Changes in Myocardial Blood Flow During Development of and Recovery From Tachycardia-Induced Cardiomyopathy

Francis G. Spinale, PhD; Ryuhei Tanaka, MD; Fred A. Crawford, MD; and Michael R. Zile, MD

Background. Chronic supraventricular tachycardia (SVT) causes a dilated cardiomyopathy and myocyte injury. Termination of SVT improves left ventricular (LV) function but is associated with LV hypertrophy. Changes in myocardial blood flow (MBF) that may accompany the development of and recovery from SVT cardiomyopathy might have a significant effect on LV function and myocyte structure. The goal of this study was to relate changes in LV function, myocyte composition, and coronary vascular structure to changes in MBF with the development and recovery of SVT cardiomyopathy.

Methods and Results. LV function and MBF were measured in three groups of conscious pigs: sham control (control; n=8), after 3 weeks of atrial pacing (SVT, 240 beats per minute; n=8), and after a 4-week recovery from SVT (post-SVT; n=8) by echocardiography catheterization and microspheres. Measurements were made under three states: 1) at rest with a basal heart rate, 2) rapid atrial pacing (240 beats per minute), and 3) during adenosine infusion (1.5 μmol/l·kg⁻¹·min⁻¹) without pacing. LV myocyte, capillary, and arteriole morphometric studies were performed in five additional pigs from each group using histochemistry and electron microscopy. LV fractional shortening was lower and left atrial pressure was significantly higher in the SVT group compared with rest, during pacing, and with adenosine (p<0.05). In the post-SVT group, fractional shortening returned to control values at rest and with adenosine, but fell from control values with pacing (p<0.05). Left atrial pressure fell in the post-SVT group but remained significantly higher than control (p<0.05). LV/body weight ratio was significantly increased in the post-SVT group (p<0.05). In all states, SVT LVMBF was significantly reduced from control values (rest, 0.8±0.3 versus 1.6±0.3 ml·min⁻¹·g⁻¹; pacing, 1.2±0.2 versus 3.1±0.3 ml·min⁻¹·g⁻¹; adenosine, 1.4±0.3 versus 4.4±0.4 ml·min⁻¹·g⁻¹, respectively, p<0.05). In the post-SVT group, LVMBF was similar to control at rest (1.3±0.2 ml·min⁻¹·g⁻¹) but was significantly lower than control with pacing and adenosine (2.0±0.4 and 2.5±0.5 ml·min⁻¹·g⁻¹, respectively, p<0.05). Myofibrillar content fell significantly with SVT compared with control (42±5 versus 61±3%, p<0.05) and returned to control values in the post-SVT group (64±3%). Capillary density remained unchanged in the SVT and post-SVT groups, but capillary luminal diameter decreased and arteriole diameter increased in the SVT group (p<0.05).

Conclusions. The LV dysfunction and myocyte injury with SVT cardiomyopathy were associated with reduced MBF. Early recovery from SVT cardiomyopathy resulted in hypertrophy with normal MBF at rest, but significantly reduced coronary reserve. (Circulation 1992;85:717–729)

Chronic incessant tachycardia has been clearly shown to cause congestive cardiomyopathy in humans and animals.¹⁻⁴ The development of this form of cardiomyopathy occurs over a relatively short time and is characterized by significant chamber dilatation, reduced wall thickness, and decreased contractile state.¹,² Recent animal studies have shown that tachycardia-induced cardiomyopathy is associated with significant structural alterations suggestive of myocyte injury.¹ Thus, reduced myocard}

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dial blood flow is a potential contributory mechanism for the alterations in myocardial structure and function with tachycardia-induced cardiomyopathy.

Unlike irreversible dilated cardiomyopathies, such as idiopathic or viral, recovery from tachycardia-induced cardiomyopathy can be achieved through pharmacological management, surgical excision of the accessory pathway, or catheter ablation.\(^5,6\) Termination of the tachycardia after the development of cardiomyopathy in humans causes the symptoms of congestive heart failure to resolve.\(^5,6\) In a recent study from our laboratory, however, we reported that recovery from supraventricular tachycardia (SVT)—induced cardiomyopathy in pigs was associated with significant hypertrophy and persistent diastolic dysfunction.\(^2\) A study by Hittinger and colleagues\(^7\) demonstrated that reduced subendocardial blood flow was a potential mechanism for the impairment in diastolic function that follows the development of hypertrophy and heart failure. Thus, it is possible that the hypertrophy and diastolic dysfunction that occur during the recovery phase of tachycardia-induced cardiomyopathy may be caused by changes in the distribution of myocardial blood flow.

Although myocardial blood flow is dependent on coronary perfusion pressure and end-diastolic pressure, it is influenced significantly by the precapillary resistance vessels.\(^8,9\) Changes in the structure and distribution of these major resistance vessels have been suggested as a potential cause of alterations in myocardial blood flow with the development of pressure overload hypertrophy.\(^9\) Thus, alterations in the structure and distribution of the coronary arterioles may be a contributing factor to the reduced myocardial blood flow with tachycardia-induced cardiomyopathy. More importantly, it is unknown whether adequate proliferation in the coronary vasculature occurs with the hypertrophic response after termination of the tachycardia.

The overall goal of the present study was to relate changes in left ventricular (LV) function, myocyte composition, and structure of the coronary vasculature to myocardial blood flow in a model of SVT-induced cardiomyopathy and recovery. Specifically, this study was designed to answer three important questions regarding tachycardia-induced cardiomyopathy. First, is there a direct relation between myocyte injury and reduced myocardial blood flow with SVT cardiomyopathy? Second, do changes in myocardial blood flow accompany the hypertrophic recovery from SVT cardiomyopathy? Finally, where myocardial perfusion abnormalities are identified during the development and recovery of SVT cardiomyopathy, are these changes primarily a hemodynamic phenomenon or are there structural alterations in the coronary vasculature that contribute to this reduction in blood flow?

**Methods**

*Experimental Preparation*

Twenty-four Yorkshire pigs matched for age and weight (23–25 kg, 5 months old) were used in the study. Eight pigs were randomly assigned to each of three groups: 1) rapid atrial pacing (240 beats per minute) for 3 weeks (SVT), 2) atrial pacing at 240 beats per minute for 3 weeks followed by deactivation of the pacemaker and a 4-week recovery period (post-SVT), and 3) sham-operated controls. The pigs were chronically instrumented so that subsequent measurements of LV pressure, dimensions, and myocardial blood flow could be made in the conscious state.

