2), vocalizing (2), and shivering, loss of balance, strange gait, obtundation, lethargy, twitching, paddling, unresponsiveness, restlessness, and dysphoria (1 each). Additional neurologic signs recorded in the 12 dogs that had only focal PAS included twitching (n = 5), ataxia (5), blindness (5), tremors (4), abnormal mentation (2), unresponsiveness (2), and circling, head bobbing, inability to ambulate, dullness, pacing, vocalization, hypersalivation, depression, juddering, and opisthotonos (1 each). Neurologic signs recorded in the 20 dogs that had PANS other than seizures included ataxia (n = 9); dullness, obtundation, depression, lethargy, or altered mentation (8); tremors (6); blindness or decreased menace response (6); twitching (5); head pressing (3); circling (3); abnormal behavior (2); hyperexcitability (2); slow anesthetic recovery (2); and disorientation, vocalization, abnormal posture, fasciculation, pacing, and shaking (1 each).

Treatment of PANS

Forty-five (90%) dogs received treatment for PANS, including 16 of the 17 dogs with generalized PAS with or without focal seizures, 10 of the 12 dogs that had only focal PAS, and 18 of the 20 with PANS other than seizures. One additional dog with PAS for which the seizure type was not recorded also received treatment for PANS.

Treatments for dogs with generalized PAS with or without focal seizures included phenobarbital (n = 12), levetiracetam (9), propofol (9), benzodiazepine (5), an α_2-adrenoceptor agonist (4), potassium bromide (4), and pregabalin (1), alone or in combination. Nine of these 16 dogs were already receiving prophylactic antiseizure medication, which consisted of levetiracetam (n = 7), levetiracetam in combination with potassium bromide (1), or levetiracetam in combination with potassium bromide and phenobarbital (1).

Treatments for dogs that had only focal PAS included benzodiazepine (n = 6), levetiracetam (5), phenobarbital (4), propofol (3), an α_2-adrenoceptor agonist (2), flumazenil (2), potassium bromide (1), and gabapentin (1), alone or in combination. Seven of these 10 dogs were already receiving levetiracetam prophylactically.

Treatments for dogs that had PANS other than seizures included phenobarbital alone (n = 12), levetiracetam alone (5), and an α_2-adrenoceptor agonist alone (1). Eight of the 18 dogs were receiving levetiracetam prophylactically.

The dog with PAS for which type of seizure activity was not recorded was treated with phenobarbital and diazepam. This dog had also received levetiracetam prophylactically.

Medical management from discharge

Forty-two (84%) dogs were receiving lactulose when discharged from the hospital (7 did not receive lactulose, and for 1, whether lactulose was administered was not recorded), 39 (78%) were receiving antimicrobial treatment (10 did not receive antimicrobials, and for 1, whether antimicrobials were administered was not recorded), and 41 (82%) were receiving antiseizure medication (8 did not receive antiseizure medication, and for 1, whether antiseizure medication was administered was not recorded). Fifteen of the 17 dogs that had generalized PAS with or without focal seizures were discharged with antiseizure medication, which consisted of phenobarbital (n = 6), phenobarbital and levetiracetam (3), potassium bromide and levetiracetam (2), and levetiracetam alone, levetiracetam and pregabalin, phenobarbital and potassium bromide, and a combination of levetiracetam, potassium bromide, and phenobarbital (1 each). Nine of the 12 dogs that had only focal PAS were discharged with antiseizure medication, which consisted of levetiracetam and phenobarbital (n = 4), levetiracetam alone (3), and levetiracetam, phenobarbital, and potassium bromide (2). The dog with unspecified PAS was discharged with levetiracetam and phenobarbital. Sixteen of the 20 dogs that had PANS other than seizures were discharged with antiseizure medication, which consisted of phenobarbital alone (n = 8), levetiracetam alone (4), and levetiracetam and phenobarbital (4).

