Left Atrial Booster Function in Valvular Heart Disease

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ABSTRACT This study was designed to assess atrial booster pump action in valvular heart disease and to dissect booster pump from reservoir-conduit functions. In five patients with aortic stenosis and six with mitral stenosis, sequential atrioventricular (A-V) pacing was instituted during the course of diagnostic cardiac catheterization. Continuous recording of valvular gradient allowed estimation of flow for each cardiac cycle by transposition of the Gorlin formula. Left ventricular ejection time and left ventricular stroke work in aortic stenosis or left ventricular mean systolic pressure in mitral stenosis were also determined. Control observations were recorded during sequential A-V pacing with well-timed atrial systole. Cardiac cycles were then produced with no atrial contraction but undisturbed atrial reservoir function by intermittently interrupting the atrial pacing stimulus during sequential A-V pacing. This intervention significantly reduced valvular gradient, flow, left ventricular ejection time, and left ventricular mean systolic pressure or stroke work. Cardiac cycles were then produced with atrial booster action eliminated by instituting synchronous A-V pacing. The resultant simultaneous contraction of the atrium and ventricle not only eliminated effective atrial systole but also placed atrial systole during the normal period of atrial reservoir function. This also significantly reduced all the hemodynamic measurements. However, comparison of the magnitude of change from these two different pacing interventions showed no greater impairment of hemodynamic state when both booster pump action and reservoir function were impaired than when booster pump action alone was impaired. The study confirms the potential benefit of well placed atrial booster pump action in valvular heart disease in man.

INTRODUCTION

In addition to serving as a conduit, the left atrium functions both as a passive reservoir storing energy in its elastic walls as it fills during ventricular systole and as a booster pump actively ejecting blood into the ventricle in presystole. The relative importance of these two components of left atrial transport function remains controversial.

Previous studies in this laboratory during atrioventricular dissociation created by right ventricular pacing demonstrated the importance of left atrial transport in patients with aortic and mitral stenosis (1, 2). However, these studies necessarily limited comparison of an appropriately timed atrial systole to an inappropriately timed one, rather than to the noncontracting atrium. It was therefore impossible to evaluate the relative importance of the atrial booster function vs. the possible deleterious effects of the interference with atrial reservoir function. With the advent of sequential A-V pacing it is now possible to manipulate the timing of atrial systole such that the booster and the reservoir function of the atrium could be studied independently of each other. Utilizing sequential A-V pacing as a control state, acute loss of the booster pump action was observed by suddenly interrupting the atrial stimulus. This produced a complete cardiac cycle without an active atrial contraction but with intact reservoir function. This intervention was then compared with acute synchronous pacing where both the atrium and the ventricle were simultaneously stimulated such that the atrium contracted against the closed mitral valve during ventricular systole. This produced a situation of possible interference with the reservoir function as well as loss of the booster function. By comparing the effects of these two interventions upon left ventricular performance, the relative roles of the booster and the reservoir function of the left atrium could be defined as well as their absolute magnitude. All observations were intentionally made during acute interventions; thereby affording little time for compensatory homeostatic mechanisms to act.

METHODS

11 patients, 5 with aortic stenosis (AS) and six with mitral stenosis (MS) were studied during the course of diagnostic

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right and transseptal left cardiac catheterization. All patients were in normal sinus rhythm. The patient population and hemodynamic findings are described in Table I. Patients were premedicated with Demerol (meperidine) (50–75 mg) and Phenergan (promethazine hydrochloride) (25 mg) intramuscularly. Xylocaine (lidocaine) local anesthesia was utilized for percutaneous cannulation or exposure of vessels. All pressures were recorded with equisensitive P 23 Db Statham transducers (Statham Instruments, Inc., Los Angeles, Calif.) with zero pressure defined 5 cm below angle of Louis. In the mitral stenosis group, left atrial pressure was recorded through a No. 9 Ross catheter placed transeptally. Left ventricular pressure was measured through a small bore polyethylene catheter (PE-90, 0.023 I.D.)[1] threaded through the Ross catheter into the ventricle or by retrograde arterial catheterization. In the aortic stenosis group, left ventricular pressure was recorded through a No. 9 Ross catheter placed transeptally and manipulated into the left ventricle. Left ventricular mean systolic pressure was obtained by planimetry of the left ventricular pressure contour. Central aortic pressure was recorded by retrograde arterial catheterization. A Telco catheter[2] was frequently used retrograde in aortic stenosis with central aortic pressure recorded through the side arm catheter and ejection time recorded from the micromanometer. A 15 cm polyethylene catheter (PE-160; 0.045 I.D.)[1] was introduced percutaneously into the left brachial artery to monitor arterial pressure and for sampling of blood. The indirect carotid pulse contour was recorded with a standard funnel-shaped pick up connected to a P 23 Db transducer placed over the point of maximum pulsation of the carotid artery except as outlined above. Left ventricular ejection time was measured as the interval from the beginning of the upstroke to the trough of the incisural notch. A No. 5 or 6 bipolar pacing catheter was placed into the apex of the right ventricle through a right antecubital venotomy. Similarly, a No. 6 Zucker pacing catheter[3] was placed in the superior right atrium to permit atrial pacing. An external electrocardiogram was recorded, usually lead II. All events were recorded on a multichannel photorecorder[4] at a paper speed of 100 mm/sec and on time lines indicating 20-msec intervals.

Before any pacing interventions, base line mitral or aortic valve gradients were recorded on equisensitive gauges. The mean valvular gradient was obtained by planimetry of 10 consecutive complexes. Cardiac outputs were determined either by the Fick method, or by the indicator dilution technique using the central injection of indocyanine green dye. The mitral or aortic valve area could then be calculated by the method of Gorlin and Gorlin (3).

A series of four pacing states were then studied in each patient using a Medtronic model 5837 pulse generator.[5] This instrument delivers pacing stimuli through two separate bipolar gates. The atrial pacing catheter was connected to the first gate and the ventricular pacing catheter to the second gate. The unit allows the operator to select both the rate of pacing and the interval or time delay between the atrial and ventricular stimulus. Valvular gradient as well as left ventricular ejection time and left ventricular pressure was simultaneously recorded on a beat-to-beat basis throughout the subsequent interventions.

State 1 represents atrial pacing (AP), see Figs. 1, 3, and 4. This consisted of atrial pacing approximately 10 beats/min faster than the patients spontaneous rate. No ventricular pacing stimulus was delivered through the ventricular pacing catheter. Activation of the ventricles occurred by propogation of the impulse through normal pathways. The atrioventricular contraction interval was determined by the patients spontaneous atrioventricular conduction delay or PR interval. Overdrive atrial pacing was necessary to permit heart rate to be held constant throughout all subsequent pacing interventions and eliminate compensatory escape rhythms that could alter the RR interval.

