Long-term Intrinsic Rhythm Evaluation in Dogs with Atrioventricular Block

R.A. Santilli, D.M. Porteiro Vázquez, T. Vezzosi, and M. Perego

Background: Atrioventricular block (AVB) is a conduction abnormality along the atrioventricular node that, depending on etiology, may lead to different outcomes.

Objectives: To evaluate variations of intrinsic rhythm (IR) in dogs that underwent pacemaker implantation (PMI).

Animals: Medical records of 92 dogs affected by 3rd degree atrioventricular block (3AVB), advanced 2nd degree AVB (2AVB), paroxysmal 3AVB, 2:1 2AVB, or 3AVB with atrial fibrillation (AF) were retrospectively reviewed.

Method: The patient IR was documented with telemetry on the day of 1 – (95% CI, 1–2), 33 – (95% CI, 28–35), 105 – (95%CI, 98–156), and 275 days (95%CI, 221–380) after PMI. According to AVB grade at different examinations, AVB was defined as progressed, regressed, or unchanged.

Results: In 48 dogs, 3AVB remained unchanged, whereas in 7 it regressed. Eight cases of 2AVB progressed, 3 regressed and 2 remained unchanged. Eight cases of paroxysmal 3AVB progressed and 3 remained unchanged. Four dogs affected by 2:1 2AVB progressed, 2 regressed, and 1 remained unchanged. All cases with 3AVB with AF remained unchanged. Regression occurred within 30 days after PMI, whereas progression was documented at any time. Variations in IR were associated with type of AVB ($P < .03$) and time of follow-up ($P < .0001$).

Conclusions and clinical importance: The degree of AVB assessed at the time of PMI should not be considered definitive because more than one-third of the cases in this study either progressed or regressed. Additional studies would be necessary to elucidate possible causes for transient AVB in dogs.

Key words: Arrhythmias; Dog; Pacemaker; Myocarditis.

Atrioventricular block (AVB) is a relatively common cardiac arrhythmia that results from conduction abnormalities along the atrioventricular node (AVN), the His-Purkinje system, or both. Atrioventricular blocks accounted for approximately 20% of all canine arrhythmias in 1 large study.[1]

Dogs with AV nodal conduction abnormalities may be asymptomatic or may experience severe clinical signs such as syncope and sudden death secondary to bradycardia, ventricular arrhythmias, or both.[2] Advanced 2nd degree AVB (2AVB) and 3rd degree AVB (3AVB) are reported in the literature as the most common indications for permanent pacemaker implantation (PMI) in dogs.[2]

Chronic fibrous or fibrous-fatty replacement of the AV bundle and branches, and acute lymphocytic–

Abbreviations:

AVB	atrioventricular block
PM	pacemaker
3AVB	3rd degree AVB
2AVB	2nd degree AVB
AF	atrial fibrillation
PMI	pacemaker implantation
CI	confidence interval
IR	intrinsic rhythm
cTnI	cardiac troponin I
HR	heart rate

plasmacytic myocarditis are reported as causes for AVB in dogs.[3–6] Chronic and progressive AVB has been reported in older dogs and is thought to be caused by AV bundle degeneration, atrophy, and loss of conduction fibers secondary to compression and distortion of the central fibrous body.[3] This condition is similar to Lev's disease in humans, in which degeneration of the AV conduction system leads to progressive and persistent AVB.[7] Conversely, a transient form of AVB, characterized by an acute onset and high resolution rate, has been reported in children affected by acute lymphocytic myocarditis.[8–10] This type of AVB also has been described in young dogs,[4–6] and is characterized by severe lymphocytic–plasmacytic myocarditis and mild fibrous-fatty replacement involving the AV node.[4–6] Other uncommon causes of AVB reported in dogs include infectious diseases (*Borrelia burgdorferi*, *Bartonella vinsonii*),[11,12] bacterial endocarditis,[13,14] parasitic diseases (*Trichinella spiralis*),[15] immune-mediated diseases (myasthenia gravis, lupus erythematosus),[16,17] neoplasia,[18–20] and non-penetrating chest trauma.[21,22] Because in human patients, different causes of AVB have been documented to lead to different outcomes,

we hypothesized that long-term analysis of the intrinsic rhythm (IR) in dogs after PMI would disclose similar changes.

Materials and Methods

Medical records of 140 dogs with symptomatic AVB, which underwent PMI at Clinica Veterinaria Malpensa between January 2006 and December 2011, were retrospectively reviewed. Dogs with long-term follow-up (at least 6 months after PMI) were included in the study. Breed, sex, age, weight, physical examination findings, 12-lead surface electrocardiogram (ECG), thoracic radiographs, and standard echocardiogram were available for each dog. AVB grade, ventricular rate, and QRS duration at the time of PMI (T0), and AVB grade and ventricular rate at each following telemetric re-evaluation,[ab] were analyzed by 1 author (RAS): T1, 1 day after PMI (95% coefficient interval [CI], 1–2); T2, 33 days after PMI (95% CI, 28–35); T3, 105 days after PMI (95% CI, 98–156); T4, 275 days after PMI (95% CI, 221–380). Atrioventricular blocks were graded as follows: 3AVB was defined as complete atrioventricular block; 2AVB was defined as second degree AVB with atrioventricular conduction ratio $\geq$3:1; 2:1 2AVB was defined as AVB with atrioventricular conduction ratio of 2:1; paroxysmal 3AVB was defined as a sudden and transient complete AVB.[23]

During telemetric ECG interrogation, pacing was set at 30 bpm for 30 seconds and IR was defined as the underlying cardiac rhythm recorded with a ventricular rate slower than the minimum pacing cycle length set. In case of lack of occurrence of IR, the dog was defined as "PM dependent".[24] The IR with a ventricular rate faster than the minimum pacing cycle length set was analyzed for the entire duration of the telemetric interrogation. Based on long-term IR evaluation, we classified the dogs in 3 groups according to the presence or absence of changes in AV conduction over time: unchanged, progressed, and regressed. The unchanged group included dogs in which IR did not change at any re-evaluations. The progressed group included dogs in which worsening of AV conduction was documented. We defined progressed as a 2:1 2AVB that became 2AVB or 2AVB that progressed to 3AVB. Paroxysmal 3AVB was considered progressed when it became a persistent 2:1 2AVB, 2AVB, or 3AVB. The regressed group included dogs in which there was an improvement in AV conduction. We defined regressed as any case of 2AVB that became a 2:1 2AVB, any 3AVB that became a 2AVB, and any AVB that regressed to sinus rhythm.

Statistical Methods

The study population consisted of 92 dogs, data on age (years), weight (kg), sex, breed, type of AVB (3AVB, 2AVB, paroxysmal 3AVB, 2:1 2AVB, and 3AVB associated with AF), outcome (progressed, regressed, or unchanged AV conduction) were recorded. Descriptive statistics were performed. On quantitative variables (age, weight, heart rate, QRS duration, T1, T2, T3, T4), normal distribution of values was assessed by the Shapiro–Wilk W-test and mean, median and standard deviation were calculated. Categorical variables (sex, type of AVB, changes in AV conduction, outcome) were expressed as percentage. A general linear model (GLM) ANOVA was used to compare QRS duration among the 3 outcome groups (progressed, regressed, unchanged AV conduction) after controlling for type of AVB, age, and weight on a subsample of 81 bradycardic dogs (11 dogs with paroxysmal 3AVB were excluded from this analysis to make the data set more homogeneous). A chi-square test was used to test associations between outcomes and the following variables: QRS duration ($\leq$75 msec, >75 msec), type of AVB, and time from PMI (T0, T1, T2, T3,

T4). Logistic regression analysis was used to investigate the association between QRS duration and outcome, age, sex, weight, type of AVB, and time from PMI.

