BENEFICIAL EFFECTS OF ATRIOVENTRICULAR SEQUENTIAL PACING ON CARDIAC OUTPUT AND LEFT VENTRICULAR FILLING ASSESSED WITH PULSED DOPPLER ECHOCARDIOGRAPHY

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There has been increased interest in the beneficial effects of atrio-ventricular (AV) pacing over ventricular (V) pacing. This study attempted to evaluate the changes in cardiac output and left ventricular filling dynamics when the pacing mode was switched from V pacing to AV pacing. Study population consisted of 26 patients with multiprogrammable AV pacemakers. Cardiac output was determined as a product of echocardiographically determined cross sectional area of the aortic annulus and Doppler-determined velocity integral of left ventricular outflow over systole. Left ventricular peak rapid filling rate (PFR) and peak atrial filling velocity to peak rapid filling velocity ratio (A/R) were determined from measurements at the mitral annulus. Cardiac output showed a significant improvement when the pacing mode was switched from V to AV pacing, and the percent change ranged from 3 to 73% (average 26%). The improvement in cardiac output brought about by AV synchrony was greater in patients with smaller PFR ($r = -0.71$, $p < 0.01$) and larger A/R ratio ($r = 0.77$, $p < 0.01$). On the other hand, PFR was greater with V pacing than with AV pacing. Greater increment of the PFR was produced by the loss of atrial contraction in patients with smaller PFR ($r = -0.82$, $p < 0.01$) and larger A/R ratio ($r = 0.76$, $p < 0.01$). Thus, AV pacing provides a great improvement in left ventricular filling, i.e., cardiac output, which cannot be obtained with V pacing even with the compensatory enhancement of left ventricular rapid filling. These beneficial effects of AV pacing seemed to be greater in patients with impaired left ventricular rapid filling.

An appropriately timed atrial contraction augments left ventricular filling and increases the left ventricular end diastolic volume, which in turn produces a shift to a more optimal position on the Frank-Starling curve and hence greater stroke volume. Thus the appropriately timed atrial contraction is quite important in maintaining optimal cardiac output. For this reason atrio-ventricular (AV) pacing is considered to be hemodynamically superior to ventricular (V) pacing; however, AV pacing has been limited by problems in generator design, and reliability and stability of the atrial electrode. Recent technical developments have solved these problems and made such pacemaker systems available.

Benefits of AV pacing over V pacing in cardiac output have been evaluated by clinical studies. However, there have been no investigations of the effects of changing the

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pacing mode on left ventricular filling dynamics in man. In this study we utilized pulsed Doppler echocardiography to measure phasic flow patterns in the left ventricular outflow and transmitial inflow. They were provided for the determination of cardiac output and the evaluation of left ventricular filling dynamics, respectively. The purposes of this study were to assess the changes in hemodynamics which occur when the pacing mode is switched from V to AV pacing, and to determine whether left ventricular diastolic function affects the degree of hemodynamic advantages of AV pacing.

METHODS

1. Subjects

Thirty patients with programmable AV pacemakers were examined by pulsed Doppler technique. Four patients were excluded in whom Doppler recordings were not satisfactorily obtained because of poor penetration of ultrasound throughout the chest wall. Thus, the study population consisted of 16 male and 10 female patients. Ages ranged from 15 to 84 years and averaged 55 years. The indication for pacing was sick sinus syndrome in 22 patients and complete AV block in the other 4 patients. Any patients with valvular heart diseases were excluded on the findings of echo Doppler examinations and/or cardiac catheterizations. Three patients had associated coronary artery disease, and three had associated hypertension. However, none had left ventricular hypertrophy or dilatation proven by left ventriculography and/or echocardiography.