State 2 represents sequential atrioventricular pacing (SEQ), see Figs. 1, 3 and 4. This was produced by instituting atrial pacing (state 1) and then causing the ventricular pacing stimulus to activate the ventricles at a time delay shorter than the patients spontaneous PR interval. The ventricles were thus activated ectopically by the ventricular pacing stimulus that arrived earlier than the stimulus propagated through the normal pathways from the atrial pacing stimulus. The atrioventricular pacing delay interval was regulated on the Medtronic unit. The delay interval was determined in the individual patient to obtain the longest PR interval possible and still produce an ectopic QRS configuration. The purpose of this pacing state was to study the effect of the selective introduction of ventricular ectopy without significantly changing the temporal relationship of atrioventricular contraction. This state 2 (SEQ) was then used as a new control state to compare the two subsequent interventions in which atrial booster action was eliminated.

State 3 is designated interrupted atrial pacing (IAP), see Figs. 2 and 5. During sequential AV pacing, i.e. state 2 described above, individual atrial pacing stimuli were intermittently interrupted and the atrium failed to contract. The reason for this can be clearly seen in Fig. 6. The sinus pause occurred when the atrial pacing was interrupted because the atrial pacing rate was faster than the patients resting rate, together with the suppressing effect of an ectopic paced atrial focus on the SA node. Since this intervention did not affect the ventricular pacing circuit, the RR interval was preserved; and in addition, the pathway of ventricular activation was consistent. This pacing state was thus designed to study the acute effect of loss of mechanical atrial contraction, the atrium remaining diastolic throughout that individual cardiac cycle.

State 4 is designated synchronous atrioventricular pacing (SYN). This pacing intervention was obtained by reestablishing pacing state 2, sequential A-V pacing. The PR delay was then abruptly reduced to zero such that both the atrium and ventricle were stimulated at the same time. Ventricular activation continued ectopic but unchanged from state 2 or 3. Since atrial contraction no longer preceded ventricular contraction, this state eliminated potential booster pump action of the atrium as did state 3. In addition, however, it substituted atrial contraction at that phase of the cardiac cycle when the atrium normally functions as a passive dilating reservoir, thus possibly producing interference with atrial reservoir function. State 4 was studied to see if interference with reservoir function and loss of atrial booster function produced any further hemodynamic deterioration over that produced solely by loss of well-timed atrial systole (state 3).

In each patient, during each pacing state, a minimum of five cycles were analyzed for: (*a*) PR interval, (*b*) systolic

[1] Clay-Adams, Inc., Parsippany, N. Y.
[2] Carolina Medical Electronics, King, N. C.
[3] United States Catheter & Instrument Corp., Glens Falls, N. Y.
[4] Electronics for Medicine, White Plains, N. Y.
[5] Medtronic Inc., Minneapolis, Minn.

TABLE I

Patient Population

Patient	Age	Sex	Cardiac index	RV pressure rest	Mean aortic systolic gradient	Aortic area	Calcification	Associated valvular lesions	Surgical description of valve
	yr		*liters/min per M²*	*mm Hg*	*mm Hg*	*cm²*			
Aortic stenosis									
W. B.	67	M	1.5	36/5	60	0.3	Moderate	Mild aortic insufficiency (AI)	A rigidly calcified and fused valve was found with central orifice incompetence.
L. B.	43	F	4.3		79	1.0	Moderate	Mild AI	
D. S.	56	M	2.8	55/6	105	0.5	Moderate	Mild to moderate AI	A greatly stenotic fixed central orifice with fusion of all three commissures. Considerable calcium was found. Orifice estimated 5 mm diameter.
M. K.	47	F	2.4	22/6	101	0.3	Heavy	0	A bicuspid heavily calcified aortic valve was found. This valve was virtually immobile and a single commissure was running at an anteroposterior direction. The orifice was a slit before excision of the valve.
J. S.	61	M	2.4	40/6	80	0.4	Heavy	Mild AI	The valve was a calcified, deformed valve.

Patient	Age	Sex	Cardiac index	Mean PA pressure		Mean mitral diastolic gradient	Mitral valve area	Calcification	Associated valvular lesions	Surgical description of valve
				Rest	Exercise					
	yr		*liters/min per M²*	*mm Hg*		*mm Hg*	*cm²*			
Mitral stenosis										
P. H.	19	M	2.4	30	—	10	1.4	0	Minimal AI	The mitral valve was soft and pliable with slightly rolled edges and fused symmetrically in the anterolateral and posteromedial commissures equally. The valve would admit one finger to the proximal interphalangeal joint.
D. P.	39	F	3.0	(RV) 43/8	—	13	1.6	0	0	The mitral valve was fairly mobile with shortened chordae tendineae and thickened rolled edge on both aortic and mural leaflets. There was fusion of the posterior medial and anterior lateral commissures leaving an opening which probably would admit two fingers.
M. C.	35	F	1.8	16	35	4	1.7	0	Minimal AI	
C. F.	28	F	2.2	(RV) 75/10	—	23	0.7	0	Mild tricuspid insufficiency	The valve itself was nicely flexible with rolled edges and with equal fusion of the posteromedial and the anterolateral commissures. The valve would barely admit the tip of one finger. There was no calcium in the valve.
L. D.	20	F	2.0	20	38	4	1.9	0	0	
J. E.	50	M	2.2	20	50	9	1.3	0	0	The mitral valve was a flexible one, with slightly rolled edges. Main fusion of the anterolateral commissure with some fusion of the posterior medial of the valve would admit the entire tip of one finger.

ejection period (in AS) or diastolic filling period (in MS), (*c*) mean valvular gradient (by planimetry), (*d*) left ventricular mean systolic pressure (LVMSP), and (*e*) left ventricular ejection time (LVET). In state 3, sequential A-V pacing with slightly shortened PR interval and ectopic ventricular depolarization with atrial pacing intermittently interrupted, the beat of the dropped atrial stimulus (diastolic atrium) was compared to the two beats immediately preceding. A minimum of five such sequences were analyzed in each patient.

