Short-term reduction in intrinsic heart rate during biventricular pacing after cardiac surgery: A substudy of a randomized clinical trial

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Background: The Biventricular Pacing After Cardiac Surgery trial investigates hemodynamics of temporary pacing in selected patients at risk of left ventricular dysfunction. This trial demonstrates improved hemodynamics during optimized biventricular pacing compared with atrial pacing at the same heart rate 1 and 2 hours after bypass and reduced vasoactive-inotropic score over the first 4 hours after bypass. However, this advantage of biventricular versus atrial pacing disappears 12 to 24 hours later. We hypothesized that changes in intrinsic heart rate can explain variable effects of atrial pacing in this setting.

Methods: Heart rate, mean arterial pressure, cardiac output, and medications depressing heart rate were analyzed in patients randomized to continuous biventricular pacing (n = 16) or standard of care (n = 18).

Results: During 30-second testing periods without pacing, intrinsic heart rate was lower in the paced group 12 to 24 hours after bypass (76.5 ± 17.5 vs 91.7 ± 13.0 beats per minute; $P = .040$) but not 1 or 2 hours after bypass. Cardiac output (4.4 ± 1.2 vs 3.6 ± 1.9 L/min; $P = .054$) and stroke volume (53 ± 2 vs 42 ± 2 mL; $P = .051$) increased overnight in the paced group. Vasoactive medication doses were not different between groups, whereas dexmedetomidine administration was prolonged over postoperative hours 12 to 24 in the paced group (793 ± 528 vs 478 ± 295 minutes; $P = .013$).

Conclusions: These observations suggest that hemodynamic benefits of biventricular pacing 12 to 24 hours after cardiopulmonary bypass lead to withdrawal of sympathetic drive and decreased intrinsic heart rate. Depression of intrinsic rate increases the apparent benefit of atrial pacing in the chronically paced group but not in the control group. Additional study is needed to define clinical benefits of these effects. (J Thorac Cardiovasc Surg 2013;146:1494-500)

PM

Biventricular pacing (BiVP) is beneficial for patients with heart failure characterized by ventricular dyssynchrony.[1] BiVP can induce resynchronization, with function optimized by adjusting the length of both atrioventricular delay (AVD) and interventricular delay (VVD). BiVP reduces morbidity and mortality and improves quality of life and walking ability for patients with mild to severe heart failure who exhibit a prolonged QRS duration (QRSd) of greater than 120 milliseconds and a left ventricular ejection fraction (LVEF) of 35% or less.[2-5] In addition, BiVP, with or without an intracardiac defibrillator, can reduce mortality and hospitalizations after implantation.[3,6] Mechanistically, BiVP has improved LVEF and reversed left ventricular (LV) remodeling characteristic of advanced heart failure.[5,7] More important, BiVP can increase contractility without increasing myocardial oxygen demand.[8]

BiVP may be beneficial for patients after open heart surgery (OHS). Previous studies that investigated temporary BiVP after OHS have used a primary eligibility criterion of low preoperative LVEF, which can independently predict risk of acute heart failure after OHS.[9] These studies have shown mixed results but suggest that BiVP is most effective immediately after cardiopulmonary bypass (CPB).[10-13] Complicating these results is that up to 30% of patients do not respond to permanent BiVP.[2,14] Optimization of permanent BiVP pacing settings can decrease this nonresponse rate,[15,16] but the optimal settings for temporary BiVP after OHS are unknown.

The Biventricular Pacing after Cardiac Surgery (BiPACS) trial is a randomized, controlled study of temporary, optimized BiVP for patients undergoing OHS.

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Abbreviations and Acronyms

AAI = atrial pacing
AVD = atrioventricular delay
BiPACS = Biventricular Pacing after Cardiac Surgery
BiVP = biventricular pacing
bpm = beats per minute
CO = cardiac output
CPB = cardiopulmonary bypass
ICU = intensive care unit
LVEF = left ventricular ejection fraction
MAP = mean arterial pressure
OHS = open heart surgery
QRSd = QRS duration
SOC = standard of care
VIS = vasoactive-inotrope score
VVD = interventricular delay

Enrollemnt criteria are described in Methods. The primary end point for this study is cardiac index, measured by thermodilution in the intensive care unit (ICU). In addition, the BiPACS trial tests optimization of BiVP for all enrolled patients at 3 time points: immediately after CPB (phase I), after chest closure (phase II), and 12 to 24 hours postoperatively (phase III). At phase I in the BiPACS trial, optimized BiVP increased cardiac output (CO) by 13% compared with no pacing, whereas atrial pacing (AAI) at the same heart rate provided no benefit.[17] Interestingly, in phase II, the effect of AAI was intermediate between no pacing and optimized BiVP[18]; and in phase III, the benefit of AAI was indistinguishable from BiVP.[18] These data indicate that BiVP increases stroke volume immediately after CPB (phase I), whereas the benefit of BiVP and AAI in the ICU (phase III) is primarily due to an increase in heart rate.

