Evaluation of the effects of transvenous pacing site on left ventricular function and synchrony in healthy anesthetized dogs

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Objective—To compare the acute effects of cardiac pacing from various transvenous pacing sites on left ventricular (LV) function and synchrony in clinically normal dogs.

Animals—10 healthy adult mixed-breed dogs.

Procedures—Dogs were anesthetized, and dual-chamber transvenous biventricular pacing systems were implanted. Dogs were paced in single-chamber mode from the right atrial appendage (RAA) alone and in dual-chamber mode from the right ventricular apex (RVA), from the left ventricular free wall (LVFW), and simultaneously from the RVA and LVFW (BiV). Standard ECG and echocardiographic measurements, cardiac output measured with the lithium dilution method (LiDCO), and tissue Doppler–derived measurements of LV synchrony were obtained during each of the pacing configurations.

Results—Placement of the biventricular pacing systems was possible in 8 of the 10 dogs. The QRS duration was significantly different among all pacing sites, and the order of increasing duration was RAA, BiV, LVFW, and RVA. Pacing sites did not differ with respect to fractional shortening; however, pacing from the RVA resulted in a significantly lower ejection fraction than pacing from all other sites. During RVA and LVFW pacing, LiDCO was significantly lower than that at other sites; there was no significant difference between RAA and BiV pacing with respect to LiDCO. Although the degree of dyssynchrony was significantly lower during pacing from the RAA versus other ventricular pacing sites, it was not significantly different among sites.

Conclusions and Clinical Relevance—Ventricular activation by RAA pacing provided the best LV function and synchrony. Pacing from the RVA worsened LV function, and although pacing from the LVFW improved it, BiV pacing may provide additional improvement. (Am J Vet Res 2009;70:455–463)

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AV</td>
<td>Atrioventricular</td>
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<tr>
<td>BIV</td>
<td>Biventricular</td>
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<tr>
<td>DECO</td>
<td>Cardiac output determined via Doppler echocardiography</td>
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<tr>
<td>LiDCO</td>
<td>Cardiac output determined via the lithium dilution method</td>
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<tr>
<td>LV</td>
<td>Left ventricle</td>
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<tr>
<td>LVA</td>
<td>Left ventricular apex</td>
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<tr>
<td>LVFW</td>
<td>Left ventricular free wall</td>
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<tr>
<td>LVIDd</td>
<td>Left ventricular internal diameter at end-diastole</td>
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<td>LVIDs</td>
<td>Left ventricular internal diameter at end-systole</td>
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<tr>
<td>RA</td>
<td>Right atrium</td>
</tr>
<tr>
<td>RAA</td>
<td>Right atrial appendage</td>
</tr>
<tr>
<td>RV</td>
<td>Right ventricle</td>
</tr>
<tr>
<td>RVA</td>
<td>Right ventricular apex</td>
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<td>TDI</td>
<td>Tissue Doppler imaging</td>
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Transvenous cardiac pacing is a common procedure performed in humans and other animals with clinical bradyarrhythmias, and the RVA is the traditional site of ventricular lead implantation because of ease of placement. As early as 1925, Wiggers\textsuperscript{1} reported that pacing at the RVA in mammals leads to asynchronous ventricular contraction and reduced cardiac function; however, there has been a surge of interest in the sequence of ventricular activation and the search for better ventricular pacing sites. Electrical activation of the ventricles via the His-Purkinje system leads to a synchronous and monophasic contraction of both ventricles, but RVA pacing causes an abnormal and dysynchronous ventricular activation and contraction pattern.\textsuperscript{2}