A calculation of stroke volume (SV) on a beat-to-beat basis across the aortic valve in aortic stenosis or in diastolic flow (DF) across the mitral valve in mitral stenosis was made. This was done by assuming the stenotic mitral or aortic valve is a fixed orifice obstruction and the formula of Gorlin and Gorlin relating pressure gradient, valve area, and flow was transposed to solve for flow. The known valve area previously determined in the usual fashion for each patient during steady-state observations in sinus rhythm was utilized in the subsequent calculations of beat-to-beat flow. Transposition of the formula of Gorlin and Gorlin in mitral stenosis follows:

$$MVA = \frac{CO/DFP \times HR}{31\sqrt{LA - LV}} \quad (1)$$

$$\frac{CO}{HR} = MVA \times DFP \times 31\sqrt{LA - LV}. \quad (2)$$

Equation 2 was then altered to solve for diastolic flow

$$DF = MVA \times DFP \times 31\sqrt{LA - LV} \quad (3)$$

where MVA = mitral valve area, cm^2, calculated from measurements made during sinus rhythm; CO = cardiac output, ml/min; DFP = diastolic filling period, sec/beat; HR = heart rate, beats/min; LA − LV = mean diastolic pressure gradient across the mitral valve, mm Hg; DF = diastolic flow, ml/beat.

Similarly, the beat to beat calculations of stroke volume in the aortic stenosis group were done as previously reported from this laboratory by Kroetz et al. (1). The formula of Gorlin and Gorlin in aortic stenosis transposes to stroke volume as follows:

$$AVA = \frac{CO/SEP \times HR}{44.5\sqrt{LV - aorta}} \quad (4)$$

$$\frac{CO}{HR} = AVA \times SEP \times 44.5\sqrt{LV - aorta}. \quad (5)$$

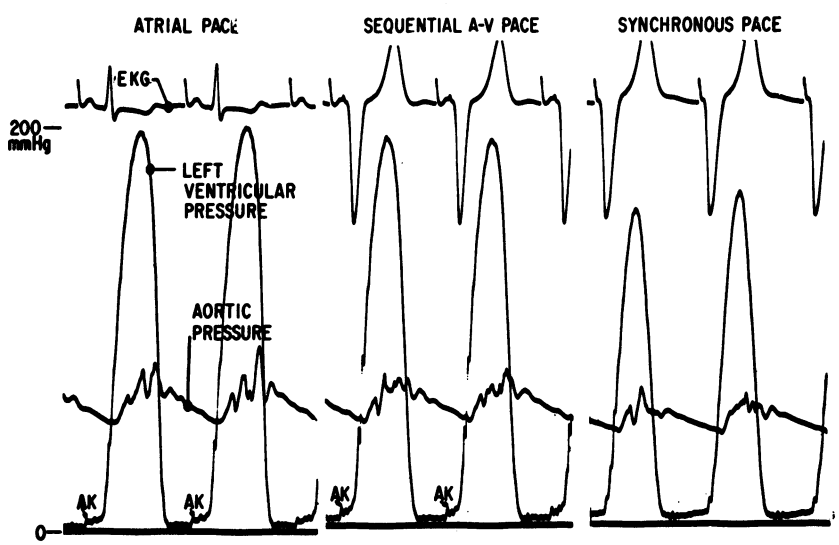

FIGURE 1 Three pacing states are shown in this patient with aortic stenosis (M.K.). Atrial pacing alone (AP) (left) demonstrates normal sequence of impulse transmission from atrial depolarization to ventricular depolarization. The contribution of atrial systole to LV filling or the atrial kick (AK) elevates left ventricular end diastolic pressure (LVEDP). Sequential A-V pacing (SEQ) with ectopic ventricular activation is shown (center). The PR interval is reduced but atrioventricular contraction interval is such that the atrial contraction still elevates LVEDP. Ectopic ventricular activation affects left ventricular peak systolic pressure (LVPSP) minimally. This state serves as the new control for subsequent interventions. Synchronous pacing (SYN) (right) eliminates the effect of the atrial kick, and both LVEDP and LVPSP are reduced. Ventricular activation is ectopic but identical to center panel. The significant intervention is elimination of effective atrial contraction, rather than the pathway of ventricular depolarization.

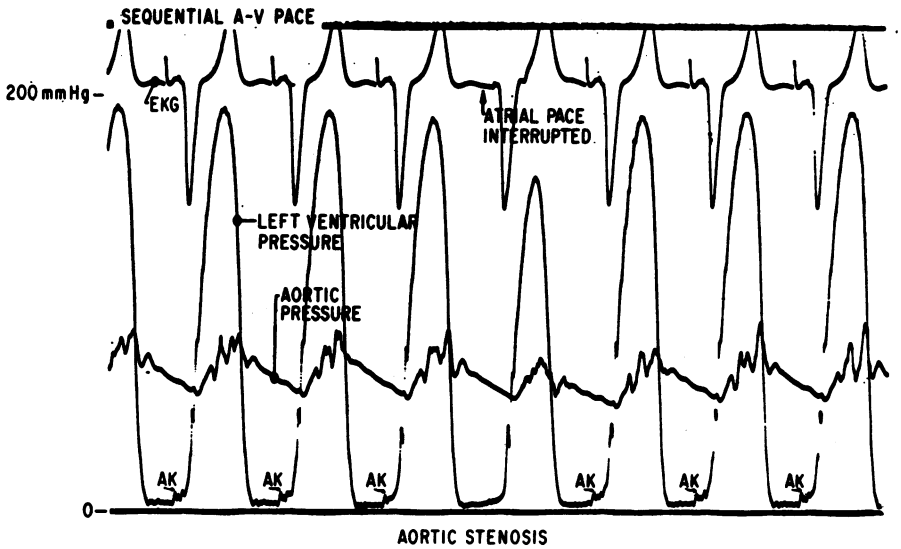

FIGURE 2 Interrupted atrial pacing (IAP) in aortic stenosis. The hemodynamic effect of atrial asystole (diastolic left atrium) in aortic stenosis is shown. During sequential A-V pacing, the atrial pacing stimulus is suddenly interrupted. In the subsequent cycle there is a marked drop in the ventricular peak pressure and mean gradient. Note also the absence of the atrial kick (AK) in this complex.

Equation 5 was then altered to solve for stroke volume

$$SV = AVA \times SEP \times 44.5\sqrt{LV - aorta} \qquad (6)$$

where AVA = aortic valve area, cm^2, calculated from measurements made during sinus rhythm; SEP = systolic ejection period, sec/beat; LV − aorta = mean systolic pressure gradient across the aortic valve, mm Hg; and SV = stroke volume, ml/beat.

