Optimized Biventricular Pacing in Atrioventricular Block After Cardiac Surgery

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Background. Temporary pacing is required after open-heart surgery for treatment of heart block. Atrioventricular delay and ventricular pacing site might be manipulated to increase cardiac output. We hypothesized that by optimizing both atrioventricular delay and ventricular pacing site a 10% improvement in cardiac output would be observed compared with a standard pacing protocol.

Methods. Seven patients in first or third degree heart block after valve replacement surgery had temporary wires sewn to the right atrium, right ventricle, and left ventricle. Cardiac output was measured by integrating flow velocity from an ultrasonic aortic flow probe. After optimization of atrioventricular delays during atrial synchronous right ventricular pacing, the effects of ventricular pacing site were tested at the optimum atrioventricular delay for 10-second intervals.

Results. Biventricular pacing was beneficial in all patients with a mean increase of 22% in cardiac index over right ventricular pacing (1.95 L/min/m² ± 0.27 standard error of the mean (SEM) to 2.38 L/min/m² ± 0.27 SEM, p = 0.0012) and 14% over left ventricular pacing (2.08 L/min/m² ± 0.22 SEM to 2.38 L/min/m² ± 0.27 SEM, p = 0.0133). Comparing optimized with standard pacing for 30-second intervals yielded a mean increase of 10% in cardiac index over three respiratory cycles (2.87 L/min/m² ± 0.33 SEM to 2.60 L/min/m² ± 0.37 SEM, p = 0.009) and 17% at the corresponding end-expiratory beats (2.76 L/min/m² ± 0.33 SEM to 2.36 L/min/m² ± 0.36 SEM, p = 0.011).

Conclusions. Biventricular pacing at optimum atrioventricular delay improves cardiac output in patients with postoperative heart block by at least 10% compared with standard pacing.

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Temporary perioperative cardiac pacing is often required after open-heart surgery for treatment of sinus bradycardia and transient heart block [1]. The effect of temporary perioperative cardiac pacing on cardiac output (CO) and stroke volume is rarely measured despite parameters that might be manipulated to the patient’s advantage including heart rate (HR), ventricular pacing site (VPS), and atrioventricular delay (AVD). Use of ultrasonic transit-time aortic flow probes makes measurement of CO and stroke volume during implementation of temporary perioperative cardiac pacing more feasible [2].

Clinical trials have confirmed that simultaneous pacing of the right ventricle (RV) and left ventricle (LV) by a second pacing lead in a lateral branch of the coronary sinus can narrow the QRS complex and improve exercise capacity and quality of life, possibly leading to reduced hospitalization in patients with severe heart failure and intraventricular conduction delays [3]. With regard to epicardial pacing, comparison of DDD and VVI modes has shown that DDD pacing improves CO at any given HR [4]. Studies in experimental animals have demonstrated that DDD pacing reduces myocardial oxygen consumption (MVO₂) when compared with VVI pacing [5]. Biventricular pacing (BiVP) has been shown to be effective with epicardial leads in both right and left bundle branch block (LBBB) [6, 7].

We sought to optimize temporary perioperative cardiac pacing in patients with atrioventricular block (AVB) after separation from cardiopulmonary bypass (CPB). We measured the effect of temporary perioperative cardiac pacing optimization on CO at a HR selected by the surgical team in order to test the following hypothesis: BiVP at optimal AVD yields a 10% improvement in CO compared with standard RV pacing at optimal AVD or no pacing.

Patients and Methods

Patient Selection

This study was approved by the Western Institutional Review Board. With the consent of the attending surgeon, patients undergoing open-heart surgery with a high probability of postoperative AVB were approached to enroll in this study. All patients gave informed consent. Candidates included patients undergoing valve replacement surgery...
and patients with known first, second, or third degree block. Patients were excluded if the surgeon did not plan to dissect the aorta or pulmonary artery in case of previous cardiac surgery. Patients with advanced calcification of the aortic arch were also excluded.

Preoperative data were obtained by chart review and included left ventricular ejection fraction (LVEF), LV diastolic dimension from echocardiograms and PR interval, QRS duration, HR, and intraventricular blocks from electrocardiogram (ECG) tracings. The results of any Holter monitoring, as well as any history of syncope or arrhythmias, were recorded. Hemodynamic or angiographic data supporting the need for surgery were also obtained. The cardiac rhythm prior to pacing, and actual surgery performed, were also recorded.