2. Apparatus

We used a duplex Doppler echocardiograph (Toshiba SDS-21A with SSH-41A or SDS-21B with SSH-40A) for both cardiac imaging and determination of flow velocity. Two-dimensional echocardiographic images, M-mode echocardiographic tracings and Doppler-determined flow velocity patterns were obtained with a transducer array of 2.4 or 3.5 MHz. Any cursor line could be interrogated for pulsed Doppler sampling and M-mode echocardiographic tracing, and ultrasound beam direction and sample volume were monitored as a bright line and a spot on the line in the two-dimensional echocardiographic image. The sample volume was a cylinder with a diameter of 5 mm and a length of 2 mm at a depth of 10 cm. The pulse repetition rate was 4 kHz or 6 kHz. Doppler recordings were obtained in the Doppler mode, and sampling position was easily checked by switching the instrument from the Doppler to the real-time imaging mode. Doppler signals from the structures were minimized by a high-pass filter, and all signals were analyzed in real time by the fast-Fourier transform, and were simultaneously displayed with an electrocardiogram, phonocardiogram and M-mode echocardiogram at a paper speed of 100 mm/sec. The flow velocity directed toward and away from the transducer was displayed above and below the baseline on the recording paper.

3. Measurement of left ventricular outflow

Each patient rested in a supine position and breathed in a relaxed way during Doppler examination. The transducer was placed at the cardiac apex and tilted medially to depict the left ventricular outflow and the ascending aorta in a left anterior oblique view (Fig. 1). Doppler recordings of flow velocity were obtained with the Doppler beam directed as parallel as possible to the long axis of the left ventricular outflow tract and with the sample volume positioned immediately proximal to the aortic orifice in the middle of the left ventricular outflow. The Doppler incident angle was determined from the mid-systolic echocardiographic image. The mid-systolic diameter of the aortic annulus was determined from mid-systolic two-dimensional echocardiographic images or M-mode echocardiograms that were recorded with the ultrasound beam directed through the aortic annulus perpendicular to the aortic root.

On the assumption that the velocity profile just at the aortic valve orifice is flat, stroke volume was determined as a product of the cross-sectional area and the velocity integral over systole. The velocity integral was determined as an area under the envelope of the Doppler shift frequency pattern with a digitizer (Cardio 80, Contron). Angle correction was performed in 16 patients in whom the Doppler incident angle was over 20 degrees. Stroke volume was calculated as an average of ten consecutive cardiac cycles, and cardiac output was determined as a product of stroke volume and heart rate.

4. Measurement of transmitial inflow

After measurement of left ventricular outflow, we recorded the transmitial inflow velocity pattern. It was obtained with the transducer placed on the cardiac apex and angled medially to depict the left ventricular inflow and left
atrium. The sample volume was carefully positioned just at the level of mitral annulus at the center of the mitral orifice. Assuming that the transmitral inflow is directed toward the apex, we measured the Doppler incident angle between the beam direction and the assumed direction of the transmitral inflow. Since the angle was less than 20 degrees in all patients studied, flow velocity was not corrected for the angle.

The transmitral inflow showed a 2-peak pattern during AV pacing in all patients studied (Fig. 2). One of the velocity peaks was in the rapid filling phase and the other was in the atrial contraction phase. On the other hand, the transmitral inflow showed one of two patterns during V pacing. The first, characterized by only one peak in the rapid filling phase, was a one-peak pattern. The other was a two-peak pattern with the second peak in the "asynchronized" atrial contraction phase. The one-peak pattern was consistently observed in 12 patients without any atrial contraction, and both patterns were observed in the sequence of Doppler recordings in the other 14 patients.

We determined left ventricular peak rapid filling velocity (R) and peak filling rate (PFR) during both AV pacing and V pacing (Fig. 1). The PFR was determined as a product of the R and mitral annulus cross sectional area. The early diastolic transverse diameter of the mitral annulus was measured on the four-chamber view at a time of maximal opening motion of the anterior leaflet. The cross sectional area of the annulus was derived as $\pi r^2$, where $r$ represents half of the annular diameter. Peak atrial filling velocity (A) to R ratio was also determined during AV pacing. The PFR, R, and A/R ratio during AV pacing were used as Doppler indexes of left ventricular filling. The average values of ten consecutive cardiac cycles were used for the analysis.