In the aortic stenosis group, left ventricular stroke work (LVSW) was derived from the equation LVSW = LVMSP × SV × 0.0136.

Differences of various parameters were compared by the method of paired means (4).

RESULTS

Representative hemodynamic recordings illustrating atrial pacing (AP), sequential A-V pacing (SEQ), and synchronous A-V pacing (SYN) are shown for aortic stenosis (Fig. 1) and mitral stenosis (Figs. 3 and 4). Interrupted atrial pacing (IAP) is shown for aortic stenosis (Fig. 2) and mitral stenosis (Fig. 5). Table II includes the individual data for all measurements during each pacing state.

In aortic stenosis, Fig. 1, change from atrial pacing to sequential A-V pacing which represents the introduction of ectopic ventricular activation had little effect on valvular gradient or parameters of left ventricular output. Sequential A-V pacing is associated with preservation of atrial booster pump action. This is shown by a late diastolic elevation of left ventricular pressure caused by the atrial booster pump effect of atrial kick (AK). This is seen both in atrial pacing and in sequential A-V pacing. In aortic stenosis, when sequential A-V pacing is changed to interrupted atrial pacing, Fig. 2, or when sequential A-V pacing is changed to synchronous A-V pacing, Fig. 1, the effect of loss of atrial booster pump action is seen. Interrupted atrial pacing or synchronous A-V pacing produces no late diastolic elevation of left ventricular pressure. A concomitant fall in aortic systolic gradient as well as LVET and LVMSP occurs.

In mitral stenosis, Figs. 3, 4, and 5, marked changes are seen in the left atrial pressure contour depending on the presence or absence and timing of atrial contraction. In mitral stenosis when atrial pacing is changed to sequential A-V pacing, Figs. 3 and 4, little change in gradient or other hemodynamic measurements is seen. When sequential A-V pacing is changed to interrupted atrial pacing, Fig. 5, the a wave in late diastole is lost, the mitral gradient falls, the calculated diastolic flow decreases, left ventricular ejection time and left ventricular mean systolic pressure decrease. When sequential A-V pacing is changed to synchronous A-V pacing, Figs. 3 and 4, the late diastolic a wave is again lost with similar reductions in gradient, calculated flow, left ventricular ejection time, and left ventricular mean systolic pressure.

Atrial pacing is compared to sequential A-V pacing in Fig. 7. The introduction of ectopic ventricular activation produces only small and variable hemodynamic changes, demonstrating that sequential A-V pacing is

TABLE II

Hemodynamic

Patient	Age	Sex	Intervention	PR	Grad	SV	LVET	LVMSP	SW
				Aortic stenosis					
D. S.	56	M	Atrial pace	170	95	65	298	178	156
			Sequential pace 1	100	89	61	291	176	146
			Interrupted atrial pace	none	55	38	232	130	67
			Sequential pace 2‡	120	93	64	297	171	148
			Synchronous pace	0	66	47	259	138	88
W. B.	67	M	Atrial pace	210	63	31	297	149	63
			Sequential pace 1	100	64	31	293	152	65
			Interrupted atrial pace	none	57	28	281	140	54
			Sequential pace 2	100	61	30	288	140	57
			Synchronous pace	020	51	26	275	126	45
L. B.	43	F	Atrial pace	170	70	93	241	156	196
			Sequential pace 1	100	61	86	239	167	196
			Interrupted atrial pace	none	51	65	197	138	122
			Sequential pace 2	104	68	92	240	154	192
			Synchronous pace	020	59	79	224	132	143
M. K.	47	F	Atrial pace	180	96	49	330	173	115
			Sequential pace 1	104	92	48	329	172	112
			Interrupted atrial pace	none	64	32	269	135	59
			Sequential pace 2	104	89	45	315	161	98
			Synchronous pace	0	68	35	282	128	61
J. S.	61	M	Atrial pace	260	74	48	285	169	110
			Sequential pace 1	160	69	46	284	158	99
			Interrupted atrial pace	none	58	38	258	137	71
			Sequential pace 2	160	71	47	285	158	101
			Synchronous pace	030	57	38	260	127	66
Group means			Atrial pace	198	80	57	290	165	128
			Sequential pace 1	128	75	54	287	165	124
			Interrupted atrial pace	none	57	40	247	136	75
			Sequential pace 2	118	76	56	285	157	119
			Synchronous pace	014	60	45	260	130	81
P values			AP vs. Seq 1	<0.005	<0.05	<0.05	>0.1	<0.01	<0.02
			Seq 1 vs. IAP	—	<0.05	<0.05	<0.02	<0.01	<0.05
			Seq 2 vs. SYN	<0.001	<0.02	<0.01	<0.01	<0.01	<0.01
			(Seq 1-IAP) vs. (Seq 2-SYN)§	—	>0.3	>0.1	>0.05	>0.5	>0.1

* PR, electrocardiographic P-R interval in msec; Grad, valvular gradient in mm Hg; SV, stroke volume in ml/beat; LVET, left ventricular ejection time in msec; LVMSP, left ventricular mean systolic pressure in mm Hg; SW, stroke work in g-m; DF, diastolic flow into the left ventricle in ml/beat.

‡ Sequential pace 2 differs from sequential pace 1 only in that the cardiac cycles of interrupted atrial pacing were compared to the two immediately preceding cycles (sequential pace 1) during continuous recording. Sequential pace 2 represents the reestablished sequential pacing before synchronous pacing.

§ (Seq 1-IAP) vs. (Seq 2-SYN) The magnitude of change brought about by the intervention of interrupted atrial pacing during sequential pacing (Seq 1-IAP) is compared to the change produced by the intervention of synchronous pacing during sequential pacing (Seq 2-SYN).

