Epicardial pacemaker placement is associated with low complications rate and improved quality of life in dogs

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Abstract

Objective

To describe complications and outcomes in dogs undergoing epicardial pacemaker (EP) implantation, to identify factors associated with survival, and to investigate improvement in clinical signs and health-related quality of life (HRQoL) following surgery.

Animals

52 client-owned dogs that underwent EP placement.

Procedures

Medical records of four UK-based referral hospitals were searched and data reviewed retrospectively between July 2010 and December 2022. Factors contributing to outcomes after EP placement were assessed.

Results

The primary reasons for referral included collapsing/syncopal episodes (36), exercise intolerance (15), and significant bradycardia (46). Third-degree atrioventricular block (39, 75%) was the predominant indication for pacemaker placement and common reasons for EP placement included previous transvenous pacemaker dislodgment/loss of capture (12) and small body size (10). Intra- and post-operative complications were documented in 11% and 23% of dogs respectively. Overall, 96% of dogs survived to discharge, and median follow-up time was 462 (range, 31-3139) days. Presence of coexistent myocardial or valvular disease at the time of EP implantation was associated with a reduced survival. Owners reported decreased clinical signs, increased activity levels and improved HRQoL.

Clinical relevance

EP is a valuable option for dogs requiring artificial cardiac pacing. Complications are common but do not impact the overall outcome. Dogs with a coexisting cardiac pathology ~~concurrent~~

61 ~~cardiac disease~~ have a shorter life expectancy after EP placement, but their HRQoL appeared
62 good with an improvement in clinical signs and increased activity levels.
63
64 **Key words**
65 Canine, epicardial, pacemaker, artificial cardiac pacing, quality of life
66

Introduction

Artificial cardiac pacing (ACP) is considered the standard treatment for certain bradyarrhythmias in cats and dogs.[1-5] The most common indications include ~~high-grade~~ atrioventricular block (AVB) such as 2nd and 3rd degree AVB; however other symptomatic bradyarrhythmias unresponsive to medical therapy are suitable for ACP, including sick sinus syndrome (SSS), atrial standstill and vasovagal syncope.[1-7]

Breeds including West Highland white terriers, miniature schnauzers and cocker spaniels are predisposed to sinus node dysfunction, while breeds such as Labrador retrievers and German shepherd dogs appear predisposed to AVBs.[5,8,9]

Artificial cardiac pacing may: prevent bradycardia-associated secondary congestive heart failure (CHF), allow a more appropriate heart rate for concurrent structural heart disease, to either manage CHF, or at least delay its onset, and protects patients against clinical signs such as syncopal episodes and sudden cardiac death due to bradyarrhythmia.[3,10]

Transvenous pacemaker implantation is generally considered the preferred method of ACP in dogs, with complication rates ranging from 13 to 33% and a risk of intraprocedural mortality of 5 to 7%.[5,8,10-14]

Small patient size, pre-existing infections ~~such as neck skin pyoderma~~of the transvenous pacemaker implantation site, endocarditis, concurrent immunosuppressive therapy, arrhythmogenic right ventricular cardiomyopathy, coagulopathy~~, and other concurrent diseases necessitating surgical intervention~~ are recognized as contraindications for transvenous pacemaker implantation.[2,3] Epicardial pacemaker (EP) is a valuable alternative to transvenous pacemaker in these instances, and may also be indicated in dogs that undergo other cardiothoracic or abdominal surgical procedures.[2,3]

Different surgical approaches have been described for the placement of permanent EP leads in dogs including thoracotomy,[3,15-18] median celiotomy with partial median sternotomy[19] and median celiotomy with transdiaphragmatic approach.[3,17,18] Recently, minimally invasive approaches including transxiphoid approach,[20] minimally invasive thoracotomy[2,3] and thoracoscopy[21] have also been described in dogs.

Historically, EP was associated with a high rate of complications (28-73%);[15,17-19] however, a more recent study reported a major complication rate in dogs of 16-25% which is comparable to the complication rate reported for transvenous pacemaker implantation.[1,3,13] Major complications reported in dogs include lead dislodgement, loss of capture, pacemaker generator failure, and cardiac arrest, whereas minor complications reported include minor self-limiting arrhythmias (i.e. ventricular premature complexes), oversensing, inappropriate programming, muscle twitching, minor hemorrhage, and seroma formation.[2,3,5]

The outcome for dogs with transvenous or epicardial ACP appears to be good with a high degree of owner satisfaction (up to 80%), including dogs in which major complications occurred, reflecting an improvement of clinical signs and health related quality of life (HRQoL).[22]

In recent years, HRQoL has emerged as a crucial treatment outcome measure in veterinary medicine with a particular emphasis on understanding its impact through decision-making for veterinary patients and aiding client decision-making with quantitative HRQoL changes following treatments.[22-25] Beyond merely affecting survival time, HRQoL instruments offer valuable insights into a patient's clinical signs and treatment efficacy, marking HRQoL as a key indicator of medical or surgical treatment success and a preferred standard primary endpoint alongside mortality rates.[21-25]

The objectives of this study were: (1) to describe complications and outcomes of dogs undergoing EP implantation by using a large-scale multicenter study; (2) to identify factors

116 associated with survival in dogs after EP implantation; (3) to use a HRQoL questionnaire to
117 determine improvement in clinical signs and in HRQoL after EP implantation in dogs. We
118 hypothesized that complication rates and outcomes for EP would be comparable to transvenous
119 ACP and the owners would report an improvement in dogs' HRQoL after EP placement.
120

Materials and Methods

This retrospective observational study used anonymized clinical data and was approved by the social science research ethical review board of the Royal Veterinary College, University of London (approval no.: URN SRXXXX-XXX). Ethical reviews were also conducted at the University of Bristol (VIN/22/010) and University of Liverpool (VREC1121).

Data collection

Electronic records from four small animal referral hospitals between July 2010 and December 2022 (Royal Veterinary College, University of Liverpool, University of Bristol, North Downs Specialist Referrals) were searched to identify dogs in which an EP was placed. The search term 'epicardial pacemaker AND dog' was used, and cases reviewed for inclusion by authors. Dogs were excluded if they had incomplete medical records, they had a transvenous pacemaker alone implanted, or follow-up was less than 14 days. Dogs presented for an EP placement after failure of a transvenous PM were classified as new cases and included in the statistical analysis. However, dogs presented for a placement of a second EP due to a problem with a previous EP were not included in the study a second time but the complication requiring a second EP was recorded. Data collected from the records included signalment, clinical history, presenting clinical signs, presence or absence of coexisting cardiac pathology ~~structural heart disease~~, primary ECG diagnosis, Troponin I concentration at diagnosis, time from diagnosis to EP placement, presence of concurrent medical conditions (cardiac and non-cardiac), reason for EP placement, anesthetic and surgical time, surgical approach, method of lead fixation, pacing mode, location of the generator, details on thoracostomy tube placement. The occurrence of any intraoperative and postoperative complication was recorded as well as the requirement of additional surgical intervention or medical treatment; these were classified according to Follette et al. (2019) and described in Supplementary Table S1.[26]

146

147 Statistical analysis

148 Descriptive statistics were computed for all variables. Continuous variables assessed were age,
149 time from diagnosis to EP placement, Troponin I concentration and survival. Categorical
150 variables assessed were body weight (< 10 kg vs > 10 kg), presenting clinical signs (collapse
151 vs others), coexisting cardiac pathology ~~coexisting cardiac disease~~, concurrent non-cardiac
152 disease, ECG diagnosis (AVB vs others), lead type (unipolar vs bipolar), concomitant
153 procedures, and any intra- or post-operative complication.
154 The Kaplan-Meier method and Cox proportional hazards analysis were used to determine the
155 association between these variables and survival time. The outcome variable was survival time,
156 and the explanatory variables were those previously listed, including occurrence of intra- and
157 post-operative complications. For each dog, survival time was determined as the time elapsed
158 from the date of EP placement to the date of censorship. Dogs were censored from survival
159 analysis if they were alive at the time of analysis, died for reasons unrelated to the presence of
160 the EP or were lost to follow-up. All variables were initially tested separately via univariate
161 Cox proportional hazards analysis, and a multivariate Cox proportional hazards model was then
162 built, which initially included the variables identified as P < .2 on univariate analysis.
163 Cox proportional hazards analysis results are reported as odds ratios, 95% CI, and the
164 associated *P*-value. The level of statistical significance was set at $P < .05$.
165 Analyses were performed using Microsoft Excel 2020 and SPSS 28.0 (IBM SPSS statistics,
166 version 26.0; IBM Corp, Armonk, New York). Normality was assessed by the Shapiro-Wilk
167 test: datasets likely to be from a normal distribution (P > .001) are reported as mean (standard
168 deviation [SD]), whereas datasets likely not to be from a normal distribution ($P < .001$) are
169 reported as median (interquartile range [IQR]). ~~The level of statistical significance was set at~~
170 ~~$P < .05$.~~

171

172 Health-related Quality of life questionnaire

173 To evaluate outcome, a two-part (preoperatively and long-term follow-up) questionnaire was
174 designed (Supplementary Material S1) based on a previously published HRQoL questionnaires
175 for dogs with congenital portosystemic shunts and cardiac diseases.[22-24]

176 For the assessment of clinical signs, six questions for the preoperative part and eight questions
177 for the long-term follow-up part were developed based on previous reported clinical signs
178 associated to cardiac pathologies that required ACP and complications reported after
179 transvenous pacemaker and EP implantation.[3,5,11] For each clinical sign the frequency was
180 recorded on a categorical scale ("never", "less than once a month", "weekly", "daily") and the
181 impact on the dog's quality of life was recorded using a visual analogue scale (VAS) from "not
182 at all" to "could not be worse".

183 Five questions in both parts of the questionnaire were designed to assess the dog's activity
184 levels and willingness to exercise, play, and interact with the owner or other pets. These
185 questions used a VAS from "not willing at all" to "could not be more willing".

186 In the long-term follow-up part of the questionnaire, six questions were designed to assess the
187 outcome of the procedure, the owners' satisfaction or concerns, and the improvement of the
188 dog's HRQoL. Individual preoperative and long-term follow-up question scores were
189 compared with the Wilcoxon signed-rank test; only owners completing both questionnaires
190 were included in the statistical analysis.

191

Results

Population data, clinical presentation, and diagnostic investigations:

Fifty-two dogs met the inclusion criteria and were included in the study. The population included 24 male dogs (16 neutered and 8 intact) and 28 female dogs (20 neutered and 8 intact), with a male-to-female ratio of 1:1.1. A variety of breeds was represented, including West Highland white terrier (5); Labrador retriever (5); cocker spaniel (5); English springer spaniel (4); miniature schnauzer (4); Jack Russell terrier (3); miniature poodle (3); crossbreed (2); great Dane (2); Maltese (2); chihuahua (2); Yorkshire terrier (2); dogue de Bordeaux (2); Nova Scotia duck tolling retriever (1); border collie (1); German shepherd (1); Staffordshire bull terrier (1); Lhasa Apso (1); sharpei (1); cavalier King Charles spaniel (1); Japanese akita (1); German wire haired pointer (1); Gordon setter (1); Spanish water dog (1).

At the time of the surgery, the median age was 9 years (IQR, 5-11), and the median weight was 14.8 kg (IQR, 8.1-30.2).