Neurologic outcome

Dogs with PANS at the time of discharge—Neurologic signs had fully resolved by the time of discharge in 24 (48%) dogs, but the remaining 26 (52%) dogs still had PANS at the time of discharge. A total of 43 neurologic signs were documented in these 26 dogs, consisting of ataxia (n = 14), blindness or impaired vision (12), tremors (4), disorientation (2), abnormal mentation (2), inability to ambulate (2), and circling, strange gait, pacing, dullness, head bobbing, twitching, and loss of balance (1 each; **Table 1**). In 18 of these 26 (69%) dogs, the neurologic signs resolved. In 7 dogs, neurologic signs resolved ≤ 30 days after surgery, and in the remaining 11 dogs, neurologic signs resolved > 30 days after surgery (within a median of 69 days; range, 34 to 754 days). In 8 (31%) dogs, neurologic signs did not completely resolve; for these dogs, mean duration of follow-up was 1,393 days (SD, 1,334 days). Of the 12 dogs reported to be blind or have impaired vision at the time of hospital discharge, only 4 had a resolution (3 ≤ 30 days and 1 by 743 days after surgery).

Table 1—Postdischarge resolution of neurologic signs other than seizures (n = 43) in 26 dogs that developed postattenuation neurologic signs after surgical treatment of a single congenital portosystemic shunt, survived at least 30 days, and still had neurologic signs present at the time of hospital discharge.

Sign[a]	Resolved	Time to resolution (d)[b]	Time sign remained present (d)[b]	Veterinary follow-up time (d)[b]	Owner follow-up time (d)[b]
Ataxia (14)	Yes (11)	28 (2–197)	NA	1,151 (699)	1,842 (785)[c,d]
	No (3)	NA	188, 1,620, 22	76, 1,657, 139	188, NOC, NOC
Blindness or impaired vision (12)	Yes (4)	2, 18, 4, ≤ 743	NA	50, 1,697, 1,063, 754	1,233, 2,029[d], 823, NOC
	No (8)	NA	1,339 (1,293)	514 (76–3,212)	1,842 (1,433)[c,d]
Tremors (4)	Yes (4)	55, 50, 93, 180	NA	2,382, 611, 737, 2,503	2,548, NOC, NOC, 4,009[d]
Disorientation (2)	No (2)	NA	3,325, 188	3,212, 76	3,325, 188
Abnormal mentation (2)	Yes (2)	2, 69	NA	1,450, 453	1,450[d], 457
Inability to ambulate (2)	Yes (2)	15, 42	NA	76, 205	188, 902
Circling (1)	Yes (1)	69	NA	453	457
Strange gait (1)	No (1)	NA	134	134	NOC
Pacing (1)	Yes (1)	30	NA	1,899	1,948
Dullness (1)	Yes (1)	21	NA	1,899	1,948
Head bobbing (1)	Yes (1)	8	NA	2,580	2,631
Twitching (1)	Yes (1)	8	NA	2,580	2,631
Loss of balance (1)	Yes (1)	34	NA	3,415	3,415[d]

NA = Not applicable. NOC = No owner contact.

[a]Numbers in parentheses indicate number of dogs with that particular sign at the time of hospital discharge or number of dogs in which the sign did or did not resolve. [b]Values represent times after surgery and are given as median (range), mean (SD), or, for cells with < 5 dogs, individual data points. [c]No owner follow-up information was available for 3 dogs. [d]For 1 dog that experienced this sign, date of last owner follow-up also represented the date of death.

Of the 43 neurologic signs present at the time of discharge in 26 dogs, 29 (67%) subsequently resolved. Fifteen signs resolved ≤ 30 days after surgery, and 14 resolved > 30 days after surgery (within a median of 69 days; range, 34 to 754 days). Overall, 27 signs resolved ≤ 6 months after surgery. Fourteen of the 43 neurologic signs were still present at the time of final follow-up (median follow-up time, 545 days; range, 134 to 3,340 days).