The pigs were anesthetized with isoflurane (2.0%, 1.5 l/min) and nitrous oxide (0.5 l/min), intubated, and ventilated at a flow rate of 22 ml/kg/min and a respiratory rate of 15 breaths per minute. A sterile left thoracotomy was performed from the fourth intercostal space, and the heart was exposed by a pericardiotomy. A polyethylene catheter (1.67-mm i.d., Becton Dickinson Co., Rutherford, N.J.) pretreated with heparin (TDMAC, Polysciences, Inc., Warrington, Pa.) was implanted in the left atrium. The catheter was exteriorized through a dorsal percutaneous puncture and filled with a heparin solution (1,000 units/cm\(^3\)). A shielded stimulating electrode was sutured onto the left atrium, connected to a programmable pacemaker modified for programming heart rates up to 300 beats per minute (Spectrax, Medtronic, Inc., Minneapolis, Minn.), and buried in a subcutaneous pocket. The pericardium was left open, the thoracotomy closed, and the pleural space evacuated of air. Using sterile technique, the left carotid artery was then exposed and a second catheter advanced into the ascending aorta. This catheter was tunneled dorsally and prepared as described above. Each pig was fitted with a nylon mesh jacket containing an instrument pocket to protect the catheters from contamination and damage. Systemic cepazolin sodium (50 mg/kg) was administered daily for 7 days after surgery. Following a 10-day recovery period, the pigs were returned to the laboratory, and a baseline echocardiogram (ECG) was obtained by procedures described in the following section. The pacemaker was activated to 240 beats per minute, and an ECG was obtained to ensure 1:1 conduction. During the pacing protocol, the pigs were auscultated daily to ensure pacemaker capture. The pigs in the SVT and post-SVT groups were paced for 3 weeks. We have previously shown that this pacing rate and duration will reliably produce LV dilatation and dysfunction.\(^1,2\) The control pigs were treated in identical fashion with the exception of pacemaker activation. All pigs were treated and cared for in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals.\(^10\)

**Ventricular Function and Myocardial Blood Flow Studies**

Pressures, LV dimensions, and myocardial blood flow were measured in these conscious pigs under three experimental conditions: 1) at a basal, spontaneous heart rate; 2) with acute atrial pacing (240 beats per minute); and 3) after vasodilatation with
adenosine at a basal heart rate. On the day of study, the pig was sedated with 10 mg of midazolam (Versed, Hoffman-La Roche, Inc., Nutley, N.J.), placed in a custom-designed sling, and brought to the laboratory. An ECG was established, the atrial and aortic catheters were flushed, and the pacemaker was deactivated. The laboratory was dimly illuminated and kept quiet to avoid disturbing the pig. After a 30-minute stabilization period, simultaneous pressures and echocardiographic recordings were performed. Pressures from the fluid-filled catheters were obtained with externally calibrated transducers (Statham P23ID, Gould, Oxnard, Calif.) and a pressure amplifier (78304A, Hewlett Packard Corp., Andover, Mass.). The ECG and pressure waveforms were recorded with a multichannel recorder (Western Graphtec, FWR3701, Irvine, Calif.). Two-dimensional and M-mode echocardiographic studies (ATL Ultramark VI, 2.5-MHz transducer, Bothell, Wash.) were used to image the LV from a right parasternal approach. Measurements were made according to the criteria of the American Society of Echocardiography. End systole was defined as the peak downward motion of the interventricular septum. End diastole was defined as the onset of the Q wave of the ECG. Dimensions, thickness, and pressure recordings were obtained simultaneously at 100 mm/sec for subsequent analysis.

Immediately after collection of echocardiographic and pressure measurements, measurements of regional myocardial blood flow were made. Microspheres 15 μm in diameter labeled with either 141Ce, 51Cr, or 103Ru (NEN Research Products, Wilmington, Del.) were used in random order in this study. The stock solutions of microspheres suspended in 10% Dextran with 0.01% Tween 80 were mixed for 30 minutes in an ultrasonic bath and vortex agitated immediately before use. The microsphere injection and aortic sampling procedures have been described previously. Briefly, 3×10⁶ microspheres were injected through the left atrial line, followed immediately by a 3-cm³ saline flush over a 10-second interval. Beginning 20 seconds before the microsphere injection and continuing for 100 seconds, a reference sample of arterial blood was collected from the aortic catheter at a constant rate of 7.34 ml/min with a withdrawal pump (600–900 V, Harvard Apparatus, South Natick, Mass.).

After pressure-echocardiographic recordings and microsphere injection at a basal, resting heart rate, the pacemaker was activated to 240 beats per minute. After a 15-minute stabilization period at this heart rate, the measurements described above were repeated. Rapid atrial pacing was discontinued 5 minutes after injection of the microspheres. After a 30-minute stabilization period, an intravenous infusion of adenosine (1.5 mg·kg⁻¹·min⁻¹) was begun. Pressure, echocardiographic, and blood flow measurements were made during the adenosine infusion after stable hemodynamics were obtained. This dosage of adenosine has been shown previously to cause maximal coronary vasodilatation in swine. Upon completion of the final set of measurements, 20 mg of pentobarbital was administered, a sternotomy was performed, and the heart was removed. The great vessels were removed at the aortic and pulmonary valves, and the LV was weighed and immersed in 10% buffered formalin for 5 days to facilitate slicing.

Ventricular function and blood flow analysis. LV fractional shortening (FS) was computed as

\[
FS(\%) = \frac{(EDD - ESD)}{EDD} \times 100
\]

where EDD is the end-diastolic dimension and ESD is the end-systolic dimension. An index of circumferential global average wall stress was computed at end-systole and end-diastole with a spherical model:

\[
\sigma(g/cm^2) = \frac{PD/4h(1 + h/D)}{1.36}
\]

where \(\sigma\) represents stress, \(P\) represents pressure, \(D\) is the minor axis dimension, and \(h\) is the wall thickness. Mean left atrial pressure was taken as an index of LV diastolic pressure. Left atrial pressure and LV end-diastolic dimension and wall thickness were used to compute an index of end-diastolic stress. Peak systolic arterial pressure and LV end-systolic dimension and wall thickness were used to compute an index of end-systolic stress. The rate-pressure product was computed as the product of heart rate and systolic aortic pressure.

The fixed LV was sectioned into three transverse sections parallel to the mitral valve ring, and each of these sections was separated into endocardial and epicardial layers. Each of these sections was weighed and placed into scintillation vials for counting. Myocardial and blood reference samples were counted on a gamma spectrometer (Gamma 8000, Beckman Instruments Co., Fullerton, Calif.) at window settings selected to correspond to the peak emissions of each radionuclide. The counts per minute were digitally recorded and transferred to an 80286 microcomputer (Z-200, Zenith Data Systems Corp., St. Joseph, Mich.) for correction of background activity, realignment with corresponding myocardial weights, and subsequent blood flow computations. Flow per gram of myocardial tissue (Qm) was computed from the following equation:

\[
Q_m = Q_r \times C_m/C_r
\]

where \(Q_r\) is the rate of withdrawal of the aortic reference blood sample, \(C_m\) is the radioactive counts per gram of myocardium, and \(C_r\) is the activity of the reference blood sample. Myocardial blood flow values were computed for the endocardial and epicardial regions, and the ratio of endocardial to epicardial blood flow was determined. Coronary vascular resistance for each region was determined from the formula:

\[
CVR = (MAP - LAP)/MCF
\]

where CVR is coronary vascular resistance (mm Hg·min/ml·g), MAP is mean arterial pressure, LAP is mean left atrial pressure, and MCF is mean coronary flow.
Myocyte and Coronary Vessel Morphometric Studies

Because of the tissue preparation requirements, fixation methods used, and the intrinsic radiation levels, sections from the myocardial blood flow study were unacceptable for coronary and myocyte morphometric studies. Accordingly, 15 additional pigs were randomly assigned to the control group (n=5), the SVT group (n=5), or the post-SVT group (n=5). The pigs were treated identically to those described in the preceding section except for chronic catheter placement. These pigs were used for morphometric examination of LV myocytes, capillaries, and coronary arterioles. On the day of study, the pigs were brought to the laboratory, an ECG was established, and the pacemaker was deactivated. After a 30-minute stabilization period, each pig was anesthetized with isoflurane (0.5%, 1.5 l/min), a carotid artery was exposed, and an externally calibrated micromanometer-tipped transducer (PPG Biomedical Systems, Pleasantville, N.Y.) was positioned in the LV. Pressure and echocardiographic data were recorded as previously described. After LV pressure and dimension measurements, 20 mg of pentobarbital was administered, a sternotomy was performed, and the heart was arrested in diastole with chilled KCl (40 meq/ml). The heart was quickly extirpated and placed in a phosphate-buffered ice slush. The left coronary artery was cannulated and perfused with isotonic saline followed by a buffered sodium cacodylate solution containing 2% paraformaldehyde and 2% glutaraldehyde (pH 7.4, 750 mosm) at a perfusion pressure of 100 mm Hg. After delivery of 1 l of perfusion solution, the LV free wall was removed and sectioned in 4-mm increments from base to apex. Sections were taken from the apex, midventricular region, and base of the LV and prepared for myocyte ultrastructural examination and morphological quantification of capillaries and precapillary arterioles. Finally, a 2 x 4-cm section was taken from the posterior LV free wall for measurement of water content. These sections were weighed, placed in a 37°C oven, dried for 48 hours, and reweighed. Water content was determined as (wet weight−dry weight)/wet weight and expressed as a percentage.

Myocyte ultrastructure. LV sections prepared for electron microscopy were finely minced, rinsed in 0.1 mol/l phosphate buffer, postosmicated for 1 hour in 1% osmium tetroxide, dehydrated, and embedded in Spurr's resin (Ted Pella Inc., Tustin, Calif.). Two grids containing three thin-sections each were prepared from each specimen. Thin-sections were stained with uranyl acetate and lead citrate and examined with a JEOL 100S electron microscope. Five random electron micrographs were taken of cross-sectional capillaries from each grid and printed at a calibrated magnification of ×5,000. These electron micrographs were coded and this code was not broken until completion of the study. Ultrastructural evaluations of myocytes within the control, SVT, and post-SVT sections were made by well-described morphometric techniques. From the circumferentially oriented micrographs, the percent volume of myofibrils and mitochondria within myocytes was analyzed morphometrically by use of a stereology sampling grid consisting of 140 sampling points.

Capillary morphometry. Recent reports have shown that histochemical staining with the lectin Griffonia simplicifolia (GSA-B4) is a sensitive and reliable method to visualize the entire capillary vasculature within skeletal and cardiac muscle. Accordingly, LV sections from the present study were stained with GSA-B4 (Sigma Chemical Co., St. Louis, Mo.) in order to examine the morphology of the capillary bed. LV sample blocks were dehydrated through graded ethanol, cleared in xylenes, and embedded in paraplast, and 10 sections 5 μm thick were cut from the blocks and mounted on glass slides. Immediately before lectin staining, the tissue was deparaffinized in xylene, rehydrated in descending series of alcohols, and placed in phosphate-buffered saline (PBS) for 30 minutes. GSA-B4 conjugated to horseradish peroxidase was diluted 1:50 in PBS and incubated on the tissue sections for 2 hours in a humidified chamber at 37°C. The slides were then thoroughly rinsed in PBS. Sites of bound lectin were visualized by incubation in a 3′,3′-diaminobenzidine–hydrogen peroxide substrate medium followed by two additional rinses in PBS. The tissue sections were then dehydrated through a graded series of ethanol and xylenes and coverslipped. Controls for lectin staining consisted of substituting nonconjugated lectin for the first step of the staining procedure. The stained LV sections were mounted on an inverted microscope (IM-35, Zeiss, Munich, FRG), and circumferentially oriented capillaries were imaged at a final magnification of ×400. The image was entered through a high-resolution video camera (Dage 68, Michigan City, Ind.) connected to a computer image analysis system (IBAS 2000, Zeiss/Kontron, Munich, FRG). For each LV section, 10 random fields with an area of 25,390 μm² per field were analyzed. Only myocardial sections cut perpendicular to the long axis were analyzed, which placed the myocytes and capillaries in a circumferentially oriented position with respect to the microscope objective and provided a reliable means to count capillary profiles. Areas of fibrosis or cutting artifact were not included in the analysis. With computer-aided stereology, the number per unit area (numerical density) and the mean diameter of the capillaries within the myocardial sample were computed. A computer-generated test frame automatically discriminated the capillary profiles and determined the number of profiles within the test area by exclusion-edge principles. Capillary diameter was computed by measuring the area of a stained vessel, transforming this area into a circle, and computing the diameter. This method for determining capillary diameter was used to avoid computational errors for vessels in a transverse orientation.