Presenting clinical signs included collapsing/syncopal episodes (36), exercise intolerance (15), lethargy (9), weakness (7), vomiting (5), diarrhea (4), anorexia/hyporexia (3), tachypnea (2), ataxia (2), melena (1), weight loss (1), pyrexia (1), cough (1), nausea (1), obtundation/abnormal mentation (2), hypersalivation (1), abdominal distension (1). In most dogs, a combination of clinical signs was reported, while seven dogs showed no clinical signs associated with the cardiovascular system.

Findings at physical examination included bradycardia (46), heart murmur (25), abdominal mass (3), arrhythmia (2), hyperdynamic pulses (2), ascites (2), jugular vein pulsation (1), vestibular syndrome (1), exophytic skin lesions on the cervical region (1), pale mucous membranes (1), muffled lungs sounds (1), peripheral edema (1), enlarged submandibular lymph nodes (1), variable pulses strength (1). Collapsing/syncopal episodes (36), exercise intolerance (15) and bradycardia (46) were the main reasons for referral.

The primary ECG diagnosis and indications for ACP were: 3rd degree AVB (39, 75%), SSS (7, 13%), high grade 2nd degree AV block/~~,~~ paroxysmal 3rd degree AV block (5, 10%) and atrial standstill (1, 2%).

Ventricular rate of all dogs prior to EP implantation ranged between 20 and 90 complexes per minute (median, 40). For dogs diagnosed with SSS, the longest pause length ranged between 4.5 to 8.6 seconds. Troponin I concentration was recorded in 21 dogs (41%) and ranged from 0.48µg/L to 180 µg/L with a median of 1.16µg/L.

At the time of the pacemaker implantation, 19 dogs (36%) had a coexisting cardiac pathology ~~concurrent cardiac disease~~ including myxomatous mitral valve disease (12), suspected myocarditis (2), dilated cardiomyopathy (2), myocardial infiltration (1, suspected neoplastic), tricuspid valve dysplasia (1), tricuspid degenerative valve disease and pulmonary hypertension (1). ~~and 13~~ Thirteen dogs (25%) had a concurrent non-cardiac disease. Coexisting cardiac and non-cardiac pathologies are summarized in ~~(~~Table 1~~)~~. In two dogs, presence of CHF was reported at the time of pacemaker implantation.

The reasons for an EP placement (Table 2) included previous transvenous PM dislodgment/malfunction (12), small body size (10), temperament (9), medical concerns about hypercoagulability/thrombus formation (7), concurrent abdominal surgery (5), unknown (2), inability to place transvenous pacemaker (2), cervical pyoderma (2), chronic otitis externa and head shaking (1), concurrent thoracic surgery (1), perforation of the right ventricle during transvenous pacemaker implantation (1).

Twelve dogs had a previous transvenous PM placed ranging from 4 days to 1275 days before EP implantation: eight dogs had one transvenous PM placed, 2 dogs had 2 transvenous PM placed. Loss of capture due to lead dislodgment (11) and perforation of the right ventricle (1) were the reasons of the EP placement in these dogs.

Surgical procedures:

Median time from diagnosis to EP implantation was one day (IQR, 1-4). All surgeries were performed by, or under the direct supervision of, a European or American College of Veterinary Surgeons (ECVS/ACVS) board-certified or Royal College of Veterinary Surgeons (RCVS) specialist surgeon. According to the American Society of Anesthesiologist (ASA) scoring system, 33 dogs (63%) were considered ASA 3, 14 dogs (27%) were ASA 4, 1 dog (2%) was ASA 5. In 4 dogs (8%) ASA status was not reported. Median surgical time was 110 minutes (IQR, 90-150), and median anesthetic time was 178 minutes (IQR, 140-240). Under general anesthetic, dogs were temporarily paced either through transthoracic stimulation using pacing pads, by temporary transvenous pacing or by using temporary epicardial leads. Epicardial pacemakers were implanted using an abdominal trans-diaphragmatic approach in 47 dogs, and a left lateral intercostal thoracotomy in five dogs (4 at the 5th intercostal space and 1 at the 6th intercostal space). A unipolar system was implanted in 23 dogs and a bipolar system in 25 dogs; in 4 dogs the system used was not recorded. The EP leads were fixed to the epicardium using two to three polypropylene (5-0 to 3-0) sutures, except for one dog where a screw-in suture-less system was used. In 39 dogs the generator was placed in a muscular pocket between internal abdominal oblique and transversus abdominis in the left body wall, in 6 dogs it was placed on the right body wall and in 5 dogs between the external and internal abdominal oblique muscles. In 2 dogs the location of the generator was not indicated in the reports.

Perioperative intravenous antibiotics were administered in 49 dogs and included cefuroxime (10-20 mg/kg every 90-120 minutes) and amoxicillin/clavulanic acid (20 mg/kg every 90-120 minutes). Antibiotic use was not recorded in 3 dogs. Fifteen concomitant surgeries were performed in sixteen dogs including removal of the previous transvenous pacemaker (5), splenectomy (3), liver biopsies (2), liver lobectomy (1), ileocecocolic resection and anastomosis (1), esophagostomy tube placement (1), partial cystectomy for a bladder mass (1),

skin biopsies (1). A chest drain was placed in 21 dogs, and it was removed from 7 hours to 3 days after surgery. In 27 dogs that underwent transdiaphragmatic EP placement, the pleural space was drained using a trans-diaphragmatic catheter, prior to abdominal closure. In 4 dogs a percutaneous thoracocentesis was repeated due to evidence of residual pneumothorax in the postoperative thoracic radiographs. The method of thoracic drainage was not recorded in 4 dogs.

Antibacterial and analgesia therapy was prescribed post-operatively at the discretion of the surgeon; 15 dogs received a course of antibiotic (20-22 mg/kg amoxicillin-clavulanic acid or 20-22 mg/kg cephalexin) postoperatively ranging from 5 to 14 days.