All statistical analyses were carried out using commercially available software[c], and the level of statistical significance was set at $P < .05$.

Results

The study population included 92 dogs (49 males and 43 females) of different breeds. Mean age was 8.8 ± 3.3 years and mean body weight was 26.5 ± 12.8 kg. Indications for PMI included: 3AVB (59.8%, 55/92), 2AVB (14.1%, 13/92), paroxysmal 3AVB (12.0%, 11/92), 2:1 2AVB (7.6%, 7/92), and 3AVB associated with AF (6.5%, 6/92).

At follow-up re-evaluations, 65.2% of dogs (60/92) had no IR changes, 21.8% (20/92) had AVB progression, and 13% (12/92) had AVB regression. Regressed cases, which converted to sinus rhythm, were 66.6% (8/12).

Changes in the type of AVB are shown in Table 1. In 87.2% of the cases (48/55), 3AVB remained unchanged during the follow-up period. In 12.7% of dogs (7/55), the 3AVB regressed in 4 cases to sinus rhythm, in 2 cases to 2:1 2AVB, and in 1 case to 2AVB. Paroxysmal 3AVBs showed progression in 72.7% of dogs (8/11) in 5 dogs to 3AVB, in 3 dogs to 2:1 2AVB, and in 3 dogs AVB remained unchanged. In all cases of 3AVB associated with AF, the IR remained unchanged. In dogs with 2AVB, progression to 3AVB was observed in 61.5% of cases (8/13), whereas 15.4% (2/13) remained unchanged. In 23.1% of the cases (3/13), 2AVB regressed to sinus rhythm in 2 dogs and to 2:1 2AVB in 1 dog. Dogs with 2:1 2AVB progressed to 3AVB in 57.1% of the cases (4/7), whereas in 28.6% (2/7) it regressed to sinus rhythm, and in 1 dog it remained unchanged.

Results of GLM ANOVA showed a difference in heart rate (HR) among types of AVB (test F 3.25 $P < .03$) and outcomes (test F 3.29; $P < .04$). The Chi-square test showed an association between changes in IR at different follow-up time points and type of AVB

Table 1. Changes of intrinsic rhythm and atrioventricular conduction in 92 dogs underwent pacemaker implantation for high grade atrioventricular block.

	Unchanged (n)	Progressed (n)	Regressed (n)	Total (n)
2:1 2AVB	1	4	2	7
Advanced 2AVB	2	8	3	13
3AVB	48	0	7	55
3AVB + AF	6	0	0	6
Paroxysmal 3AVB	3	8	0	11
Total	60	20	12	92
%	65,2	21,7	13	100

2:1 2AVB, 2:1 second degree atrioventricular block; 2AVB, second degree atrioventricular block; 3AVB, third degree atrioventricular block; AF, atrial fibrillation.

($P < .03$). Concerning timing of variations in AV conduction (Table 2), no changes were observed at T1. Progression was observed at any time point in the follow-up, whereas all regressions occurred within T2 ($P < .0001$).

A Chi-square test showed an association between type of AVB and outcome ($P < .0001$). Pacemaker dependency was documented in 40 of 92 dogs (43.5%). Complete AVB, either alone or associated with AF, showed more frequently showed pacemaker (PM) dependency, respectively 52.7% (29/55) and 50% (3/6), whereas in the other types of AVB PM dependency was less frequent: paroxysmal 3AVB (27.3%, 3/11), 2:1 2AVB (28.6%; 2/7), and 2AVB (23.1%, 3/13).