5. Experimental protocols (pacing modes)

Measurements were done under AV and V pacings of 80 or 82 bpm in a random order in each patient. During AV pacing, the AV interval in this study ranged from 140 to 165 msec (mean 148 msec). Rhythms and heart rates were confirmed by limb lead electrocardiogram. In all patients spontaneous cardiac activity was less than the pacing rate, and the heart rates were identical in both pacing modes. All measurements were performed at least 5 minutes after changing pacing mode.

6. Statistical analysis
A-V sequential Pacing

ECG

AWAY

-2KHz

Ventricular Pacing

Fig. 2 Flow velocity patterns in the left ventricular outflow (left) and transmitral inflow (right) in a 43-year-old female with sick sinus syndrome. The top panels were recorded during atrioventricular (A-V) sequential pacing at an atrioventricular delay of 150 msec. The bottom panels were recorded during ventricular pacing. Both recordings were performed at a paced rate of 80 bpm. Note that peak flow velocity in left ventricular outflow is higher during atrioventricular sequential pacing and that peak rapid filling velocity is higher during ventricular pacing. Abbreviations: ECG = electrocardiogram, PCG = phonocardiogram, SV = sample volume.

To test reliability of the measurements, we selected 10 patients from the 26 and determined cardiac output, PFR, R, and A/R ratio by one observer on two occasions (intraobserver variability). Another observer independently performed the determination for the same 10 patients (interobserver variability). The observers were blinded to each other’s results. Mean absolute differences between observations (expressed as a percentage of the first observer’s first observation) were all less than 10%.

Results are expressed as mean ± SD. Paired t-test was applied for statistical comparison of paired differences. The relation between two variables was examined using least squares linear regression analysis and a correlation coefficient was calculated in the standard fashion.

RESULTS

1. Comparison of hemodynamic parameters during AV and V pacing.

The cardiac output during AV pacing was 5.2 ± 1.0 liters/min, which was significantly greater than that during V pacing (4.1 ± 0.8 liters/min, p < 0.01 in Fig. 3). The AV synchrony provided a mean improvement of 26 percent in cardiac output compared with V pacing at the rate of 80 or 82 bpm.

The mitral annulus cross sectional area in the AV pacing was 3.2 ± 0.7 cm², which was not significantly different from that in the V pacing (3.2 ± 0.7 cm²). The R was significantly higher in the V pacing (56 ± 11 cm/sec) than in the AV pacing (43 ± 13 cm/sec, p < 0.01 in Fig. 3). The PFR was 201 ± 53 ml/sec in the AV pacing. It was 260 ± 44 ml/sec in the V pacing. The difference between these values was also significant (p < 0.01 in Fig. 3).

2. Doppler indexes of left ventricular filling and improvement in cardiac output with AV pacing.

The relation between Doppler indexes of left ventricular filling and the percent change in cardiac output was examined (Fig. 4). The per-
cent change in cardiac output correlated well with R and PFR during AV pacing ($r = -0.66$, $p < 0.01$; $r = -0.71$, $p < 0.01$, respectively). The percent change in cardiac output also correlated well with the A/R ratio during AV pacing ($r = 0.77$, $p < 0.01$). Thus, the improvement in cardiac output with AV pacing seemed to be greater in patients with impaired left ventricular rapid filling.

3. **Doppler indexes of left ventricular filling and the change in PFR brought about by the loss of atrial contraction.**

The percent change in the PFR from AV pacing to V pacing was compared with Doppler indexes of left ventricular filling (Fig. 5). The percent change in the PFR correlated significantly with R and PFR during AV pacing ($r = -0.82, -0.82$, $p < 0.01$), and with the A/R ratio during AV pacing ($r = 0.76$, $p < 0.01$). Thus the increment of PFR with the loss of atrial contraction was greater in patients with impaired left ventricular rapid filling.