Atrial pacing is, thus, increasingly effective from phase I to phase III, but the mechanism for this trend is undefined. We hypothesized that this increasing AAI efficacy might be related to changes in intrinsic heart rate over time after CPB. The pacing rate in AAI and BiVP modes was 90 beats per minute (bpm) or 10 bpm higher than the patient's intrinsic heart rate if the intrinsic rate exceeded 90 bpm. Thus, a decrease in intrinsic heart rate could augment the percentage increase in heart rate during AAI pacing, in turn increasing the fractional change in cardiac output.

This substudy analyzes changes in intrinsic heart rate and related variables in phases I, II, and III of the BiPACS trial. Because enrollment in the trial is complete, we are also able to compare these variables across randomization groups.

METHODS

BiPACS Study Population

The BiPACS protocol is approved by the Columbia University Medical Center Institutional Review Board and supported by the National Institutes of Health under an investigational device exception from the Food and Drug Administration (No. G050189). The protocol has been described in detail previously.[17] Adult patients undergoing elective surgery on CPB are screened for inclusion in the BiPACS trial by trained study coordinators and investigators, with permission from the attending surgeon. All patients in the study give written, informed consent. Eligibility criteria include preoperative congestive heart failure, an LVEF of 40% or lower and a QRSd of 100 milliseconds or greater, or combined mitral and aortic valve replacement. Patients are excluded for atrial fibrillation, second- or third-degree AV block, congenital heart disease, intracardiac shunts, or heart rate greater than 120 bpm after CPB.

Study Design and Protocol

All BiPACS patients undergo BiVP optimization during phases I, II, and III, defined above. Randomization is done after phase I. In addition, patients in the BiVP group are paced continuously between phases I and III. The primary end point is cardiac index measured by thermodilution in the ICU. The present study does not examine primary end point data.

In phase I, 38 settings of BiVP with varying AVD, VVD, and ventricular placing sites are tested in randomized order to determine an optimal BiVP protocol designated P1, optimized with an aortic flow probe. P1 is tested against AAI at the same heart rate and against the patient's intrinsic sinus rhythm at the end of phase I.

In phase II, BiVP settings are again tested in a different randomized order to determine a second optimal BiVP protocol, P2. P1 and P2 are then compared against each other and against AAI and no pacing, at the end of phase II. Mean arterial pressure (MAP) is a surrogate marker for CO in phase II, because chest closure precludes use of flow probes and time constraints obviate use of thermodilution.

Patients in the BIVP group are paced from the end of phase I to the start of phase II under protocol P1. The BIVP group is then paced from phase II to phase III with the optimum phase II protocol (either P1 or P2), as determined using MAP. Patients in the standard-of-care (SOC) group are not paced between phases. The primary end point at the start of phase III is CO by thermodilution, using a Swan-Ganz catheter.

At the start of phase III, the active pacing protocol is again compared with AAI and no pacing using thermodilution CO; 212 settings of AVD and VVD are then tested in random order. The 10 settings yielding the highest MAP are retested to determine an optimal phase III setting, P3. P3 is finally compared with AAI and no pacing by thermodilution CO.

Data Analysis

At all phases, electrocardiographic and arterial pressure tracings are recorded. In phase I, flow velocity is recorded using an aortic flow probe. Data are converted to digital form with a PowerLab AD system (ADInstruments, Inc, Colorado Springs, Colo) and stored on a personal computer (Apple Computer, Inc, Cupertino, Calif) with MacLab software (ADInstruments, Inc). Data are then loaded into Matlab (The MathWorks, Inc, Natick, Mass), where heart rate, CO, and MAP are averaged and recorded over one respiratory cycle toward the end of no pacing, AAI, and optimized BiVP segments.[17,18] Doses of vasoactive medications and duration of sedative infusions are obtained from the Eclipsys patient record system (Allscripts Healthcare Solutions, Inc, Chicago, Ill) at New York–Presbyterian Hospital. Vasoactive-inotrope scores were calculated as described in a prior substudy[22]: