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Increased Sympathetic Activity After Atrioventricular Junction Ablation in Patients With Chronic Atrial Fibrillation

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OBJECTIVES The aim of this study was to determine the changes in sympathetic nerve activity (SNA) after atrioventricular junction (AVJ) ablation in patients with chronic atrial fibrillation (AF).

BACKGROUND Polymorphic ventricular tachycardia (PMVT) has been reported after AVJ ablation in patients paced at a rate of ≤70 beats/min. We hypothesized that AVJ ablation results in sympathetic neural changes that favor the occurrence of PMVT and that pacing at 90 beats/min attenuates these changes.

METHODS Sympathetic nerve activity, 90% monophasic cardiac action potential duration (APD_{90}), right ventricular effective refractory period (ERP) and blood pressure measurements were obtained in 10 patients undergoing AVJ ablation. Sympathetic nerve activity was analyzed at baseline and during and after successful AVJ ablation for at least 10 min. Data were also collected after ablation at pacing rates of 60 and 90 beats/min. The APD_{90} and ERP were measured before and after AV block during pacing at 120 beats/min.

RESULTS Sympathetic nerve activity increased to 134 ± 16% of the pre-ablation baseline value ($p < 0.01$) after successful AVJ ablation plus pacing at 60 beats/min and decreased to 74 ± 8% of baseline ($p < 0.05$) with subsequent pacing at 90 beats/min. Both APD_{90} and ERP increased significantly.

CONCLUSIONS 1) Ablation of the AVJ followed by pacing at 60 beats/min is associated with an increase in SNA. 2) Pacing at 90 beats/min decreases SNA to or below the pre-ablation baseline value. 3) Cardiac APD and ERP increase after AVJ ablation. The increase in SNA, along with the prolongation in APD, may play a role in the pathogenesis of ventricular arrhythmias that occur after AVJ ablation. (J Am Coll Cardiol 2000;36:151–8) © 2000 by the American College of Cardiology

Catheter ablation of the atrioventricular junction (AVJ) with implantation of a ventricular pacemaker is now an acceptable treatment option in the management of drug-refractory atrial fibrillation (AF). This procedure was first performed using direct current energy, which resulted in several complications, including ventricular fibrillation (VF) (1,2). Currently, radiofrequency (RF) energy is the method of choice because it is less painful and delivers a smaller, more homogeneous lesion that is considered to be safer. Ventricular fibrillation and sudden death, however, continue to be reported in up to 7% of patients undergoing this procedure, suggesting that factors other than the method of AVJ ablation can play a role in the occurrence of these ventricular arrhythmias (2–5).

Since the original observation of VF after AVJ ablation, several reports have indicated that the arrhythmia seemed to be pause- and bradycardia-dependent (4,5). Geelen et al. (5) recently reported a decrease in the incidence of VF or sudden death with high rate ventricular pacing. Ventricular fibrillation or sudden death occurred in 6% of patients paced at a rate of ≤70 beats/min after the procedure, compared with 0% in those paced at a rate of 90 beats/min for one to three months. The authors concluded that the occurrence of this malignant ventricular arrhythmia might be prevented with such a period of rapid pacing. The purpose of this study was to investigate the sympathetic neural changes that accompany AVJ ablation. We hypothesized that changes in sympathetic nerve activity (SNA), either directly, associated with AVJ ablation or indirectly, in response to hemodynamic changes, enhance the risk of sudden cardiac death, and that pacing at 90 beats/min attenuates these changes. To test this hypothesis, muscle SNA, evaluated by microneurography, monophasic cardiac action potential duration (APD) and effective refractory period (ERP) were measured in patients undergoing AVJ ablation for drug-refractory AF.

METHODS

Study patients. The study was performed at the Dallas Veterans Affairs Medical Center. Written, informed consent was obtained from all patients, and the procedures were in accordance with institutional guidelines. All patients with drug-refractory chronic AF referred for AVJ ablation were screened for the study. Patients were excluded if they had a history of insulin-dependent diabetes mellitus or a history or

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Abbreviations and Acronyms

AF	=	atrial fibrillation
APD	=	action potential duration
AVJ	=	atrioventricular junction
BP	=	blood pressure
ERP	=	effective refractory period
HR	=	heart rate
MAP	=	monophasic action potential
PMVT	=	polymorphic ventricular tachycardia
RF	=	radiofrequency
RV	=	right ventricular
SNA	=	sympathetic nerve activity
VF	=	ventricular fibrillation

signs of peripheral neuropathy. A total of 12 patients were enrolled, and successful muscle SNA recordings were obtained in 10 patients. In the remaining two patients, peroneal nerve recordings were technically difficult and could not be obtained. The data on the 10 patients in whom the experimental protocol was conducted comprise the material of this study.

Electrophysiologic study. Patients were studied in the drug-free, postabsorptive state after informed consent was obtained. In patients receiving beta-blocker therapy, these drugs were discontinued at least five half-lives before the study. Local anesthesia was achieved with 2% procaine hydrochloride, and conscious sedation was avoided, if possible, until the end of the research protocol. In patients who needed sedation, intravenous midazolam was given at the beginning of the study before any baseline measurements were made. Central venous access was obtained from the femoral veins, and continuous arterial blood pressure (BP) monitoring was obtained from a 5F catheter positioned in the right femoral artery. One quadripolar catheter was inserted percutaneously and positioned in the right ventricular (RV) apex. A monophasic action potential (MAP) catheter (EP Technologies, Sunnyvale, California) was placed in the RV apex on the interventricular septum. Ventricular pacing thresholds were then measured from both catheters. When APD and ERP were being measured, pacing was always performed from the MAP catheter; all other pacing was performed from the RV catheter. Radiofrequency ablation was performed using a 5-mm tip catheter (EP Technologies). The end point of ablation was complete AV block that persisted at least 30 min.

Experimental protocol. Muscle SNA, arterial pressure and MAP signals were recorded continuously throughout the protocol. At least 5 min of baseline AF was recorded before the first RF ablation attempt. Radiofrequency ablation was performed as many times as necessary until successful ablation was accomplished (producing sustained AV block). A new baseline was recorded for at least 1 min before each RF application. The baseline value preceding the successful ablation was compared with the initial baseline value, and all physiologic measures were not significantly different ($p > 0.46$); therefore, the baseline values preceding ablation were used for all analyses. Once AV block was achieved, RV pacing was performed at 60 beats/min for 10 min. This was followed by pacing at 90 beats/min for 2 min. Arterial pressure and SNA data were averaged over a 1-min period before ablation (baseline), during the first and tenth minutes after AV block while pacing at 60 beats/min and during the second minute of pacing at 90 beats/min. During AF, the diastolic and systolic pressures were defined on the basis of whether a given QRS complex produced a significant pressure pulse (increase of >10 mm Hg). In each patient, the average values during AF were obtained from at least 70 heart beats. In addition, physiologic and MAP data were obtained during RV pacing at 120 beats/min for 1 min before and after AV block. Pacing at 120 beats/min after AV block was performed ~20 min after successful AVJ ablation. The APD_{90} (defined subsequently) and ERP at a pulse width of 2 ms and at twice the diastolic threshold were obtained from the MAP catheter recordings. A rate of 120 beats/min was chosen to avoid competition during AF before ablation. The MAP recordings were obtained at the beginning of the study. If the MAP tracing changed during the study, the catheter was gently advanced to improve the signal. If the signal failed to improve and required repositioning of the catheter, the data were disregarded because comparison with baseline values was no longer feasible.

Measurements. Efferent, postganglionic muscle SNA was recorded from the right peroneal nerve, as described previously (6). Quantitation of SNA was assessed as the sum of the area of SNA bursts/10 s. These values were derived from 1-min sampling periods and extrapolating to activity/10 s by dividing by 6. For each 1-min sampling period, data were quantified in consecutive 10-s sampling epochs, and analysis of variance with repeated measures was performed to ensure that SNA did not change significantly during the 1-min sampling period, and this was confirmed for all measurement periods. Burst area was used because it more appropriately reflects the changes in SNA, often producing broad, irregular bursts of SNA associated with wide fluctuations in arterial pressure during AF or rapid ventricular pacing. Sympathetic nerve activity during pacing at 60 and 90 beats/min was reported as the percent baseline value during AF before RF ablation (i.e., baseline SNA during AF was reported as 100%). Arterial BP was directly recorded with a catheter inserted into the right femoral artery. Heart rate (HR) was derived from continuous electrocardiographic recording of at least two leads (II and V_1). We measured APD_{90}, defined as the action potential duration at 90% repolarization, from the MAP catheter during pacing at 120 beats/min before and after ablation. The APD_{90} was derived from the average of 10 consecutive heart beats for each subject. The ERP was measured from the MAP catheter as the longest coupling interval at which a ventricular premature stimulus failed to capture twice after an eight-beat drive train.

Follow-up. After the procedure, all patients underwent implantation of a permanent pacemaker, except for one

Table 1. Clinical Characteristics of Patients Undergoing AVJ Ablation

Patient No.	Age (yrs)	EF	Mitral Regurgitation	No. of RFA Lesions	Cardiac Medications Before RFA	MAP Reading
1	56	>50%	None	9	Digoxin	No
2	72	>50%	Trac	4	Digoxin, metoprolol	No
3	71	>50%	None	4	Digoxin, diltiazem	No
4	58	>50%	Trace	2	Digoxin, metoprolol	No
5	46	>50%	Trace	2	Metoprolol, amiodarone	Yes
6	67	20%	Moderate	10	Digoxin	Yes
7	69	20%	Mild	5	Digoxin, metoprolol	Yes
8	42	>50%	None	5	Digoxin, verapamil	Yes
9	68	35%	Mild	3	Digoxin, metoprolol	Yes
10	61	20%	Mild	3	Digoxin, metoprolol	Yes

EF = ejection fraction; MAP = monophasic action potential; RFA = radiofrequency ablation.

patient who already had a pacemaker implanted for symptomatic bradycardia. They were then admitted to a telemetry unit for at least 24 h and discharged at a heart rate of 90 beats/min. Follow-up was done at one week, six weeks and every three months thereafter. The pacing rate was decreased to 70 beats/min after six weeks for the remaining duration of the follow-up period.

Statistical analysis. All data were processed to produce mean values for the last 30-s segments of each phase of the protocol. All data sets were normally distributed, as determined by a Kolmogorov-Smirnov test. Comparisons of the effect of RF ablation on all variables were performed using analysis of variance with repeated measures. When a main effect difference was observed, a post hoc evaluation was performed with a least significant difference test. Comparisons of the responses to pacing at 120 beats/min before and after ablation, as well as between postablation pacing at 60 and 90 beats/min, were performed with a paired *t* test. All significant differences reflect a p value < 0.05.

RESULTS

Patient characteristics. All patients were men (mean age 61 ± 11 years). Left ventricular function was normal in six patients, moderately depressed in one and severely depressed in three. The mean average HR before RF ablation was 92 ± 5 beats/min. Successful RF ablation of the AVJ using the right-sided approach was accomplished in all patients. The median number of RF lesions applied per patient was four. A junctional escape rhythm with a rate of <60 beats/min was noted after ablation in two patients. A summary of the clinical characteristics and number of RF lesions applied is provided in Table 1.

Effect of RF ablation without AV block. Successful AVJ ablation was achieved on the first attempt in two patients. In the other eight patients, a total of 10 RF lesions were applied to the anteroseptal region, with a good temperature rise but no AV block. These unsuccessful RF applications had no effect on SNA, HR or arterial BP, as illustrated in the sample tracing in Figure 1 and as summarized in Table 2.

Sympathetic nerve activity and arterial pressure after successful AVJ ablation. A typical SNA and BP response associated with successful AVJ ablation plus pacing at 60 beats/min is shown in Figure 2. A summary of the SNA and BP changes is provided in Figure 3. For these analyses, SNA is reported as the percent baseline value during AF before RF ablation. In all patients, SNA increased significantly during the first minute after successful AVJ ablation plus pacing at 60 beats/min (ΔSNA = 134 ± 16%, $p < 0.01$). This increase in SNA was sustained for the entire duration of the nerve recording period after successful ablation (20 to 45 min). A small drop in arterial BP accompanied the increase in SNA, with a gradual recovery to baseline.

Effect of pacing rate on SNA and arterial pressure after successful AVJ ablation. Ten minutes after successful AVJ ablation, the effect of pacing at 90 beats/min was compared with the effect of pacing at 60 beats/min (Fig. 4). At this time, SNA during pacing at 60 beats/min remained elevated from the preablation baseline value (126 ± 16%), but decreased significantly below the preablation baseline value during pacing at 90 beats/min (74 ± 8%). Thus, pacing at 90 beats/min resulted in a decrease in SNA that was significant relative to both pacing at 60 beats/min and the preablation baseline value. The BP response was in the opposite direction. Diastolic and mean arterial pressure increased from 77 ± 5 and 99 ± 7 mm Hg during pacing at 60 beats/min to 85 ± 6 and 105 ± 8 mm Hg during pacing at 90 beats/min, respectively. These findings are summarized in Figure 4.

Changes in APD and ERP after successful AVJ ablation. Stable MAP recordings throughout the entire study were available in six patients. In the remaining four patients, the tracings changed during the study (decrease in amplitude and unstable diastolic baseline values), making the measurements unreliable. Therefore, APD_{90} was measured before and ~20 min after successful AVJ ablation during pacing at a rate of 120 beats/min in six patients. The APD_{90} increased in every patient (242 ± 17 ms before ablation vs. 261 ± 12 ms after ablation, $p < 0.01$). Similarly, the ERP at a pacing rate of 120 beats/min increased significantly after

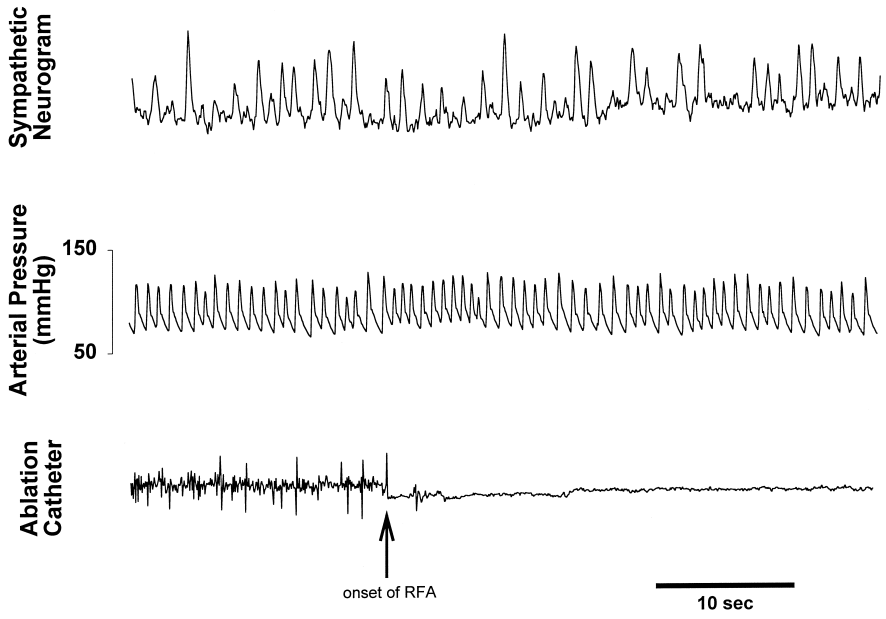

Figure 1. Sample tracings of integrated SNA, femoral artery pressure and ablation catheter. These tracings show a 20-s period before the onset of RF ablation (RFA) and ~40 s of RF ablation without AV block. The **arrow** indicates the onset of RF ablation. No significant changes in arterial pressure or SNA were produced by unsuccessful RF ablation (see Table 2).

ablation (215 ± 14 ms before ablation vs. 233 ± 16 ms after successful AVJ ablation, $p < 0.01$) (Fig. 5). Blood pressure and SNA, however, did not change significantly during pacing at 120 beats/min before and after ablation. A summary of the APD and ERP changes is provided in Table 3.

Follow-up. During a mean follow-up period of 9.5 ± 5 months, all patients did well, except for one who presented with multiple episodes of polymorphic ventricular tachycardia (PMVT) soon after the procedure. This particular patient had a history of sustained monomorphic ventricular tachycardia requiring placement of an implantable cardioverter-defibrillatory 10 months before his AVJ ablation. The episodes of PMVT were treated with beta-blockers and by increasing the pacing rate to 100 beats/min for 24 h. Several weeks after hospital discharge, the patient died at home. A postmortem device interrogation and autopsy were not performed.

DISCUSSION

The main findings of this study are: 1) AVJ ablation followed by pacing at 60 beats/min is associated with an increase in SNA; 2) pacing at 90 beats/min decreases SNA; and 3) APD and ERP in the RV apex are prolonged after AVJ ablation. To our knowledge, this is the first study in which SNA was measured directly during RF ablation. The increase in SNA at 60 beats/min and the prolongation of APD may predispose patients to early afterdepolarizations and PMVT, known complications of AVJ ablation. The decrease in SNA with pacing at 90 beats/min compared to 60 beats/min may contribute to the lower incidence of PMVT in patients paced at faster rates.

Table 2. Effect of Unsuccessful Radiofrequency Lesions

	DBP (mm Hg)	SBP (mm Hg)	MBP (mm Hg)	HR (beats/min)	SNA (%)
Baseline	83 ± 4	140 ± 7	101 ± 4	92 ± 5	100 ± 0
RFA, no block	79 ± 4	142 ± 9	100 ± 6	87 ± 7	93 ± 14

Data are presented as the mean value ± SEM.
DBP = diastolic blood pressure; HR = heart rate; MBP = mean blood pressure; RFA = radiofrequency ablation, SBP = systolic blood pressure; SNA = sympathetic nerve activity.

Hemodynamic changes after AVJ ablation. Radiofrequency ablation of the AVJ has been shown to improve the quality of life in patients with drug-refractory AF (7–9). Although several studies indicate improvement in left ventricular function after AVJ ablation (1,10–13), some authors have reported no change or even hemodynamic deterioration at follow-up (8,14,15). Vanderheyden et al. (15) observed hemodynamic deterioration related to worsening mitral regurgitation in 7.4% of patients undergoing AVJ ablation. Brignole et al. (14) recently reported that although symptoms improved with AVJ ablation and pacemaker implantation, cardiac performance, as evaluated by standard echocardiography and exercise testing, remained stable over time.

In the present study, we observed a subtle decrease in the mean and diastolic arterial pressure initially after AV block, but this pressure recovered to pre–RF ablation levels within 10 min in all patients. We did not measure cardiac output or assess left ventricular function immediately after ablation, but we believe that the decrease in BP after AV block can be explained by the negative hemodynamic effect of RV apex pacing and the decrease in ventricular rate. Right ventricular apex pacing results in aberrant activation of the papillary muscle, which may lead to mitral regurgitation (9). In

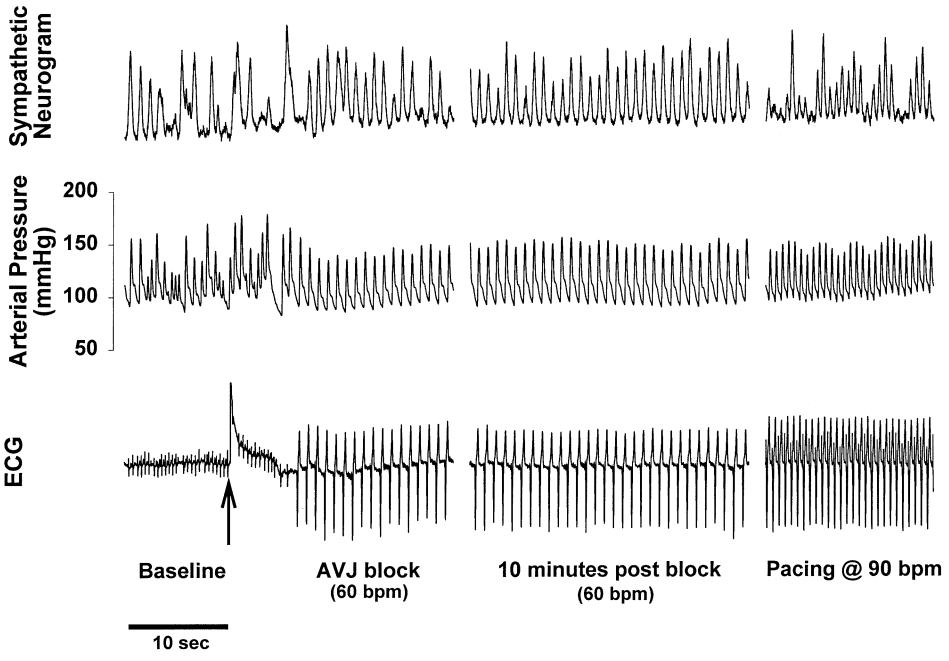

Figure 2. Sample tracings of integrated SNA, femoral artery pressure and surface ECG for one patient. The periods shown include a baseline period (during AF) just before the beginning of RF ablation and during RF ablation (**arrow** on ECG panel) in which AV block was achieved within 10 s, 10 min after AV block (pacing at 60 beats/min) and 12 min after AV block (pacing at 90 beats/min).

addition, the altered sequence of activation associated with RV pacing results in changes in coronary blood flow and elevation in tissue catecholamine levels, which can all lead to a negative effect on left ventricular function (14).

Changes in SNA after AVJ ablation. Unsuccessful RF energy delivery at the AVJ had no effect on SNA, HR or BP. This was true of RF attempts that produced sustained elevations of temperature. Therefore, neither the acute

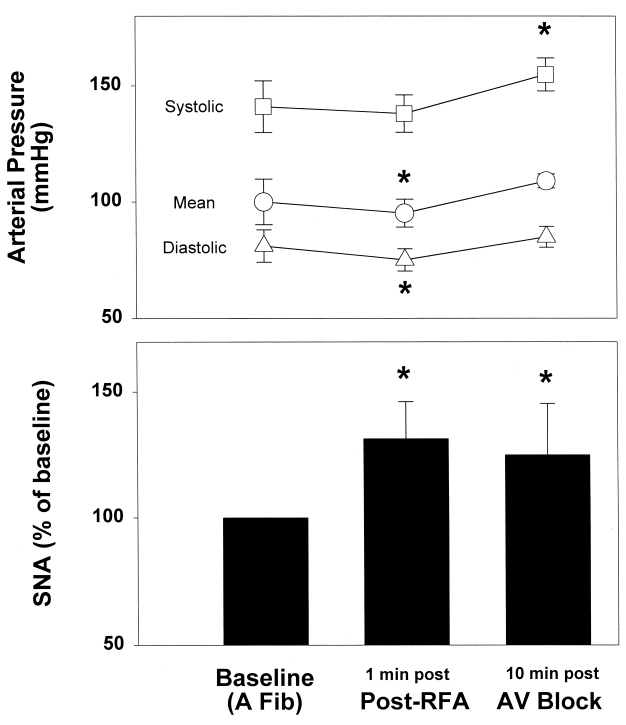

Figure 3. Mean (±SEM) arterial pressures and SNA levels for all 10 patients at baseline (with atrial fibrillation [AFib]), during RF ablation (RFA) with AV block (first minute) and 10 min after AV block was achieved. **Asterisks** indicate significant differences from baseline ($p < 0.05$).

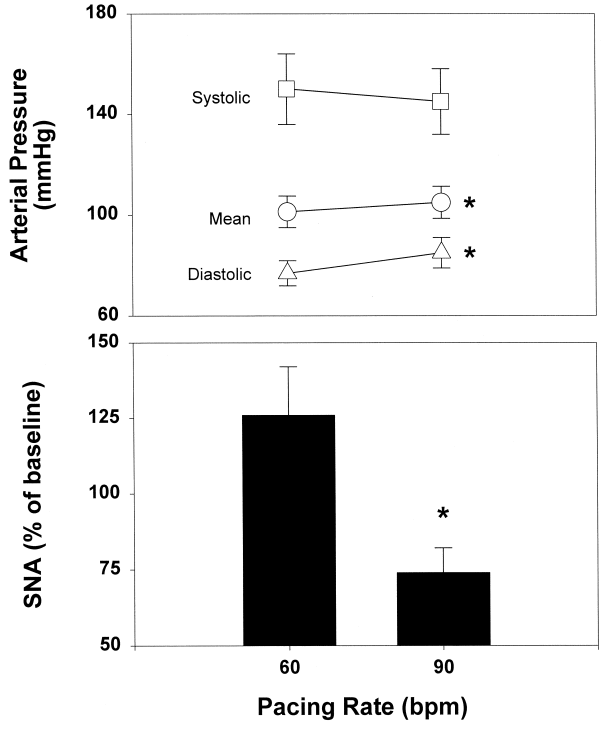

Figure 4. Mean (±SEM) arterial pressures and SNA levels for all 10 patients during pacing rates of 60 and 90 beats/min after complete AV node block was achieved by RF ablation. The data for pacing at 60 beats/min were collected immediately before pacing at 90 beats/min. **Asterisks** indicate significant differences between pacing rates ($p < 0.05$).