Discussion

Our study analyzed data from long-term follow-up of 92 dogs with AVB that underwent PMI, and identified changes in AV nodal conduction over time. In our population, 87% of cases showed persistent (65.2%) or progressive (21.8%) AV conduction disturbance, whereas in 13% of the dogs improvement of AV block was recorded. The majority of dogs reported here presented with similar changes in AV conduction disturbances over time as have been described in human patients, where 83% of the cases affected by AVB and treated with permanent PMI show persistent and progressive AVB at long-term follow-up.[25–27] Progressive idiopathic fibrosis of the conduction system related to aging of the cardiac skeleton (Lev's disease) is the most common cause of chronic acquired AVB in humans.[7,8] Presumably, most of our cases of unchanged or progressive AVB suffered from chronic fibrous or fibrous-fatty replacement of the AV bundle and branches, as previously reported in the veterinary literature.[3] In our study, paroxysmal 3AVB progressed to permanent 3AVB in

the majority of the dogs, and in all cases of 3AVB with AF improvement in AV conduction disturbances was not documented. On the basis on these results, we speculate that these conditions may represent the initial and terminal phases of chronic progressive conduction system degeneration.

In our study, most cases of 2:1 2AVB progressed to 3AVB in a variable period of time that ranged from 33 to 105 days. These results are not in agreement with findings in human patients where 2:1 2AVB is considered a stable AV conduction disturbance.[26] These findings support the need for PMI in dogs with 2:1 2AVB, if other causes of AVB have been ruled out.

Interestingly, 13% of dogs in our study had transient AVB. Improvement in AV conduction is reported to occur in approximately 15% of human patients diagnosed with AVB,[9,25–27] whereas in veterinary medicine only 1 study described 2 cases of transient AVB that reverted to sinus rhythm within 6 months after PMI.[28] The most common cause of transient AVB in humans is acute myocarditis.[8–10] The pathogenesis of transient AVB secondary to acute myocarditis implies the presence of myocardial interstitial edema and a correlation between severity of myocardial hypertrophy and grade of AVB has been described.[29] Experimental models of acute myocarditis, as well as human patients with spontaneously occurring acute lymphocytic myocarditis, very often present with AVB that occurs within a few days or, less frequently, after 2–3 weeks, and regresses completely during the convalescent stage at 2–4 weeks in 67–96% of the patients.[9,10,29–31] Similarly, in all dogs reported here that showed regression of AVB, improvement was recorded within 1 month after PMI. The prevalence of persistent AVB after acute myocarditis is approximately 4%,[29] and in these patients permanent PMI is required. In children, the occurrence of persistent AVB secondary to resolved acute myocarditis is higher (28%).[10] Chronic myocarditis as a cause of long-standing AVB in human beings is considered somewhat uncommon. The presence of chronic myocarditis was proven in 3 (6%) of 50 patients with idiopathic AVB in 1 study.[32]

The prevalence of myocarditis-related AVB in dogs is unknown. In the veterinary literature, only a few case reports have described acute myocarditis in dogs with AVB, but solely based on postmortem examination.[4–6] In 1 of these case reports, very high serum concentration of cardiac troponin I (cTnI) was documented (44.65 ng/mL), and the authors suggested that this biomarker may help detect dogs with AVB secondary to active myocarditis.[4]

In human medicine, endomyocardial biopsy is the gold standard for in vivo diagnosis of myocarditis, and increased serum concentrations of troponin I and T are considered reliable to confirm this diagnosis because of their high specificity but limited sensitivity.[33,34] Interestingly, 1 study indicated that cTnI concentration was significantly higher in patients with myocarditis and symptoms lasting ≤1 month, suggesting a higher sensitivity of the test in the acute phase of the disease.[35] Cardiac troponin I concentration >99%

Table 2. Timing of variations of intrinsic rhythm and atrioventricular conduction in 92 dogs underwent pacemaker implantation of high grade atrioventricular block.

	T1 (CI 1–2 days)	T2 (CI 8–35 days)	T3 (CI 98–156 days)	T4 (CI 221–380 days)
2:1 2AVB	0 P	2 P	2 P	0 P
	0 R	2 R	0 R	0 R
Advanced 2AVB	0 P	6 P	2 P	0 P
	0 R	3 R	0 R	0 R
Paroxysmal 3AVB	0 P	4 P	3 P	1 P
	0 R	0 R	0 R	0 R
3AVB	0 P	0 P	0 P	0 P
	0 R	7 R	0 R	0 R

2:1 2AVB, 2:1 second degree atrioventricular block; 2AVB, second degree atrioventricular block; 3AVB, third degree atrioventricular block; P, progressed; R regressed. The chi-square test showed an association between changes in intrinsic rhythm at different follow-up time-points and the type of AVB ($P < .03$).

of the normal reference range is indicative of acute myocardial necrosis, although different extracardiac causes for increases in serum cTnI concentration have been reported.[36–38]

In veterinary medicine, cTnI serum concentration is a sensitive and specific marker of myocardial injury and has been used to quantify the extent of cellular injury in dogs.[38–40] A few studies showed that dogs with AVB frequently have cTnI serum concentrations above the reference range. This is likely secondary to decreased cardiac output, structural remodeling secondary to volume overload, presence of congestive heart failure, or underlying cardiomyopathy or myocarditis.[41–43] In 1 study, myocarditis was suspected in dogs with AVB that had very high serum cTnI concentrations and concurrent positive *Bartonella* spp. serology or in dogs that developed a dilated-hypokinetic phenotype after PMI with persistently increased cTnI serum concentrations.[41] Other possible explanations, besides chronic myocarditis,[34,44] for these cases include cardiomyopathy with secondary AVB or pacing-induced cardiomyopathy.[45–47]

In our study, PM dependency was found in 43.5% of the cases, similar to what has been reported in the human literature, where the time of onset is approximately 3 years.[24,26,48]

Limitations of this study include its retrospective nature, which influenced particularly the timing of re-evaluation: T1 and T2 were homogeneous whereas T3 and T4 had wider CI. Intrinsic rhythm was evaluated during a limited time frame, and for this reason paroxysmal AVB could not be completely ruled out. Furthermore, this study lacked information on QRS duration and intraventricular conduction abnormalities at re-evaluations. This parameter should have been considered because in human beings with AV nodal conduction disturbances, intraventricular conduction changes over time and its assessment assists in staging progression of AVB.[25,30] Finally, serum cTnI concentrations and endomyocardial biopsy were not performed in the dogs reported here. These tests could have been particularly useful in dogs with transient AV nodal conduction abnormalities in an attempt to rule out acute myocarditis in this subset of dogs.

Conclusion

Based on our results, AV nodal conduction disturbances remained unchanged or progressed in 87% of dogs with AVB, suggesting the presence of a chronic and progressive degenerative process affecting the conduction system (likely similar to Lev's disease). For this reason, PMI should be considered as the first line of treatment not only in dogs with 2AVB and 3AVB but also in dogs with 2:1 2AVB. Conversely, AVB regressed within 1 month after diagnosis in 13% of cases, 67% of which returned to sinus rhythm. Additional studies would be necessary to assess the prevalence of acute lymphocytic myocarditis in this subset of dogs.

Footnotes

Acknowledgments

References

1. Patterson DF, Detweiler DK, Hubben K, et al. Spontaneous abnormal cardiac arrhythmias and conduction disturbances in the dog. A clinical and pathologic study of 3,000 dogs. Am J Vet Res 1961;22:355–369.

2. Schrope DP, Kelch WJ. Signalment, clinical signs, and prognostic indicators associated with high-grade second- or third-degree atrioventricular block in dogs: 124 cases (January 1, 1997-December 31, 1997). J Am Vet Med Assoc 2006;228:1710–1717.

3. Kaneshige T, Machida N, Yamamoto S, et al. A histological study of the cardiac conduction system in canine cases of mitral valve endocardiosis with complete atrioventricular block. J Comp Pathol 2007;136:120–126.

4. Church WM, Sisson DD, Oyama MA, et al. Third degree atrioventricular block and sudden death secondary to acute myocarditis in a dog. J Vet Cardiol 2007;9:53–57.

5. Atwell RB, Sutton RH. Focal lymphocytic non-suppurative myocarditis and 3 degrees heart block in a 2-year-old dog. Aust Vet J 1990;67:265.

6. Kaneshige T, Machida N, Nakao S, et al. Complete atrioventricular block associated with lymphocytic myocarditis of the atrioventricular node in two young adult dogs. J Comp Pathol 2007;137:146–150.

7. Barold SS. Atrioventricular block revisited. Compr Ther 2002;28:74–78.

8. Lev M. Anatomic basis for atrioventricular block. Am J Med 1964;37:742–748.

9. Wang JN, Tsai YC, Lee WL, et al. Complete atrioventricular block following myocarditis in children. Pediatr Cardiol 2002;23:518–521.

10. Batra AS, Epstein D, Silka MJ. The clinical course of acquired complete heart block in children with acute myocarditis. Pediatr Cardiol 2003;24:495–497.

11. Levy SA, Duray PH. Complete heart block in a dog seropositive for *Borrelia burgdorferi*. Similarity to human Lyme carditis. J Vet Intern Med 1988;2:138–144.

12. Breitschwerdt EB, Atkins CE, Brown TT, et al. *Bartonella vinsonii* subsp. berkhoffii and related members of the alpha subdivision of the Proteobacteria in dogs with cardiac arrhythmias, endocarditis, or myocarditis. J Clin Microbiol 1999;37:3618–3626.

13. Robertson BT, Giles HD. Complete heart block associated with vegetative endocarditis in a dog. J Am Vet Med Assoc 1972;161:180–184.

14. Sykes JE, Kittleson MD, Chomel BB, et al. Clinicopathologic findings and outcome in dogs with infective endocarditis: 71 cases (1992-2005). J Am Vet Med Assoc 2006;228:1735–1747.

15. Sleeper MM, Bissett S, Craig L. Canine trichinosis presenting with syncope and AV conduction disturbance. J Vet Intern Med 2006;20:1228–1231.

16. Hackett TB, Van Pelt DR, Willard MD, et al. Third degree atrioventricular block and acquired myasthenia gravis in four dogs. J Am Vet Med Assoc 1995;206:1173–1176.

17. Malik R, Zunino P, Hunt GB. Complete heart block associated with lupus in a dog. Aust Vet J 2003;81:398–401.

18. Gallay J, Bélanger MC, Hélie P, et al. Cardiac leiomyoma associated with advanced atrioventricular block in a young dog. J Vet Cardiol 2011;13:71–77.

19. Dupuy-Mateos A, Wotton PR, Blunden AS, et al. Primary cardiac chondrosarcoma in a paced dog. Vet Rec 2008;163:272–273.

20. Stern JA, Tobias JR, Keene BW. Complete atrioventricular block secondary to cardiac lymphoma in a dog. J Vet Cardiol 2012;14:537–539.

21. Abbott JA, King RR. Third degree atrioventricular block following non-penetrating chest trauma in a dog. J Small Anim Pract 1993;34:377–380.

22. Nicholls PK, Watson PJ. Cardiac trauma and third degree AV block in a dog following a road accident. J Small Anim Pract 1995;36:411–415.

23. Epstein AE, Dimarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: executive summary. Heart Rhythm 2008;5:934–955.

24. Nagatomo T, Abe H, Kikuchi K, et al. New onset of pacemaker dependency after permanent pacemaker implantation. Pacing Clin Electrophysiol 2004;27:475–479.

25. Uga S. A study on electrocardiographic changes during long-term cardiac pacing. Jpn J Surg 1978;8:79–85.

26. Staessen J, Ector H, De Geest H. The underlying heart rhythm in patients with an artificial cardiac pacemaker. Pacing Clin Electrophysiol 1982;5:801–807.

27. Shaw DB, Kekwick CA, Veale D, et al. Survival in second degree atrioventricular block. Br Heart J 1985;53:587–593.

28. Shih AC, Maisenbacher HW, Barreirinha A, et al. Effect of routine cardiovascular catheterization on cardiac troponin I concentration in dogs. J Vet Cardiol 2009;11:S87–S92.