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The ventricular dyssynchrony that occurs during RVA pacing is associated with a decrease in systolic and diastolic function of the LV.3-5 The reduction in systolic performance may be attributable to several mechanisms, including mechanical interference between early and late activation of the myocardium,6 premature contraction of the LV leading to paradoxical septal motion with abnormal interventricular coupling,8 and mitral valve regurgitation caused or worsened by dys-synchronous LV and papillary muscle activation.9,10 In addition to functional abnormalities, chronic RVA pacing induces considerable cardiac abnormalities such as aberrant myocardial perfusion, an increase in myocardial catecholamine concentrations, and heterogeneity between perfusion and sympathetic innervation of the myocardium.11-13 Histologic evaluations of the myocardium of children4 and dogs14 paced from the RVA have revealed myofiber disarray, dystrophic calcification, disorganized mitochondria, fibrosis, and fat deposition.15 Because of the negative consequences of RVA pacing, potentially better RV pacing sites such as the RV septum or outflow tract have been explored, and although some studies16-18 have revealed an improvement in LV function over that induced via RVA pacing, other studies19,20 have yielded inconclusive and conflicting results. There is no consensus on the potential benefits of pacing from other RV sites. In contrast, numerous studies in humans and other animals have consistently revealed that LV pacing sites are superior to RV pacing sites. Generally, results of studies19-22 in various animals indicate that pacing from epicardial sites in the LV results in improved LV performance over RVA pacing, with the LVA being the optimal LV pacing site. Although one of these studies21 revealed additional improvement with simultaneous pacing of RV and LV sites (BiV pacing) in nonfailing hearts, other studies23-25 did not. In agreement with those experimental data in animals, the LVA appears to be the optimal ventricular pacing site in pediatric human patients.21

Because it is now possible to transvenously pace the LVFW via the coronary venous system without a surgical approach to the thorax, the LVFW has been explored as an alternative pacing site in adult humans. In humans with refractory atrial fibrillation undergoing AV node ablation and ventricular pacing for rate control, LVFW pacing improves function of the LV over that of RVA pacing in patients with and without systolic dysfunction.24-26 Cardiac resynchronization therapy is the use of a transvenous BiV pacing system to simultaneously pace an RV site and the LVFW for human patients with heart failure, LV systolic dysfunction, and a left bundle branch block. This treatment approach reportedly improves morbidity and mortality rates, LV function, LV volume overload, and mitral valve regurgitation by increasing synchronization of LV contraction.20-28 In a study29 of humans with clinically normal or abnormal function of the LV, RV pacing worsened LV performance in both groups, whereas LV or BiV pacing improved function in patients with LV dysfunction and preserved it in those with normal function. To the authors’ knowledge, there are no published reports of studies on transvenous LVFW or BiV pacing in nonhuman animals.

The purpose of the study reported here was to compare the short-term effects of cardiac pacing from various transvenous pacing sites on LV function and synchrony in clinically normal, anesthetized dogs. The specific transvenous pacing sites evaluated were the RAA, RVA, LVFW, and BiV (simultaneous pacing of the RVA and LVFW). Because placement of RAA and RVA pacing leads is routine in dogs but placement of LVFW leads is not and may be difficult or impossible in some human patients, an additional objective of the study was to determine whether the procedure was possible in healthy dogs.

Materials and Methods

Animals—The study sample consisted of 10 adult mixed-breed dogs, including 3 castrated males and 8 sexually intact females, none of which were pregnant or in estrus. Age ranged from 1 to 3 years, and body weight ranged from 19.7 to 29.8 kg. All dogs were healthy with unremarkable results of cardiovascular examinations, and none of the dogs were receiving any form of treatment. An initial lead II ECG for each dog revealed a typical sinus rhythm.

Pacemaker implantation—Dogs were treated with a high dose of hydromorphone (0.2 mg/kg, IM) to induce sinus bradycardia and first-degree AV block. Anesthesia was induced with propofol (2 to 4 mg/kg, IV) and maintained with isoflurane in 100% oxygen administered via an endotracheal tube. Dogs were mechanically ventilated at 8 to 10 breaths/min, and end-tidal isoflurane and CO2 concentrations were monitored to maintain an end-tidal isoflurane concentration of 1.0% to 1.5% and an end-tidal CO2 partial pressure of 30 to 40 mm Hg. Additionally, heart rate, direct arterial blood pressure, arterial oxygen saturation, and rectal temperature were monitored to allow anesthetic depth assessment and maintain a stable plane of anesthesia throughout the pacemaker implantation and data collection procedures. Once a surgical plane of anesthesia was attained, the right lateral aspect of the neck was surgically prepared and the right jugular vein was surgically exposed. Transvenous leads were placed via a venotomy incision with fluoroscopic guidance. To place the LVFW lead, the coronary sinus was first cannulated with a steerable electrophysiology catheter and this catheter was used to position a disposable guide catheter within the coronary sinus. Next, a retrograde venogram was performed through the guide catheter by use of a balloon-tipped end-hole catheter to obtain a map of the coronary venous system and select the appropriate coronary vein for lead placement. A unipolar or bipolar over-the-wire LVFW lead34-36 was placed in the selected coronary vein through the guide catheter with the aid of a 180-cm-long guidewire (diameter, 0.014 in.). The guide catheter was then simultaneously removed and cut from the LVFW lead with the supplied cutting device.

