Effects of atrial pacing site on atrial and atrioventricular nodal function¹

Fernando Amat y Leon, Pablo Denes, Delon Wu, Raymond J. Pietras, and Kenneth M. Rosen

From the Section of Cardiology, Department of Medicine, Abraham Lincoln School of Medicine, University of Illinois College of Medicine, Chicago, Illinois, U.S.A.

The effects of the site used for atrial pacing on atrial and atrioventricular nodal conduction were assessed in 16 patients. In 13 patients, three atrial pacing sites were used: high right atrium, low lateral right atrium, and midcoronary sinus. Two recording sites were used: low septal right atrium, including His electrogram, and high right atrium. Stimulus (S) to high right atrium interval was longest with coronary sinus pacing (76 ± 7 ms) ($P < 0.001$), and shortest with high right atrial pacing (41 ± 3 ms) ($P < 0.05$). There was no significant difference in stimulus to low septal right atrium from all three pacing sites. Atrial functional and effective refractory periods were not significantly different. Mean low septal right atrium to His was significantly shorter from the coronary sinus (93 ± 8 ms) ($P < 0.001$), as compared to high right atrium (139 ± 16 ms), and low lateral right atrium (129 ± 13 ms) pacing. AV nodal functional and effective refractory periods, and the paced rate producing AV nodal Wenckebach were not significantly different when comparing the three sites.

Left atrial appendage and high right atrium were similarly compared in three additional patients, and no significant differences were found in conduction times and refractory periods.

Electrophysiological studies in the catheterization laboratory are used to study conduction physiology, pathophysiology, and pharmacology. In these studies, conduction intervals and their responses to atrial pacing are measured. Refractory periods are determined using the atrial extra-stimulus technique. Previous studies suggest that atrial stimulation site might influence electrophysiological findings (Waldo *et al.*, 1970; Leon *et al.*, 1970; Lau *et al.*, 1970; Lancaster *et al.*, 1965; Janse, 1969). In this study, we have systematically studied the effects of atrial pacing site on atrial and AV nodal conduction times and refractory periods.

Methods

This study was conducted in 16 patients: 12 had electrophysiological evaluation because of intraventricular conduction disease, and 4 had electrophysiological studies performed after diagnostic cardiac catheteriza-

tion. Informed consent was obtained. Clinical data in the 16 patients are summarized in Table 1.

All patients were studied in the post-absorptive, non-sedated state. A tripolar electrode catheter was introduced percutaneously into the right femoral vein and placed across the tricuspid valve for His bundle recording (Scherlag *et al.*, 1969). A quadripolar electrode catheter was introduced into the left femoral vein and advanced into the high lateral right atrium for both recording of atrial electrograms and for atrial stimulation. A bipolar electrode catheter, introduced via the antecubital vein, was used for pacing the low lateral right atrium and coronary sinus. The interelectrode distances in the bi, tri, and quadripolar catheters were 1 cm. Refractory periods were determined using the atrial extra-stimulus technique (Denes *et al.*, 1974). Previous definitions of atrial and AV nodal effective and functional refractory periods were used (Denes *et al.*, 1974). Stimuli were 2 ms in duration and twice diastolic threshold in intensity, delivered by a digital programmable pulse generator.¹ Intracardiac electrograms, as well as electrocardiographic standard leads I, II, III, and chest lead V₁ were simultaneously displayed on an oscilloscope and recorded on a multichannel photographic recorder (Electronics for Medicine DR-16, White Plains, New York) at paper speeds of 100 and 200 mm/s.

¹M. Bloom, Philadelphia, Pa., U.S.A.

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TABLE 1 Clinical, electrocardiographic, and electrophysiological data in 16 patients

Case No.	Age (yr)	Sex	Diagnosis	ECG	HR (beats/min)	P-A (ms)	A-H (ms)	H-V (ms)
1	56	F	ASHD	CRBBB+LAH	70	26	125	72
2	42	F	PCD	IRBBB+LPH	68	26	93	43
3	71	M	PCD	CRBBB+LAH	56	40	110	43
4	72	M	HCVD	CRBBB+LAH	71	34	101	63
5	26	F	RHD	LVH+1° A-V	76	26	145	52
6	62	M	ASHD	LBBB+1° A-V	66	21	168	83
7	70	F	HCVD	CRBBB	73	45	107	49
8	65	M	HCVD	CRBBB+LAH	83	49	76	65
9	38	M	PCD	IRBBB+LAH	55	32	154	44
10	64	M	HCVD	CRBBB+LAH	46	40	107	43
11	66	M	PCD	CRBBB+LAH	67	46	104	32
12	26	M	RHD	Normal	82	28	105	46
13	45	F	RHD	Normal	75	32	105	42
14	47	M	PCD	IRBBB	44	40	84	50
15	68	M	ASHD	CRBBB+LAH	82	45	82	77
16	32	F	NoHD	QT Prolongation	65	25	83	38

Abbreviations: M, male; F, female; ASHD, arteriosclerotic heart disease; PCD, primary conduction disease; HCVD, hypertensive cardiovascular disease; RHD, rheumatic heart disease; NoHD, no organic heart disease; LBBB, left bundle-branch block; CRBBB, complete right bundle-branch block; IRBBB, incomplete right bundle-branch block; LAH, left anterior hemiblock; LPH, left posterior hemiblock; LVH, left ventricular hypertrophy; HR, heart rate; 1° A-V, 1st degree atrioventricular block.

Location of pacing and recording sites used

The locations of pacing and recording electrode catheters are shown in Fig. 1. Three stimulation sites were studied in 13 of the patients, these being: 1) high lateral right atrium at the junction of the superior vena cava and right atrium; 2) low lateral right atrium just above the junction of the inferior vena cava and low right atrium, and 3) the midportion of the coronary sinus (a posterior left atrial pacing site). The position of the

catheter in the coronary sinus was confirmed by its posterior location in the lateral view and by the presence of inverted P waves in leads II and III during stimulation. In addition, in a separate group of three patients, the left atrial appendage was paced and compared to the high right atrium. In these three patients, the left atrium could be entered via a patent foramen ovale.

The following two atrial recording sites were used (Fig. 1): 1) high right atrium, recorded from the quadri-

FIG. 1 Location of pacing and recording sites utilized. HRA=high right atrium; LRA=low lateral right atrium; CS=midportion of the coronary sinus; P=pacing site; R=recording sites; RA=right atrium; RV=right ventricle.

polar catheter; and 2) low septal right atrium, recorded from the His bundle catheter.

Protocol

The following protocol was used. In 13 patients, the three pacing sites were studied sequentially, beginning with the high right atrium, then with the low lateral right atrium, and concluding with the coronary sinus. In

three patients, the left atrium was studied and compared to the high right atrium. At each site, the atria were paced at increasing rates until AV nodal Wenckebach periods were observed. The following intervals were then measured and compared at a cycle length of 667 ms: 1) S-H, from stimulus to His bundle electrogram. This measured total conduction time from stimulus (at a given pacing site) to His bundle: 2) A-H from low septal right

TABLE 2 Conduction times and refractory periods in 16 patients

Case No.	Atrial conduction times and refractory periods					AV nodal conduction times and refractory periods				
	Pacing site	S-HRA (ms)	S-A (ms)	FRP-atr (ms)	ERP-atr (ms)	S-H (ms)	A-H (ms)	W (beats/min)	FRP-AV (ms)	ERP-AV (ms)
1	HRA	33	41	250	230	149	110	130	490	370
	LRA	54	37	280	250	196	160	120	540	380
	CS	60	40	300	280	145	103	130	500	404
2	HRA	32	58	270	260	158	100	120	590	450
	LRA	90	85	240	230	255	170	120	580	490
	CS	65	45	310	250	135	90	110	610	540
3	HRA	50	80	< 350	< 350	215	135	170	420	< 350
	LRA	52	90	—	—	228	138	160	—	—
	CS	60	50	310	260	168	118	160	410	< 310
4	HRA	36	79	280	260	185	107	170	360	< 280
	LRA	37	39	270	240	123	86	190	360	< 270
	CS	72	38	280	255	121	83	190	350	< 280
5	HRA	43	60	290	280	232	173	140	470	300
	LRA	45	71	280	270	236	166	140	460	310
	CS	79	39	320	300	176	138	150	450	< 320
6	HRA	83	96	—	—	301	202	130	—	—
	LRA	—	68	—	—	200	135	140	—	—
	CS	149	122	—	—	258	132	150	—	—
7	HRA	29	39	270	240	131	92	170	430	< 270
	LRA	36	57	260	240	166	110	170	420	< 260
	CS	89	52	290	220	139	87	170	420	< 290
8	HRA	38	49	210	200	146	97	160	460	320
	LRA	52	73	320	300	140	67	170	430	340
	CS	79	42	290	270	78	35	160	440	320
9	HRA	41	46	320	190	325	285	150	470	320
	LRA	76	69	300	240	274	211	150	400	300
	CS	145	58	305	300	216	155	150	460	320
10	HRA	70	70	350	340	242	172	130	530	445
	LRA	100	110	340	210	272	165	140	520	440
	CS	91	77	300	230	192	110	130	530	450
11	HRA	49	81	350	300	208	129	120	500	410
	LRA	52	52	280	240	152	102	140	420	310
	CS	65	43	300	260	144	100	130	470	370
12	HRA	40	52	180	155	162	107	110	580	360
	LRA	32	38	260	210	130	91	110	620	550
	CS	59	41	270	220	122	77	100	640	550
13	HRA	35	46	250	230	134	94	160	405	< 250
	LRA	48	40	250	210	105	70	180	390	< 250
	CS	43	42	240	200	118	76	170	410	255
14	HRA	34	45	295	275	167	120	170	400	295
	LA	35	50	300	250	169	125	180	415	300
15	HRA	45	45	300	220	155	109	180	440	< 300
	LA	67	76	330	275	182	107	190	420	< 330
16	HRA	38	50	260	235	170	115	160	460	< 260
	LA	39	57	230	160	169	111	160	420	< 230

Abbreviations: FRP-atr, functional refractory period of the atrium; ERP-atr, effective refractory period of the atrium; W, paced rate producing AV nodal Wenckebach; FRP-AV, functional refractory period of the AV node; ERP-AV, effective refractory period of the AV node.

atrial electrogram to His bundle electrogram, the usual measure of AV nodal conduction time; 3) S-HRA, from stimulus to high right atrial electrogram, and 4) S-A, from stimulus to low septal right atrial electrogram. The value assigned to each interval represented the mean of 10 measurements in consecutive beats.

Refractory periods were measured using the atrial extra-stimulus technique at a cycle length of 667 ms from the three stimulation sites. In 6 patients, the refractory periods from high right atrium were also repeated at the end of the procedure, and were noted to be similar to the initial measurements. Statistical analysis was done using analysis of variance, in those patients in whom the measured variables were available for all three pacing sites. The Student *t*-test was used to compare left atrium against high right atrium.

Results

The detailed results obtained in the 16 patients are given in Table 2.

Intra-atrial conduction (Table 3)

Stimulus to high right atrium conduction times were (mean $\pm$ SEM) 41 ± 3 , 56 ± 6 , and 76 ± 7 ms with high right atrium, low lateral right atrium, and coronary sinus pacing, respectively. Stimulus to high right atrium was significantly shorter with high right atrial pacing when compared to both coronary sinus and low lateral right atrium pacing. S-A

conduction times were 61 ± 5 , 64 ± 6 , and 53 ± 6 ms with high right atrium, low lateral right atrium, and coronary sinus pacing, respectively. These means were not significantly different.

Mean atrial functional refractory period was 265 ± 19 , 280 ± 9 , and 291 ± 7 ms from high right atrium, low lateral right atrium, and coronary sinus, respectively (NS). Mean atrial effective refractory period was 244 ± 16 , 240 ± 8 , and 253 ± 10 ms from high right atrium, low lateral right atrium, and coronary sinus pacing, respectively (NS).

AV nodal conduction (Table 4)

Mean S-H interval was 199 ± 17 , 190 ± 16 , and 162 ± 13 ms from high right atrium, low lateral right atrium, and coronary sinus, respectively (Fig. 2). Mean A-H interval was 139 ± 16 , 129 ± 13 , 93 ± 8 ms from high right atrium, low lateral right atrium, and coronary sinus, respectively. Both S-H and A-H were significantly shorter with coronary sinus pacing, with *P* values of 0.05 and 0.001, respectively. The decrease in A-H was responsible for the decrease in S-H. There was no significant difference in S-H and A-H when high and low lateral right atrial pacings were compared.

Mean AV nodal functional refractory period was 480 ± 21 , 467 ± 26 , and 480 ± 26 ms from high right atrium, low lateral right atrium, and coronary sinus,

TABLE 3 Intra-atrial conduction

Stimulation site	S-HRA			S-A			FRP- <i>atr</i>			ERP- <i>atr</i>		
	HRA	LRA	CS	HRA	LRA	CS	HRA	LRA	CS	HRA	LRA	CS
No. of patients	12	12	12	13	13	13	11	11	11	11	11	11
Range (ms)	29-70	32-100	43-145	39-96	37-110	38-122	180-350	240-340	240-310	155-350	210-300	200-300
Mean $\pm$ SEM (ms)	41 ± 3	56 ± 6	76 ± 7	61 ± 5	64 ± 6	53 ± 6	265 ± 19	280 ± 9	291 ± 7	244 ± 16	240 ± 8	253 ± 10
<i>P</i>	<0.05			NS			NS			NS		

Abbreviations: HRA, high right atrium; LRA, low lateral right atrium; CS, coronary sinus.

TABLE 4 AV nodal conduction

Stimulation site	S-H			A-H			FRP-AV		
	HRA	LRA	CS	HRA	LRA	CS	HRA	LRA	CS
No. of patients	13	13	13	13	13	13	11	11	11
Range (ms)	131-325	105-274	78-258	94-285	67-211	35-155	360-590	360-260	350-640
Mean $\pm$ SEM (ms)	199 ± 17	190 ± 16	162 ± 13	139 ± 16	129 ± 13	93 ± 8	480 ± 21	467 ± 26	480 ± 26
<i>P</i>	<0.05			<0.001			NS

FIG. 2 Case 9. His bundle recordings obtained by pacing the atrium at three atrial sites and at identical cycle lengths of 667 ms. Note: 1) The significant shortening of S-H and A-H intervals by coronary sinus pacing. 2) The minimal changes in S-A interval between the three pacing sites, 3) The lengthening of the S-HRA interval by coronary sinus pacing. HRA = high right atrium; LRA = low lateral right atrium; CS = coronary sinus; HBE = His bundle recordings.

respectively (NS). Mean AV nodal effective refractory period was 382 ± 20 , 401 ± 36 , and 422 ± 36 ms from the high right atrium, low lateral right atrium, and coronary sinus respectively (NS).

The mean pacing rates inducing AV nodal Wenckebach periods were 143 ± 6 , 148 ± 7 , and 146 ± 7 beats/min from the high right atrium, low lateral right atrium, and coronary sinus, respectively (NS).

Left atrial pacing

In the three patients in whom the left atrial appendage was paced and compared against high right atrium, mean stimulus to high right atrium was 39 ± 5 ms from high right atrium and 47 ± 10 ms from the left atrium (NS). The mean S-A was 47 ± 2 ms from the high right atrium, and 61 ± 8 ms from the left atrium (NS). Mean atrial functional refractory period was 285 ± 13 ms from the high right atrium, and 287 ± 30 ms from the left atrium (NS).

Mean atrial effective refractory period was 243 ± 16 and 288 ± 35 ms for high right atrium and left atrium, respectively (NS). Mean S-H was 164 ± 4 ms from the high right atrium and 173 ± 4 ms from the left atrium (NS). Mean A-H was 115 ± 3 and 114 ± 5 ms from high right atrium and left atrium, respectively (NS). Wenckebach periods occurred at 170 ± 5 beats/min from the high right atrium and 177 ± 9 beats/min from the left atrium (NS). The mean AV nodal functional refractory period was 433 ± 18 and 418 ± 2 ms from the high right atrium and left atrium, respectively (NS). In these patients, the AV nodal effective refractory period could not be measured because of limiting atrial refractoriness.

Discussion

Intra-atrial conduction

In 1911 Sir Thomas Lewis, in a classic experiment in dogs, was able to demonstrate that the conduction time from the sinoatrial node was longer to the left atrial appendage than that to the right atrial appendage, establishing a direct correlation between the distance an impulse has to travel with the time required to traverse the same tissue (Lewis, 1925). Lewis suggested that atrial depolarization was radial, originating from the sinus node. In contrast, James (James, 1963; James and Sherf, 1971) has emphasized the importance of the internodal tracts, suggesting that these atrial pathways facilitate orderly atrial depolarization and uniform input to the AV node.

ERP-AV			Paced rate producing AV nodal Wenckebach (beats/min)		
HRA	LRA	CS	HRA	LRA	CS
7	7	7	13	13	13
300-450	310-550	255-550	110-170	110-190	100-190
382 ± 20	401 ± 36	422 ± 36	143 ± 6	148 ± 7	146 ± 7
NS			NS		

In this study, two stimulation sites were selected in the right, and two in the left atrium (coronary sinus being equivalent to posterior left atrium). Stimulus to high right atrial conduction time was shortest with high right atrial pacing and longest with coronary sinus pacing, findings consistent with the location of pacing and recording sites. S-A was similar with the high right atrial, low lateral right atrial, and coronary sinus pacing, suggesting that the low right atrial septal recording site with the His bundle recording was equivalently remote from the three sites of stimulation.

The measurement of the atrial refractory periods with the extra-stimulus technique was performed with a quadripolar electrode catheter in which the distal pair of electrodes was used for pacing while the proximal pair was used for recording of local electrograms. Whether the measurements obtained represented the whole atrium or only that part of the atrium surrounding the electrode is not clear. In individual patients, there were variations in refractoriness at different atrial sites (Table 2). However, these differences were not significant when analysed for the entire group.

AV nodal conduction

Janse (1969) has suggested that the route of entry of the atrial wave front into the AV node is a partial determinant of AV nodal conduction and excitation. In the isolated rabbit heart, he was able to demonstrate that by changing the stimulation site from the crista terminalis to the interatrial septum, conduction disturbances appeared in the form of 2:1 AV block. Our findings by pacing from four pacing sites revealed a significant shortening of S-H interval with coronary sinus pacing. This reflected shortening of A-H interval, since S-A was not significantly different. This finding corroborates earlier observations by Leon *et al.* (1970) as well as Lau *et al.* (1970) and Batsford *et al.* (1973) who observed shortening of the PR when pacing the coronary sinus. Waldo *et al.* (1970) noted PR intervals less than 0.12 s when directly stimulating the low right atrium and coronary sinus.

The decrease in A-H interval with coronary sinus pacing can be explained in several ways, depending upon what basic assumptions are made. 1) If it is assumed that the low right atrial septum (the A recording site) is the final common pathway for any atrial stimulus into the AV node, and that A-H is thus a relatively direct measure of AV nodal conduction time, then the decrease in A-H with coronary sinus stimulation should reflect a true decrease in AV nodal conduction time. 2) If it is assumed that A is not necessarily the final common pathway for an atrial impulse into the AV node, and

thus that A-H is not a relatively direct measure of AV nodal conduction time, then this decrease could reflect delivery of the impulse into the distal AV node (bypassing the proximal AV node), perhaps by preferential pathway (posterior internodal tract). This explanation seems unlikely, since coronary sinus stimulation did not result in any other significant facilitation of AV nodal conduction, e.g. shortening of AV nodal effective or functional refractory periods, or decrease in the paced rates producing AV nodal Wenckebach periods. 3) The decrease in A-H with coronary sinus pacing could also reflect simultaneous activation of the low atrial septum and the AV node itself, because of anatomical proximity to the pacing site. Under these circumstances, AV nodal conduction could be unchanged, despite the decrease in A-H with coronary sinus pacing. This would be compatible with the lack of change in other indices of AV nodal function with coronary sinus pacing.

Implications regarding electrophysiological studies

This study suggests the following conclusions: 1) stimulus-atrium intervals can vary, depending upon atrial recording and stimulation sites. 2) Atrial refractory periods can vary in an individual patient, when measured from different stimulation sites. However, no specific atrial stimulation site appears to have an intrinsically shorter or longer atrial refractory period. 3) Changes in A-H interval can be expected when pacing from different atrial sites in a given patient. A-H is shorter with coronary sinus stimulation. 4) AV nodal refractory periods may vary in an individual patient, when studied from different atrial stimulation sites. In the group as a whole, no specific atrial site is associated with significantly longer or shorter AV nodal refractory periods.

The results imply that when performing electrophysiological studies in which the patient serves as his own control (for example, during a drug study), then the stimulation site should be kept constant. When comparing different groups of patients, it is probably also advisable to use similar pacing sites. The high right atrial pacing site seems to be the most physiological site, since this most closely approximates to the normal sequence of atrial activation.

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Requests for reprints to Dr. Kenneth M. Rosen, Cardiology Section, University of Illinois Hospital, P.O. Box 6998, Chicago, Illinois 60680, U.S.A.