TITLE: Survival in feline epilepsy: the long and short of it

AUTHORS: Rowena M. A. Packer

JOURNAL TITLE: Veterinary Record

PUBLISHER: BMJ Publishing Group

PUBLICATION DATE: 2 November 2017 (online)

DOI: 10.1136/vr.j5025

EDITORIAL

Survival in feline epilepsy: the long and short of it

Rowena M.A. Packer BSc PhD

Royal Veterinary College, Hawkshead Lane, Hatfield, AL9 7TA

rpacker@rvc.ac.uk

Both quality and quantity of life are of importance to the owners of companion animals (Sandøe and Christiansen 2007), and in ideal circumstances, each veterinary treatment would ensure high quality of life *and* increase longevity (Oyama and others 2008). Understanding which disease and treatment related factors influence survival in diseased animals may help guide their management, for example, whether a treatment that compromises quality of life provides sufficient additional lifespan to justify its use. In animals with life-limiting diseases, mismatches may exist between owners' expectations of survival versus reality. For example, in a study of dog and cat owners' perceptions of medical treatment for cancer, a mismatch was observed between the number of owners expecting treatment to extend their pet's lifespan (87.0%) and the actual number that experienced this (60.9%) (Brønden and others 2003). As such, robust estimates of survival time are potentially valuable statistics for guiding owner expectations post-diagnosis. Indeed, in a study of owner perceptions of quality versus quantity of life for dogs with heart disease, owners' reported high levels of concern regarding their inability to know how long their pet was going to live (Oyama and others 2008).

Survival analysis was developed to examine mortality data and risks associated with time until death, and allows for censoring where the outcome (usually death or euthanasia) is not recorded at a point in time for a particular subject. Canine epilepsy is a common, chronic neurological disorder in dogs and survival analyses have demonstrated that it can significantly reduce lifespan (Berendt and others 2007). Epileptic seizures are also a common presenting complaint in cats, affecting 1-2% of the general feline population (Schriefl and others 2008). Seizure manifestations may be different to those typically seen in dogs, but the underlying causes of seizure activity appear to be similar, with both idiopathic and structural epilepsies described (Pákozdy and others 2010; Stanciu and others 2017). Of those cats presenting with seizures, between 22-54% are classified as idiopathic (also termed 'epilepsy of unknown cause', or EUC) (Pákozdy and others 2010; Schriefl and others 2008; Wahle and others 2014). To date, little data have been published documenting survival in feline EUC. In a recent small-scale study of n=18 cats with EUC, the 1-year survival rate was 73%, which was significantly higher than the survival rate of cats with structural epilepsy or acute symptomatic seizures (35%; 22/63 cats) (Wahle and others 2014). A new study is summarised on p*X* of this issue of *Veterinary Record* (Szelecsenyi and others 2017) which builds upon these findings in a larger population of 76 cats with EUC.

In a retrospective study of cats presenting with seizures over a 15 year period, Szelecsenyi and others explored the effects of seizure semiology and type upon treatment outcome and survival. The authors demonstrate that of 76 cats with EUC, the majority were alive at follow up (68%), with a median follow up time of 3.2 years. The longest follow up of a live cat with EUC was 11 years, and from Kaplan-Meyer analysis, the median survival time of cats with EUC was 4.9 years. This is markedly higher than studies of canine epilepsy, where in a multi-breed study, the median lifespan with epilepsy was 2.3 years (Berendt and others 2007), and in a study of Border Collies with EUC was 2.07 years (Hülsmeyer and others 2010). Szelecsenyi and others report that of the cats that died during the study period (24/76), the majority were epilepsy-related (66.6%, n=16). This was defined as the authors as euthanasia motivated by circumstances directly associated with seizures. Similar findings have been reported in canine epilepsy, for example more than 60% of Irish Wolfhounds (Casal and others 2006) and 70% of Belgian Shepherds with idiopathic epilepsy were reported to die of epilepsy-related reasons (Gulløv and others 2012). Whether euthanasia was elected for by the cat owners in this study due to uncontrolled seizures, intolerable side effects of AEDs or other factors perceived to impair cat and/or owner quality of life was not investigated in this study, but exploring where owners' 'limits' lie for these factors *a priori* may aid in the management of owner and feline quality of life. As attitudes to companion animal euthanasia may be culturally driven (Miura and others 2000), and all cats in this study were derived from a hospital population in Switzerland, similar studies from other countries may provide further insights into end of life decision-making in feline epilepsy.