Once the LVFW lead was in place, a tined or screw-in bipolar atrial lead was placed in the RVA and a tined or screw-in bipolar J-shaped atrial lead33 was placed in the RAA (Figure 1). After each lead was placed, impedance, sensitivity, and threshold measure-
ments were obtained with a pacing system analyzer to ensure adequate lead position and function. The leads were secured within the jugular vein by means of encircling ligatures, and a subcutaneous pocket was dissected dorsal to the jugular vein. The leads were then connected to the appropriate ports of a dual-chamber BiV pulse generator. Finally, the remaining portions of the leads and the generator were placed in the subcutaneous pocket, and the incision was closed routinely. The neck was wrapped with a sterile bandage during data collection.

Data collection—First, a 6-lead ECG in sinus rhythm was obtained to confirm that the rate of sinus node discharge was < 80 pulses/min and the duration of the PR interval exceeded 160 milliseconds. When this was not the situation, an additional dose of hydromorphone (0.1 mg/kg, IV) was administered and another ECG was obtained to confirm the aforementioned criteria were met. These actions were taken to ensure that all dogs would be paced at the programmed lower rate and that ventricular activation occurred completely by ventricular pacing and not by antegrade conduction through the AV node.

All ECG, echocardiographic, and cardiac output data were collected in each of 4 pacing configurations after 5 minutes of stable pacing had been achieved. The first pacing configuration was in single-chamber mode, with pacing from the RAA alone, which provided control data for natural ventricular activation via the His-Purkinje system. The remaining pacing configurations were all in dual-chamber mode with sequential pacing from the RAA followed by the RVA alone, LVFW alone, and the RVA and LVFW simultaneously (BiV). The programmed pacing settings were standardized for all dogs. These pacing configurations were as follows: mode switch, off; lower rate, 90 pulses/min; upper tracking rate, 160 pulses/min; paced AV interval, 150 milliseconds; sensed AV interval, 120 milliseconds; rate adaptive AV interval, off; first chamber paced for BiV pacing, LV; interventricular pace delay, 4 milliseconds; ventricular sense response, off; postventricular atrial refractory period, 210 milliseconds; postventricular atrial refractory period, off; ventricular blanking period, 28 milliseconds; RA amplitude, 3.50 V; RA pulse width, 0.40 milliseconds; RA sensitivity, 0.50 mV; RA pace and sense polarity, bipolar; RV amplitude, 3.50 V; RV pulse width, 0.40 milliseconds; RV sensitivity, 2.80 mV; RV pace and sense polarity, bipolar; LV amplitude, 5.00 V; LV pulse width, 0.50 milliseconds; LV pace polarity, LVtip/ RVring; and all additional features, off. Although data were not collected in a blinded manner, all measurements were obtained by the same observer (HWM), who was unaware of the pacing configuration.

A 12-lead ECG was obtained and the heart rate, PR interval, and QRS duration were measured from 5 consecutive beats in lead II. Echocardiographic examinations were performed by use of an ultrasonographic system with a 2- to 5-MHz phased array transducer. All echocardiographic variables were measured from 5 consecutive beats. Standard echocardiographic M-mode measurements of the LV (LVIDd, LVIDs, and fractional shortening) were obtained from the right parasternal short-axis view at the level of the papillary muscles. The diameter of the aorta at the hinge points of the aortic valve was measured from the right parasternal long-axis LV outflow view. Left ventricular end-diastolic volume, end-systolic volume, and ejection fraction were calculated by means of the modified Simpson

Figure 1—Lateral fluoroscopic image of the thorax of a clinically normal dog indicating the position of dual-chamber BiV pacing leads in the RAA, the RVA, and a coronary vein over the LVFW via the coronary sinus.