Arteriolar morphometry. Three full-thickness LV blocks (endocardium to epicardium) from each pig.
were dehydrated in alcohols and embedded in paraplast. From these embedded blocks, 10 sections 5 μm thick were cut and stained with hematoxylin and eosin. These sections were viewed with the image analysis system described in the preceding paragraph at a final magnification of ×200. Cross-sectional profiles of arterioles were digitized, and the lumen diameter and wall/lumen ratios were determined as previously described.21,23 The entire section was scanned, and all precapillary vessels less than 100 μm in diameter were digitized and analyzed. To minimize the effects of measuring some of these vessels at an oblique angle, the smallest diameter of the vessel was considered representative of lumen diameter.23 Wall thickness was determined from the same axis used to determine lumen diameter and was computed as the length of the line extending from the luminal surface of the endothelial cell to the exterior surface of the tunica media. With this sampling scheme, 30 full-thickness sections were analyzed from each pig. In a pilot study using control sections, this sampling scheme resulted in less than a 5% coefficient of variation for arteriolar lumen diameter and wall thickness.

Data Analysis and Statistics

Indexes of LV function and myocardial blood flow values were compared among the sham control group, the SVT group, and the post-SVT group under the three different experimental conditions used in the study (basal, rapid pacing, and adenosine infusion) by multiway ANOVA. If ANOVA revealed significant differences, pairwise tests of individual group means were compared by Tukey’s procedure.24 Indexes of LV function obtained from the pigs used in the capillary morphometry study were compared by one-way ANOVA.24 Analysis of the myocyte, capillary, and arteriole morphological data used the average measurements obtained for each pig, and the control and experimental groups were compared by ANOVA. Before ANOVA was performed on the morphometric data, homogeneity of variances of each morphometric variable for the three groups was confirmed by Bartlett’s test.24 If ANOVA revealed significant differences, pairwise tests of individual group means were compared by Tukey’s procedure.24 In addition to determining an overall mean for arteriolar diameter, the vessels were classified into one of four size classes: <25, 25–49, 50–74, and 75–100 μm. Comparison of the distribution of these size classes for the three groups was made by χ² analysis. Results are presented as mean±SEM. Values of p<0.05 were considered to be statistically significant.

Results

All of the pigs in the pacing protocol developed congestive heart failure as evidenced by dyspnea, ascites, and peripheral edema within 22–26 days of pacemaker activation. These symptoms and signs resolved in the post-SVT group within 7–10 days after pacemaker deactivation.

Ventricular Function

There was no significant difference in LV mass–to–body weight ratio between the control and SVT group (2.6±0.2 g/kg versus 2.9±0.3 g/kg, respectively, p=0.45). In contrast, termination of SVT and a 4-week recovery period resulted in a significant increase in LV mass–to–body weight ratio (4.2±0.2 g/kg, p<0.05). Indexes of LV function and hemodynamics at a basal spontaneous heart rate, during acute rapid atrial pacing, and following adenosine infusion are summarized in Table 1.

Basal state. In the SVT group, heart rate was significantly higher and mean arterial pressure significantly lower than in the control group. The rate–pressure product was significantly higher in the SVT group than in the control group. Chronic SVT resulted in increased left atrial pressure, significantly increased LV dimensions, reduced LV wall thickness, and significantly lower fractional shortening. These changes in LV architecture and pressure resulted in significantly higher indexes of wall stress in the chronic SVT group (p<0.05). In the post-SVT group, LV fractional shortening returned to control values. LV dimensions, atrial pressure, and wall stress, however, remained significantly higher than in controls. Thus, at this basal resting state, the determinants of myocardial oxygen demand (increased heart rate, rate–pressure product, and LV wall stress) were higher in the SVT group than in controls. In the post-SVT group, these indexes of myocardial oxygen demand declined significantly.

Rapid atrial pacing. In the control pigs, rapid atrial pacing at 240 beats per minute increased left atrial pressure, decreased LV dimensions, increased LV wall thickness, and decreased fractional shortening. In the SVT group, rapid atrial pacing did not change these parameters compared with the basal state. In the post-SVT group, left atrial pressure increased significantly compared with control values and was equivalent to SVT atrial pressures. A significant increase from basal-state values in the rate–pressure product during pacing was observed in all three groups.

Adenosine infusion. In the control group, adenosine administration resulted in increased fractional shortening, reduced mean arterial pressure, and a decline in the rate–pressure product. Similarly, in the chronic SVT group, adenosine infusion resulted in improved fractional shortening, reduced mean arterial pressure, and reduced rate–pressure product from basal conditions. Heart rate, the rate–pressure product, and LV wall stress all remained significantly higher in the SVT group versus the control group, however. In the post-SVT group, fractional shortening and left atrial pressure returned to basal-state values.
Myocardial Blood Flow

LV endocardial and epicardial blood flow values are summarized in Table 2. In the control group, rapid atrial pacing caused a twofold increase and adenosine infusion nearly a threefold increase in myocardial blood flow from the basal, resting state. In the chronic SVT group, basal myocardial blood flow was significantly lower than in the control group. Rapid atrial pacing significantly increased myocardial blood flow in the SVT group, but this value remained 50% lower than in the control group. In the SVT group, adenosine infusion did not increase myocardial blood flow above rapid pacing values. In the post-SVT group, myocardial blood flow was similar to that in the control group in the basal, resting state.

Acute rapid atrial pacing increased myocardial blood flow in the post-SVT group, but this value remained significantly lower than in the control group. During adenosine infusion, myocardial blood flow was 40% lower in the post-SVT group than in the control group.

Using average LV myocardial blood flow values, coronary vascular resistance was computed and is shown in Figure 1. In the control group, coronary vascular resistance fell significantly during acute rapid atrial pacing compared with the basal state and fell further during adenosine infusion. Coronary vascular resistance was higher in both the SVT and post-SVT groups in the basal state, but this did not reach statistical significance (p=0.25). Coronary vas-
Morphometry

Myocardial and during pacing significantly higher than control was used in the control group.

