Utility of Two-Dimensional and Doppler Echocardiography in Dual-Chamber Pacing for the Cardiomyopathies

Rick Nishimura, John Symanski, David Hurrell, A. Jamil Tajik

Rochester, Minnesota - USA

Implantation of a permanent pacemaker is a well accepted mode of therapy for patients with arrhythmias. However, there has recently been interest generated in implanting dual-chamber pacemaker for improvement of hemodynamics in patients with various cardiomyopathies. In patients with hypertrophic cardiomyopathy, dual-chamber pacing has been shown to reduce the left ventricular outflow tract gradient, improve symptoms, and even cause regression of hypertrophy. In patients with severe congestive heart failure due to dilated cardiomyopathy, implantation of a dual-chamber pacemaker has been shown to improve symptoms and enhance systolic performance of the left ventricle.

The use of dual-chamber pacemaker in cardiomyopathies is early and at the present time, should still be considered investigational. The very early reports of dramatic improvements in symptomatology and hemodynamics with this modality has recently been tempered by subsequent studies indicating a lesser degree of benefit. Results from randomized multicenter trials need to be known before the ultimate role of dual-chamber pacing in these cardiomyopathies is known.

Two-dimensional and Doppler echocardiography have come to play essential roles in elucidating the pathophysiologic mechanism by which dual-chamber pacing provides hemodynamic benefit. Echocardiography is also important in identifying candidates who may benefit from this procedure as well providing information about technical considerations for achieving an optimal result. Finally, echocardiography is an excellent method for providing noninvasive follow-up following implantation. The purpose of this monography is to provide an overview of the role that two-dimensional and Doppler echocardiography play in this new indication for permanent pacemakers in the treatment of selected patients with cardiomyopathies.

**Dual-chamber pacing in patients with hypertrophic cardiomyopathy**

**Background** - In 1975 Hassenstein et al demonstrated a reduction in the severity of left ventricular outflow tract obstruction and improvement in symptomatology in several patients with hypertrophic obstructive cardiomyopathy following implantation of a dual-chamber pacemaker. For the next two decades, isolated case reports and small series emerged which confirmed that implantation of a dual-chamber pacemaker could reduce the gradient and relieve symptoms in these patients with hypertrophic obstructive cardiomyopathy. The proposed mechanism for benefit is a reduction in left ventricular outflow tract obstruction due to altered septal activation from pacing the right ventricular apex. This interrupts the sequence of events (septal encroachment into the outflow tract with resultant systolic anterior motion of the mitral valve) that causes the outflow obstruction. There may also be a longer term remodeling effect from continuous pacing causing ventricular dilatation and even regression of hypertrophy. In an initial three-month follow-up study of 44 patients published in 1992 as well as a larger 2-3 years follow-up of 84 patients published in 1994, Fananapazil et al from the National Institutes of Health described the first large cohort of patients with hypertrophic obstructive cardiomyopathy in whom a dual-chamber pacemaker was implanted. After over two years of follow-up, these authors showed a significant reduction in symptomatology in near 90% of patients, a reduction in left ventricular outflow tract gradient, and a suggestion of a regression in left ventricular hypertrophy. Based upon these studies, the authors suggested that "dual-chamber pacing be considered the therapeutic procedure of choice in patients with severely symptomatic hypertrophy obstructive cardiomyopathy who failed medical therapy".

These results generated great enthusiasm in the cardiology community. Certainly, implantation of a dual-chamber pacemaker is much less invasive and risky than surgical myectomy. If over 90% of patients could obtain symptomatic relief, many agree it would be appropriate for all patients with severely symptomatic hypertrophic obstructive cardiomyopathy to undergo implantation of a dual-chamber pacemaker. However, subsequent follow-up studies have shown that this high success rate could not be obtained in all patients. Up to 20-40% of patients in these other studies did not obtain relief of symptoms and 5-10% of patients actually experienced deterioration following implantation of a dual-chamber pacemaker. Symptomatic benefit has not been shown to be related to a change in left ventricular outflow tract gradient, which has raised questions as to the actual pathophysiologic mechanism by which dual-cham-
ber pacing works. In addition, there has been the question of a symptomatic relief from the placebo effect of simply implanting a permanent pacemaker\textsuperscript{10}. The long-term outcome of these patients is not yet known and it has been speculated that any therapeutic modality which produces ventricular dilatation could eventually be deleterious by causing the end stage systolic dysfunction that may occur during the natural history of these patients\textsuperscript{13,12}.

Therefore, there are many questions that remain to be answered before dual-chamber pacing can be recommended to all patients with hypertrophic obstructive cardiomyopathy. The decision to implant a dual-chamber pacemaker must be weighed against the excellent results of surgical myectomy\textsuperscript{21,22}. The results from randomized multicenter studies with long-term follow-up are required to determine the ultimate role of dual-chamber pacing in this subgroup of patients.

**Preimplant evaluation of patients with hypertrophic obstructive cardiomyopathy** - Two-dimensional and Doppler echocardiography are important in the evaluation of a patient with severely symptomatic obstructive hypertrophic cardiomyopathy in whom a dual-chamber pacemaker is being considered. At the present time, two-dimensional echocardiography should be considered the “gold standard” for the diagnosis of hypertrophic cardiomyopathy\textsuperscript{24-27}, in which there is severe hypertrophy of the myocardium in the absence of a known etiology. Doppler echocardiography can be used to measure the left ventricular outflow tract gradient by application of the modified Bernoulli equation\textsuperscript{24-27} (fig. 1). Due to catheter entrapment which may occur in these patients with small hyperdynamic ventricular cavities, Doppler echocardiography can be more accurate than cardiac catheterization in assessing the severity of obstruction. In addition, if there is only a labile obstruction with no or minimal gradient at rest, maneuvers in the echocardiographic laboratory such as inhalation of amyl nitrate or exercise can demonstrate the dynamic nature of this obstruction (fig. 1). Concomitant mitral regurgitation may be the key pathophysiologic mechanism producing symptoms of dyspnea in some patients and its presence and severity can readily be assessed by Doppler echocardiography. Finally, diastolic filling of the heart can be determined by Doppler echocardiography by interrogating both mitral inflow and pulmonary venous flow\textsuperscript{28,29}.

A major role of two-dimensional and Doppler echocardiography in these patients is to rule out other causes of left ventricular outflow tract obstruction. There have been patients referred for consideration of dual-chamber pacemaker with erroneous diagnosis of hypertrophic cardiomyopathy which was made based upon significant hypertrophy and an increase in left ventricular outflow tract velocity. Discrete fixed subvalvular aortic stenosis may mimic hypertrophic cardiomyopathy. In fixed subvalvular aortic stenosis, there will be an absence of systolic anterior motion of the mitral valve. The continuous wave velocity across the outflow tract will be an early to mid peak rather than the late peaking “dagger shaped” velocity seen in patients with true hypertrophic obstructive cardiomyopathy (fig. 2). Secondary subvalvular dynamic obstruction in response to pressure overload from valvular stenosis can also be recognized by two-dimensional and Doppler echocardiography. In these patients, dual-chamber pacing would not be expected to provide benefit in terms of gradient relief.

There is a subset of patients with hypertrophic cardio-

---

**Fig. 1** - Catheter pressures in the left ventricular (LV) base and left ventricular apex demonstrating the dynamic left ventricular outflow tract obstruction in a patient with hypertrophic cardiomyopathy. The simultaneous continuous wave Doppler velocity across the left ventricular outflow tract shown with calculated gradient (in parenthesis) as derived from modified Bernoulli equation. The baseline gradient of 21mm is shown (left). After amyl nitrate is given, there is an increase in the gradient to 30mmHg (center) and 70mmHg (right). There is a corresponding increase in the Doppler derived gradient.
myopathy who have severe mitral regurgitation secondary to intrinsic mitral valve disease. This may be due to chordal rupture with flail mitral valve leaflets. In patients with severe mitral regurgitation, either a detailed transthoracic echocardiogram or even a transesophageal echocardiography should be performed to rule out intrinsic mitral valve disease. If there is severe mitral regurgitation from a primary abnormality of the mitral valve apparatus, dual-chamber pacing would not be expected to benefit.

Technical considerations of pacemaker implantation and setting - Obtaining an optimal benefit from dual-chamber pacing requires knowledge of the technical considerations implicit to this therapeutic modality. Two factors of major importance include lead placement and optimization of the atrioventricular interval, both of which are guided by two-dimensional and Doppler echocardiography.

In order for dual-chamber pacing to produce the optimal decrease in left ventricular outflow tract gradient, it is necessary to place the pacing lead in the most distal right ventricular apex. It has been shown that pacing either the mid septal area or right ventricular outflow tract area may not result in optimal changes in hemodynamics. In some patients, there may actually be a deterioration in hemodynamics if the pacemaker lead is not placed in the distal right ventricular apex. Two-dimensional echocardiography is useful for assuring that the pacemaker lead is truly in the apex of the right ventricle, as fluoroscopic guidance is an imprecise marker of lead position.

It is essential to optimize the atrioventricular interval of the pacemaker in these patients with hypertrophic obstructive cardiomyopathy. When the atrioventricular interval is too short, there will be deterioration of both systolic and diastolic function from inadequate atrial contribution to ventricular filling. In patients with very short atrioventricular intervals, atrial contraction occurs after the closure of mitral valve, resulting in an increase in mean left atrial pressure. Conversely, if the atrioventricular interval is too long, there will be deterioration in hemodynamics if the pacemaker is not placed in the distal right ventricular apex.
interval is set too long so that native atrioventricular conduction occurs, there will be suboptimal relief of the gradient.

Doppler echocardiography can aid in determining whether or not the atrioventricular interval is too short causing elevation of left atrial pressure by examining the duration of the mitral flow velocity curve at atrial contraction (fig. 6). When the atrioventricular interval is too short, there will be a shortening of the duration of the mitral flow velocity curve at atrial contraction, as left ventricular pressure rapidly exceeds left atrial pressure closing the mitral valve and causing cessation of forward transmitial flow. The optimal atrioventricular interval is present when the atrioventricular interval is short enough to provide complete pre-excitation of the right ventricle but not to cause a shortening of the velocity at atrial contraction on the transmitial mitral flow velocity curve. It must be understood that optimization of the atrioventricular interval in the resting supine state may not reflect what occurs in the upright position during exertion. Therefore, similar optimization is necessary during upright exercise in addition to that obtained during the supine resting state.

Follow-up - Follow-up of patients after receiving a dual-chamber pacemaker for hypertrophic obstructive cardiomyopathy can be best performed by two-dimensional and Doppler echocardiography. Continuous wave Doppler across the left ventricular outflow tract is able to assess the effect of the pacemaker on the left ventricular outflow tract gradient (fig. 7). It is important to measure the systolic blood pressure during echocardiographic evaluation, as there are some patients who may have a slight reduction in total gradient but overall hemodynamic deterioration due to a reduction in systolic performance from inappropriate atrial timing (fig. 8). Care must be taken to assure that there is no contamination of the left ventricular outflow velocity by the mitral regurgitation signal (fig. 9).

The mitral flow velocity curve should be obtained at each echocardiographic study. An increase in the initial E velocity indicates a rise in left atrial pressure. A shortening
Utility of echocardiography in pacing for cardiomyopathies

Nishimura e col

Fig. 7 - High fidelity left ventricular (LV) and aortic (AO) pressures in a patient with hypertrophic cardiomyopathy. The simultaneous wave Doppler flow velocity across the left ventricular outflow tract is shown. The beneficial effect of pacing on the outflow tract gradient is shown. There is a gradient of over 100mmHg during normal sinus rhythm (left) as compared to a much lower gradient (36mmHg) during pacing at an atrioventricular interval of 60msec (right).

Fig. 6 - Doppler velocity curves of the mitral inflow with simultaneous left ventricular (LV) and left atrial (LA) pressures. Left - during atrial pacing, there is appropriate timing of atrial and ventricular contraction and there is an A wave duration of 140msec from the mitral flow velocity curve; center - during atrioventricular pacing at 60msec, there is inadequate contribution from atrial contraction as the atrioventricular interval is too short. There is a rise in left atrial pressure. A shortening of the duration of the mitral flow velocity curve at atrial contractions is present. Right - at an optimal atrioventricular interval of 140msec, there is an appropriate timing of atrial and ventricular contraction so that there is a duration of the A duration of the mitral flow velocity curve of 130msec.

of the A duration of the mitral flow velocity curve is indicative that the atrioventricular interval is too short.

The question has arisen as to whether or not dual-chamber pacing actually cause regression of hypertrophy in these patients with hypertrophic cardiomyopathy. Two-dimensional echocardiography should be an ideal method to noninvasively assess serial changes in the wall thickness of the entire myocardium.

Dual-chamber pacing in patients with dilated cardiomyopathy

Background - In 1990 and subsequently in 1992, Hochleitner et al reported on the beneficial effect of implantation of a dual-chamber pacemaker in patients with severe heart failure due to dilated cardiomyopathy. At both short and intermediate term follow-up, the authors reported...
Fig. 8 - High fidelity left ventricular (LV) and aortic pressures in a patient with hypertrophic cardiomyopathy. The simultaneous continuous wave Doppler flow velocity curve across the left ventricular outflow tract is shown. Although the Doppler velocity curve is unchanged at 5 m/sec, there is a significant deterioration during P synchronous pacing at 60 msec (right) as compared to normal sinus rhythm (left) from inappropriate atrial timing causing a fall in cardiac output and a decrease in aortic pressure.

Fig. 9 - Overestimation of the Doppler derived left ventricular outflow tract gradient caused by misplacement of the continuous wave sample volume in the mitral regurgitation jet (left). With appropriate position of the continuous wave cursor, Doppler derived left ventricular outflow tract gradient correlated well with catheter generated measurements (right).
Follow-up prospective studies have shown that dual-chamber pacing does not produce benefit in most patients with severe left ventricular dysfunction. Thus, there has been controversy as to whether or not this proposed therapeutic modality may provide any benefit for these severely ill patients with dilated cardiomyopathy.