Study Design
Prior to separation from CPB, patients with normal atrial rates had standard temporary wires sewn to the right atrial appendage, anterior RV, and obtuse margin of the LV. Lead placement was consistent in all patients. Patients were connected to a 5388 Medtronic Dual Chamber temporary pacemaker (Medtronic, Inc, Minneapolis, MN). Sensing and pacing functions of these wires were tested and confirmed. An appropriately sized real-time ultrasonic flow probe (Transonic Systems, Inc, Ithaca, NY) was placed on the ascending aorta. When the patient had been successfully weaned from CPB and volume loading and pressor support had been optimized, the protocol was initiated at a HR defined by the surgical team. During the period of data acquisition, there were no changes in pressor support. Data acquisition was initiated within 5 minutes after separation from CPB.

Data Acquisition and Analysis
ECG measurements, arterial pressure, and flow velocity tracings were sampled and transferred through a 16-channel analog-to-digital converter (PowerLab, ADInstruments, Inc, Milford, MA) to a personal computer (iMac, Apple Computer, Cupertino, CA). During atrial and RV pacing (DDD), AVD was increased by 30 ms increments from 90 ms to 270 ms, and then decreased incrementally to 90 ms for 10-second intervals. Optimum AVD was determined by comparing CO values displayed by the flowmeter. Effects of VPS (RV, BiV, LV) were then tested at the optimum AVD for 10-second intervals. After determining the optimum (OPT) VPS, pacing was then alternated between the OPT and baseline (BL) VPS for 30-second intervals. The BL setting, as determined by the surgeon, was either RV pacing or no pacing. Table 1 shows the pacing protocol and elapsed time in seconds. Representative tracings are shown in Figure 1. After data collection, instrumentation was removed and temporary perioperative cardiac pacing was controlled by the clinical team.

For the 10-second intervals, CO data were obtained by integrating flow velocity tracings over paired beats at end-expiration using MacLab software (ADInstruments Inc, Milford, MA). For the 30-second intervals, CO data were obtained by integrating flow velocity tracings over three respiratory cycles as well as the corresponding end-expiratory beats for each of the three cycles. Using custom designed routines in MATLAB (The MathWorks, Inc, Natick, MA), beat-to-beat CO and mean arterial pressure (MAP) were calculated across three respiratory cycles for the OPT and BL settings. Each respiratory cycle was defined as the time between successive end-expiratory points (point of minimum MAP). The CO values from the three respiratory cycles for each setting were averaged and time expressed as percentage of the respiratory cycle. All CO data were indexed by body surface area.

Statistical Analysis
A mixed model methodology (PROC MIXED) was used to analyze the effect of AVD on cardiac index (CI) as well as the effect of VPS on CI. To discern differences among the three sites, contrast statements were utilized. This test controls the type I comparisonwise error rate, not the experimentwise error rate. With the assumption that CI

<table>
<thead>
<tr>
<th>AVD test</th>
<th>AVD</th>
<th>Time (sec)</th>
<th>VPS test</th>
<th>VPS</th>
<th>Time (sec)</th>
<th>OPT/BL test</th>
<th>Time (sec)</th>
</tr>
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<tr>
<td>VPS = RV</td>
<td>90</td>
<td>10</td>
<td>AVD = OPT</td>
<td>RV</td>
<td>140</td>
<td>OPT</td>
<td>220</td>
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<td></td>
<td>120</td>
<td>20</td>
<td></td>
<td>BiV</td>
<td>150</td>
<td>BL</td>
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<td></td>
<td>150</td>
<td>30</td>
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<td>LV</td>
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<td></td>
<td>BiV</td>
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</table>

AVD = atrioventricular delay; BiV = biventricular; BL = baseline; LV = left ventricle; OPT = optimum; RV = right ventricle; VPS = ventricular pacing site.
data follow a normal distribution, a paired t test was utilized to analyze the effect of OPT and BL settings on CI. To discern whether there were differences in CI across the respiratory cycle and between BL and OPT settings, a two factor, repeated measures analysis of variance design was performed, with repeated measures analyzed for both factors; ie, pacing setting and percentage of the respiratory cycle. In addition, a paired t test was utilized to compare CI values at end-expiration with the mean for other time points in the respiratory cycle. All data were analyzed using SAS system software (SAS Institute, Inc, Cary, NC).

Results

Study Population

A total of 15 patients were enrolled in this study. Eight patients were excluded because they did not develop heart block. Upon separation from CPB, the protocol was initiated in 7 patients. Six patients developed complete heart block and one patient remained in first-degree heart block. Table 2 lists baseline clinical characteristics for these patients including primary pathologic lesions.