Initially, all pacemakers were set to a ventricular demand pacing mode (VVI) with rates ranging from 60 to 80 beats per minute. Approximately four weeks later, the pacemakers were reprogrammed to a rate-responsive ventricular demand pacing mode (VVIR), tailored to each patient's needs as determined by the cardiologist's preference.

Complications and outcome:

Surgery was uncomplicated in 46 dogs (89%). Six dogs (11%) suffered an intraoperative complication including seizure-like activity under general anesthetic (1), minor self-limiting bleeding from the epicardial sutures (1), hypoxemia with ST-segment depression on ECG after lead suturing (1), profuse hemorrhage due to perforation of the left ventricular wall during suturing followed by ventricular fibrillation that failed to respond to cardiopulmonary resuscitation (1), self-resolving paroxysms of ventricular tachycardia (1), occasional ventricular premature complexes and runs of accelerated idioventricular rhythm during epicardial suturing (1).

Fifty-one dogs (98%) survived the surgical procedure, one dog developed refractory ventricular fibrillation and died intraoperatively.

In the postoperative period, 12 dogs (23%) suffered a total of 24 complications (Table 3), of which 8 dogs (15%) suffered 9 pacing-related complications. Of these 9 dogs, f~~F~~our dogs required only adjustment of the PM settings whereas 5 dogs required a surgical intervention including placement of a transvenous PM due to lead displacement (3), replacement of the PM leads due to lead fracture (1), and replacement of the generator (1). Except for one dog (8.4kg), all these dogs weighted more than 10 kg.

There were three dogs that had an EP replaced by a transvenous PM. One was a Labrador with a 3rd AVB, which had a splenic mass removed through a midline celiotomy and an EP was placed under the same general anesthetic episode. The dog was represented two weeks after surgery with bradycardia and lack of pacing due to the dislodgment of the EP. The second was a crossbred with a 3rd AVB had ~~a~~an EP placed due to boisterous temperament; represented 13 days after surgery with a lack of ventricular capture and evidence of lead displacement. Third was a West Highland white terrier diagnosed with SSS had a transvenous PM initially placed however due to intermittent pacing, an EP was placed; four days post-operatively inadequate pacing was detected despite correct lead positioning.

In total fifty dogs (96%) survived to discharge, indicating a total perioperative mortality of 4%. The dog who died during hospitalization developed a presumptive thromboembolic event characterized by an acute onset pain and pelvic limb paresis with absent femoral and metatarsal pulses followed by seizures and cardiac arrest on the same day of the surgery.

Follow-up was available for all dogs and ranged from 31 to 3139 days (median, 462). Thirty-two dogs (64%) died or were euthanized during the follow-up period between 104 and 3139 days, thirteen (26%) of which were for heart-related conditions. The causes of death for these thirteen dogs are reported in Table 4. The 1-, 2-, and 3- year survival rates were 90%, 82%, and 74%, respectively (Figure 1).

Risk factors associated with survival for EP implantation.

Cox proportional hazards analysis was used to determine factors associated with survival when possible confounding factors were considered. After the initial model was refined by backward-stepwise elimination, the best-fit model was one that included 3 variables (age, coexisting cardiac pathology ~~coexisting cardiac disease~~, postoperative complication). In the final multiple-regression model (Supplementary Table S2), the only factor associated with increased risk of death was coexisting cardiac pathology ~~coexisting cardiac disease~~. Dogs with a coexisting cardiac pathology ~~coexisting cardiac disease~~ had a median survival time of 806 days (95% CI, 339-1272) whereas the median survival time for dogs without a coexisting cardiac pathology ~~coexistent structural cardiac disease~~ was not reached.

Health-related Quality of life questionnaires

Thirty-three owners (63%) completed both preoperative and follow-up questionnaires. Results comparing scores for each individual question between the two time points were reported in Figure 2. No statistical difference was noted regarding clinical signs including wobbliness/weakness, and vomiting, or activities like interaction with other pets or interaction with the owners. Scores from four questions (collapsing/syncope [$P < .001$], inappetence [$P = .033$], lethargy [$P < .001$], and rapid breathing [$P < .001$]) were significantly decreased (indicating improvement) between the two time points after EP placement. No episodes of hiccups were reported in the postoperative period, whereas muscle twitching less than once a month was reported in two dogs, however, quality of life was not adversely affected (both scored "0").

Owners reported a good improvement in their dogs' general condition following EP implantation, with average score of 8.4 out of 10. Additionally, they expressed a good degree of satisfaction with their dog's response to surgery, averaging 9.2 of 10. However, a relatively

342 high level of worry or concern about their dogs' condition persisted, with an average score of
343 7.4 out of 10. There was a significant (all $P < .001$) increase in level activity, level of playing
344 and overall HRQoL score in dogs undergoing EP placement from preoperatively to long-term
345 follow-up.
346

Discussion

The results of this study confirmed (1) that EP placement was an effective therapy for ACP in dogs; (2) that dogs diagnosed with coexisting cardiac pathology ~~coexisting cardiac disease~~ at the time of the EP implantation had a shorter life expectancy compared to dogs without such changes; and (3) that post-EP implantation, HRQoL for dogs improved with an increased level of activity accepting our initial hypothesis.

The patient characteristics in this study were consistent with previous reports, including signalment, presenting clinical signs, ECG diagnosis, and concurrent heart diseases.[1,3,5,8,11-14,27,28] Bradyarrhythmias, unresponsive to medical management, including AVBs and sick sinus syndrome were the most common indications for ACP in dogs, aligning with findings from prior studies.[8,11-13,19]

While transvenous pacemakers, which are minimally invasive, are generally favored over EP there are currently no clear guidelines as to when EP is preferable to transvenous pacemakers. Historically, EP was the preferred option for small dogs and cats; however recent studies have shown a body weight range for dogs undergoing transvenous pacemaker placement that is comparable to the population of dogs in the study reported here.[10,31] This suggests that EP should be reserved for dogs where strong contraindications for endocardial pacemakers exist such as a known hypercoagulable state, pre-existing infection of the pacemaker implantation site or a protein-losing condition.[11-13] An advantage of EP is the avoidance of direct contact with blood and intracardiac structures, reducing the risk of certain complications, such as pacemaker-lead associated thrombosis, right ventricular outflow tract obstruction, tricuspid stenosis, caval fibrosis, cardiac perforation, chylothorax and embolic pulmonary hypertension.[2,13] Although none of these specific complications were observed in this study, there was a suspicion of a thromboembolic event in four dogs during the postoperative period

(range, <24 hours to 210 days), with one leading to the death of a patient. Only one the four dogs had a preexistent risk factor (protein losing enteropathy) for thromboembolism.

~~In all dogs, a single-chamber system was used with the leads fixed to the left ventricle and programmed in VVI or VVIR mode. Dual-chamber pacing is linked to more physiological pacing and favorable hemodynamics by restoring AV synchrony and allowing variable pacing rates. Dual-chamber pacing using an EP has been reported in only two dogs via a standard right thoracotomy with lead complications reported in one dog.[29] In veterinary medicine, the use of dual-chamber pacing modality is not widely performed currently, and existing studies comparing dual- versus single-chamber pacing have not demonstrated a significant difference in terms of quality of life and survival rates in dogs.[28,30,31]~~

Previous studies on EP in dogs have documented a high complication rate (up to 71%), with dislodgment of the EP pacing lead being the most common major complication and perioperative ventricular ectopy as the most common minor complication.[3,19] Visser et al. (2013) reported an increased incidence of major complications in dogs >10kg, potentially associated with the surgical approach and the distance between the left ventricular apex or the left ventricular free wall and the abdominal incision during a transdiaphragmatic approach.[3] All dogs that had a loss of capture had a median celiotomy and transdiaphragmatic approach and, except for one dog (8.4kg), were over 10 kg. As previously suggested, it is possible that the use of a lateral thoracotomy could provide more consistent access to suture epicardial electrodes in larger dogs, thus reducing the risk of lead dislodgment and loss of capture.[2,3] However, the limited number of dogs undergoing lateral thoracotomy precludes any meaningful statistical investigation. It is also possible that EP was less commonly used in dogs due to the prevailing preference for transvenous pacemakers, thereby presenting a challenge for surgeons who need to execute the placement of epicardial leads on the beating heart, very infrequently.

This current study revealed that postoperative complications after EP placement are lower than previously reported but still relatively common (23%) and comparable to those associated with transvenous pacemaker implantation (13-33%).[5,8,10-12,14]

Loss of capture or non-capture remains the most common complications after EP implantation in dogs.[2,3,32] As in human patients, causes for the loss of capture are highly correlated with timing: acute causes (hours to weeks) are cardiac in nature including lead dislodgment or malposition, premature lead failure, premature battery depletion and programming errors with suboptimal output.[32] Whereas long-term causes (months to years) can be cardiac (lead fracture, fibrosis/inflammation, cardiomyopathy, exit block, breach in insulation, end of life battery) or non-cardiac (electrolytes imbalances, acidemia, hypoxemia, medication-induced alterations of the capture threshold, external electrical stimulus).[32,33] At times, reasons for the loss of capture are reversible with an increase of the pacemaker voltage output or pulse duration settings, whereas, when the cause cannot be reversed, lead or generator replacement / repositioning / revision are needed.[32] In this study, loss of capture occurred in eight dogs with three of them requiring a transvenous PM. Notably, seven dogs in this population had an EP placed due to loss of capture from a previous transvenous PM. In this study, no association between complications and survival was found, and none of the dogs experiencing postoperative complications died as a result. This contrasted with previous studies showing an association[1] or a trend toward[3] a shorter survival time in dogs with major complications. Postoperative monitoring, regular rechecks, and pulse generator interrogation are recommended for early detection and timely management of possible PM malfunction or complication.

Various negative prognostic factors for dogs undergoing endocardial PM implantation have been reported, including age, high serum troponin I concentration, severe azotemia, the use of a second-hand pacemaker, presence of CHF, the occurrence of complications and a concurrent cardiac disease.[1,5,11,12,27]

In this study only the presence of a coexisting cardiac pathology ~~coexisting cardiac disease~~ showed a strong association with survival; suggesting that dogs without coexisting cardiac pathology ~~coexisting cardiac disease~~ were more likely to have a longer survival. Epicardial pacemaker implantation in young human adults without coexisting cardiac pathology ~~concurrent cardiac diseases~~ has a survival similar to an age-matched control population.[34] It seems plausible that dogs with coexisting cardiac pathology ~~concurrent cardiac diseases~~ also have shorter life expectancy due to the progression of their underlying condition rather than the placement of an EP itself. Most cardiac diseases in dogs, such as mitral valve disease and cardiomyopathy, are progressive and reduce the lifespan of severely affected dogs. Given the retrospective nature of this study, it was not possible to thoroughly verify if the reason for death was strictly associated with the EP. Nonetheless, all the EPs were regularly interrogated and found to be working satisfactorily with adequate battery life during the follow-up period. In human medicine, HRQoL is considered a crucial outcome measure when evaluating the success of an intervention, with human patients valuing their QoL as much as the overall survival time.[34-36] Similarly, owners of dogs with heart disease place high value on their pet's HRQoL over the quantity of life.[22,25,35] Dogs with advanced heart disease may experience reduced HRQoL due to respiratory distress, poor appetite, and reduced activity.[22,37] Therefore, it is important to demonstrate that survival time is associated with a good HRQoL in dogs undergoing cardiac surgery, such as EP implantation. Oyama et al. (2001) reported that 80% of owners rated their satisfaction after transvenous pacemaker implantation as high, assuming that there was resolution of syncope, improved exercise intolerance and a perceived improvement in HRQoL.[22] This study successfully investigated, for the first time, HRQoL as outcome measure for dogs undergoing EP implantation, utilizing a comprehensive questionnaire to assess clinical signs and an HRQoL post-surgery. The results showed a significant decreased in total score between the preoperative and postoperative time points

reflecting a resolution of collapse/syncope, breathing difficulties, inappetence and lethargy with an increased activity level and enhanced HRQoL post EP implantation.

The main limitation of this study was its multi-institutional retrospective nature, with unavoidable variation in the management and treatment of cases across different institutions. Incomplete medical records and inconsistent follow-up data could have affected the accuracy of the results. Minor complications could have been missed, as minor cardiac rhythm changes can be transient and self-limiting and potentially not recorded. The outcome measures for the dogs in our study were based entirely on a non-validated owner-based questionnaire; this assessment may be less reliable, because of a bias on behalf the owner. The wide range of follow-up periods may have introduced recall bias, with owners who completed the questionnaire long after their dog's surgery potentially having less accurate recall of their dog's clinical outcome. There was also a possibility of selection bias, in that owners may have been more inclined to complete the questionnaire if their dogs were clinically better.

In conclusion, this study provided valuable evidence supporting the use of EP as a viable means to achieve ACP in dogs. Despite the occurrence of complications, they were comparable to those seen with transvenous pacemaker implantation and did not significantly impact the outcome. Dogs with a coexisting cardiac pathology ~~coexisting cardiac disease~~ had a shorter life expectancy, but their HRQoL appeared good following EP implantation, with an improvement in clinical signs, and increased activity levels, which is of crucial for client decision-making.

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587 Figure 1. Kaplan-Meier survival curve for dogs undergoing epicardial pacemaker implantation
588 with coexisting cardiac disease (MST: 806 days) or without coexisting cardiac disease (MST
589 not reached).
590 MST = Median survival time.
591
592 Figure 2. Bar chart indicating the impact of EPM placement in dogs on the clinical signs,
593 activity levels and quality of life (mean values)
594

595

596 Table 1. Coexisting cardiac pathologies ~~Coexisting cardiac disease~~ and concurrent extra-cardiac conditions in dogs undergoing epicardial

597 pacemaker placement.

Coexisting cardiac pathologies ~~Coexisting cardiac conditions~~ (19 dogs)		Concurrent extra-cardiac conditions (13 dogs)	
Myxomatous mitral valve disease	12	Splenic mass	2
Tricuspid ~~valve regurgitation~~degenerative valve disease and pulmonary hypertension	~~1~~6	Chronic skin disease	2
~~Pulmonary hypertension~~	~~3~~	Otitis externa	2
~~Systolic dysfunction~~	~~2~~	Chronic kidney disease	1
Suspected myocarditis	2	Chronic enteropathy	2
~~Four chambers dilatation~~	~~1~~	Urinary incontinence	1
~~Myocardial fibrosis~~	~~1~~	Immuno-mediated keratopathy	1
Tricuspid valve dysplasia	1	Thymoma	1
~~AV node~~Myocardial infiltrative disease (suspected neoplastic)	1	Polycythemia	1
Dilated cardiomyopathy	2	Right external iliac thrombus	1
		Hepatic cyst	1
		Hepatic neoplasia	1
		Prostatomegaly	1
		Right idiopathic Horner's syndrome	1
		Hyperadrenocorticism	1
		Chronic hepatopathy	1
		Protein losing nephropathy	1

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600 Table 2. Reason for epicardial pacemaker placement in 52 dogs.

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Reason for epicardial pacemaker implantation	N of cases (%)
Transvenous pacemaker implantation associated complication:	15 (29%)
dislodgment/loss of capture	12
failure to place transvenous pacemaker	2
perforation of the right ventricle during placement	1
Dog size	10 (19%)
Dog temperament	9 (17%)
Concern for thrombus formation	7 (13%)
Concurrent surgery	6 (12%)
Abdominal	5
Thoracic	1
Dermatological condition:	3 (6%)

Cervical pyoderma	2
Chronic otitis externa and head shaking	1
Unknown	2 (4%)

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605 Table 3. Postoperative complications, time, treatment and classification in dogs undergoing epicardial pacemaker placement.

Case	Signalment	Complication	Treatment	Time	Classification
1	Nova Scotia duck tolling retriever, FE, 4y, 15kg	• VPCs and runs of accelerated idioventricular rhythm (rate of 150/minute) • Exercise intolerance and unexplained loss of VVIR mode leaving her in basic VVI mode	None Changed from VVI to VVIR mode	<24 hours 1917 days	Mild Mild
2	WHWT, FN, 11y, 12.8kg	• Colitis • Serosanguinous discharge from sternotomy incision	Dietary modification and metronidazole None	1 day 1 day	Mild Mild
3	Lhasa Apso, MN, 11yr, 4.7kg	• Haematuria • Pain	None Tramadol	2 days 4 days	Mild Mild
4	Sharpei, ME, 10y, 14.8kg	• Pelvic limb weakness, thrombus in right femoral artery • PM lead microdisplacement (loss of capture and increased impedance of pacing system). • Collapse, bradycardia 30bpm, 3rd degree AVB ~~block~~	Clopidogrel Pacing voltage increased, and output increased to 7.5V Pacemaker reset to 7.5V, 0.75ms in order to gain consistent capture. VVI mode at 65bpm.	14 days 142 days 157 days	Moderate Mild Mild
4	WHWT, FN, 11y, 8.4kg	• Hypoxia and dyspnoea (pulmonary thromboembolism suspected) • Inadequate pacing despite correct lead positioning	Oxygen therapy, dalteparin, aspirin and clopidogrel Transvenous PM placed	< 24 hours 4 days	Moderate Severe
5	WHWT, FN, 14y, 9.8kg	• Acute onset pain and pelvic limb paresis, absent femoral and metatarsal pulses • Seizure, CPA	None CPR, unsuccessful	<24 hours <24 hours	Mild Death
6	German wire haired pointer, FN, 7y, 26.7kg	• Systemic Hypertension • Short tonic seizure • Moderate haemorrhagic pleural effusion (PCV 30%).	Amlodipine, clopidogrel, low molecular weight heparin. None Above medications stopped	< 24 hours < 24 hours 1 days	Moderate Mild Moderate
7	Japanese Akita, MN, 8y, 52.9kg	• Pleural effusion and embolism of the right caudal pulmonary vein • Unexplained 3rd degree AVB relapse	Clopidogrel Increase in pacing amplitude	1 day 60 days	Moderate Mild