We and others have recently looked at the mechanism of dual-chamber pacing in patients with severe left ventricular dysfunction using combined cardiac catheterization and Doppler flow velocity curves. From the results of these investigations, it is concluded that the mechanism by which dual-chamber pacing works in selected patients is optimization of atrioventricular synchrony. In those patients who already have adequate...
Utility of echocardiography in pacing for cardiomyopathies

**Identification of patients who respond to dual-chamber pacing** - The mechanism by which dual-chamber pacing can provide hemodynamic benefit for patients with severe left ventricular dysfunction is optimization of atrioventricular synchrony. The patients who respond best to dual-chamber pacing are those in whom the atrial contraction occurs prematurely in relation to the ventricular contraction. In these patients, left atrial pressure falls below left ventricular pressure in mid diastole during atrial relaxation, causing cessation of forward transmitral flow. In patients with concomitant mitral regurgitation, diastolic mitral regurgitation occurs and blood flows retrogradely from left ventricle to left atrium before the onset of ventricular contraction. The overall result of this dysynchrony between atrial and ventricular contraction is a relatively low preload at the time of ventricular contraction which results in a low forward cardiac output from the Starling mechanism. If dual-chamber pacing can restore appropriate atrioventricular timing, atrial contraction occurs just prior to the onset of ventricular contraction. Filling of the left ventricle throughout all of diastole is restored and abolition of the presystolic mitral regurgitation occurs. Thus at the onset of ventricular contraction, there is a relatively higher preload in the left ventricle and forward cardiac output increases.

We have found that those patients who respond to dual-chamber pacing can be identified on the basis of both transmitral Doppler flow velocity curves and continuous wave Doppler of the mitral regurgitation. On the transmitral flow velocity curve, there will be early cessation of diastolic filling well before to the onset of the QRS complex. This frequently results in fusion of the E and A wave. On the continuous wave signal of the mitral flow velocity curve, presystolic mitral regurgitation is a key indicator that inappropriate atrioventricular synchrony is present.

**Technical considerations** - As with patients who undergo dual-chamber pacing with hypertrophic cardiomyopathy, there are critical technical considerations for pacemaker therapy in patients with dilated cardiomyopathy. It appears that the site of the pacemaker implantation is less important than for patients with hypertrophic cardiomyopathy. Future investigation into multilead systems to optimize ventricular contraction synchrony is currently under way.

The optimal atrioventricular interval must be determined following implantation of the dual-chamber pace-
maker. If the atrioventricular interval is too short, there will be deterioration of diastolic filling of the left ventricle, as atrial contraction occurs on top of a closed mitral valve raising left atrial pressure. This is assessed by examining the mitral flow curve with a shortening of the transmitral velocity duration at atrial contraction. Conversely, if the atrioventricular interval is too long, there will be dysynchrony of atrial and ventricular contraction. This can be identified on the pulsed or continuous wave flow velocity curve across the mitral valve when early cessation of flow is seen in conjunction with diastolic mitral regurgitation.

Assessment of results - There are many parameters which can be measured by echocardiography to assess the improvement obtained by dual-chamber pacing. Measurement of volumetric flow or stroke volume from the left ventricular outflow tract is useful. Assessing the transmitral flow velocity curve to assure that diastolic filling occurs throughout the entire diastole without shortening of the duration at atrial contraction is important. It is the continuous wave Doppler of the mitral regurgitation signal which provides the optimal assessment of hemodynamic results. The continuous wave mitral regurgitation signal is determined by the pressure gradient between the left ventricle and left atrium during systole. Thus, improvement of hemodynamics will result in a higher left ventricular systolic pressure and lower atrial pressure resulting in an increase in the mitral regurgitation peak velocity (fig. 10). Conversely, patients with deterioration of hemodynamics have either a drop in left ventricular systolic pressure or an elevation of left atrial pressure, in which mitral regurgitation peak velocity will be decreased as compared to sinus rhythm (fig. 11).

Conclusion

Dual-chamber pacing in patients with both hypertrophic and dilated cardiomyopathies should still be considered an investigative technique. The results of long-term randomized multicenter trials are necessary before widespread application of these therapeutic modalities. However, there are clearly some patients who may benefit from this technique. Two-dimensional and Doppler echocardiography are critical in the evaluation of these patients preoperatively, optimizing the technical aspects of pacemaker implantation and programming and providing a noninvasive assessment of follow-up.

Bibliography

23. Sigwart U - Non-surgical myocardial reduction for hypertrophic ob-
Utility of echocardiography in pacing for cardiomyopathies

1. Arq Bras Cardiol volume 68, (nº 5), 1997


