Optimized temporary biventricular pacing acutely improves intraoperative cardiac output after weaning from cardiopulmonary bypass: A substudy of a randomized clinical trial

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Objective: Permanent biventricular pacing benefits patients with heart failure and interventricular conduction delay, but the importance of pacing with and without optimization in patients at risk of low cardiac output after cardiac surgery is unknown. We hypothesized that pacing parameters independently affect cardiac output. Accordingly, we analyzed aortic flow measured with an electromagnetic flowmeter in patients at risk of low cardiac output during an ongoing randomized clinical trial of biventricular pacing (n = 11) versus standard of care (n = 9).

Methods: A substudy was conducted in all 20 patients in both groups with stable pacing after coronary artery bypass grafting, valve surgery, or both. Ejection fraction averaged 33% ± 15%, and QRS duration was 116 ± 19 ms. Effects were measured within 1 hour of the conclusion of cardiopulmonary bypass. Atrioventricular delay (7 settings) and interventricular delay (9 settings) were optimized in random sequence.

Results: Optimization of atrioventricular delay (171 ± 8 ms) at an interventricular delay of 0 ms increased flow by 14% versus the worst setting (111 ± 11 ms, $P < .001$) and 7% versus nominal atrioventricular delay (120 ms, $P < .001$). Interventricular delay optimization increased flow 10% versus the worst setting ($P < .001$) and 5% versus nominal interventricular delay (0 ms, $P < .001$). Optimized pacing increased cardiac output 13% versus atrial pacing at matched heart rate (5.5 ± 0.5 vs 4.9 ± 0.6 L/min, $P = .003$) and 10% versus sinus rhythm (5.0 ± 0.6 L/min, $P = .019$).

Conclusions: Temporary biventricular pacing increases intraoperative cardiac output in patients with left ventricular dysfunction undergoing cardiac surgery. Atrioventricular and interventricular delay optimization maximizes this benefit. (J Thorac Cardiovasc Surg 2011;141:1002-8)

Supplemental material is available online.

Biventricular pacing (BiVP) is an established therapy for congestive heart failure (CHF), and it is currently the standard of care for select patients with advanced CHF associated with left ventricular (LV) dysfunction and intraventricular conduction delay (IVCD).[1] Permanent BiVP improves LV dimension and function and decreases morbidity and mortality, although it is associated with a nonresponse rate of up to 30%.[2-5] Although the long-term benefits of BiVP are typically not appreciated until several months after implantation, hemodynamic effects of changes to pacing parameters are reflected acutely by metrics such as stroke volume, ventricular dyssynchrony, and the maximal first derivative of pressure (dP/dt_{max}).[6,7] These properties have facilitated the study of the optimization of programmable BiVP parameters, such as atrioventricular delay (AVD) and interventricular delay (VVD), to maximize the hemodynamic benefit of BiVP and to reduce its nonresponse rate.[8-10]

The acute hemodynamic effects of BiVP also enable the study of temporary BiVP as a treatment for low output states after cardiac surgery. Low left ventricular ejection fraction (LVEF) is an independent risk factor for poor outcomes after cardiac surgery.[11] BiVP improves hemodynamics without increasing myocardial oxygen consumption,[7] and therefore it is particularly appealing as a potential therapy in patients undergoing cardiac surgery. Prior studies have assessed temporary perioperative BiVP in heterogeneous groups of patients with varying results.[12-24] Moreover, the

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Abbreviations and Acronyms

AAI = atrial pacing
AVD = atrioventricular delay
BiPACS = BiVP After Cardiac Surgery
BiVP = biventricular pacing
CABG = coronary artery bypass grafting
CHF = congestive heart failure
CO = cardiac output
CPB = cardiopulmonary bypass
dP/dt_{max} = maximal first derivative of pressure
IVCD = intraventricular conduction delay
LV = left ventricle
LVEF = left ventricular ejection fraction
NSR = sinus rhythm with no pacing
RA = right atrium
RV = right ventricle
VVD = interventricular delay

role of optimization of temporary BiVP parameters in the perioperative setting is unclear.[25,26]

The BiVP After Cardiac Surgery (BiPACS) trial is a randomized clinical trial to study the effect of optimized temporary BiVP on cardiac output (CO) in postoperative cardiac surgery patients with preoperative LV systolic dysfunction and an IVCD. Patients undergo BiVP optimization at multiple time points in the intraoperative and postoperative periods and are randomized to continuous optimized BiVP versus standard of care. The hypothesis underlying the BiPACS trial is that CO will increase 15% in patients undergoing temporary BiVP. In this substudy of the BiPACS trial, we hypothesized that optimization of pacing parameters would increase CO. Accordingly, we assessed the contribution of AVD and VVD optimization to the effect of BiVP optimization in the intraoperative period after separation from cardiopulmonary bypass (CPB) and evaluated the effect of optimized BiVP on CO compared with atrial pacing (AAI) and with sinus rhythm with no pacing (NSR).

