English springer spaniels with significant bradyarrhythmias—presentation, troponin I and follow-up after pacemaker implantation

OBJECTIVES: English springer spaniels (ESS) are one of the most frequently presented breeds for pacemaker implantation in the UK and may do so at an early age. In comparison to dogs of other breeds (non-ESS) presenting for pacemaker implantation, cardiac troponin I (cTnI), the outcome and survival of ESS were investigated.

METHODS: Case records of dogs receiving pacemaker implantation were retrospectively reviewed.

RESULTS: Between September 2004 and October 2008, 58 dogs were presented to the Small Animal Teaching Hospital, University of Liverpool for pacemaker implantation. ESS (n=10) was the second most commonly presented breed. ESS were significantly younger than non-ESS (P=0.022). cTnI values were elevated on presentation and a significant reduction was present after pacemaker implantation (P=0.008) in all dogs. No significant difference in initial cTnI was identified comparing ESS and non-ESS (P=0.45) and median survival times were similar (P=0.37).

CLINICAL SIGNIFICANCE: ESS may be predisposed to bradyarrhythmias requiring pacemaker implantation. They present at a significantly younger age than non-ESS. Survival times between ESS and non-ESS were similar, despite ESS being paced at a younger age. However, pacemaker implantation is recommended in ESS as median survival times of 30 months with a good quality of life were achieved.

INTRODUCTION

Pacemaker implantation is the recommended treatment for significant bradyarrhythmias in dogs (Sisson and others 1991, Oyama and others 2001, Wess and others 2006, Johnson and others 2007, Hildebrandt and others 2009).

The most common canine arrhythmias requiring pacemaker implantation are high grade second and third degree atrioventricular block (AVB) and sick sinus syndrome (SSS) (Sisson and others 1991, Oyama and others 2001, Wess and others 2006, Johnson and others 2007). Recent literature reports Labradors as the breed most commonly affected with third degree AVB and West Highland white terrier (WHWT) and miniature schnauzer being most commonly affected with SSS (Moneva-Jordan and others 2001, Oyama and others 2001, Wess and others 2006, Johnson and others 2007). Interestingly, English springer spaniels (ESS) and Labradors are the most frequent breeds presented for pacemaker implantation in the UK (Johnson and others 2007), whereas in American publications only single cases of ESS have been reported (Sisson and others 1991, Oyama and others 2001, Wess and others 2006). In the experience of the authors, ESS with significant bradyarrhythmias show a distinct clinical feature as some seem to be present at a young age (<5 years), whereas most dogs present for pacemaker implantation at an age of 7 to 10 years (Oyama and others 2001, Wess and others 2006, Johnson and others 2007, Hildebrandt and others 2009).

The primary causes of significant bradyarrhythmias in dogs are often not identified, but fibrosis of the atrioventricular (AV) node and conduction system or myocarditis is usually suspected. In ESS and also Labradors, dilated cardiomyopathy (DCM), myocardial inflammation, fibrofatty replacement of the myocardium...
Pacemaker implantation is now a routine procedure in referral centres. There is no apparent difference in outcome whether using used or new pacemakers and whether these are implanted either passively or actively. Survival after pacemaker implantation is in most situations good. Complications after surgery can be divided into major (lead dislodgement, loss of capture, infections of the pacemaker site and sudden death) and minor complications (e.g. seroma production at the implantation site), which are more frequent, but resolve in nearly all cases. Several studies have reviewed the rates of complication and no breed predisposition to such events was reported (Oyama and others 2001, Wass and others 2006, Johnson and others 2007, Hildebrand and others 2009). However, in the authors’ experience, ESS seem to more frequently develop major complications after pacemaker implantation when compared to other breeds.

This retrospective study aimed to compare presentation, cTnI concentrations, complications and survival of ESS with dogs of other breeds presented with bradyarythmias requiring pacemaker implantation.

**MATERIALS AND METHODS**

For this retrospective study, records of dogs presented for pacemaker implantation to the University of Liverpool Small Animal Teaching Hospital (ULIV-SATH) between September 2004 and October 2008 were reviewed. Investigations of dogs included signalment, history, presenting signs, physical examination, complete blood count (CBC), biochemistry (BC), six lead electrocardiogram (ECG) and Doppler echocardiographic investigation. A 24-hour Holter monitoring was performed in cases requiring further documentation of episodic arrhythmias. cTnI was analysed in animals where myocardial inflammation or infiltration was suspected (from the history, haematology, BC results or echocardiographic findings). cTnI measurements were repeated at revisits 1 to 24 months (median four months) after pacemaker placement. T4/TSH was analysed if hypothyroidism was suspected. Samples were collected for polymerase chain reaction (PCR) screening of endemic tick borne diseases (Ehrlichia/Borrelia/Rickettsia/Babesia/Bartonella) and Neospora and Toxoplasma antibody titres from patients evidencing clinical features suggestive of infectious myocarditis or with a history of previous tick infestation.