Figure 2—Diagrams of the 3 left apical echocardiographic views (top) used to analyze the displacement of 12 myocardial segments by tissue tracking in dogs in which the effects of pacing at various sites were evaluated. The right parasternal short-axis diagrams (bottom) include the circumferential locations of the 12 myocardial segments at the base and midpoint of the LV (bottom). The standardized nomenclature is based on the 16- or 17-segment model for analysis of regional LV function as recommended by the American Society of Echocardiography (1 = basal anteroseptal, 2 = basal anterior, 3 = basal anterolateral, 4 = basal inferolateral, 5 = basal inferior, 6 = basal inferoseptal, 7 = mid anteroseptal, 8 = mid anterior, 9 = mid anterolateral, 10 = mid inferolateral, 11 = mid inferior, and 12 = mid inferoseptal). LA = Left atrium. Ao = Aorta. MV = Mitral valve.
rule from the left apical 4-chamber view. Pulsed-wave spectral Doppler signals at the level of aortic valve were recorded from the left apical 5-chamber view, and the velocity time integral was measured. Cardiac output as measured via Doppler echocardiography was then calculated with the formula:

\[ \text{DECO} = \text{AoVTI} \times (\text{aortic valve diameter}/2)^2 \times \pi \times \text{HR} \]

in which AoVTI represents the aortic velocity time integral and HR represents heart rate.

Cardiac output was also determined by use of the lithium dilution method. The lithium sensor for the LiDCO computer was connected to a previously placed peripheral arterial catheter, and to measure cardiac output, 0.15 mmol of lithium chloride was injected into a previously placed central venous catheter. The LiDCO was determined 3 times. When one of the LiDCO values was identified as an outlier, it was eliminated leaving 2 measurements.

To evaluate synchronization of LV contraction, TDI examinations were performed with the aforementioned ultrasonographic system and transducer. Real-time color TDI was superimposed on the 2-dimensional grayscale image of the LV from the left apical window, and 3 digital loops of 1 cardiac cycle each were recorded from the 4-, 5-, and 2-chamber views. Evaluation of 4 myocardial segments (2 at the base and 2 at the mid-point of the LV) in each view allowed circumferential analysis of LV synchrony (Figure 2). These loops were then analyzed on an off-line system with tissue-tracking software. A 3 X 3-mm gate was used to evaluate each segment, and a graph of longitudinal myocardial displacement over time was displayed by the software. To quantify synchronization of LV contraction, interval to peak displacement from the onset of the QRS complex was measured for each myocardial segment in each stored loop (Figure 3). The value of dyssynchrony was calculated as the SD of the interval to peak displacement for all 12 segments.

Pacemaker removal and recovery—Once data collection was complete, the right lateral aspect of the neck was again surgically prepared, the incision was reopened, and the generator and leads were gently removed. The right jugular vein was ligated, the incision was flushed, and the incision was closed routinely. The dogs were allowed to recover from anesthesia and were monitored overnight with hydromorphone (0.1 mg/kg, IM) administered for analgesia, as needed.

Statistical analysis—The primary outcomes of the study were the variables measured at each of the 4 pacing configurations, and outcome values were compared among and between pairs of configurations. Statistical analyses were performed with a statistical software package. Generalized linear mixed models were used to adjust for the repeated measures for each dog and to test for overall significant differences in each variable among the pacing configurations. After assessing the impact of including various covariance matrices to account for the repeated measurements in the model and selecting the structure that minimized the value of the Akaike information criterion, the covariate structure was assumed to be compound symmetric. For variables that were significant on the basis of a value of \( P \leq 0.05 \), pairwise comparisons between
effects of the pacing configurations were generated with the Tukey-Kramer method for adjustment.

Results

Implantation of the BiV pacing system was possible with no serious procedural complications in 8 of the 10 dogs. Although retrograde venography revealed considerable variation in the anatomy of the coronary vein among dogs, most dogs had only 1 straight coronary vein overlying the LV with a lumen that would readily accept the LVFW lead (Figure 4). This vessel was identified as the great cardiac vein. Two dogs did not have coronary veins that were adequate for placement of the LVFW lead. One dog was a 29.1-kg female with multiple branches of coronary veins overlying the LV (arrowheads), but none were of adequate diameter to accept an LVFW lead. The second dog was a 22.9-kg male with several acute angles in the target coronary vein that could not be traversed and with partial drainage of the vessel via an anomalous connection directly to the RA. These 2 dogs were allowed to recover from anesthesia without placement of the pacing system, and no additional data were collected. The results were based on the 8 dogs in which the entire BiV pacing system could be implanted.