*Observations**

Mitral stenosis								
Patient	Age	Sex	Intervention	PR	Grad	DF	LVET	LVMSP
C. F.	28	F	Atrial pace	250	23	36	259	90
			Sequential pace 1	145	23	36	264	90
			Interrupted atrial pace	none	16	30	248	85
			Sequential pace 2	146	22	35	252	86
			Synchronous pace	056	14	30	228	78
J. E.	50	M	Atrial pace	270	13	39	254	104
			Sequential pace 1	160	12	39	258	94
			Interrupted atrial pace	none	6	28	207	80
			Sequantial pace 2	160	11	38	250	89
			Synchronous pace	020	5	28	221	78
D. P.	39	F	Atrial pace	220	11	48	240	—
			Sequential pace 1	130	16	48	234	135
			Interrupted atrial pace	none	9	35	202	116
			Sequential pace 2	120	12	41	227	—
			Synchronous pace	020	7	38	202	—
M. C.	35	F	Atrial pace	260	22	75	274	93
			Sequential pace 1	180	16	75	272	93
			Interrupted atrial pace	none	9	53	250	89
			Sequential pace 2	180	21	83	268	85
			Synchronous pace	050	12	69	242	76
L. D.	20	F	Atrial pace	140	14	54	234	99
			Sequential pace 1	130	15	57	235	98
			Interrupted atrial pace	none	10	54	216	94
			Sequential pace 2	054	14	54	231	92
			Synchronous pace	0	10	48	224	90
P. H.	19	M	Atrial pace	180	15	64	295	114
			Sequential pace 1	—	—	—	—	—
			Interrupted atrial pace	—	—	—	—	—
			Sequential pace 2	115	13	60	295	100
			Synchronous pace	030	9	54	274	92
Group means			Atrial pace	220	16	53	259	100
			Sequential pace 1	149	16	51	253	102
			Interrupted atrial pace	none	10	40	225	93
			Sequential pace 2	129	15	52	254	90
			Synchronous pace	029	10	45	232	83
P values			AP vs. Seq 1	<0.001	>0.05	>0.6	<0.05	<0.02
			Seq 1 vs. IAP	—	<0.001	<0.05	<0.02	<0.05
			Seq 2 vs. SYN	<0.005	<0.01	<0.01	<0.001	<0.01
			(Seq 1-IAP) vs. (Seq 2-SYN)	—	>0.6	>0.2	>0.3	>0.6

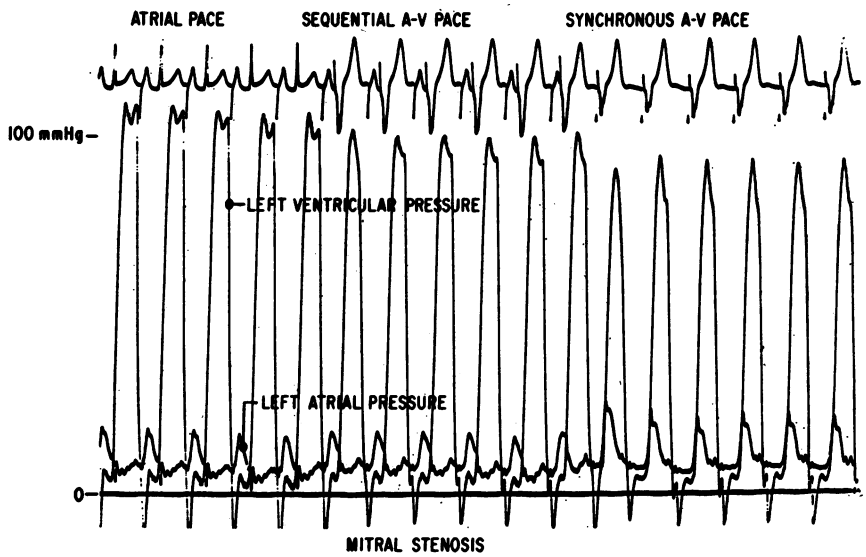

FIGURE 3 A continuous hemodynamic recording of the same three pacing states as shown in Fig. 1 here in a patient with mitral stenosis (M.C.). Sequential A-V pacing (SEQ) (center) introduces ectopic ventricular activation but preserves the PR interval. Ectopic ventricular activation causes only a minor decrease in left ventricular peak systolic pressure. In the synchronous A-V pacing state (SYN) (right) the presystolic component of the diastolic gradient is lost. This is associated with a significant decrease in left ventricular peak systolic pressure.

only a slightly different physiologic state from atrial pacing. Therefore, in all subsequent comparisons, sequential A-V pacing will now serve as the new control state.

Comparison of the hemodynamic effect of well-timed atrial contraction, (which obtains during sequential A-V pacing) to no atrial contraction (interrupted atrial pacing), or to inappropriate atrial contraction (synchronous A-V pacing) for the two groups is summarized graphically in Figs. 8 and 9. Loss of effective atrial contraction through interrupted atrial pacing or though synchronous A-V pacing significantly reduces all parameters recorded in patients with either valvular lesion. In aortic stenosis, Fig. 8, aortic valvular systolic gradient, calculated stroke volume, LVET, and LVSW all decrease significantly when effective atrial contraction is excluded. In mitral stenosis, Fig. 9, the mitral valvular diastolic gradient, calculated diastolic flow, LVET, and LVMSP all decrease significantly when atrial contraction is removed. In Figs. 8 and 9, absolute values for the group means for each parameter are inscribed in the bars and statistical values are indicated.

In addition to showing the effect of loss of atrial contraction, Figs. 8 and 9 allow comparison of the magnitude of change brought about by the two different techniques of interfering with effective atrial systole. As demonstrated in Figs. 8 and 9, the *P* values at the top of the bar graphs designated with an asterisk compare the magnitude of change produced by the intervention of interrupted atrial pacing to the change produced by the intervention of synchronous A-V pacing. There is no significant difference between these two interventions indicating that they produce an effect of similar magnitude.

Since transposition of the Gorlin formula in aortic stenosis yields stroke volume, it was possible to calculate stroke work. A 55% increase in LVSW occurred with well placed atrial contraction due to the product of a 29% increase in SV and a 21% increase in LVMSP. In mitral stenosis, the transposed Gorlin formula yields diastolic flow. This is modified on a beat-to-beat basis by the ejection fraction of the ventricle into stroke volume. It was thus not possible to calculate stroke work in the mitral stenosis group and LVMSP is reported. However, the LVMSP increased with well placed atrial contraction as did LVET. In view of Harley, Starmer, and Greenfield's work (5) the increase in LVET indicates an increase in SV. Therefore, the LVSW would also be increased in the mitral stenosis group with well placed atrial contraction, although it was not possible to quantitate the increase.

DISCUSSION

Animal experiments in the past decade have shown that well-timed atrial contraction improves ventricular filling. This has not been adequately studied in humans. Previous

experience investigating active atrial transport in valvular disease in man made clear to us the need for an experimental design in which the hemodynamic effect of the presence or absence of atrial systole could be evaluated acutely independently of other variables. Use of sequential A-V pacing in conjunction with left heart catheterization in humans as described above approaches the controlled heart block animal studies of Mitchell, Sarnoff, and others (6–10). Using this approach, the heart rate was held constant, the pathway of ventricular activation was constant, inotropic state was as constant as achievable in the intact awake patient while cardiac cycles were produced with well placed atrial contraction, poorly placed atrial contraction, and no atrial contraction. This experimental design demonstrates active atrial transport function in patients with stenotic valvular disease.

The potential contribution of active atrial transport to increased cardiac output was shown in both groups of patients with a spectrum of severity of disease. In the aortic stenosis group, three patients had very severe and symptomatic calcific aortic stenosis, one patient having syncope at rest. Nevertheless, well-timed atrial contraction increased SV 24% and LVMSP 16%. Similarly in the mitral group a spectrum from mild to severe stenosis was present. In the three patients with moderate to severe mitral stenosis, C.F., J.E., P.H., (all of whom required mitral commissurotomy) well-timed atrial systole augmented diastolic gradient 66%, diastolic flow 19%, and LVMSP 11%. LVET also increased 10%. As can be seen by inspection of the pressure contour in Fig. 5, well placed atrial systole produces a striking change in the mean mitral diastolic gradient, dependent on the area under the a wave. The change in mean mitral gradient that accrues from the a wave should relate to flow in the manner described by the Gorlin formula in which flow is proportional to the square root of the gradient, as long as the valve remains open (11). This exponential relationship of pressure and flow should be emphasized. For example, in patient C.F. with tight mitral stenosis (0.7 cm^2) a 7 mm Hg augmentation of mean mitral gradient produced a 6 ml/beat increase in diastolic flow

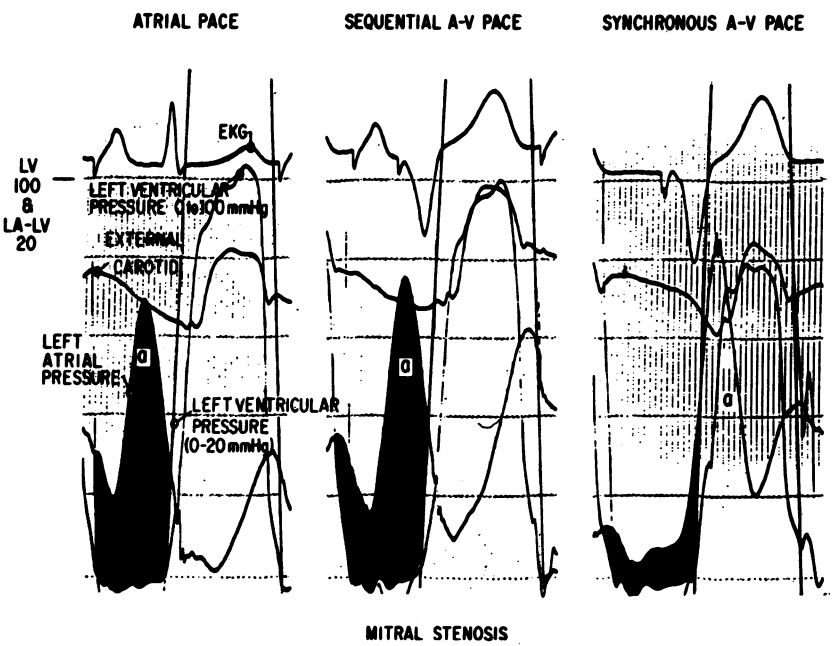

FIGURE 4 Atrial (AP), sequential A-V (SEQ), and synchronous (SYN) pacing are shown in another patient with mitral stenosis (J.E.). The mitral gradient (solid) is shown at full scale 20 mm Hg while LV pressure is also displayed at 100 mm Hg to record left ventricular peak systolic pressure. LVET is measured from the external carotid pulse contour. In the left and center panels with PR interval preserved, note the large presystolic atrial a wave contributing significantly to the mean mitral diastolic gradient. During synchronous A-V pacing (right) this presystolic component is lost. The mean gradient is reduced as is left ventricular peak systolic pressure. The displaced atrial contraction during synchronous pacing generates a large atrial pressure wave during ventricular systole when the atrium normally is passively expanding.

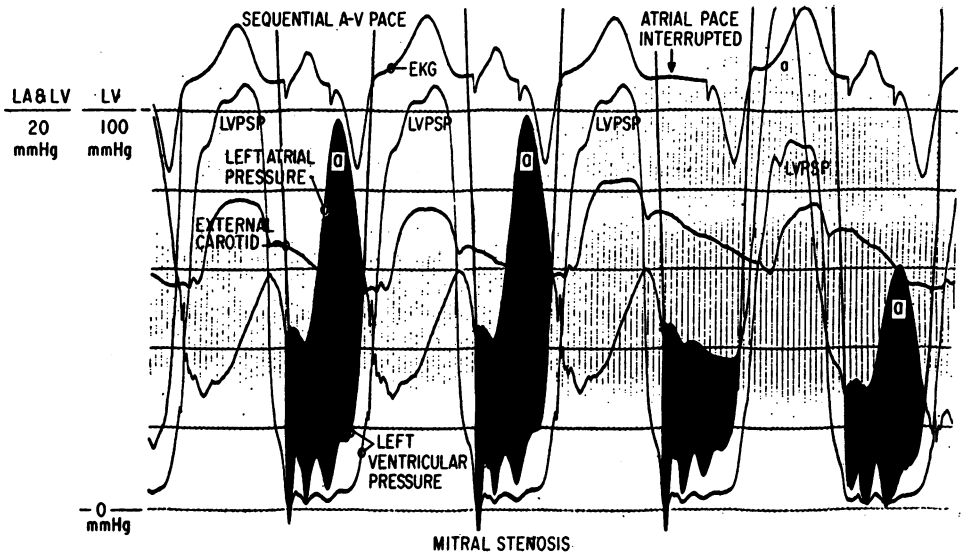

FIGURE 5 Interrupted atrial pacing (IAP) in mitral stenosis. The effect of atrial asystole (diastolic left atrium) in mitral stenosis is shown. In the third complex from the left, the atrial pacing is suddenly interrupted. The large presystolic left atrial a wave seen in the preceding complexes does not occur. This results in a marked reduction in the mean mitral diastolic gradient (solid). The reduction in left ventricular peak systolic pressure and LVET can be seen in the subsequent beat.

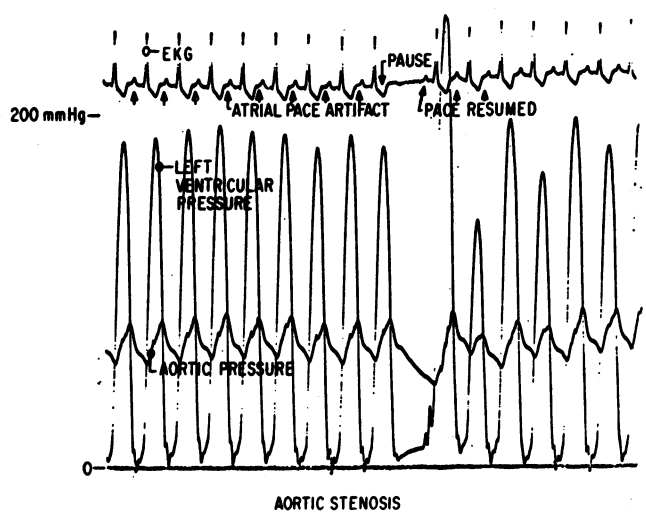

FIGURE 6 Atrial pacing (AP) in aortic stenosis with left ventricular and central aortic pressures recorded showing the aortic valvular gradient. The atrial pacing stimulus was temporarily interrupted (center of the figure). After the abrupt cessation of atrial pacing, a sinus pause occurred (see text). The intervention of intermittently interrupting atrial pacing during sequential A-V pacing was used to take advantage of the above phenomenon to produce cardiac cycles with no atrial contraction.

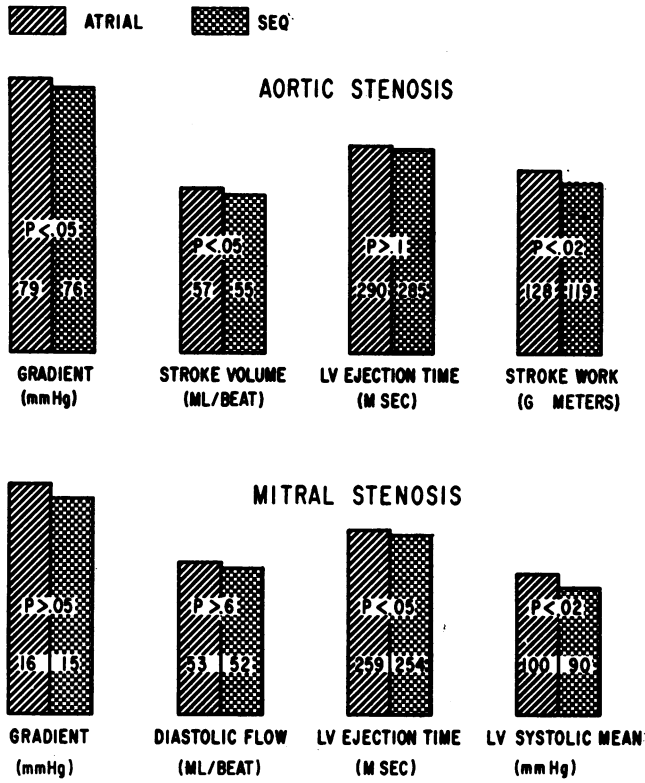

FIGURE 7 Comparison of atrial pacing (AP) to sequential A-V pacing (SEQ) by group means for both valvular lesions is shown. Minimal but occasionally significant changes in the various parameters of ventricular performance occur with ectopic ventricular activation.

whereas patient D.P. with less severe mitral stenosis (1.6 cm^2) the same pressure increase produced a 13 ml/beat increase in diastolic flow.

Comparison of the relative importance of atrial systole in the two valvular lesions is difficult. Patients with mitral and aortic stenosis were chosen because the fixed orifice obstruction acts as a flowmeter allowing calculation of flow change on a beat-to-beat basis as the timing of atrial systole is varied. In this study we have shown that the atrium can function even in the presence of severe valvular stenosis. Carleton and Graettinger (12) studied atrial function in a group of patients with mitral stenosis. They observed cardiac output in a steady-state fashion during sequential A-V pacing with well placed atrial contraction and compared it to cardiac outputs repeated 3–19 min after elimination of effective atrial contraction by synchronous A-V pacing. They concluded atrial function is not significant in mitral stenosis. As previously stated, it is unlikely that the timing of atrial systole is a prime determinant of cardiac output. Compensatory mechanisms maintain homeostasis tending to obscure the effect of a hemodynamic intervention unless sensitive acute parameters are recorded. Recording such sensitive parameters acutely in this group of 11 patients unmasked atrial function in severe valvular stenosis.

As can be seen in the tracing in aortic stenosis (Figs. 1 and 2), the atrial booster effect markedly elevates left ventricular end diastolic pressure (LVEDP). Such dramatic change in LVEDP was not seen in the mitral stenosis patients in spite of the significant change in calculated diastolic flow. In the patients with severe aortic stenosis, there is decreased compliance of the left ventricle. The ventricle is operating on the steep portion of its length tension curve and inflow of a small additional amount of blood volume to the ventricle produces marked pressure change. In the mitral stenosis group, the compliance of the left ventricle is presumably normal. Due to the inflow obstruction, the ventricle in mitral stenosis is on the flat portion of its length tension curve. Because of this, increases in ventricular volume are less well reflected in pressure increases. The increase in LVMSP, LVET,

and LVSW with well placed atrial contraction again underscores the importance of ventricular filling and not LVEDP per se.

Our calculation of the increase in flow with well placed atrial contraction of 31% in aortic stenosis and 22% in mitral stenosis compares with increases of 36% in SV in dogs reported by Brockman (13) and 20% in SV in calves with a flowmeter implanted about the mitral annulus (14). In our study LVMSP increased 21% in aortic stenosis and 9% in mitral stenosis compared with 19% pressure augmentation with well placed atrial contraction in heart block humans (15). In aortic stenosis in our study LVSW increased 56% with well placed atrial systole compared to 37% increase in LVSW in dogs (12) and 42% increase in LVSW in heart block humans (16).

The innovation of interrupting the atrial pace to produce cycles in which the atrium fails to contract defines the relative role of the atrium as a booster pump and as a reservoir. Previous A-V dissociation studies (1, 2) necessarily compared well placed atrial contraction to atrial contraction during ventricular contraction when the atrium normally functions as a passive dilating reservoir. It was of some concern that changes seen with A-V dissociation possibly reflected on interference with reservoir function rather than the loss of the booster pump. Grant, Bunnell, and Greene (17) attributed nearly all atrial function to the passive distensible reservoir rather than to atrial contraction. This study produced cycles with no atrial contraction to show essentially identical changes whether the atrium contracted during ventricular systole or did not contract at all. The loss of the well placed active contraction was the most important variable.