All blood samples were collected from the jugular vein. 2-ml ethylenediaminetetraacetic acid (EDTA) blood was taken for CBC and tick borne diseases (1 ml each), 1 ml of blood was taken into a serum tube for BC. For analyses of cTnI, T4/TSH, Neospora and Toxoplasma further serum samples were obtained if needed. Samples were centrifuged within one hour, submitted for BC (in house) and sent by post at room temperature the same day to external laboratories for cTnI analysis (Beaufort Cottage Laboratories, Newmarket), T4/TSH (CSLS, Cambridge) and EDTA samples were sent for tick borne diseases (Acarus; Bristol) and/or Neospora and Toxoplasma (Biobest; Penicuik).

**Pacemaker implantation**

Pacemaker implantation was performed as previously described (Oyama and others 2001, Wass and others 2006, Johnson and others 2007). Briefly, temporary pacing was obtained in small breed dogs by placing external pacing patches, in large breed and broad-chested dogs a temporary pacing lead was placed into the right ventricle via the lateral or medial saphenous vein. The dogs were positioned in left lateral recumbency and the pacemaker lead was placed into the right ventricle via the right jugular vein under fluoroscopic guidance. The pulse generator was placed into a subcutaneous pouch on the right dorsolateral aspect of the neck. Pacemaker placement was analysed postsurgery by thoracic radiographs.

Dogs with high grade second and third degree AVB and atrial stand still (ASS) received new Sorin Neway SR bipolar system pacemakers with rate responsive mode and active fixation leads. Dogs with SSS sometimes received pacemakers without rate responsive mode (VVI). The ESS of this study received new Sorin Neway SR bipolar pacemakers and active fixation leads, except for one where a used pacemaker and a passive...
fixation lead was placed. The pacemaker was initially set in VVI mode at a basic rate of 70 beats per minute (for second and third degree AVB and ASS) and 50 beats per minute in case of SSS. The dogs were initially paced at 2.5 V (pulse duration of 0.4 ms) with sensitivity set at 2.0 mV. Pacemaker settings were checked one month after surgery (with start of VVIR mode except in SSS cases), three months after surgery and every six months thereafter. For this study, follow-up was based on revisits or telephone contact with the owners.

Complications and survival time
Complications of procedures were recorded and separated into major and minor complications as reported previously (Oyama and others 2001, Wess and others 2006, Johnson and others 2007). Major complications included lead dislodgement or pacemaker failure needing a pacemaker and/or lead replacement, and wound infections. Survival time and outcome was assessed and dogs were separated into alive at the end of the study, cardiac-related and non-cardiac-related death. cTnI levels were measured at presentation of the dog (before pacemaker placement) and at revisits (after pacemaker placement) and concentrations were correlated with survival time of dogs.

Age, cTnI and survival time of ESS (n=10) was compared to other dogs (non-ESS; n=48) of this study.

Statistical analysis
Data were entered into Excel spreadsheets (Microsoft Corporation) and statistical analysis was performed using Minitab 15 (Minitab Inc, State College, PA, USA). Following basic descriptive statistics (mean, median, variance, standard deviation, interquartile range, confidence interval), some variables were log transformed as required to give normal distribution of data. Differences in age of animals and cTnI concentrations were compared using Kruskal–Wallis and Mann-Whitney U tests as appropriate. Differences between repeat samples were expressed as “after minus before” and examined using the Wilcoxon 1-sample signed Rank test. Survival analysis used the Kaplan–Meier method (log Rank test). Dog were censored if they were lost to follow-up or died of non-cardiac causes. Association of survival time and cTnI values with 0.3 and 0.5 ng/ml as cutoff were analysed using the Kaplan–Meier method (log Rank test). Statistical significance was defined as P<0.05.

RESULTS
Between September 2004 and October 2008, 58 animals were presented for pacemaker implantation at ULIV-SATH. Main presenting problems were collapsing episodes, exercise intolerance and bradycardia. Most dogs were presented with a high grade second and third degree AVB (n=42, 72.4%) and SSS (n=13, 22.4%). Three dogs (one ESS and two Labradors; 5.2%), were presented with ASS.