Myocardial Morphometry

LV size, mass, and function for the control and SVT pigs used in the morphometric studies are shown in Table 3. These data indicate that the pigs used to examine myocyte composition, capillary distribution, and arteriolar density and size were very similar to those used to study myocardial blood flow. Myocyte ultrastructure, capillary density, and arteriolar distribution were similar within the subendocardium, midmyocardium, and epicardium. In addition, there was no difference in morphometric parameters between sections taken from the LV apex or midventricular regions. Thus, these regions were combined for final analysis and data presentation. A summary of the morphometric measurements computed from the LV free wall of the control, SVT, and post-SVT groups is presented in Table 4.

Myocyte ultrastructure. In total, 520 electron micrographs were examined from the control, SVT, and post-SVT sections. Representative electron micrographs from each of these groups are shown in Figure 2. Myocytes from control tissue contained normal-appearing mitochondria and a dense distribution of myofibrils (Figure 2A). In the SVT myocytes, evidence of cell injury included clumping and margin-

![Graph showing coronary vascular resistance](image)

**Table 2.** Left Ventricular Myocardial Blood Flow in Conscious Pigs

<table>
<thead>
<tr>
<th></th>
<th>Basal state</th>
<th>Rapid atrial pacing</th>
<th>Adenosine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocardial blood flow (ml/min/g)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.7±0.3</td>
<td>3.0±0.3†</td>
<td>4.1±0.3†‡</td>
</tr>
<tr>
<td>Chronic SVT</td>
<td>0.8±0.2*</td>
<td>1.1±0.3†‡</td>
<td>1.2±0.7†‡</td>
</tr>
<tr>
<td>Post-SVT</td>
<td>1.4±0.4</td>
<td>1.9±0.3*</td>
<td>2.4±0.6†‡</td>
</tr>
<tr>
<td>Epicardial blood flow (ml/min/g)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.5±0.3</td>
<td>3.2±0.3†</td>
<td>4.6±0.4†‡</td>
</tr>
<tr>
<td>Chronic SVT</td>
<td>0.7±0.2*</td>
<td>1.4±0.3†‡</td>
<td>1.8±0.2†‡</td>
</tr>
<tr>
<td>Post-SVT</td>
<td>1.2±0.3</td>
<td>2.1±0.4†‡</td>
<td>2.6±0.3†‡</td>
</tr>
<tr>
<td>Endocardial/epicardial ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.1±0.2</td>
<td>0.9±0.1</td>
<td>0.9±0.2†</td>
</tr>
<tr>
<td>Chronic SVT</td>
<td>1.1±0.2</td>
<td>0.7±0.1†</td>
<td>0.8±0.1†</td>
</tr>
<tr>
<td>Post-SVT</td>
<td>1.2±0.1</td>
<td>0.8±0.2†</td>
<td>0.8±0.2†</td>
</tr>
</tbody>
</table>

Control, sham-operated controls (n=8); SVT, supraventricular tachycardia; chronic SVT, rapid atrial pacing for 3 weeks (n=8); post-SVT, chronic SVT followed by 4-week recovery period (n=8); basal state, resting basal heart rate; rapid atrial pacing, acute atrial pacing at 240 beats/min; adenosine, intravenous adenosine infusion (1.5 mg/kg/min).

*pSignificantly different from control values at respective state, p<0.05.
†Significantly different from control, SVT, and post-SVT values, p<0.05.
‡Significantly different from paced-state values, p<0.05.

![Graph showing coronary vascular resistance](image)

**Figure 1.** Bar graph shows that coronary vascular resistance was increased in the supraventricular tachycardia (SVT) group and the post-SVT group at rest compared with the control group but did not reach statistical significance (p=0.21). Coronary vascular resistance fell significantly from basal heart rate values with rapid atrial pacing and after adenosine infusion in the control, SVT, and post-SVT groups (p<0.05). However, coronary vascular resistance was significantly higher in the SVT and post-SVT group than in controls during pacing and adenosine infusion. bpm, Beats per minute. *p<0.05.

**Table 3.** Left Ventricular Function and Hemodynamics in Pigs Used in Morphometric Studies

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Chronic SVT</th>
<th>Post-SVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal heart rate (bpm)</td>
<td>98±5</td>
<td>148±7*</td>
<td>96±7</td>
</tr>
<tr>
<td>LV peak pressure (mm Hg)</td>
<td>88±5</td>
<td>76±5*</td>
<td>89±5</td>
</tr>
<tr>
<td>LV end-diastolic pressure (mm Hg)</td>
<td>5±2</td>
<td>26±4*</td>
<td>12±3*</td>
</tr>
<tr>
<td>LV fractional shortening (%)</td>
<td>33±3</td>
<td>13±5*</td>
<td>35±2</td>
</tr>
<tr>
<td>LV end-diastolic dimension (cm)</td>
<td>3.8±0.2</td>
<td>5.6±0.8*</td>
<td>5.3±0.4*</td>
</tr>
<tr>
<td>LV mass/body weight ratio (g/kg)</td>
<td>2.6±0.2</td>
<td>2.9±0.4</td>
<td>4.1±0.2*</td>
</tr>
<tr>
<td>Sample size</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

bpm, Beats per minute; LV, left ventricular; control, sham-operated controls; SVT, supraventricular tachycardia; chronic SVT, rapid atrial pacing for 3 weeks; post-SVT, chronic SVT followed by 4-week recovery period.

*Significantly different from control values, p<0.05.
TABLE 4. Myocardial Morphometry With the Development and Regression of SVT-Induced Cardiomyopathy

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Chronic SVT</th>
<th>Post-SVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capillaries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Density (no./mm²)</td>
<td>2,525±123</td>
<td>2,295±107</td>
<td>2,240±162</td>
</tr>
<tr>
<td>Diameter (µm)</td>
<td>7.8±0.2</td>
<td>7.3±0.3</td>
<td>7.9±0.4</td>
</tr>
<tr>
<td>Arterioles†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter (µm)</td>
<td>26±3</td>
<td>34±4*</td>
<td>25±4</td>
</tr>
<tr>
<td>Wall thickness (µm)</td>
<td>15±2</td>
<td>16±2</td>
<td>14±3</td>
</tr>
<tr>
<td>Wall/lumen ratio</td>
<td>0.68±0.04</td>
<td>0.56±0.03*</td>
<td>0.65±0.04*</td>
</tr>
<tr>
<td>Myocytes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myofibrils (%)</td>
<td>61±3</td>
<td>42±5*</td>
<td>64±3</td>
</tr>
<tr>
<td>Mitochondria (%)</td>
<td>20±2</td>
<td>22±5</td>
<td>26±3</td>
</tr>
<tr>
<td>Mitochondria/myofibrils</td>
<td>0.32±0.08</td>
<td>0.52±0.12*</td>
<td>0.41±0.09</td>
</tr>
<tr>
<td>Sample size</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

SVT, supraventricular tachycardia; control, sham-operated controls; chronic SVT, rapid atrial pacing for 3 weeks; post-SVT, chronic SVT followed by 4-week recovery period.
*Significantly different from control values, p<0.05.
†Arterioles defined as precapillary vessels with 100-µm minimal diameter or less.