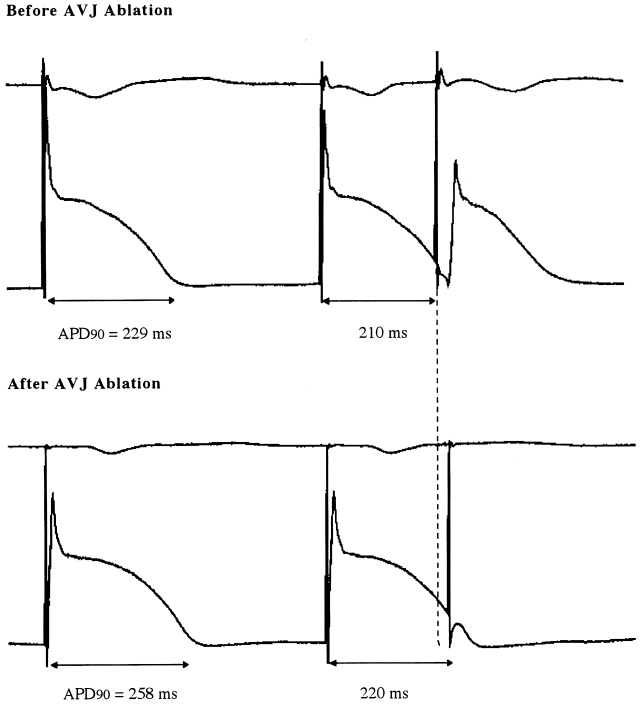

Figure 5. Monophasic action potential recordings obtained from the MAP catheter positioned at the RV apex during pacing at 120 beats/min. **Top,** Before ablation, APD_{90} was 229 ms and ERP was 200 ms, with evidence of capture at a coupling interval equal to 210 ms. **Bottom,** After ablation, APD_{90} increased to 258 ms and premature stimuli delivered at a coupling interval of 220 ms failed to capture. The ERP increased from 200 ms before ablation to 220 ms after ablation.

application of RF energy nor the resulting lesion that was presumably produced appeared to affect basal SNA or hemodynamic conditions. However, when AV block was achieved and pacing was performed at 60 beats/min, SNA increased significantly above the preablation baseline value during AF (by ~30%). This was associated with a small, but significant decrease in mean and diastolic BP, suggesting that the sympathoexcitation was partly due to a reflex-mediated effect. However, the elevation of SNA persisted throughout the postablation period of measurement, despite a return of both mean and diastolic BP to preablation levels. This may reflect that baroreflex-mediated sympathoexcitation adequately corrected the modest hypotension after successful ablation; however, other explanations may also be involved. A direct effect of RV pacing on cardiopulmonary receptors is a possible explanation that we think is very unlikely. Smith et al. (16) have shown that RV pacing produces similar hemodynamic and SNA responses to spontaneous ventricular tachycardia of the same rate. Direct activation of SNA by a small cardiac lesion could occur as a result of disruption of cardioinhibitory afferent signals, resulting in sympathoexcitation. Although this scenario is possible, we believe this is unlikely because of the size of the lesion. Another possible related mechanism could be a change in cardiac filling pressures—the stimulus for cardiopulmonary baroreceptors. We did not measure intracardiac pressures during this study because of the required additional venous access and the risk of dislodging the temporary pacemaker during manipulation of the pulmonary artery catheter. However, the hemodynamic effects of AF and ventricular pacing at 60 beats/min after AVJ ablation have been reported: Clark et al. (17) showed no significant change in right atrial and pulmonary capillary wedge pressures in patients with AF after AVJ ablation and pacing at 60 beats/min. Blood pressure fluctuations during AF are variable and include periodic, large elevations, as shown in Figure 1. Because all the patients studied had very high basal SNA, these periodic increases in arterial pressure tend to inhibit SNA. Therefore, successful AVJ ablation may serve to stabilize these arterial pressure fluctuations, so that the patient's high basal SNA is allowed to run uninhibited. This is consistent with preliminary data from our group suggesting that the net SNA response to high rates of ectopy (e.g., bigeminy) is a *reduction* in SNA in patients with very high basal SNA, which is in contrast to a normal *increase* in SNA during high rates of ectopy in most patients.

When the postablation ventricle was paced at 90 beats/min, mean and diastolic BPs were increased significantly, compared with pacing at 60 beats/min, and this resulted in a reflex-mediated decrease in SNA. This decrease in SNA was to a level that was below the preablation baseline levels during AF. These data show that one of the hemodynamic benefits of an elevated pacing rate is a reduction in the chronically elevated SNA level, not only in relation to postablation pacing at 60 beats/min but also in relation to the preablation state. The potential clinical relevance of these findings are discussed subsequently.

Alterations in autonomic innervation after RF ablation. Several authors have described an increase in the sinus rate after ablation of para-Hisian accessory pathways (18), after AV node modification using the posterior approach and after ablation of posteroseptal accessory pathways (19–21). In an effort to investigate the autonomic changes that follow RF ablation, analysis of HR variability has been used

Table 3. Pacing at 120 Beats/Min

	APD_{90} (ms)	ERP (ms)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	SNA (U/10 s)
Before RF ablation	242 ± 17	215 ± 14	133 ± 14	79 ± 7	97 ± 10	642 ± 59
After AV block	261 ± 12	233 ± 16	136 ± 16	81 ± 8	99 ± 11	621 ± 48
p Value	< 0.01	< 0.01	NS	NS	NS	NS

Data are presented as the mean value ± SEM.
APD_{90} = duration of action potential at 90% repolarization; AV = atrioventricular; ERP = effective refractory period; NS = not significant; RF = radiofrequency; other abbreviations as in Table 2.