8	Staffordshire bull terrier, FN, 11y, 25.1kg	• Frequent episodes of paroxysmal atrial flutter	Sotalol	<14 days	Moderate
9	Labrador, ME, 10y, 30.5	• PM lead macro dislodgment (lack of pacing and bradycardia)	Transvenous PM placed	14 days	Severe
10	Crossbreed, MN, 2y, 18kg	• PM lead macro dislodgment (lack of ventricular capture).	Transvenous PM placed	13 days	Severe
11	Great Dane, ME, 3y, 57kg	• Two partial collapse episodes and PM lead fracture at lead-header interface	Epicardial PM lead replaced	60 days	Severe
12	Labrador, MN, 7y, 40kg	• 100% PM dependency and complete 3rd AVB • Generator battery not working	Changed from VVI to VVIR mode 70 bpm Battery replaced	60 days 120 days	Mild Severe

606 AVB = atrioventricular block; FE = female entire; FN = female neutered; ME = male entire; MN = male neutered; PCV = packed cell volume;

607 PM = pacemaker; VPCs = Ventricular premature complexes; VVI = ventricular demand pacing mode; VVIR = rate-responsive ventricular demand

608 pacing mode WHWT = West Highland White Terrier;

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Table 4. Cause of death or euthanasia and ~~surgical~~ survival time in dogs undergoing epicardial pacemaker placement.

Case	Cause of death or euthanasia	Survival (days)
1	Sudden death due to a suspected myocarditis	104
2	~~Euthanised due to~~ V~~v~~entricular arrhythmias, deterioration, ascites	115
3	Sudden death suspected cardiac related	193
4	Cardiac arrest following dyspnoea, severe pneumonia and pulmonary thromboembolism in the right main pulmonary artery	210
5	Deterioration due to atrioventricular muscular dystrophy	397
6	MMVD, CHF (EPM reported working well)	462
7	Acute deterioration, suspected cardiac	488
8	Dyspnoea, suspected cardiac	766
9	CHF (EPM reported working well)	806
10	CHF (EPM reported working well)	993
11	Lethargy, ascites, CHF	1248
12	Deterioration due to MMVD, ~~Stage C and~~ CHF	1761
13	DCM ~~with poor systolic function~~	1925

CHF = congestive heart failure; DCM = dilated cardiomyopathy EPM = epicardial pacemaker; MMVD = myxomatous mitral disease;

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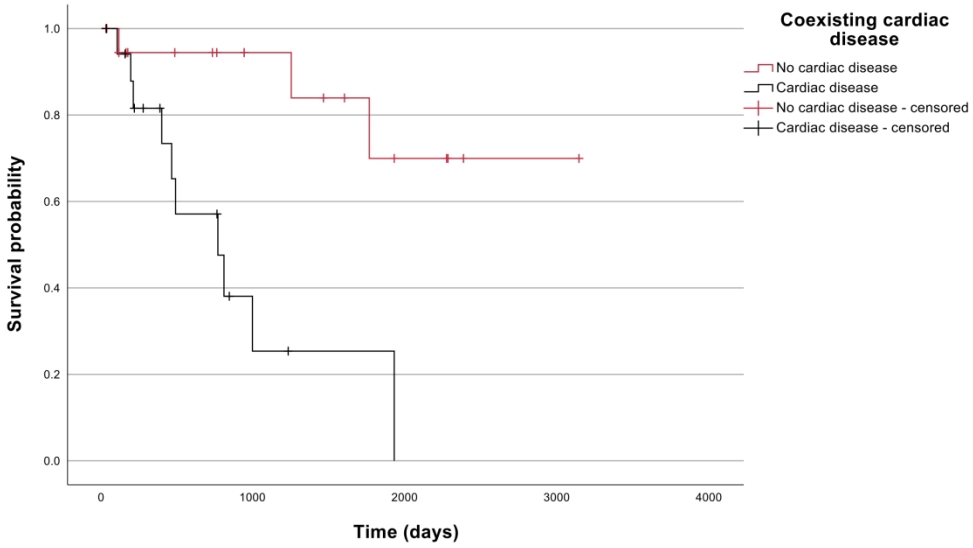

Figure 1. Kaplan-Meier survival curve for dogs undergoing epicardial pacemaker implantation with coexisting cardiac disease (MST: 806 days) or without coexisting cardiac disease (MST not reached).
MST = Median survival time.