Of the 18 dogs that had complete resolution of neurologic signs, 8 developed new neurologic signs that were not part of original episode of PANS; within a mean of 1,447 days after surgery (SD, 1,401 days). These signs subsequently resolved in 2 dogs. One dog had tremors 39 days after surgery that resolved within 24 hours; the other dog developed pacing 58 days after surgery that had resolved by 553 days after surgery. In the remaining 6 dogs, the new neurologic signs did not resolve after a mean follow-up time of 2,011 days (SD, 1,181 days) after surgery.

Twelve of the 24 dogs in which PANS had resolved prior to hospital discharge developed new neurologic signs a mean of 1,808 days (SD, 1,106 days) after surgery. These signs subsequently resolved in 2 dogs. One dog had tremors 440 days after surgery that resolved within 24 hours; the other dog developed head pressing and a depressed mentation by 103 days after surgery, which resolved by 110 days after surgery. In the remaining 10 dogs, the new neurologic signs did not resolve after a mean follow-up time of 2,120 days (SD, 997 days) after surgery.

Dogs with PAS—Of the 30 dogs with PAS, 15 (50%), including 7 with a history of preoperative seizure activity, had a reoccurrence of seizure activity following discharge. Of the 12 dogs that had only focal PAS, 6 had a reoccurrence of focal seizure activity after discharge, of which 4 continued to experience seizures > 30 days postoperatively and 2 only had seizures ≤ 30 days postoperatively **(Table 2)**. Two of the 4 dogs with long-term seizure activity were euthanized 1,450 and 2,936 days postoperatively; one was euthanized because of ongoing seizure activity and the other was euthanized because of a cardiac condition and ongoing seizure activity.

Of the 17 dogs that had generalized PAS with or without focal seizures, 8 had a reoccurrence of seizure activity after discharge, including 3 with focal seizures, 2 with generalized seizures, 1 with generalized and focal seizures, and 2 with unspecified seizure activity. Seven of these 8 dogs continued to have seizure activity in the long term, whereas the remaining dog had seizure activity only in the short term. Three of the 7 dogs with long-term seizure activity died or were euthanized 1,015, 1,078, and 737 days postoperatively; the cause of death or euthanasia was not related to the PANS in 2 dogs and was not recorded in 1 dog. The 1 dog that had PAS but for which seizure type was not recorded continued to have seizure activity in the long term.

Dogs with new neurologic signs following discharge—Twenty-five (50%) dogs developed new neurologic signs after hospital discharge. A total of 53 neurologic signs were recorded in these 25 dogs, consisting of lethargy or weakness (n = 6), disorientation (6), unresponsiveness or vacant episodes (6), seizure activity (5), head pressing (5), aggressive behavior (4), collapse (3), wobbliness (3), circling (2), tremors (2), dullness (2), vocalization (2), and pacing, paralysis, blindness, hypermetria, paresis, lip smacking, and depressed mentation (1 each). Four dogs had complete resolution of these new neurologic signs within a mean of 300 days (SD, 271 days)

Table 2—Reoccurrence of seizures and time to last recorded seizure activity for 30 dogs that developed postattenuation seizures (PAS) after surgical treatment of a single congenital portosystemic shunt and survived at least 30 days after surgery.

PAS type[a]	Reoccurrence[a]	Type of recurrent seizures[a]	Time to last known seizure (d)[b]	Veterinary follow-up time (d)[b]	Owner follow-up time (d)[b]
Focal only (12)	Yes (6)	Focal (6)	1,282 (1,514)[c]	1,080 (969)	2,468 (793)[d,e]
	No (6)	NA	NA	1,857 (1,411)	2,179 (1,163)
Generalized with or without focal (17)	Yes (8)	Generalized (2)	1,015, 161	419, 161	1,015[f], NOC
		Focal (3)	27, 337, 1,444	3,415, 737, 1,446	3,415[f], NOC, 3,962
		Generalized and focal (1)	1,306	1,657	NOC
		Unknown (2)	100, 902	171, 205	100, 902
	No (9)	NA	NA	611 (76–3,212)	1,858 (1,242)[g]
Unspecified (1)	Yes (1)	Generalized (1)	615	619	254

NA = Not applicable. NOC = No owner contact.