Preoperatively, 4 patients were in normal sinus rhythm and 3 patients were in first-degree heart block. Left ventricular diastolic dimensions were available in only 2 patients and were abnormal in both cases (5.8 cm, 6.7 cm). The QRS duration on preoperative ECG was greater than 140 ms in 5 patients and less than 120 ms in 2 patients. Preoperative LVEF was greater than 35% in 6 patients. All patients underwent either aortic or mitral valve replacement surgery. One patient underwent both aortic and mitral valve replacement surgery. None of the patients required permanent pacemaker implantation postoperatively as complete heart block was transient.

Table 2. Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>Study Number</th>
<th>Primary Lesion</th>
<th>Pre-op EF</th>
<th>QRS duration (msec)</th>
<th>Operation</th>
<th>Heart Block</th>
</tr>
</thead>
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<tr>
<td>HB-1</td>
<td>Severe AI, SBE</td>
<td>40%</td>
<td>140</td>
<td>AVR</td>
<td>3rd degree</td>
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<tr>
<td>HB-2</td>
<td>Severe AS</td>
<td>40%</td>
<td>106</td>
<td>AVR/CABGx4</td>
<td>3rd degree</td>
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<td>HB-3</td>
<td>Severe AI</td>
<td>45%</td>
<td>148</td>
<td>AVR</td>
<td>3rd degree</td>
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<tr>
<td>HB-4</td>
<td>Severe MR</td>
<td>23%</td>
<td>164</td>
<td>MVR/CABGx1</td>
<td>3rd degree</td>
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<tr>
<td>HB-5</td>
<td>Severe MR/TR</td>
<td>35%</td>
<td>146</td>
<td>MVR/TV repair</td>
<td>3rd degree</td>
</tr>
<tr>
<td>HB-6</td>
<td>Severe AS/AI</td>
<td>55%</td>
<td>164</td>
<td>AVR</td>
<td>1st degree</td>
</tr>
<tr>
<td>HB-7</td>
<td>Severe AS/MR</td>
<td>45%</td>
<td>100</td>
<td>AVR/MVR</td>
<td>3rd degree</td>
</tr>
</tbody>
</table>

AI = aortic insufficiency; AS = aortic stenosis; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; EF = ejection fraction; MVR = mitral valve replacement; QRS = Q, R, and S waves in electrocardiogram; SBE = subacute bacterial endocarditis; TR = tricuspid regurgitation.
Clinical Results

The AVD significantly affected CI for all patients \((p = 0.0002)\). Post-tests revealed significant differences in CI at AVD values of 90, 210, 240, and 270. Optimum AVD was 150 ms in 3 patients, 120 ms in 2 patients, 180 ms in 1 patient, and 210 ms in 1 patient. The individual effect of VPS on CI for all patients is shown in Figure 2. At optimum AVD, BiVP was beneficial in all patients with a mean increase in CI of 22% over RV pacing \((1.95 \text{ L/min/m}^2 \pm 0.27 \text{ SEM, } p = 0.0012)\) and a mean increase of 14% in CI over LV pacing \((2.08 \text{ L/min/m}^2 \pm 0.22 \text{ SEM to 2.38 L/min/m}^2 \pm 0.27 \text{ SEM, } p = 0.0133)\). Testing at OPT/BL settings for 30-second intervals was performed in 5 of 7 patients. As shown in Figure 3, OPT was beneficial in all patients with a mean increase of 10% in CI compared with BL over three respiratory cycles \((2.87 \text{ L/min/m}^2 \pm 0.33 \text{ SEM to 2.60 L/min/m}^2 \pm 0.37 \text{ SEM, } p = 0.009)\). When comparing the average of three corresponding end-expiratory beats from the three respiratory cycles, OPT was beneficial by 17% over BL \((2.76 \text{ L/min/m}^2 \pm 0.33 \text{ SEM to 2.36 L/min/m}^2 \pm 0.36 \text{ SEM, } p = 0.011)\). Figure 4 illustrates the relation between MAP and CI during three successive respiratory cycles averaged across the 5 patients. Average MAP and CI measurements when these cycles are combined are shown in Figure 5. There was significant variation of CI and MAP over the respiratory cycle for both OPT and BL, with cyclic changes about the mean \((p = 0.0001)\). Both CI and MAP increased with inspiration. The pattern of variation relating CI to the respiratory cycle appeared different for OPT and BL and approached statistical significance \((p = 0.0715)\). Specifically, CI increased and decreased more rapidly for OPT. The pattern of variation relating MAP to the respiratory cycle was not different for OPT and BL \((p = 0.9787)\).

Comment

This study indicates that BiVP at optimum AVD significantly enhances CO in patients with AVB during open-heart surgery. Although optimum AVD setting was patient specific, in each case BiVP was associated with significant improvement in CO compared with RV or LV.
pacing. The present study systematically studies acute effects of pacing protocol modification at constant heart rate in patients who require pacing for AVB after CPB during open-heart surgery. In this study, we focused primarily on the effect of AVD and VPS on CO. Physiologically, lead placement may be as or more important to optimizing ventricular function. The effect of lead placement should be investigated in future studies.