Smitted in a significantly higher mitochondrial/myofibril ratio compared with the control group. Thus, the significant LV dysfunction observed in the SVT group was associated with a reduction in the percent volume of contractile material within the myocytes. In the post-SVT group, myofibrillar percent area increased significantly from SVT values. There was no significant difference in myofibril or mitochondrial percent area between the post-SVT group and the control group. Thus, the improved LV function observed in the post-SVT group was associated with a normalization of myofibrillar content.

Myocardial water content increased significantly with SVT compared with controls (80±4% versus 71±5%, respectively, p<0.05). Therefore, the reduced LV myofibril volume with SVT cardiomyopathy was associated with increased myocardial edema. In the post-SVT group, myocardial water content returned to control values (73±6%).

Capillary density. Histochemical staining of LV sections with the lectin GSA-B4 resulted in selective and uniform staining of the capillary vasculature in control, SVT, and post-SVT sections (Figure 3). Capillary density was reduced in the SVT group compared with control values; this difference, however, did not reach statistical significance (p=0.35). The overall average capillary luminal diameter was lower in the SVT group but did not reach statistical significance (p=0.25). Analysis of the frequency distribution for capillary diameter, however, revealed much higher frequency of capillaries with a diameter less than 5 µm in the SVT group than in controls.

FIGURE 2. Electron micrographs of histochemical staining with the lectin GSA-B4 reveal a uniform staining of capillaries within the left ventricular (LV) free wall sections taken from control, chronic supraventricular tachycardia (SVT), and post-SVT hearts. There was no significant difference in LV capillary density within the three groups. Representative electron micrographs from a control (panel A) and after 3 weeks of SVT (panel B) are shown. The identical procedure using unconjugated GSA-B4 resulted in abolution of all staining of the capillary vasculature (panel C). Original magnification, ×400.
Thus, in the SVT group, there was a significantly higher number of smaller capillaries within the LV free wall. There were no significant differences in capillary distribution or lumen diameter in the post-SVT group compared with controls.

**Arteriole morphometry.** In total, 1,150 arterioles were digitized from control sections, 1,375 from SVT sections, and 1,075 from post-SVT sections. A summary of arteriole diameter and wall thickness is shown in Table 4. Arteriole diameter was significantly higher in the SVT group than in the control and post-SVT groups. A frequency distribution of arteriole diameter for the three groups is shown in Figure 4. The number of arterioles less than 25 μm in diameter was significantly decreased in the SVT group compared with the control or post-SVT groups (Figure 4). There was no significant difference in arteriole wall thickness in the control, SVT, or post-SVT groups. As a result of the significantly increased lumen diameter, however, there was a significantly lower arteriole wall-to-lumen ratio in the SVT group than in the control or post-SVT groups.

**Discussion**

The objective of this study was to examine the relation between changes in LV function, myocyte composition, and myocardial blood flow with the development and recovery of SVT-induced cardiomyopathy. A second objective was to determine whether there was an association between structural changes in the coronary vasculature and changes in myocardial blood flow. The important findings of this study were that 1) the LV dysfunction and myocyte degeneration caused by chronic SVT were associated with a significant reduction in myocardial blood flow; 2) the hypertrophic response that followed early recovery from SVT cardiomyopathy normalizes LV function and myocardial blood flow at rest but results in significant LV dysfunction and reduced blood flow with stress; 3) the hypertrophy that followed recovery from SVT cardiomyopathy resulted in reduced coronary reserve; and 4) minimal changes in the coronary vasculature occurred with the development and recovery of SVT cardiomyopathy, suggesting that structural changes in the myocardial vascular bed were not the primary mechanism for the changes in myocardial blood flow patterns observed.

As previously reported by this laboratory and others,1,2,4–6 chronic SVT produced significant chamber dilatation, increased wall stress, and no change in LV/body weight ratio. Termination of chronic tachy-
Cardia resulted in a resolution of symptoms of congestive heart failure and significantly improved LV systolic function but was accompanied by persistent chamber dilatation and hypertension. We have previously reported that the early recovery phase from SVT cardiomyopathy in swine is associated with significant hypertension and diastolic dysfunction.\(^2\)

The present study builds upon these past studies by examining LV function with the development and recovery of SVT cardiomyopathy not only at rest but also during the acute onset of pacing and after maximal coronary vasodilatation. Results from this study demonstrated little change in hemodynamics or LV function during pacing or vasodilatation with SVT cardiomyopathy. In the early recovery phase from SVT cardiomyopathy (post-SVT), however, the acute onset of pacing resulted in significantly elevated left atrial pressure and reduced LV fractional shortening. These findings suggest that although a normalization of LV function may occur during the early recovery phase from SVT cardiomyopathy at rest, persistent abnormalities in LV systolic and diastolic function may exist with demand.

It has been demonstrated that in normal dog and swine hearts, myocardial blood flow increased significantly with acute rapid pacing.\(^25^-^27\) In the present study, the control pigs exhibited a similar increase in myocardial blood flow with acute pacing. In the SVT group, however, myocardial blood flow was reduced by more than 55% at rest as well as with pacing compared with control pigs. Thus, despite a significant increase in the determinants of myocardial oxygen demand with SVT cardiomyopathy, myocardial blood flow was significantly reduced. In the present study, rapid pacing in these post-SVT hearts was associated with reduced myocardial blood flow. Thus, a potential mechanism for the reduction in LV function after the acute onset of pacing in these post-cardiomyopathic hearts is a reduction in myocardial blood flow.