[a]Numbers in parentheses indicate number of dogs. [b]Values represent times after surgery and are given as median (range), mean (SD), or, for cells with < 5 dogs, individual data points. [c]For 1 dog, the specific date of last seizure activity could not be obtained and January 1 of the last year the dog was known to have had focal seizure activity before being euthanized was used. [d]For 2 dogs, date of last owner follow-up also represented the date of death. [e]No owner follow-up information was available for 1 dog. [f]Date of last owner follow-up also represented the date of death. [g]No owner follow-up information was available for 3 dogs.

postoperatively, whereas 18 dogs did not have complete resolution of these new neurologic signs after a mean follow-up time of 1,909 days (SD, 1,095 days) postoperatively. For 3 dogs, including 2 dogs with seizure activity, it was unknown whether neurologic signs resolved.

Of the 53 new neurologic signs that developed, 14 (26%) subsequently resolved. Five (36%) signs resolved within 24 hours (tremors, n = 2; vocalizing, 1; collapsing, 1; and seizure activity, 1), and 9 (64%) resolved within 110 days (range, 3 to 2,631 days) after surgery (circling, 2; dullness, 2; head pressing, 2; depressed mention, 1; pacing, 1; and vocalizing, 1). Thirty-four (64%) of the 53 new neurologic signs were reportedly still present a mean of 1,937 days (SD, 1,077 days) postoperatively (lethargy or weakness, n = 6; disorientation, 6; unresponsive or vacant episodes, 6; aggressive behavior, 4; head pressing, 3; wobbliness, 3; collapse, 2; seizure activity, 2; paralysis, 1; and blindness, 1). It was not known whether the remaining 5 (9%) new neurologic signs resolved (seizure activity, n = 2; hypermetria, 1; paresis, 1; and lip smacking, 1). Seven of the 25 (28%) dogs that developed new neurologic signs died or were euthanized a mean of 1,893 days (SD, 1,134 days) postoperatively. The cause of death or euthanasia was related to PANS in 1 dog, unrelated to PANS in 4 dogs, and not recorded in 2 dogs.

Owner questionnaire and survival time

Thirty-three of the 50 (66%) owners completed the owner questionnaire **(Supplementary Tables S1 and S2)**. Twenty-nine (88%) dogs were alive at the time of questionnaire completion a mean of 1,986 days (SD, 1,237 days) postoperatively, whereas 4 (12%) dogs had died or been euthanized (3 dogs were euthanized, but whether the remaining dog died or was euthanized was not recorded) a mean of 1,997 days (1,045 days) postoperatively. For 3 of these dogs, death or euthanasia was not related to PANS, and for 1, death or euthanasia was related to seizure activity. Two dogs that were recorded as alive at the time of owner questionnaire completion were found to have been euthanized 34 and 330 days later (4,009 and 2,661 days postoperatively, respectively) at the time of further follow-up telephone contact with the owner. The cause of euthanasia in these 2 dogs could not be ascertained from the owners. Seven (21%) dogs were recorded as receiving antiseizure medication (5 that were alive and 2 that received antiseizure medication until the time of death). Three (9%) dogs were recorded as receiving lactulose (2 that were alive and 1 that received lactulose until the time of death). One (3%) dog was receiving antimicrobial treatment until the time of death. Prior to surgery, 18 (55%) of 33 owners graded their dog's QOL as low (ie, a score of 0 to 3), 14 (42%) graded it as moderate (ie, a score of 4 to 7), and 1 (3%) recorded it as high (ie, a score of 8 to 10). At the time of questionnaire completion, 1 of 33 (3%) owners graded their dog's QOL as low, 5 (15%) graded it as moderate, and 27 (82%) graded it as high.