(19,20). Most of these studies revealed a significant reduction in the high frequency components of the HR frequency spectra, indicating that parasympathetic denervation of the sinus node may have occurred, which was then reversed within one to six months, suggesting that reinnervation may have occurred. Although most of these studies suggested parasympathetic denervation, some data were also suggestive of sympathetic denervation (19–22).

In our study, we could not use measures of HR variability owing to the presence of AF and postablation complete AV block. Therefore, we used cardiac electrophysiologic properties to assess changes in cardiac autonomic function. We demonstrated an increase in right ventricular APD and ERP after successful AVJ ablation. These findings were present in every patient, and the changes reached statistical significance. In our opinion, this could be explained by downstream myocardial denervation. Transmural myocardial infarction has been shown to interrupt sympathetic and vagal transmission over axons located within the region of infarction and produce "downstream" sympathetic and vagal denervation at non–infarct-related sites apical to the infarction (23,24). If RF ablation results in myocardial denervation, our findings of prolonged RV APD and ERP would suggest predominance of sympathetic innervation. Another possible explanation for the APD and ERP prolongation after AVJ ablation may be the effect of sustained tachycardia during AF on ventricular refractoriness. Recently, Krebs et al. (25) demonstrated, for the first time in humans, that short-term rapid ventricular pacing prolongs ventricular refractoriness. In patients with poorly controlled AF, you would expect the tachycardia-induced changes in ventricular refractoriness to be present even before AVJ ablation. In our study, we found a change in APD and ERP after AV block. Therefore, unless tachycardia-induced changes in ventricular refractoriness manifest only after slowing of the heart rate, we find it hard to explain our results with the latter hypothesis.

Ventricular arrhythmias after AVJ ablation. Ventricular fibrillation was reported after RF ablation and was attributed to the slow HR associated with AV block. Interestingly, patients with AF and spontaneous AV block, paced at 60 beats/min, do not experience a similar incidence of sudden death. In this latter group, we think the decrease in HR is gradual, and as such, these patients are less likely to have acute hemodynamic, neural and electrophysiologic changes. In addition, one cannot exclude a proarrhythmic effect of the RF ablation itself, as previously discussed. In our present study, one patient of 10 had frequent episodes of PMVT two weeks after the procedure. It is conceivable that these episodes had nothing to do with the procedure. However, the presence of only one event before AVJ ablation, the occurrence of >20 episodes after the procedure and the mode of initiation (long–short) with every episode suggest that this was a complication.

Clinical implications. Our findings help explain the mechanism responsible for malignant ventricular arrhythmias after AVJ ablation. The increase in SNA in the setting of prolonged APD creates a milieu that favors early afterdepolarizations and triggered activity, which can result in PMVT, a known complication of AVJ ablation. The decrease in SNA and shortening of APD with rapid pacing may also explain the lower incidence of PMVT with rapid pacing. These results indicate that increased SNA may play a role in the pathogenesis of PMVT, and that bradycardia is not the only factor involved. In fact, if cardiac denervation occurs after ablation, then the increase in SNA can be potentially proarrhythmic in many ways, as denervated tissue may become supersensitive to certain agents such as catecholamines.

Study limitations. There are limitations of this study: 1) We did not measure APD and ERP at 60 beats/min before ablation, and therefore an increase in APD duration after ablation at 60 beats/min can only be assumed to be true, on the basis of measurements obtained at 120 beats/min. The APD and ERP were not measured at 60 beats/min because the ventricular response during AF was significantly higher than 60 beats/min. 2) We did not assess the SNA response during RF ablation at other sites to see whether the changes were specific to anteroseptal ablation. Although this is true, the lack of any change in SNA during unsuccessful ablation indicates to us that the increase in SNA was secondary to AV block and was not a direct effect of the RF lesions. Thus, these unsuccessful lesions served as our control data. 3) We did not measure right and left atrial pressures during the study. Although some authors have shown no change in central venous pressure after AVJ ablation, changes in cardiac filling pressures might have played a role by changing the input to the cardiopulmonary baroreceptors and their modulation of SNA. 4) Finally, the number of patients was small. However, the changes in this study were present in every patient, were very consistent and were statistically significant.

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