**DISCUSSION**

In this study, cardiac output and left ventricular filling dynamics were evaluated by pulsed Doppler echocardiography to determine the beneficial effects of AV pacing over V pacing. The results of this study indicate that AV pacing provides greater improvement in cardiac output in patients with impaired left ventricular rapid filling, and that during V pacing left ventricular rapid filling increases to compensate.

1. **Accuracy of Doppler measurement of cardiac output.**

The accuracy and usefulness of Doppler-determined cardiac output have been well studied\(^{11-14}\). Most of the previous studies have noted that accurate cardiac output is obtained as a product of echocardiographically determined cross sectional area and Doppler-determined flow velocity integral over cardiac cycles. The effects
Fig.4. The percent change in cardiac output (CO) from ventricular to atrioventricular (A-V) sequential pacing is compared with left ventricular peak rapid filling velocity (R), peak filling rate (PFR) and the peak atrial filling velocity to peak rapid filling velocity ratio (A/R). Any Doppler indexes of left ventricular diastolic filling correlate well with the percent improvement in cardiac output with atrioventricular pacing.

Fig.5. The percent change in the left ventricular peak rapid filling rate (PFR) from atrioventricular (A-V) sequential pacing to ventricular pacing is compared with Doppler indexes of left ventricular diastolic filling: peak rapid filling velocity (R), PFR and peak atrial filling velocity to peak rapid filling velocity ratio (A/R). There are significant correlations between them.

of the velocity profile, instantaneous changes in the size of the valve orifice and Doppler incident angle were found to be little.\textsuperscript{11,14} Cardiac output can be determined by Doppler echocardiography from measurement of any level of aortic valve, pulmonary valve and mitral valve\textsuperscript{11–14} ; however,
mitral valve orifice area varies significantly during diastole\(^1\)\(^\text{3,14}\) and measurement of the pulmonary valve orifice area is sometimes difficult\(^1\)\(^\text{11}\) For these reasons measurements at the aortic valve orifice seem most constant, accurate and easy. In the present study we measured aortic flow velocity using the apical window. With this approach we could easily align the Doppler beam nearly parallel to the long axis of the left ventricular outflow tract, while we failed to set the Doppler incident angle within 20 degrees in 16 of 26 cases. Previous studies\(^1\)\(^\text{2,14}\) have demonstrated that cardiac output measured using the present method correlated well with cardiac output determined by the thermodilution method. Further, the value of cardiac output obtained with this method is not affected by mitral regurgitation, which is frequently observed in patients with pacemakers\(^1\)\(^\text{15}\)

2. Doppler indexes of left ventricular diastolic filling.

In the present study, we evaluated left ventricular diastolic filling with Doppler-determined R, PFR, and A/R ratio. Rokey et al\(^1\)\(^\text{16}\) have reported that Doppler measurements of mitral inflow correlate well with angiographic measurements of left ventricular volume change, and that the Doppler technique can be used to assess left ventricular filling dynamics in the absence of inflow obstruction or aortic regurgitation. Kitabatake et al\(^1\)\(^\text{17}\) have reported that Doppler measurements of mitral inflow closely reflect left ventricular relaxation as well as diastolic performance of left ventricle. Thus, we evaluated left ventricular diastolic filling with Doppler measurements of mitral inflow.

3. Improvement in cardiac output with AV pacing.

In the present study, cardiac output was larger during AV pacing which held the atrial contraction in the late diastole. Several mechanisms have been suggested to account for the observation that atrial contraction provides a significant increment to left ventricular filling and hence cardiac output. An appropriately timed atrial contraction may maintain a low mean atrial pressure, thus facilitating venous return. It may also coordinate mitral valve closure, thus minimizing mitral regurgitation. Last, it may augment left ventricular filling, which improves ventricular contractile state according to the Frank-Starling principle.

4. Enhanced left ventricular rapid filling brought about by the loss of atrial contraction.

To examine the effects of the loss of atrial contraction on left ventricular filling in detail, we also studied the changes in transmural inflow when the pacing mode was switched from AV pacing to V pacing. PFR was significantly higher during V pacing than during AV pacing. While the PFR might usually be used as an index of left ventricular diastolic function, especially of left ventricular relaxation\(^1\)\(^\text{17-19}\) it seemed improbable that left ventricular relaxation was more prolonged during AV pacing than during V pacing, because the asynchrony of ventricular contraction that would most affect left ventricular relaxation occurred in both pacing modes. The enhanced left ventricular rapid filling during V pacing would be produced by effects of hemodynamic parameters such as left ventricular filling pressure and/or left ventricular preload rather than by changes in the left ventricular relaxation. Left atrial pressure was reported to be higher during V pacing than during AV pacing\(^5\)\(^,\)\(^6\) The elevation of left atrial pressure during V pacing may be a primary cause of the enhanced left ventricular rapid filling.

5. Relation of left ventricular diastolic filling to the advantageous effects of AV pacing.

The percent change in cardiac output brought about by switching the pacing mode from V to AV pacing varied widely from 3% to 73%; thus, we further examined which factors influenced the degree of improvement in cardiac output with AV pacing. Several papers\(^6\)\(^,\)\(^8\)\(^,\)\(^10\) have studied whether the degree of impairment of left ventricular systolic function correlates with the beneficial effects of AV pacing. This problem remains unresolved. In the present study, we examined the relation between the beneficial effects of AV pacing and left ventricular diastolic filling and found that the improvement in cardiac output with AV pacing was greater in patients with impaired left ventricular rapid filling. In such patients decreased left ventricular rapid filling is usually compensated for by ventricular filling caused by atrial contraction during AV pacing; the loss of the atrial contraction may lead to a decrease in left ventricular filling and hence cardiac output.

The increment of PFR by V pacing also varied widely from \(-5\%\) to \(78\%\). The degree correlated well with Doppler indexes of left ventricular diastolic filling (Fig. 5). These findings suggest

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that the increase in left ventricular rapid filling brought about by the loss of atrial contraction appears more prominent in patients with impaired left ventricular rapid filling. Considering that left ventricular filling, i.e., cardiac output is more dependent on the atrial filling in patients with impaired left ventricular rapid filling, even the greater enhancement of the ventricular rapid filling during V pacing in patients with impaired left ventricular rapid filling may not be sufficient.

6. Clinical implications.

Our study indicates that AV pacing is superior to V pacing, especially in patients with impaired left ventricular rapid filling. Continuous adaptation to V pacing might improve hemodynamic performance; however, Kruse et al? have shown that the major adaptation to a change in pacing mode is rapid and that one should be able to draw conclusions on the long-term effects of a particular mode of pacing from acute studies. Therefore, the beneficial changes in cardiac output and left ventricular filling dynamics brought about by AV pacing may last even in to a chronic stage. Thus, AV pacing should be used in patients with sick sinus syndrome as well as complete AV block, especially when the left ventricular rapid filling is expected to be impaired.

REFERENCES


5. GREENBERG B, CHATTERJEE K, PARMLEY WW, WERNER JA, HOLLY AN: The influence of left ventricular filling pressure on atrial contribution to cardiac output. Am Heart J 98: 742, 1979


15. ZUGIBE FT, NANDA NC, AKIYAMA T, BAROLD S: Doppler detection and quantitation of mitral regurgitation during ventricular and atrioventricular sequential pacing. J Am Coll Cardiol 3: 508, 1984 (abstr)


18. HAMMERMEISTER KE, WARBAESE JR: The

Japanese Circulation Journal Vol. 50, September 1986
rate of change of left ventricular volume in man. II. Diastolic events in health and disease. Circulation 47: 739, 1974

19. KITABATAKE A, INOUE M, ASAO M, TANOUCHI J, MASUYAMA T, ABE H, MORITA

H, SENDA S, MATSUO H: Transmirtal blood flow reflecting diastolic behavior of the left ventricle in health and disease: a study by pulsed Doppler technique. Jpn Circ J 46: 92, 1982