Seventeen of the 50 (34%) owners could not be contacted and the referring veterinarian or contributing surgeon provided the necessary follow-up information. Eleven (65%) of these 17 dogs were recorded as alive a mean of 648 days (SD, 502 days) postoperatively and 6 (35%) had died or been euthanized (1 dog was euthanized, and 1 dog died, but whether the remaining 4 dogs died or were euthanized was not recorded) a mean of 1,150 days (SD, 979 days) postoperatively. For 5 of these dogs, death or euthanasia was not related to PANS, but the cause of death or euthanasia was not recorded for the remaining dog. Five dogs were receiving antiseizure medication at the time last recorded alive (n = 3) or the time of death (2). For 1 additional dog, information regarding whether the dog was receiving antiseizure medication was not available. Neurologic signs were recorded in 5 dogs at the time last recorded alive (n = 4) or at the time of death (1), including blindness or impaired vision (3), proprioceptive deficits (2), pare-

sis (2), and strange gait, tremors, hypermetria, ataxia, lip smacking, and focal seizure activity (1 each). On the basis of information provided by the owner, referring veterinarian, or contributing surgeon, 12 of 50 (24%) dogs were receiving antiseizure medication at the time of last follow-up or the time of death.

In total, 38 of 50 (76%) dogs were recorded as alive a median of 1,255 days (range, 121 to 3,962 days) postoperatively, whereas 12 (24%) dogs had died or been euthanized a mean of 1,790 days (SD, 1,219 days) postoperatively. For 8 dogs that died or were euthanized, the cause of death or euthanasia was unrelated to PANS. The median survival time was not reached after a median postoperative follow-up of time of 1,324 days (range, 61 to 4,009 days). Forty-five (90%) dogs survived > 6 months.

Discussion

The main findings of the present study were that most (45/50 [90%]) dogs that developed PANS after surgical ligation of a congenital PSS and were still alive 30 days after surgery survived > 6 months, most owners (27/33 [82%]) graded their dog's long-term QOL as high (ie, a score of 8 to 10 on a scale from 0 to 10), half (15/30 [50%]) of all dogs that had PAS had a reoccurrence of seizures, and most (29/43 [67%]) neurologic signs present at the time of hospital discharge resolved, with just over half (15/29 [52%]) resolving ≤ 30 days postoperatively.

Our first hypothesis was that most dogs with PANS that were still alive 30 days after surgery would have survival times of > 6 months. This hypothesis was based on a number of previous reports[2,3,5,6,9,15,17] indicating that if affected dogs survive to hospital discharge, most will have survival times of at least 6 months. These previous reports, however, have a number of important limitations. The largest is a retrospective case series involving only 5 dogs, with long-term survival information provided for only one dog in that report,[2] and follow-up information beyond 6 months was available for only 7 dogs.[2,3,5,15,17] Despite their limitations, these reports corroborate findings in our study in which 45 of 50 (90%) dogs had survival times of > 6 months. Median survival time could not be calculated in our study because more than half of the dogs remained alive at the time of last follow-up, with just 12 (24%) dogs having died or been euthanized. For 8 of the 12 dogs that died or were euthanized, the cause of death or euthanasia was unrelated to PANS.

Most (27/33 [82%]) owners who completed the questionnaire in our study graded their dog's QOL as high at the time of questionnaire completion. The questionnaire used in our study was a modification of one used in previous studies.[24,26] One of these studies[26] compared the health-related QOL preoperatively and at long-term follow-up in dogs with a congenital PSS and a control population. A limitation of the use of this questionnaire is that it has not yet been validated. A shortened version of the original questionnaire, which focused on neurologic signs and excluded questions related to gastrointestinal and urinary signs, was used in our study. This questionnaire was also not completed by all owners in our study. On the basis of the absence of previous studies evaluating the long-term QOL of dogs with PANS, our results are difficult to compare with others.