The most common breed were ESS (n=10, 17.2%) and Labradors (n=9, 15.5%) with third degree AVB and ASS, and WHWT (n=11; 19%) with SSS (Fig 1). Thirty-two dogs were female (55%; 24 neutered, eight intact), 26 were male (45%; 13 neutered, 13 intact). The ESS genders included eight females (six neutered, two intact) and two males (one neutered, one intact; Table 1).

The age of all dogs presented ranged between 2 and 14 years (mean 8.1 years, median 9 years; 95% confidence interval [CI] 7 to 10 years). ESS (n=10) were between 2 and 11 years old (median 4 years, 95% CI 2 to 10·3 years) and were significantly younger (P=0·022) than non-ESS (n=48), which were between 2 and 14 years old (median 9 years, 95% CI 8 to 10 years; Fig 2). None of the dogs showed muscle wasting or neurological abnormalities. All cases tested negative for tick borne diseases, hypothyroidism and Neospora/Toxoplasma.

cTnI
cTnI concentration was analysed in 39 dogs and ranged between 0.02 and 180 ng/ml with a median of 0.53 ng/ml (95% CI 0·3 to 0·89 ng/ml). Only five dogs had a cTnI concentration within the normal range (<0.15 ng/ml; Spratt and others 2005). No significant difference was present comparing cTnI concentrations in ESS (n=8, median cTnI 0.7 ng/ml; 95% CI 0·25 to 2·19 ng/ml) and dogs of other breeds (non-ESS; n=31; median cTnI 0.53 ng/ml; 0·27 to 0·89 ng/ml; P=0·45; Fig 3).

In 11 dogs follow-up cTnI concentrations were obtained. These revealed a significant reduction comparing cTnI values before pacemaker placement (median 3·0 ng/ml, 95% CI 0·29 to 12·4 ng/ml) and after pacemaker placement (median 0·42 ng/ml, 95% CI 0·19 to 0·89 ng/ml; P=0·008; Fig 4). However in most dogs, cTnI (9/11) remained higher than the reference range (i.e. >0·15 ng/ml).
Complications

All animals survived the procedure and immediate recovery after surgery was unremarkable. Pacemaker settings after surgery were satisfactory and marked improvement of clinical signs was seen in all animals.

Major complications including lead dislodgement, infection and loss of capture occurred in eight (14%), five (8.6%) and six (10%) animals, respectively. Major complications occurred in all two years old ESS (n=3). One developed an infected fistula over the jugular vein at the incision site two months after pacemaker implantation. The pacemaker was removed and an abdominal pacemaker and epicardial lead was placed. This animal developed generalised cardiomegaly and myocardial failure and congestive heart failure (CHF) four months after pacemaker placement, but his condition

Table 1. Signalment, cardiac troponin I (cTnI) diagnosis, pacemaker, complications and outcome of ESS presented with bradyarrhythmia to the University of Liverpool Small Animal Teaching Hospital

<table>
<thead>
<tr>
<th>ESS</th>
<th>Age (years)</th>
<th>Sex</th>
<th>cTnI (ng/ml)</th>
<th>Diagnosis</th>
<th>Pacemaker</th>
<th>Complication</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>F</td>
<td>0.27</td>
<td>ASS</td>
<td>New, active fixation lead</td>
<td>Infection after two months, epicardial lead placed, MF and CHF after four months, stable on medication</td>
<td>Alive three years after pacemaker placement</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>F</td>
<td>1.62</td>
<td>AVB</td>
<td>New, active fixation lead</td>
<td>Seroma, infection after one week, lead dislodgement after four months, loss of capture after six months (resolved after four months)</td>
<td>Died two years after pacemaker placement</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>MN</td>
<td>180</td>
<td>AVB</td>
<td>New, active fixation lead</td>
<td>Seroma, lead dislodgement after two weeks</td>
<td>Died two years after pacemaker placement</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>FN</td>
<td>n.d.</td>
<td>SSS</td>
<td>New, active fixation lead</td>
<td>No</td>
<td>Alive five years after pacemaker placement</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>FN</td>
<td>11.1</td>
<td>AVB</td>
<td>New, active fixation lead</td>
<td>No</td>
<td>Alive six months after pacemaker placement</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>FN</td>
<td>0.02</td>
<td>AVB</td>
<td>New, active fixation lead</td>
<td>Lead dislodgement after 24 hours</td>
<td>Alive six months after pacemaker placement</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>FN</td>
<td>0.83</td>
<td>AVB</td>
<td>New, active fixation lead</td>
<td>No</td>
<td>Alive two years after pacemaker placement</td>
</tr>
<tr>
<td>8</td>
<td>10</td>
<td>FN</td>
<td>n.d.</td>
<td>AVB, CHF</td>
<td>New, active fixation lead</td>
<td>Seroma</td>
<td>Died three years after pacemaker placement</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td>FN</td>
<td>n.d.</td>
<td>AVB</td>
<td>New, active fixation lead</td>
<td>No</td>
<td>Developed neuropathy, died after one month</td>
</tr>
<tr>
<td>10</td>
<td>11</td>
<td>M</td>
<td>0.3</td>
<td>SSS</td>
<td>Second hand, passive fixation lead</td>
<td>No</td>
<td>Alive three years after pacemaker placement</td>
</tr>
</tbody>
</table>