29. Morimoto S, Kato S, Hiramitsu S, et al. Role of myocardial interstitial edema in conduction disturbances in acute myocarditis. Heart Vessels 2006;21:356–360.

30. Kishimoto C, Matsumori A, Ohmae M, et al. Electrocardiographic findings in experimental myocarditis in DBA/2 mice: complete atrioventricular block in the acute stage, low voltage of the QRS complex in the subacute stage and arrhythmias in the chronic stage. J Am Coll Cardiol 1984;3:1461–1468.

31. Mahoney LT, Marvin WJ Jr, Atkins DL, et al. Pacemaker management for acute onset of heart block in childhood. J Pediatr 1985;107:207–211.

32. Uemura A, Morimoto S, Hiramitsu S, et al. Endomyocardial biopsy findings in 50 patients with idiopathic atrioventricular block: presence of myocarditis. Jpn Heart J 2001;42:691–700.

33. Cooper LT Jr. Myocarditis. N Engl J Med 2009;360:1526–1538.

34. Kindermann I, Barth C, Mahfoud F, et al. Update on myocarditis. J Am Coll Cardiol 2012;59:779–792.

35. Smith SC, Ladenson JH, Mason JW, et al. Elevations of cardiac troponin I associated with myocarditis. Experimental and clinical correlates. Circulation 1997;95:163–168.

36. Alpert JS, Thygesen K, Antman E, et al. Myocardial infarction redefined–a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol 2000;36:959–969.

37. Oyama MA, Sisson DD. Cardiac troponin-I concentration in dogs with cardiac disease. J Vet Intern Med 2004;18:831–839.

38. Smith KF, Quinn RL, Rahilly LJ. Biomarkers for differentiation of causes of respiratory distress in dogs and cats: Part I - Cardiac diseases and pulmonary hypertension. J Vet Emerg Critical Care 2015;25:311–329.

39. Spratt DP, Mellanby RJ, Drury N, et al. Cardiac troponin I: evaluation I of a biomarker for the diagnosis of heart disease in the dog. J Small Anim Pract 2005;46:139–145.

40. Burgener IA, Kovacevic A, Mauldin GN, et al. Cardiac troponins as indicators of acute myocardial damage in dogs. J Vet Intern Med 2006;20:277–283.

41. Trafny DJ, Oyama MA, Wormser C, et al. Cardiac troponin-I concentrations in dogs with bradyarrhythmias before and after artificial pacing. J Vet Cardiol 2010;12:183–190.

42. Fonfara S, Loureiro JF, Swift S, et al. English springer spaniels with significant bradyarrhythmias–presentation, troponin I and follow-up after pacemaker implantation. J Small Anim Pract 2010;51:155–161.

43. Fonfara S, Loureiro J, Swift S, et al. Cardiac troponin I as a marker for severity and prognosis of cardiac disease in dogs. Vet J 2010;184:334–339.

44. Adachi K, Fujioca S, Fujiwara H, et al. Guideline for diagnosing chronic myocarditis. Japanese Circulation Society (JCS) Task Force Committee on Chronic Myocarditis. Jpn Circ J 1996;60:263–264.

45. Prinzen FW, Cheriex EC, Delhaas T, et al. Asymmetric thickness of the left ventricular wall resulting from asynchronous electric activation: a study in dogs with ventricular pacing and in patients with left bundle branch block. Am Heart J 1995;130:1045–1053.

46. Dreger H, Maethner K, Bondke H, et al. Pacing-induced cardiomyopathy in patients with right ventricular stimulation for >15 years. Europace 2012;14:238–242.

47. Bank AJ, Gage RM, Burns KV. Right ventricular pacing, mechanical dyssynchrony, and heart failure. J Cardiovasc Transl Res 2012;5:219–231.

48. Grendahl H, Miller M, Kjekshus J. Overdrive suppression of implanted pacemakers in patients with AV block. Br Heart J 1978;40:106–113.