Szelecsenyi and others identified two major risk factors that predicted survival in cats with EUO: age at time of seizure onset and remission. In contrast, AED treatment, seizure semiology and seizure type were not associated with survival. Seizure freedom is considered the primary treatment goal in the therapeutic management of canine and feline epilepsy patients (Potschka and others 2015), and data suggests that seizure control is also beneficial for survival in canine epilepsy (Weissl and others 2012); although remission rates are generally low in the dog at ~14-15% (Berendt and others 2007; Packer and others 2014). In contrast, Szelecsenyi and others report relatively high rates of remission in their feline study; complete remission (defined by a seizure-free period of at least one year with or without AED therapy) was achieved in 34% of cats with AED therapy and 79% of cats without AED therapy. In a previous study, 40-50% of phenobarbital treated cats with EUC were reported to become seizure-free (Pakozdy and others 2012), and in a second population of treated and untreated cats, 44% of cats (8/18) became seizure-free (Wahle and others 2014). From these data it appears that feline EUC is manageable and may have a more favourable outcome than canine epilepsy. Remission rates being higher in the untreated group was initially considered unexpected by Szelecsenyi and others; however, a previous canine study did not identify positive effects of AED treatment on remission (Berendt and others 2007). It is likely that untreated animals of both species have a less severe epileptic phenotype and thus a better prognosis for survival compared to those whose epilepsy phenotype necessitated treatment.

Szelecsenyi and others' data add to our understanding of survival and treatment outcomes in feline EUC; however, unknown variation in survival remains, and further research is necessary to understand animal, disease and treatment-related risk factors. Clinical variables including a history of status epilepticus (SE) and cluster seizures (SE) have previously been associated with reduced survival time in canine epilepsy patients (Arrol and others 2012; Berendt and others 2007; Fredso and others 2014; Monteiro and others 2012; Saito and others 2001). Several other signalment-based risk factors for survival have been identified in dogs that could be further explored in cats, including sex (bitches lived longer than dogs) (Berendt and others 2007) and neuter status (intact dogs are at an increased risk of epilepsy-related euthanasia compared to neutered) (Berendt and others 2008).

As recently stated by the International Veterinary Epilepsy Task Force, no information is available yet about SUDEP (sudden unexpected death in epilepsy) and life expectancy in feline epilepsy patients (Potschka and others 2015). Cases of presumed SUDEP have been reported in dogs (Berendt and others 2007; Gulløv and others 2012) and life expectancy has been estimated to be around 7 years (Berendt and others 2007; Proschowsky and others 2003). Similar data for cats could aid clinicians in the management of EUC patients, and in managing client expectations of their animal's disease.

Clinical importance for practitioners

- Epilepsy of unknown origin exists in a proportion of cats with seizures and has a good long-term prognosis for many cats, with complete remission in 42% and a median survival time of 4.9 years
- Cats that achieve complete remission (at least 1 year seizure free) have an increased survival time
- Epilepsy follows a self-remitting course in a proportion of cats without the use of AEDs, with long (1 year+) seizure free periods; however, previous studies indicate anti-epileptic therapy should be continued to avoid seizure recurrence (Pakozdy and others 2012)

References

ARROL, L., PENDERIS, J., GAROSI, L., CRIPPS, P., GUTIERREZ-QUINTANA, R. & GONÇALVES, R. (2012) Aetiology and long-term outcome of juvenile epilepsy in 136 dogs. Veterinary Record 170, 335

BERENDT, M., GREDAL, H., ERSBØLL, A. K. & ALVING, J. (2007) Premature Death, Risk Factors, and Life Patterns in Dogs with Epilepsy. Journal of Veterinary Internal Medicine 21, 754-759

BERENDT, M., GULLOV, C., CHRISTENSEN, S., GUDMUNDSDOTTIR, H., GREDAL, H., FREDHOLM, M. & ALBAN, L. (2008) Prevalence and characteristics of epilepsy in the Belgian shepherd variants Groenendael and Tervueren born in Denmark 1995-2004. Acta Veterinaria Scandinavica 50, 51

BRØNDEN, L. B., FLAGSTAD, A., RUTTEMAN, G. R. & TESKE, E. (2003) Study of dog and cat owners' perceptions of medical treatment for cancer. Veterinary Record 152, 77-80

CASAL, M. L., MUNUVE, R. M., JANIS, M. A., WERNER, P. & HENTHORN, P. S. (2006) Epilepsy in Irish Wolfhounds. Journal of Veterinary Internal Medicine 20, 131-135

FREDSO, N., KOCH, B. C., TOFT, N. & BERENDT, M. (2014) Risk Factors for Survival in a University Hospital Population of Dogs with Epilepsy. J Vet Intern Med

GULLØV, C. H., TOFT, N. & BERENDT, M. (2012) A Longitudinal Study of Survival in Belgian Shepherds with Genetic Epilepsy. Journal of Veterinary Internal Medicine 26, 1115-1120

HÜLSMEYER, V., ZIMMERMANN, R., BRAUER, C., SAUTER-LOUIS, C. & FISCHER, A. (2010) Epilepsy in Border Collies: Clinical Manifestation, Outcome, and Mode of Inheritance. Journal of Veterinary Internal Medicine 24, 171-178

MIURA, A., BRADSHAW, J. W. S. & TANIDA, H. (2000) Attitudes Towards Dogs: A Study of University Students in Japan and the UK. Anthrozoös 13, 80-88

MONTEIRO, R., ADAMS, V. & KEYS, D. (2012) Canine idiopathic epilepsy: prevalence, risk factors and outcome associated with cluster seizures and status epilepticus. J Small Anim Pract 53, 526-530

OYAMA, M. A., RUSH, J. E., O'SULLIVAN, M. L., WILLIAMS, R. M., ROZANSKI, E. A., PETRIE, J.-P., SLEEPER, M. M. & BROWN, D. C. (2008) Perceptions and priorities of owners of dogs with heart disease regarding quality versus quantity of life for their pets. Journal of the American Veterinary Medical Association 233, 104-108

PACKER, R. M., SHIHAB, N. K., TORRES, B. B. & VOLK, H. A. (2014) Clinical risk factors associated with anti-epileptic drug responsiveness in canine epilepsy. PLOS ONE 9

PÁKOZDY, Á., LESCHNIK, M., SARCHAHI, A. A., TICHY, A. G. & THALHAMMER, J. G. (2010) Clinical comparison of primary versus secondary epilepsy in 125 cats. Journal of Feline Medicine and Surgery 12, 910-916

PAKOZDY, A., SARCHAHI, A. A., LESCHNIK, M., TICHY, A. G., HALASZ, P. & THALHAMMER, J. G. (2012) Treatment and long-term follow-up of cats with suspected primary epilepsy. Journal of Feline Medicine and Surgery 15, 267-273

POTSCHKA, H., FISCHER, A., LÖSCHER, W., PATTERSON, N., BHATTI, S., BERENDT, M., DE RISIO, L., FARQUHAR, R., LONG, S., MANDIGERS, P., MATIASEK, K., MUÑANA, K., PAKOZDY, A., PENDERIS, J., PLATT, S., PODELL, M., RUSBRIDGE, C., STEIN, V., TIPOLD, A. & VOLK, H. A. (2015) International veterinary epilepsy task force consensus proposal: outcome of therapeutic interventions in canine and feline epilepsy. BMC Veterinary Research 11, 177

PROSCHOWSKY, H. F., RUGBJERG, H. & ERSBØLL, A. K. (2003) Mortality of purebred and mixed-breed dogs in Denmark. Preventive Veterinary Medicine 58, 63-74

SAITO, M., MUNANA, K. & NJ, S. (2001) Risk factors for development of status epilepticus in dogs with idiopathic epilepsy and effects of status epilepticus on outcome and survival time: 32 cases (1990-1996). J Am Vet Med Assoc 219, 618-623

SANDØE, P. & CHRISTIANSEN, S. B. (2007) The value of animal life: how should we balance quality against quantity? Animal Welfare 16, 109-115

SCHRIEFL, S., STEINBERG, T. A., MATIASEK, K., OSSIG, A., N., F. & FISCHER, A. (2008) Etiologic classification of seizures, signalment, clinical signs, and outcome in cats with seizure disorders: 91 cases (2000–2004). J Am Vet Med Assoc 233, 1591–1597

STANCIU, G.-D., PACKER, R. M. A., PAKOZDY, A., SOLCAN, G. & VOLK, H. A. (2017) Clinical reasoning in feline epilepsy: Which combination of clinical information is useful? The Veterinary Journal 225, 9-12

153 WAHLE, A. M., BRÜHSCHWEIN, A., MATIASEK, K., PUTSCHBACH, K., WAGNER, E.,
154 MUELLER, R. S. & FISCHER, A. (2014) Clinical Characterization of Epilepsy of Unknown Cause in
155 Cats. Journal of Veterinary Internal Medicine 28, 182-188

156 WEISSL, J., HULSMEYER, V., BRAUER, C., TIPOLD, A., KOSKINEN, L. L., KYOSTILA, K.,
157 LOHI, H., SAUTER-LOUIS, C., WOLF, M. & FISCHER, A. (2012) Disease progression and
158 treatment response of idiopathic epilepsy in Australian Shepherd dogs. Journal of veterinary internal
159 medicine / American College of Veterinary Internal Medicine 26, 116-125

160