492x277mm (144 x 144 DPI)

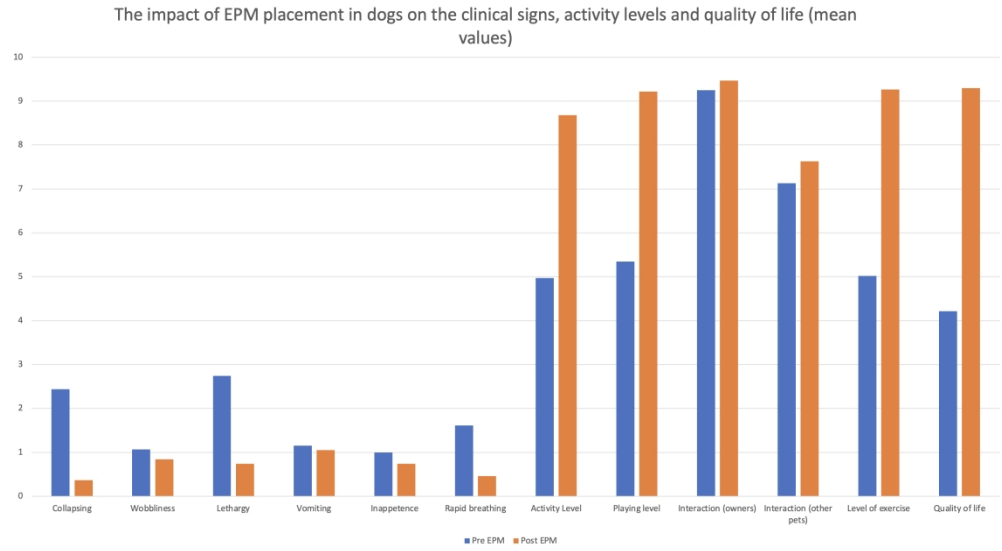

Figure 2. Bar chart indicating the impact of EPM placement in dogs on the clinical signs, activity levels and quality of life (mean values)

516x290mm (144 x 144 DPI)

Epicardial pacemakers in dogs Quality of Life Questionnaire: Part 1: BEFORE SURGERY

1. How often approximately did your dog show the following signs (BEFORE surgery and BEFORE receiving any medical treatment from us or your vet)?

a. Collapse

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

b. Wobbliness/difficulty walking properly

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

c. Lethargy/weakness

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

d. Vomiting

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

e. Inappetence

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————————— **10** | Could not be worse

f. Rapid breathing/ short of breath

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————————— **10** | Could not be worse

2. How active was your dog?

Not active at all | **1** ——————————————————————— **10** | Could not be more active

3. How willing was your dog to:

a. Play

Not willing at all **1** ——————————————————————— **10** | Could not be more willing

b. Interact with yourselves

Not willing at all | **1** ——————————————————————— **10** | Could not be more willing

c. Exercise

Not willing at all | **1** ——————————————————————— **10** | Could not be more willing

d. Interact with other dogs

Not willing at all | **1** ——————————————————————— **10** | Could not be more willing

4. Did your dog receive medical treatment prior to surgery? Details

No Yes

Epicardial pacemakers in dogs Quality of Life Questionnaire: Part 2: AFTER SURGERY

Part 1: How is your dog now?

1. How often approximately does your dog show the following signs?

g. Collapse/Syncope

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

h. Wobbliness/difficulty walking properly

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

i. Lethargy/weakness

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

j. Vomiting

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

k. Inappetance

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

l. Rapid breathing/ short of breath

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

m. Muscle twitching

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

n. Hiccups

Never Less than once a month Monthly Weekly Daily

Please mark on the below scale how severely this impacted your dog's quality of life:

Not at all | **1** ——————————————————— **10** | Could not be worse

2. How active was your dog?

Not active at all | **1** ——————————————————— **10** | Could not be more active

3. How willing was your dog to:

e. Play

Not willing at all **1** ——————————————————— **10** | Could not be more willing

f. Interact with yourselves

Not willing at all | **1** ——————————————————— **10** | Could not be more willing

g. Exercise

Not willing at all | **1** ——————————————————— **10** | Could not be more willing

h. Interact with other dogs

Not willing at all | **1** ——————————————————— **10** | Could not be more willing

4. How improved is your dog since the surgery generally

Not at all | **1**——————————————————— **10** | Could not have improved more

5. How satisfied are you with your dog's response to surgery

Not at all | **1**——————————————————— **10** | Could not be more satisfied

6. From 1 to 10:

a) how you feel your dog's quality of life was prior to diagnosis

Worst imaginable | **1**——————————————————— **10** | Best imaginable

b) how you feel your dog's quality of life is now

Worst imaginable | **1**——————————————————— **10** | Best imaginable

7. Do you still worry/have concerns about your dog's condition?

Not at all | **1**——————————————————— **10** | Could not be more worried

Supplement 1. Classification of complications according with Follette et al. (2019)

Level	Definition
Mild	Requires only minor invasive procedures that can be performed at bedside such as insertion of intravenous lines, urinary catheters, nasogastric tubes, and drainage of wound infections. Physiotherapy and the following drugs are allowed: antiemetics, antipyretics, analgesics, diuretics, and electrolytes.
Moderate	Requires pharmacologic treatment with drugs other than those allowed for minor complications (e.g. antibiotics); blood transfusions and total parenteral nutrition are also included.
Severe	All complications requiring endoscopic or interventional radiologic procedures or reoperation as well as complications resulting in failure of one or more organ systems.
Death	Postoperative death

Supplment 2. Multiple logistic regression results determining factors associated with after epicardial pacemaker placement in dogs.

Logistic regression	**Survival**		
	OR[1]	95% CI[2]	*P* value
Age	1.01	0.99-1.02	.113
Postoperative complication	0.35	0.05-2.25	.271
Coexisting cardiac pathology~~Coexisting cardiac disease~~	**5.80**	**1.27-26.30**	**.023**

[1] OR = odds ratio [2] 95% CI = ninety-five percent confidence