Although all dogs were paced at 90 pulses/min, the heart rate was slightly but significantly lower during RAA pacing than it was during pacing at all other sites (P < 0.001 vs RVA, P = 0.003 vs LVFW, and P < 0.001 vs BiV; Table 1). This was attributable to the severely and significantly (P < 0.001) increased PR interval during RAA pacing induced by administration of a high dose of opioid. The QRS duration was significantly (P < 0.001) different among all pacing configurations, and the order of shortest to longest duration was RAA, BiV, LVFW, and RVA.

Echocardiographic values of LVIDd and end-diastolic volume were not significantly different among pacing configurations; however, values for LVIDd (P = 0.02) and end-systolic volume (P < 0.001) were significantly greater with RVA pacing, compared with respective values at all other sites (Table 1). Fractional shortening was not significantly different among all pacing sites, but ejection fraction was significantly lower with RVA pacing, compared with ejection fractions at all other sites (P = 0.005 vs RAA, P < 0.001 vs LVFW, and P < 0.001 vs BiV). There were no significant changes in DECO by pacing site. The LiDCO during RVA and LVFW pacing was significantly lower than that during RAA pacing (P < 0.001 vs RVA and P < 0.001 vs LVFW).

Figure 4—Lateral fluoroscopic images of the thorax with retrograde coronary venography via the coronary sinus of 3 clinically normal dogs. A—In the first dog, the great cardiac vein (arrow) was of adequate diameter and anatomic characteristics for placement of an LVFW lead. B—The second dog had multiple branches of coronary veins overlying the LV (arrowheads), but none were of adequate diameter to accept an LVFW lead. C—The third dog had a great cardiac vein with 2 acute angles (arrowheads) that could not be navigated with the LVFW lead and partial anomalous drainage directly to the RA (arrow).
and BiV pacing ($P < 0.001$ vs RVA and $P = 0.002$ vs LVFW pacing), whereas the LiDCO during BiV pacing was not significantly different from the LiDCO during RAA pacing.

Tissue-tracking measurements revealed no significant differences in the interval to peak displacement among all pacing sites (Table 1). The degree of dyssynchrony was significantly lower during RAA pacing ($P < 0.001$), compared with the value during pacing from any other site, but there were no significant differences in degree of dyssynchrony among ventricular pacing sites.

**Discussion**

The results of the study reported here, along with other results reported by the authors,\(^3\) suggest that it is feasible to implant transvenous BiV or LVFW pacing systems in most medium to large breed dogs. However, there is tremendous variation among dogs with respect to anatomic characteristics of the coronary vein, which makes performing retrograde venography imperative prior to attempting LVFW lead placement. Vessel size and course primarily dictate whether it is possible to place an LVFW lead in a given patient, and generally, only 1 large vein without acute bends overlying the LVFW is necessary for successful lead placement. The anatomic findings reported in the present study are corroborated by those of other studies\(^31,32\) on the variability in anatomic characteristics of human coronary veins. For the 8 dogs in which the full BiV pacing system could be implanted, only the most cranial vein (the great cardiac vein) was adequate for LVFW lead placement (Figure 4). This vessel is not ideal for cardiac resynchronization therapy in humans because it is too far anterior. The optimal lead position is over the lateral LVFW in a vessel between the great cardiac and middle cardiac veins.\(^33\) Therefore, the LV stimulation site used in the present study may have affected the results, although only 1 site was possible in each dog and the effect of the LVFW stimulation site can vary greatly among human patients.\(^34\)

Systolic LV function was assessed via echocardiography and invasive monitoring of cardiac output, and results of both techniques indicated that RVA pacing consistently and temporarily worsened systolic LV performance. This finding is similar to results of other studies involving humans\(^3,23\) and other animals.\(^2,4,23\) Analysis of the echocardiographic measurements did not reveal any significant differences between LVFW and BiV pacing, and this result was also consistent with findings of other studies\(^3,20,22\) involving animals. An additional improvement in LV systolic function with BiV pacing, compared with that achieved with LVFW pacing, was detected via measurements of LiDCO. Only 1 other study\(^21\) has revealed similar findings in dogs with clinically normal myocardial function. No changes based on pacing site were evident via measurements of DECO, but this variable does not correlate as well with the clinical standard of thermodilution as does LiDCO in dogs.\(^3,30\)