The relationship between AVD and CO is related to chamber mechanics through optimization of ventricular filling [8]. An excessively long or short interval is known to result in suboptimal chamber filling which contributes to mitral regurgitation [9]. The AVD testing in this study supported this premise by demonstrating that extreme values (90 ms, 270 ms) were detrimental to CO. The effect of VPS on parameters of acute systolic function has been studied in patients with LBBB. These studies showed that in patients with dilated cardiomyopathy or congestive heart failure, BiV stimulation was significantly more beneficial than RV pacing alone [10–12]. The present study examined the effect of VPS on CO in patients with AVB after CPB during valvular heart surgery. Using direct real-time measurements of CO from an ultrasonic aortic flow probe, this study showed a significant benefit of BiVP over RV or LV pacing alone. This suggests that typical protocols utilized for perioperative pacing in patients with regular atrial rhythm consisting of DDD mode pacing with temporary bipolar right atrial and RV wires should be questioned.

During longer testing intervals, BiVP remained superior to BL with an average improvement of 10% in CI over three respiratory cycles. The improvement was greater (17%) over the average of the corresponding end-expiratory beats in each of the three respiratory cycles. The difference between CI values over three respiratory cycles and the corresponding end-expiratory beats in each cycle is shown by Figure 5. In this figure, CI values varied over the respiratory cycle with lowest values at end-expiration and highest values at end-inspiration. Innes and colleagues [13] similarly found that when LV stroke volume data from several respiratory cycles were fit with the fundamental and first harmonic of a sine wave at the frequency of respiration, increased values of LV stroke volume during positive pressure ventilation occurred during lung inflation.

Left bundle branch block has been shown to correlate with left ventricular dysfunction [14]. Grines and colleagues [15] confirmed that altered ventricular activation secondary to LBBB resulted in delayed LV contraction with a decline in LVEF and abnormal interventricular septal motion. This study also implicated interventricular asynchrony as a mechanism for diminished cardiac function. In a canine model of LBBB, BiVP improved cardiac function by resynchronization of LV excitation and contraction [16]. The mechanism of the observed effects of VPS on CO in the present study was not formally investigated. We speculate that the majority of the benefit seen with BiVP is due to the deleterious effects of single-site ventricular pacing. This effect changes the activation sequence, generating regions of early and delayed contraction [17–19]. Early shortening at the pacing site is wasted work as ejection has not occurred. Late activation of the region remote to the pacing site occurs at higher stress as the paced region has already developed tension [20]. We have been investigating the effects of optimized pacing on interventricular synchrony in experimental models of acute ventricular failure using LV and RV pressure signals. We have found that during RV pressure overload, pacing at an optimal setting improved interventricular synchrony compared with a suboptimal one [21]. We are also beginning to investigate intraventricular synchrony in these models by echocardiography using M-mode and tissue Doppler imaging. Such analyses would be appropriate for clinical studies.

Historically, definition of mechanisms and treatment of arrhythmias have been accelerated in the operating room by direct exposure of the epicardium to mapping and interventions. This advantage might resolve issues in endocardial BiVP like whether localization of wall motion abnormalities or conduction delays defines an optimum site for LV electrode placement and whether lead localization is critical [12, 22, 23]. There may be patients with isolated RV
dysfunction in whom there is no role for BiVP [24]. Correlations between preoperative QRS duration and hemodynamic benefit and between QRS shortening and improved ventricular function have also been described [25]. These potentially fruitful areas for future studies are beyond the present design and population size.

With respect to technical aspects of the study, we are concerned about application and removal of the ultrasonic flow probes. The housing of these probes is rigid and requires manual compression of the ascending aorta during both application and removal. For this reason, we have decided to use scissor-type electromagnetic probes to avoid this manipulation. Previous studies suggest that absolute flow measurement is somewhat less accurate with electromagnetic probes, but sensitivity to small changes in flow appears sufficient. Calibration against thermodilution measurements will be done when feasible.

The present study suggests that the traditional perioperative protocol of DDD mode pacing with temporary right atrial and RV wires in patients with AVB during open-heart surgery may be suboptimal. The BiVP with AVD optimization should be utilized in the acute setting after separation from CPB.

Little objective data are available regarding the benefits of BiVP in the perioperative setting. We believe that further clinical trials should be undertaken to investigate whether the effects we have seen are sustained over time. We also propose that these trials should investigate any additional benefit of right-left ventricular delay and LV pacing site in optimization of CO in patients with perioperative AVB.

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References