We hypothesized that most dogs that developed PAS would experience a reoccurrence of seizures. A limitation of the previous literature reporting long-term (> 30 days) outcomes of dogs with PAS is that case numbers are small and follow-up times are very inconsistent. Most of this literature consists of small retrospective case series and case reports, the largest of which includes only 5 dogs with PAS,[2,3,5,6,8,9,15,17] and long-term outcomes are reported for only 14 dogs with PAS. The duration of long-term follow-up in these reports ranges from 2 months to 4 years, with follow-up times of > 6 months provided for only 8 of these 14 dogs.[2,3,5,8,15,17] In these reports,[2,3,5,6,8,9,15,17] reoccurrence of seizure activity is common, with 8 of 14 dogs for which long-term follow-up information is reported having a reoccurrence of seizures. This formed the basis of our third hypothesis and was supported by our results, with 15 of 30 (50%) dogs that had PAS having a reoccurrence of seizures. Three of the 15 dogs with a reoccurrence had seizures only in the short-term (ie, < 30 days after surgery), with long-term follow-up information for all 3 dogs (follow-up times of 1,948, 139, and 3,415 days postoperatively), whereas the remaining 12 dogs continued to experience seizure activity in the long-term (ie, ≥ 30 days after surgery), with a median follow-up time of 1,233 days (range, 161 to 3,962 days). The overall rate of reoccurrence of seizures in our study was similar for dogs that had generalized (8/17) versus only focal (6/12) PAS. Four of the 6 dogs that had only focal PAS and had a reoccurrence continued to have seizure activity in the long-term, whereas 7 of the 8 dogs that had generalized PAS with or without focal seizures and had a reoccurrence continued to have seizure activity in the long-term. A strength of our study was the long follow-up times, with 45 of 50 (90%) dogs confirmed as surviving > 6 months. These data are novel and difficult to compare with others owing to the lack of similar studies.

Our fourth hypothesis was that most neurologic signs present at the time of hospital discharge in dogs with PANS would resolve. This hypothesis was based on our experience and results of 5 retrospective case series[2,3,5,8,9] and a single case report.[17] In these reports,[2,3,5,8,9,17] information regarding whether neurologic signs present at the time of hospital discharge resolved is available for only 9 dogs. In some other reports,[3,6,8,15] no neurologic signs were present at hospital discharge[6,15] or it is unclear whether signs were present at discharge or developed after discharge.[3,8] Blindness resolved in 3 of 7 dogs that had it at the time of discharge and improved in another dog.[2,3,5,8,9] In our study, most (29/43 [67%]) individual neurologic signs present at the time of discharge resolved, with just over half (15/29 [52%] doing so within 30 days and most (27/29 [93%]) doing so within 6 months. Conversely, blindness did not resolve in 8 of the 12 dogs in which it was reported to be present at the time of hospital discharge, disorientation did not resolve in either of

the 2 dogs in which it was reported to be present, and strange gait did not resolve in the 1 dog in which it was reported to be present. It is difficult to compare times to resolution of signs present at the time of discharge in our study with previously reported times[2,3,5,8,9,17] because of inconsistent follow-up and lack of standardization of follow-up times. Thus, it is not possible to determine an accurate percentage of individual neurologic signs that will resolve within 30 days; however, it appears that most individual signs resolve within 6 months.[2,3,5,8,9,17]

Eight of 18 dogs in our study in which neurologic signs present at the time of hospital discharge resolved developed new neurologic signs that were not part of original episode of PANS, with 2 developing new neurologic signs < 6 months and 6 developing new neurologic signs ≥ 6 months postoperatively. It is possible that such signs developed as a result of reoccurrence or persistence of hepatic encephalopathy related to persistent shunting, and in most (6/8) dogs, these new neurologic signs did not resolve during the extended follow-up period available in our study. Therefore, although these dogs may have experienced a resolution of neurologic signs present at the time of discharge, they did not necessarily become neurologically normal. It is worthy of note that most new neurologic signs were reported by the owners at the time of questionnaire completion. We acknowledge the limitation of this and the possibility of overinterpretation or misinterpretation of information provided in the questionnaire.