The hypertrophy that occurred after termination of chronic SVT was associated with normal myocardial blood flow in the basal, resting state. With rapid atrial pacing, however, myocardial blood flow was 33% lower than in the control group despite a significantly elevated rate–pressure product. Moreover, the endocardial/epicardial ratio fell, suggesting that an endocardial perfusion deficit occurred with rapid atrial pacing in these post-SVT hypertrophied hearts. These findings are similar to other forms of pressure overload hypertrophy where there is no apparent abnormality of myocardial blood flow at rest but myocardial blood flow fails to reach normal values with the acute onset of rapid pacing.\(^7^-^28\) The results from this study suggest that during the early recovery phase of SVT cardiomyopathy, increased demand (such as rapid pacing) cannot be met with an adequate increase in myocardial blood flow. Thus, an elevation in myocardial oxygen demand in these post-SVT hearts may result in underperfusion and myocardial ischemia.

Myocardial blood flow measurement during intravenous administration of adenosine is a well-established method to evaluate coronary reserve and minimal coronary vascular resistance.\(^7^-^13\) In the present study, adenosine infusion doubled myocardial blood flow in the control pigs compared with the basal state. With SVT cardiomyopathy, adenosine-mediated vasodilatation resulted in a relative increase in myocardial blood flow from the basal state. However, the absolute myocardial blood flow remained significantly lower in the SVT group than in the control pigs during adenosine. Also, myocardial blood flow during adenosine-mediated vasodilatation remained unchanged from rapid pacing values in the SVT cardiomyopathy group. These results suggest that during chronic SVT, myocardial blood flow was maximal. The increase in myocardial blood flow during adenosine administration was also significantly blunted in the post-SVT group compared with the control group. Maximal myocardial blood flow during adenosine was 45% lower in the post-SVT hearts than in controls. Thus, findings from the present study suggest that in the development of and during recovery from SVT cardiomyopathy, there is a significant impairment of myocardial blood flow reserve.

Capillary density with the development of and recovery from SVT cardiomyopathy did not change significantly from control values. In experimental models of hypertrophy, capillary density has been reported to increase, decrease, or remain unchanged depending on the etiology and duration of the heart failure.\(^20^-^22\) Tomanek et al\(^21\) reported that after renal hypertension in dogs, capillary density decreased. In volume overload hypertrophy, Wright and colleagues\(^29\) observed a significant decline in capillary density. In thyroxine-induced hypertrophy in the rat, Chilian et al\(^30\) reported an increase in capillary bed size. Finally, in cardiomyopathic Syrian hamsters, Figulla et al\(^31\) reported no change in capillary density compared with control animals. Although capillary density remained unchanged, capillary luminal diameter decreased significantly with SVT cardiomyopathy. One potential mechanism for this reduction in capillary luminal diameter in the SVT group may be increased compressive forces within the LV free wall. In the present study, SVT-induced cardiomyopathy was associated with increased myocardial water content. Increased extravascular water may have increased extravascular compression upon the capillaries. The hypertrophy associated with recovery from SVT cardiomyopathy resulted in no change in capillary density or diameter compared with control hearts. Therefore, results from the present study suggest that the development of and recovery from SVT cardiomyopathy was not associated with significant capillary rarefaction.

Arteriolar luminal diameters were increased in the SVT group compared with the control or the post-SVT groups. It is possible that SVT cardiomyopathy resulted in an increased distribution of larger-diam
arterioles as a result of long-standing smooth muscle dilatation. However, this parameter must be viewed with caution. The LV myocardium was perfusion fixed at a constant pressure of 100 mm Hg in vitro in all three groups. Therefore, intrinsic wall tension and ventricular volumes and pressures, which were different among the three groups, were not in force during fixation. Increased arteriolar compliance resulting from decreased smooth muscle patency of these vessels may also have influenced arteriolar diameter measurements. Thus, changes in arteriolar compliance may have occurred in the SVT cardiomyopathy group and allowed artificially increased luminal diameters after in vitro perfusion. While a large number of arterioles were examined in the present study, arteriolar numerical density was not computed. Actual numerical density of arterioles is much lower than that of capillaries and would therefore require a larger region of the myocardium be sampled from the three groups than was used in the present study. In addition, the arteriolar system is a highly branched network, and actual numerical density may be underestimated if only arteriole profile density is computed. Using a more rigorous geometric approach, Anversa and Capasso recently reported a reduction in the numerical density of medium-sized arterioles in rats with long-term renal hypertension. Results from the present study suggest that a redistribution of arteriolar size occurred with SVT cardiomyopathy. A future study directed at quantifying the specific changes in arteriolar density and distribution with SVT cardiomyopathy would be appropriate.

Although hemodynamic alterations contributed significantly to the changes in myocardial blood flow with SVT cardiomyopathy and recovery, changes in myocardial structure and composition may also have contributed to these changes. The collagen network surrounding capillaries provides extracellular support and maintains capillary patency throughout the cardiac cycle. Recent reports have identified significant changes in the extracellular matrix with chronic tachycardia. Weber et al reported interstitial edema and disruption of the collagen weave between myocytes with the development of tachycardia-induced heart failure in dogs. Our laboratory reported previously that SVT cardiomyopathy was associated with disruption and dissolution of the fibrillar collagen network surrounding adjoining myocytes and capillaries. In the present study, a significant increase in myocardial water content was observed with SVT cardiomyopathy. This reduction in collagen-mediated capillary support, interstitial edema, and increased LV wall stress that occurred with chronic SVT may have resulted in increased capillary and arteriolar compression. Weber and colleagues also reported that ventricular tachycardia was associated with arteriolar smooth muscle degeneration. These changes in arteriolar composition may also play a role in the reduced myocardial blood flow with SVT-induced cardiomyopathy.

Myocardial blood flow is determined primarily by the pressure gradient across the vascular bed, extravascular pressure, and local autoregulatory responsiveness of arteriolar smooth muscle. In the present study, SVT cardiomyopathy resulted in a decrease of more than 50% in the myocardial perfusion gradient (the difference between mean arterial pressure and left atrial pressure) at rest, with rapid pacing, and during adenosine infusion. During diastole, the intraventricular pressure constitutes a major source of extravascular coronary resistance. Diastolic pressure (as estimated by left atrial pressure) was significantly increased with chronic SVT; therefore, extravascular resistance was increased. In addition, extravascular compression forces, which include physical compression and twisting of the coronary vessels, may impede myocardial perfusion. The significant LV dilatation and wall thinning that occurred with chronic SVT may have resulted in increased exposure of the coronary vasculature to these compressive and shear forces. The increased diameter of the arteriolar bed with SVT cardiomyopathy after in vitro perfusion suggested decreased elastance of these capillary vessels. Thus, with increased extravascular compression and reduced perfusion pressure, these vessels may have reduced patency in vivo.