In the present study in dogs with clinically normal LV function before pacing, RVA pacing resulted in LV systolic dysfunction, whereas LVFW or BiV pacing maintained better LV performance. Biventricular pacing provided even more improvement, compared with LVFW pacing. However, no ventricular pacing site improved LV systolic function beyond that of ventricular activation by atrial pacing or sinus rhythm, which is reportedly the situation in the human heart as well.\(^29\)

The QRS duration has been used as a measurement of interventricular dyssynchrony (ie, a temporal difference between activation of the RV and LV),\(^31\) and the results of the present study indicated that ventricular activation by RAA pacing led to the greatest interventricular synchrony in dogs. PACing from the RVA caused the most interventricular dyssynchrony, but the dysynchrony was improved with LVFW pacing, and BiV pacing led to additional improvement. Left ventricular function increased as QRS duration decreased in the present study, but this finding has not been consistent in other studies.\(^19,20,22\) The discrepancy is likely attributable to the assumption that QRS duration is not associated with intraventricular dyssynchrony of the LV\(^37\) and that LV function may be more directly associated with

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**Table 1.—Mean ± SEM electrocardiographic, echocardiographic, cardiac output, and tissue-tracking measurements in 8 dogs paced transvenously in single-chamber mode from the RAA, and in dual-chamber mode from the RVA and LVFW and simultaneously from the RVA and LVFW (BiV).**

<table>
<thead>
<tr>
<th>Variable</th>
<th>RAA</th>
<th>RVA</th>
<th>LVFW</th>
<th>BiV</th>
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<tbody>
<tr>
<td>Dyssynchrony (ms)</td>
<td>42.2 ± 2.4*</td>
<td>57.4 ± 3.4</td>
<td>59.9 ± 3.2</td>
<td>61.9 ± 3.5</td>
</tr>
<tr>
<td>End-systolic volume (mL)</td>
<td>18.9 ± 0.5</td>
<td>21.1 ± 0.6*</td>
<td>18.6 ± 0.7</td>
<td>18.3 ± 0.7</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>57.1 ± 1.1</td>
<td>53.7 ± 1.0*</td>
<td>58.0 ± 0.8</td>
<td>59.0 ± 1.2</td>
</tr>
<tr>
<td>DECO (L/min)</td>
<td>3.5 ± 0.1</td>
<td>3.5 ± 0.1</td>
<td>3.4 ± 0.1</td>
<td>3.3 ± 0.1</td>
</tr>
<tr>
<td>LiDCO (L/min)</td>
<td>3.7 ± 0.2†</td>
<td>2.7 ± 0.1</td>
<td>2.8 ± 0.1</td>
<td>3.6 ± 0.3†</td>
</tr>
<tr>
<td>Interval to peak displacement (ms)</td>
<td>369.6 ± 4.4</td>
<td>355.5 ± 5.7</td>
<td>366.9 ± 5.3</td>
<td>361.1 ± 6.0</td>
</tr>
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*Value is significantly ($P < 0.05$) different from those of other pacing sites. †Value is significantly ($P < 0.05$) different from those of the RVA and LVFW.

HR = Heart rate.
intraventricular rather than interventricular dyssynchrony. This assumption is corroborated by the findings of other studies involving cardiac resynchronization therapy in human patients, in which measurement of QRS duration alone also failed to predict response to treatment. Therefore, QRS duration cannot be used to measure intraventricular synchrony of the LV or predict changes in LV function.

Several echocardiographic modalities have been evaluated to assess intraventricular synchronization of LV contraction, including M-mode and 2-dimensional echocardiography, but TDI has been evaluated most extensively. Myocardial velocity, displacement, strain, and strain rate are all TDI-based modalities that have been used to analyze LV synchrony. Regardless of the TDI-based modality evaluated, most indices of dysynchrony have been calculated either as the difference in the interval to peak from the onset of the QRS complex between myocardial segments or the SD of the interval to peak for all measured segments.

Several color-coded TDI-derived measures of intraventricular dyssynchrony of the LV are good predictors of response to cardiac resynchronization therapy in human heart failure patients. Tissue tracking allows measurement of myocardial displacement and was chosen by the authors to evaluate LV synchrony on the basis of their training and experience with the software and the results of another study in which tissue tracking was able to identify human patients with LV dysfunction who would benefit from cardiac resynchronization therapy. The results of the present study indicated that the calculated measure of dysynchrony was significantly less during RAA pacing than during pacing from any other ventricular pacing site in dogs, but there were no significant changes in dysynchrony among the various ventricular pacing sites. The lack of significant changes may have been attributable to suboptimal placement of the LVFW lead, as mentioned previously. However, pacing at any ventricular site leads to ventricular activation that is abnormal when compared with natural activation via the His-Purkinje system. Indeed, 2 studies involving dogs revealed that the sequence of ventricular activation is more important for determining LV function than temporal synchronization of contraction. Therefore, it is possible that the improvement in LV function by LVFW or BiV pacing, compared with that of RVA pacing, may have been related to normalization of the ventricular activation sequence (which was not measured in the present study) instead of an increase in synchronization of contraction as was hypothesized.

Optimization of 2 important pacing variables considerably affects LV function, and these variables warrant discussion because they were standardized across all dogs in the present study. First, AV interval has a profound effect on stroke volume by affecting ventricular filling. This variable can be optimized echocardiographically and should be optimized on an individual basis and reoptimized when the ventricular pacing site is altered. Optimization of the interventricular pace delay also has an important effect on LV dyssynchrony and systolic function. Once again, this variable may be optimized echocardiographically, and the optimal interventricular pace delay varies, necessitating individual optimization. If these parameters had been optimized for each dog and pacing site in the study, then it is possible that additional improvement in LV performance and synchrony would have occurred and affected the results.

The clinical importance of optimizing ventricular pacing sites is illustrated by the results of several long-term human studies in which the detrimental functional and pathologic effects of RVA pacing translated into negative clinical consequences. These detrimental effects have been associated with increased morbidity and mortality in humans with sick sinus syndrome treated with dual-chamber RVA pacing versus atrial pacing. Many young patients paced from the RVA for complete congenital AV block develop reduced LV function, deleterious LV remodeling, and reduced exercise tolerance, compared with exercise tolerance in healthy humans, although these characteristics are not evident in all such patients. Similar findings are evident in elderly humans with AV block. Sick sinus syndrome and AV block are the 2 most common indications for pacemaker implantation in dogs, and typically, the RVA is the pacing site of choice for both conditions. Therefore, it is possible that clinical outcomes in human and veterinary patients may be improved if pacing sites that maximize ventricular function and minimize pathologic changes are used.

The results of the study reported here suggested that LVFW or BiV pacing temporarily improved LV function in clinically normal dogs, compared with the effects of RVA pacing. Given the evidence of the detrimental effects of RVA pacing and superiority of LVFW or BiV pacing, perhaps these pacing sites should be used whenever a ventricular pacemaker is implanted in animals. More likely, these findings will be particularly relevant for dogs with structural cardiac disease (eg, mitral valve regurgitation or systolic dysfunction) and low cardiac reserve because such dogs might not tolerate additional decreases in LV function by RVA pacing. In those dogs, LVFW or BiV pacing may preserve or possibly even increase LV function and improve outcome. New evidence in humans with heart failure who require pacing for bradyarrhythmias supports this supposition as well; however, additional studies designed to explore the long-term consequences of various transvenous ventricular pacing sites in dogs are necessary before definitive recommendations can be made. Finally, because natural ventricular activation provides the best LV function and synchrony, whenever possible, the natural intraventricular conduction pathways should be used with atrial pacing whenever pacemaker implantation is indicated in veterinary patients.

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a. RP Marinir SCXL steerable electrophysiology catheter (5 F), Medtronic Inc, Minneapolis, Minn.
b. Attain guide catheter (9 F) model 6218, Medtronic Inc, Minneapolis, Minn.
c. Attain venogram balloon catheter (6 F) model 6215, Medtronic, Inc, Minneapolis, Minn.
d. Attain OTW unipolar pacing lead (4 F) model 4193, Medtronic Inc, Minneapolis, Minn.
e. Attain OTW bipolar pacing lead (6 F) model 4194, Medtronic Inc, Minneapolis, Minn.
f. Capture SP Novus tined pacing lead (3.3 F) model 4092, Medtronic Inc, Minneapolis, Minn.
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30. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–1463.