We acknowledge a number of important limitations in this study. This was a retrospective study, and therefore the accuracy of the recorded data relied on the completeness of the medical records. Factors such as the timing of follow-up examinations could not be standardized owing to the study's retrospective nature. In dogs for which there was an extended period between follow-up examinations, the exact timing of resolution of neurologic signs could not be determined. This may have led to both over- and underestimation of the time to resolution of such signs. Similarly, neurologic signs reported at the time of last follow-up may have been related to other neurologic or non-neurologic disorders (eg, meningitis or osteoarthritis) separate from PANS. The description of neurologic signs experienced by dogs in the present study relied on the clinician's interpretation and what was recorded in the medical record. It is possible that some dogs may have experienced neurologic signs that were not witnessed or that dogs experienced other more subtle neurologic signs that were not recognized or recorded. This may have resulted in underreporting of neurologic signs. The timing of onset of PANS may have been affected by failure to recognize earlier, more subtle neurologic signs. We did not report the time of resolution of PANS that had resolved by the time of hospital discharge, and we did not have information regarding the first occurrence of seizure activity after discharge. We also did not have information regarding the frequency of seizure activity other than at the time of owner questionnaire completion. Similarly, the accuracy of timing of the development of new neurologic signs depended on the frequency of follow-up examinations and the owners' ability to recall when signs commenced. Information regarding follow-up confirmation of complete shunt closure and the absence of multiple acquired shunts by means of imaging (eg, abdominal ultrasonography or scintigraphy) and biochemical testing (eg, pre- and postprandial bile acid concentrations) was not recorded and likely would not have been standardized on the basis of the multi-institutional nature of the study. Furthermore, owners of dogs that had PANS may have been reluctant to perform additional diagnostic testing, and such testing may not have been ethically indicated unless results would directly impact therapeutic decision-making. However, this created the possibility that neurologic signs present in the long-term could have been related to reoccurrence or persistence of hepatic encephalopathy because of persistent or acquired shunting. For dogs for which the owner could not be contacted and the referring veterinarian or contributing surgeon provided the necessary follow-up information, we did not have information regarding the number that were receiving medical management apart from antiseizure medication. Nine institutions were included in this study, and therefore treatment of PANS, including administration of antiseizure medication at the time of onset and in the long-term, was not standardized. Factors that may have influenced a decision to euthanize a dog, such as the owner's willingness to continue treatment and provide care for a dog with persistent neurologic signs and the clinician's perception of the prognosis for neurologic recovery in the long-term, could not be controlled in this study. Owner QOL assessments were obtained by means of a previously published, nonvalidated, health-related QOL questionnaire.[26] In some cases in the present study, owners were contacted by telephone to complete the QOL questionnaire, and we recognize that this means of communication, versus email, could have influenced the responses provided. In situations when the owner could not be contacted, the primary veterinarian was contacted to provide information related to the final outcome on the basis of information recorded in the medical record. Furthermore, in situations where the primary veterinarian could not be contacted, the contributing surgeon had to provide the information on the basis of available records. Serum concentrations of glucose, ammonia, and electrolytes at the time PANS occurred were not reported in this study as they were not available for all dogs and were obtained from multiple diagnostic laboratories with different reference ranges.

Results of this study may provide valuable prognostic information for owners of dogs with PANS that survive > 30 days after surgery. Our findings highlighted that survival times of > 6 months and a high QOL can be achieved in most dogs with PANS that survive at least 30 days. Most neurologic signs resolved within 1 month postoperatively; however, vision loss was frequently permanent or persisted longer. Half (15/30) of all dogs with PAS had a reoccurrence of seizures. On the basis of this frequency of continued seizure activity, close monitoring of such dogs is warranted.

Acknowledgments

No third-party funding or support was received in connection with this study or the writing or publication of the manuscript. The authors declare that there were no conflicts of interest related to this study.

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Supplementary Materials

Supplementary materials are posted online at the journal website: avmajournals.avma.org