ASS Atrial stand still, AVB Third degree atrioventricular block, MF Myocardial failure, CHF Congestive heart failure, F Female, FN Female neutered, M Male, n.d. Not determined, SSS Sick sinus syndrome.

Complications

All animals survived the procedure and immediate recovery after surgery was unremarkable. Pacemaker settings after surgery were satisfactory and marked improvement of clinical signs was seen in all animals.

Major complications including lead dislodgement, infection and loss of capture occurred in eight (14%), five (8.6%) and six (10%) animals, respectively. Major complications occurred in all two years old ESS (n=3). One developed an infected fistula over the jugular vein at the incision site two months after pacemaker implantation. The pacemaker was removed and an abdominal pacemaker and epicardial lead was placed. This animal developed generalised cardiomegaly and myocardial failure and congestive heart failure (CHF) four months after pacemaker placement, but his condition

FIG 2. Numbers of ESS (left y-axis) and other than ESS (non-ESS, right y-axis) in different age groups presented for pacemaker implantation. ESS were significantly younger than non-ESS (P=0.022), presenting most commonly at an age of 0 to 4 years with a second presentation “peak” at 9 to 12 years, whereas other breeds present mainly between 9 and 12 years
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improved and became stable after initiating therapy (Table 1). Two ESS experienced lead dislodgement (two weeks and four months after placement) and repeat surgery with lead replacement was performed (Table 1). One of them developed infection of the surgery site (one week after pacemaker replacement), which was treated conservatively, and loss of capture six months after placement. The pacing voltage was increased (to 5.5 V) to ensure continuous pacing and could be reduced again to 2.5 V after four months.

Survival

Twenty-six dogs were alive at the end of the study. Cardiac-related death occurred in 19 dogs and 11 dogs died of non-cardiac causes, five of these due to neoplasia. Two dogs were lost to follow-up. The median survival time of all dogs was 22 months (mean 24 months 95% CI 19.6 to 29.7 months). Dogs dying of cardiac-related causes had median survival times of 30 months (mean 28.4 months, 95% CI 22.6 to 34.3 months), whereas dogs dying of non-cardiac causes had a median survival time of 9 months (mean 11.75 months, 95% CI 8.2 to 15.2 months; P<0.001, log Rank test; P = 0.002 Wilcoxon).

Excluding non-cardiac causes of death, no significant difference in survival time comparing ESS (n=8) and non-ESS (n=38) was present (P=0.93 log Rank test, P=0.37 Wilcoxon; Fig 5). The median survival time for ESS was 30 months (mean 32.4 months, 95% CI 21.9 to 42.9 months) and for non-ESS also 30 months (mean 27.6 months, 95% CI 20.7 to 34.5 months). The survival probabilities for ESS were 85%, 68% and 34% one, two and three years after pacemaker implantation and 79%, 59% and 29% for non-ESS.

DISCUSSION

Seventy per cent of dogs presented for pacemaker implantation to ULIV-SATH were diagnosed with high grade second or third degree AVB, 22% had SSS. This is similar to results reported before with 59% to 64% of animals presenting with grade second degree AVB and third degree AVB and around 40% with SSS (Oyama and others 2001, Wess and others 2006, Johnson and others 2007). A slight predominance of female dogs (55%) was present, which has been reported by others (Oyama and others 2001, Wess and others 2006, Johnson and others 2007).