In the early recovery phase from SVT cardiomyopathy, LV hypertrophy occurred with a normalization of coronary perfusion pressure and myocardial blood flow at rest. In these post-SVT pigs, however, myocardial blood flow was significantly attenuated with rapid pacing. With the acute onset of pacing in these hypertrophied hearts, left atrial pressure increased significantly with no change in aortic pressure, thereby reducing coronary driving pressure. Indeed, net coronary perfusion pressure fell 57% with the acute onset of pacing in the post-SVT group compared with controls. We have previously reported that the early recovery from SVT cardiomyopathy was associated with diastolic dysfunction. In the present study, the significantly increased LV diastolic pressures observed with acute rapid pacing in these post-SVT hearts are most likely caused by this persistence in diastolic dysfunction. During adenosine infusion, presumably in the absence of autoregulation, myocardial blood flow remained significantly lower in the post-SVT group than in controls. With adenosine, the net coronary driving pressures remained lower in the post-SVT pigs than in control pigs because of a persistent elevation in left atrial pressure. These findings suggest that one major mechanism for reduced myocardial blood flow with rapid pacing or with vasodilatation during the early recovery period of SVT cardiomyopathy is increased extravascular resistance caused by elevated LV diastolic pressures.

It has been reported previously that plasma norepinephrine levels are significantly increased with pacing-induced cardiomyopathy. Moreover, elevated plasma norepinephrine levels persist after termination of pacing. Several studies have identified...
a significant relation between catecholamine stimulation and the development of hypertrophy.37,38 Jalil et al37 reported significant hypertrophy and collagen accumulation in rats after chronic isoproterenol administration. We have reported previously that the hypertrophic response during recovery from SVT-induced cardiomyopathy is associated with increased collagen content.34 Thus, increased catecholamine stimulation may be a possible mechanism for the development of hypertrophy during recovery from SVT cardiomyopathy.

Coronary vascular resistance was higher in the SVT and post-SVT groups than in the control group. This elevated coronary vascular resistance persisted during adenosine administration. This suggests that in addition to the hemodynamic and extravascular forces contributing to the overall reduction in myocardial blood flow, increased coronary vascular resistance may also have played a role. This increased coronary vascular resistance occurred in the absence of significant structural or distributional changes to the arterioles, the major contributor to vascular resistance. These findings suggest that normal autoregulatory and myogenic responsiveness of the coronary vasculature may be affected during the development of and recovery from SVT cardiomyopathy.

Although coronary vascular resistance is an important determinant of myocardial blood flow, the practical application of this concept can be problematic.8 The formula used for coronary vascular resistance in the present study was chosen because it takes into consideration changes in driving pressure and left atrial pressure and normalizes the resistance value per gram of LV tissue. The changes in coronary vascular resistance observed in the SVT and post-SVT hearts probably resulted from a combination of physiological and computational causes. What is clear from this analysis, however, is that vascular angiogenesis failed to occur in either the SVT or post-SVT hearts, which would have reduced vascular resistance and created a more favorable condition for adequate myocardial blood flow.

Although the present study demonstrated an association between reduced myocardial blood flow and myocyte injury with SVT-induced cardiomyopathy, a cause-and-effect relation could not be clearly established. It remains unclear whether these changes in myocardial blood flow and myocyte structure are the primary initial mechanisms responsible for the development of SVT cardiomyopathy. Findings from the present study suggest that reduced myocardial blood flow may not be an initial mechanism responsible for the development of this form of cardiomyopathy. In the control group, acute rapid atrial pacing was associated with increased myocardial blood flow. This increased myocardial blood flow occurred despite a significant increase in left atrial pressure. Thus, tachycardia and elevated intracavitary pressure failed to reduce blood flow in the control pigs. This suggests that with the initial onset of SVT, blood flow increases to meet myocardial oxygen demand. The reduction in myocardial blood flow observed with chronic SVT probably results from the changes in LV function and geometry that occurred with chronic tachycardia.

Several limitations to the present study must be recognized. First, with SVT cardiomyopathy, the reduction in myocardial blood flow during adenosine administration may have resulted, in part, from a shift in dose responsiveness. In the present study, however, administration of adenosine resulted in an equivalent reduction in mean arterial pressure in all three groups. A future study examining the effects of intracoronary administration of adenosine or other vasodilators on myocardial blood flow in the setting of tachycardia-induced cardiomyopathy would be appropriate. Second, the ultrastructural identification of myofibrils and mitochondria was done at a relatively low magnification compared with previous studies.20 Sections from all three groups were quantified in identical fashion, however, and the statistically significant decrease in myofibrillar content observed with SVT cardiomyopathy probably exceeded any systematic error that may have been associated with this technique.

Clinical Significance

Two findings from this study have direct and important clinical implications. First, SVT cardiomyopathy resulted in a significant decline in myofibrillar content and myocardial blood flow. Thus, this condition should be treated promptly to avoid additional myocyte injury and potential permanent damage to the LV myocardium. Second, recovery from SVT cardiomyopathy resulted in hypertrophy, reduced coronary reserve, and reduced subendocardial perfusion with acute pacing. Thus, episodic increases in myocardial oxygen demand in these post-SVT hearts (such as a second episode of tachycardia) may result in reduced myocardial blood flow and reduced LV function.

Summary

The major objective of the present study was to examine the relation of changes in LV function and myocyte composition to myocardial blood flow and structure of the coronary vasculature in a model of SVT-induced cardiomyopathy and recovery. The LV dysfunction and myocyte injury with SVT cardiomyopathy was associated with reduced myocardial blood flow and coronary reserve. Early recovery from SVT cardiomyopathy resulted in hypertrophy and normalization of LV systolic function and myocyte structure. However, whereas early recovery from SVT cardiomyopathy resulted in normal myocardial blood flow at rest, significantly reduced blood flow occurred with acute pacing tachycardia and during maximal vasodilation. Capillary and arteriole density remained unchanged with the development and recovery of SVT cardiomyopathy, suggesting that these changes in myocardial perfusion were not caused by significant remodeling of the coronary vasculature.
References


Key Words • chronic pacing • blood flow • coronary vasculature • ventricular function
Changes in myocardial blood flow during development of and recovery from tachycardia-induced cardiomyopathy.
F G Spinale, R Tanaka, F A Crawford and M R Zile

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