In these intact, awake patients with a functioning autonomic nervous system, institution of synchronous A-V pacing with its concomitant reduction in central aortic pressure frequently resulted in compensatory sinus tachycardia, due to SA node escape. Thus, an atrial pace rate 10–15 beats/min faster than the resting heart rate in each individual patient was used to ensure atrial capture throughout the whole study. The necessity for overdrive pacing emphasizes the hemodynamic impact of synchronous pacing. In the patients with se-

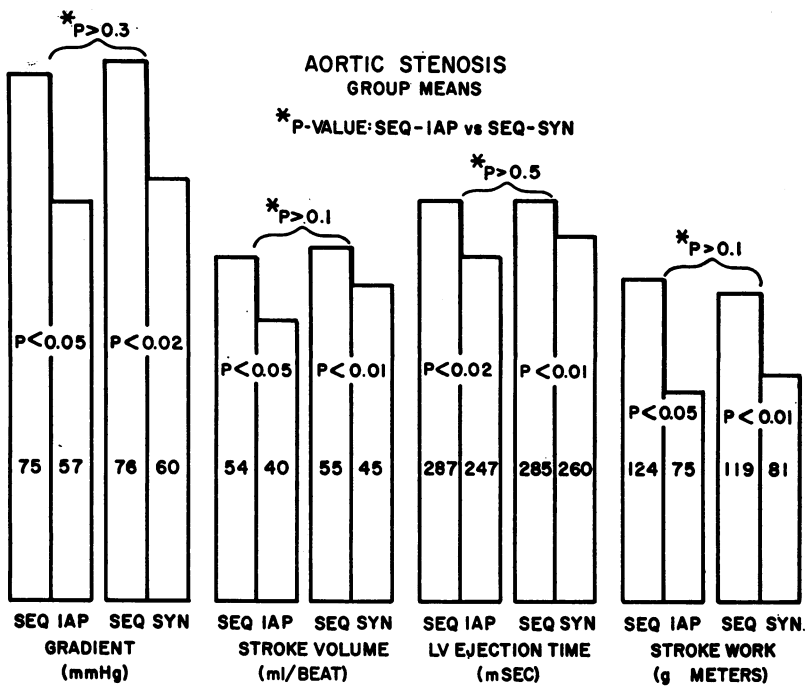

FIGURE 8 In aortic stenosis during sequential A-V pacing (SEQ), effective atrial contraction either through intermittent interruption of atrial pacing (IAP) or through synchronous A-V pacing (SYN) reduced all hemodynamic parameters recorded. This figure also shows the similar magnitude of change produced by these two different methods of eliminating atrial contraction. The *P* value designated with an asterisk at the top of the columns indicates there is not statistically significant difference in these two ways of eliminating effective atrial contraction.

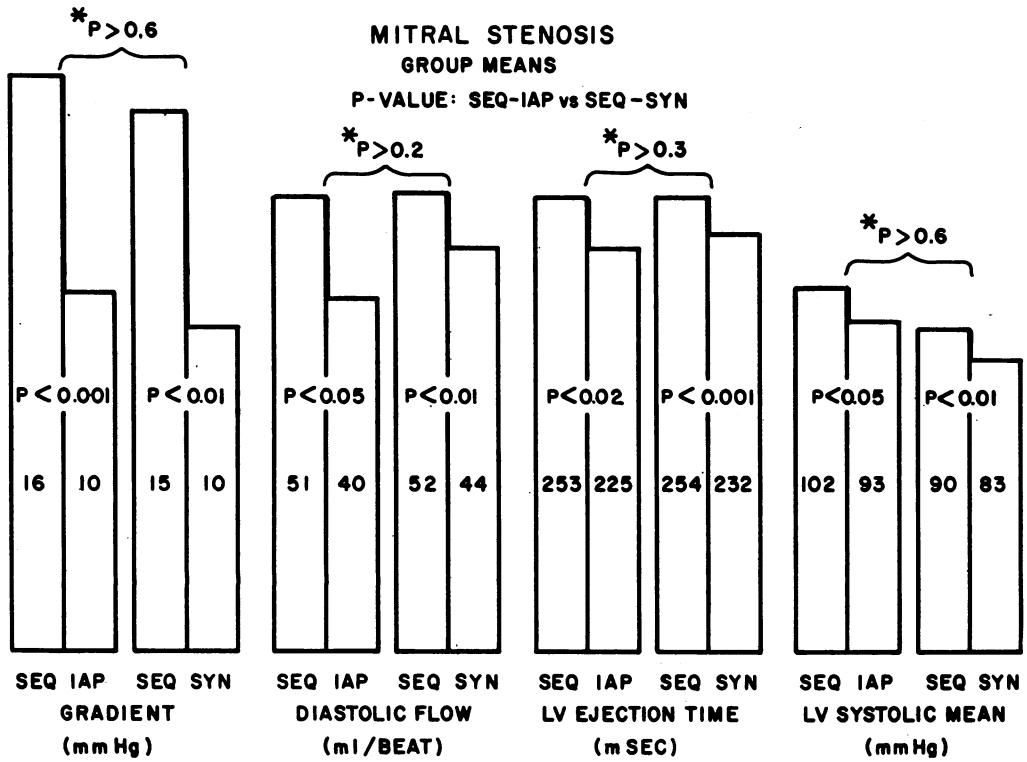

FIGURE 9 In mitral stenosis during sequential A-V pacing (SEQ), elimination of effective atrial contraction by either interrupted atrial pacing (IAP) or by synchronous A-V pacing (SYN) reduced all parameters recorded. Comparison of the magnitude of change caused by the two different means of eliminating effective atrial contraction (*P* values designated with asterisk) show no statistical difference.

vere aortic or mitral stenosis who are very ill, when other compensatory mechanisms are already stressed, it is tempting to speculate that the onset of atrial fibrillation is a negative hemodynamic change that can no longer be compensated. This would agree with the well known clinical deterioration of some patients with the onset of atrial fibrillation. The benefit of atrial systole shown in this patient group, many of whom may well have had pathologic anatomical changes in the atrium, supports efforts to maintain normal sinus rhythm (NSR) in these patients with severe valvular disease.

The unsettled question of the effect of ectopic ventricular activation was circumvented in the present study by utilizing sequential pacing to establish a new steady state for subsequent comparisons. However, examination of the bar graphs (Fig. 7) show that with the PR preserved, institution of ectopic right ventricular activation produced only minor changes in LV parameters. This would agree generally with studies previously reported indicating variable low magnitude deleterious effects of ectopic ventricular activation per se (18–21).

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