MATERIALS AND METHODS

BiPACS Trial Study Population

The study protocol was approved by the Columbia University Medical Center Institutional Review Board. Adult patients undergoing elective cardiac surgery on CPB were screened for eligibility to enroll in the BiPACS trial. All patients provided written informed consent. Recruitment was done before the day of the operation by qualified and trained study coordinators and investigators on the study team with permission of the attending surgeon. Inclusion criteria included the following: preoperative CHF, LVEF of 40% or less, and a QRS duration of 100 ms or greater or patients undergoing combined mitral and aortic valve surgery. LVEF and QRS criteria were liberalized from values of 35% and 120 ms, respectively, in the original protocol. Exclusion criteria included the following: atrial fibrillation, second- or third-degree atrioventricular block, congenital heart disease, intracardiac shunts, or heart rate of greater than 120 beats/min after separation from CPB. Preoperative data obtained by means of chart review included the following: LVEF, as measured by means of echocardiographic or left ventriculogram analysis; heart rhythm, QRS duration, and intraventricular blocks from electrocardiographic tracings; the type of operation performed; and demographic characteristics. The BiPACS trial is ongoing, and end points will not be examined until 212 patients have been randomized.

Study Design and Optimization Protocol

Patients in the BiPACS trial are randomized to the 2 treatment groups at the end of phase 1 (within 1 hour of the conclusion of cardiopulmonary bypass) by using randomly permuted blocks of 4, 6, and 8 to avoid imbalances that can occur with simple randomization. A treatment allocation ratio of 1:1 was used; each group will be of equal size. The phase 1 testing described here occurs in all patients before randomization. Optimization of AVD, ventricular pacing site, and VVD are tested in random sequences. Randomization and testing sequences are determined based on forms in sealed envelopes that are not opened until needed. These forms were prepared before enrollment of the first patient. Before separation from CPB, temporary epicardial pacing leads were sewn to the right atrial (RA) appendage, anterior right ventricle (RV), and 2 randomized sites of 6 possible sites on the LV. One of the LV leads (LV1) was placed at the basal LV at either the obtuse margin, circumflex, or posterior regions; the second LV lead (LV2) was placed at either the midinferomedial, midinferolateral, or apical LV. Data from BiVP using LV1 were analyzed in this study. The leads were attached to a Medtronic InSync III permanent biventricular pacemaker (Medtronic, Inc, Minneapolis, Minn) mounted in an external housing unit, and their sensing and pacing functions were tested and confirmed. An appropriately sized electromagnetic flow probe (Carolina Medical Electronics, East Bend, NC) was placed on the ascending aorta. After separation from CPB and establishment of stable inotrope and vasopressor dosing, the BiVP optimization protocol was initiated. The pacing rate was set at 90 beats/min or at 10 beats/min greater than the patient's intrinsic heart rate if greater than 90 beats/min to ensure atrial capture up to a maximum of 120 beats/min. These heart rates were selected empirically. A wider range of heart rates is studied in phase 3 of the BiPACS trial, including cardiac resynchronization therapy at the intrinsic heart rate.

Real-time aortic volume flow, echocardiograms, and arterial pressure signals were collected with an analog-to-digital converter (PowerLab; ADInstruments, Inc, Milford, Mass) and recorded on a personal computer (iMac; Apple Computer, Inc, Cupertino, Calif; Figure 1). CO was measured by integrating aortic volume flow tracings over 1 respiratory cycle with MacLab software (ADInstruments, Inc) and custom-designed routines in Matlab (The MathWorks, Inc, Natick, Mass).

BiVP optimization was performed by optimizing AVD, followed by VVD. All pacing settings during optimization were conducted over 10-second intervals and were tested twice. The use of a rapid optimization protocol measuring changes in cardiac mechanics over brief intervals has been described previously.[14,27] AVD optimization was performed during sequential RA BiVP, with a VVD of 0 ms. AVD was varied in 30-ms increments, ranging from 90 to 270 ms, in randomized order. AVDs that were longer than the patient's intrinsic paced AVD were not tested. The AVD yielding the highest CO was selected as the optimum AVD. AVD optimization data from a representative patient are shown in Figure 2. VVD optimization was then performed with the optimum AVD by varying the VVD by 20-ms increments, ranging from –80 ms (LV first) to +80 ms (RV first) in randomized order. CO as a function of VVD was plotted, and the VVD yielding the highest CO was selected as the optimum VVD (Figure 3), thereby defining the optimum BiVP parameters for the patient. Optimized BiVP was then compared with RA pacing (AAI mode) at the same heart rate and with NSR with no pacing, in randomized order, and over 30-second intervals. The aortic flow probe was then removed, and the temporary pacing leads were externalized for further BiVP optimization in subsequent phases of the BiPACS trial.

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