In the present study, ESS was the second most commonly presented breed (n=10; 17.2%). This is similar to other UK studies but different from American studies where ESS were only sporadically reported (Sisson and others 1991, Moneva-Jordan and others 2001, Oyama and others 2001, Wess and others 2006, Johnson and others 2007). A slight predominance of female dogs (55%) was present, which has been reported by others (Oyama and others 2001, Wess and others 2006, Johnson and others 2007).
A suspicion is raised in ESS of an underlying genetic basis but despite this genetic cause have not been identified in veterinary patients (Oyama and others 2001, Wess and others 2006, Johnson and others 2007). In people with AVB of idiopathic familial clustering has been noted and autosomal dominant inheritance was found (reviewed by Benson 2004). Furthermore, neuromuscular diseases can be associated with arrhythmias in young adults (Stevenson and others 1990, Benson 2004, Fazelifar and others 2005, Wessely and others 2005). A suspicion is raised in ESS of an underlying genetic basis. Some present significantly younger than other breeds and one of these presented with ASS. Reports of cardiomyopathy and destruction of the conduction system with associated AVB in ESS exist (Jeraj and others 1980, Holland and others 1991). However, echocardiographic parameters of ESS were not markedly different from the non-ESS with significant bradyarrhythmias in this study (data not shown). Furthermore, there was no clinical evidence of neuromuscular disease in dogs of this study. However, one ESS died of neuropathy one month after pacemaker placement, but this dog was 10 years old (Table 1).

Infectious causes of cardiomyopathy were not detected in dogs of this study. However, cTnI concentrations measured in dogs before pacemaker implantation were elevated revealing a median of 3.0 ng/ml (95% CI 0.29 to 12.4 ng/ml) and only five dogs had a cTnI within the normal range (<0.15 ng/ml; Spratt and others 2005). Increased cTnI concentrations might be associated with third degree AVB and acute myocarditis (Church and others 2007, Fonfara and others in press). However, no significant difference in cTnI concentrations between ESS and non-ESS was present (Fig 3) and no correlation of cTnI concentrations to survival time was detected (P=0.06 log Rank test), but larger numbers might be necessary to increase statistical power.

cTnI measurements taken at revisits after a median time period of four months after pacemaker placement revealed a significant reduction (P=0.008, Fig 4), which suggests reduction of myocardial damage (Maisel and others 2006, Wells and Sleeper 2008, Fonfara and others in press). These data may support the fact that the bradyarrhythmia resulted in myocardial hypoxia and cardiomyocyte injury, which improved in part following pacemaker implantation. However, in 9 of 11 cases cTnI concentrations were still higher than the reference range. Persistent elevation of cTnI blood concentrations suggest irreversible and sustained myocardial cell damage (Stanton and others 2005, O’Brien and others 2006, Wells 2008). Progressive underlying disease or myocardial damage due to non-physiological cardiac contraction from single chamber pacing are also possible causes for the continued elevation in cTnI levels (Frias and others 2003, Bulmer and others 2006, Hildebrandt and others 2009).

The rate of major complications in this study group was similar to other reports in the literature (Sisson and others 1991, Oyama and others 2001, Wess and others 2006, Johnson and others 2007). However, the three 2-year old ESS all developed major complications including lead dislodgement, surgery wound infection and pacemaker dysfunction. Unfortunately, causes were not identified and post-mortem examinations are not available. Johnson and others (2007) reported increased risk of lead dislodgement with passive fixation leads and increased risk of pacemaker dysfunction with used pacemakers. This was not evident in this study, as only one 11-year-old ESS received a used pacemaker and passive fixation lead and did not experience any complications (Table 1).

The survival probability after pacemaker implantation was similar to reports in the literature (Oyama and others 2001, Wess and others 2006, Johnson and others 2007). There was no difference in median survival times of ESS and non-ESS. Analysis of survival probabilities between the two groups showed that ESS seemed to have higher probabilities, but this difference did not achieve statistical significance. However, considering the significantly younger age of some ESS in
comparison to non-ESS, longer survival times of ESS would have been expected. Limitations of this study were inherent to all retrospective studies, in that investigations or sample times were not standardised. Only small numbers of ESS were present, which will have limited the power of statistical analyses. The number of animals in which repeat cTnl samples were taken was small and no fixed time interval between sampling was present. Post-mortem examinations of ESS are necessary to get more information about possible underlying cardiac pathology.

Conclusion

ESS are predisposed to bradyarrhythmias requiring pacemaker implantations in the UK. They are significantly younger than other breeds on presentation. cTnl concentrations were not significantly higher in comparison to other breeds and survival times were similar. Longer survival times in these dogs of young age might have been expected. However, pacemaker implantation is recommended in ESS as median survival times of 30 months (mean 32 months) with a good quality of life can be achieved.

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