Sustained Ventricular Tachycardia Is Associated with Regional Myocardial Sympathetic Denervation Assessed with ^{123}I-Metaiodobenzylguanidine in Chronic Chagas Cardiomyopathy

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Cardiac sympathetic denervation and ventricular arrhythmia are frequently observed in chronic Chagas cardiomyopathy (CCC). This study quantitatively evaluated the association between cardiac sympathetic denervation and sustained ventricular tachycardia (SVT) in patients with CCC. **Methods:** We prospectively investigated patients with CCC and left ventricular ejection fraction (LVEF) greater than 35% with SVT (SVT group: n = 15; mean age ± SD, 61 ± 8 y; LVEF, 51% ± 8%) and patients without SVT (non-SVT group: n = 11; mean age ± SD, 55 ± 10 y; LVEF, 57% ± 10%). Patients underwent myocardial scintigraphy with ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG) for the evaluation of sympathetic innervation and resting perfusion with ^{99m}Tc-methoxyisobutylisonitrile (^{99m}Tc-MIBI) for the evaluation of myocardial viability. A visual semiquantitative score was attributed for regional uptake of each radiotracer using a 17-segment left ventricular segmentation model (0, normal; 4, absence of uptake). A mismatch defect was defined as occurring in segments with a ^{99m}Tc-MIBI uptake score of 0 or 1 and a ^{123}I-MIBG score of 2 or more. **Results:** Compared with the non-SVT group, the SVT group had a similar ^{99m}Tc-MIBI summed score (6.9 ± 7.5 vs. 4.4 ± 5.2, respectively, P = 0.69) but a higher ^{123}I-MIBG summed score (10.9 ± 7.8 vs. 22.4 ± 9.5, respectively, P = 0.007) and a higher number of mismatch defects per patient (2.0 ± 2.2 vs. 7.1 ± 2.0, respectively, $P <$ 0.0001). The presence of more than 3 mismatch defects was strongly associated with the presence of SVT (93% sensitivity, 82% specificity; P = 0.0002). **Conclusion:** In CCC, the amount of sympathetically denervated viable myocardium is associated with the occurrence of SVT. Myocardial sympathetic denervation may participate in triggering malignant ventricular arrhythmia in CCC patients with relatively well-preserved ventricular function.

Key Words: chronic Chagas cardiomyopathy; sympathetic denervation; ventricular arrhythmias; ^{123}I-metaiodobenzylguanidine imaging

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Chronic Chagas cardiomyopathy (CCC) is the most serious form of Chagas disease in Latin American countries (*1*). It is a dilated cardiomyopathy that in many patients leads to severe heart failure (*2*). Another outstanding clinical feature of this disease is the striking prevalence of complex ventricular arrhythmia that leads to a high risk of sudden death (*3*). Similar to other forms of cardiac disease, severe left ventricular dysfunction and extensive areas of regional fibrosis are considered important substrates for triggering ventricular arrhythmia in CCC patients (*4,5*). However, an intriguing aspect of CCC is the high incidence of sudden death and malignant ventricular arrhythmia also in young individuals running through the early phase of the disease, when global systolic function is normal or only mildly depressed (*6*).

The mechanisms involved in the genesis of ventricular arrhythmias in the early phases of CCC have not been elucidated. Autonomic denervation may play a central role in triggering sudden death in patients with CCC (*3,7*). Previous studies have demonstrated that cardiac autonomic denervation—both parasympathetic and sympathetic—is a common finding among patients with CCC and occurs at the early phases of the disease (*7,8*). However, no previous report has focused on the association between cardiac autonomic denervation and ventricular arrhythmia in CCC.

The objective of the present study was to investigate the presence and extent of regional myocardial sympathetic denervation using ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG) scintigraphy in CCC patients with preserved or only slightly depressed ventricular function who had sustained ventricular tachycardia (SVT), compared with CCC patients with a similar degree of left ventricular dysfunction not showing SVT episodes.

MATERIALS AND METHODS

Patients

The diagnosis of CCC required 2 positive serologic tests for antibodies against *Trypanosoma cruzi* (indirect immunofluorescence

reaction, enzyme-linked immunosorbent assay), associated with typical segmental or global left ventricular dysfunction determined by 2-dimensional echocardiogram or the characteristic 12-lead electrocardiogram changes (advanced right bundle-branch block, usually with left anterior hemiblock).

The patients were recruited from the population attending the cardiac arrhythmia outpatient clinic of the University Hospital of the Faculty of Medicine of Ribeirao Preto, University of São Paulo. CCC patients with recent episodes of spontaneous SVT or presenting with this arrhythmia during electrophysiologic examination performed for the investigation of syncope were actively identified. Those exhibiting a left ventricular ejection fraction (LVEF) of 35% or more as determined by 2-dimensional echocardiogram were included in the study (SVT group, $n = 15$ patients).

For a comparative analysis of the results obtained, another group of patients with CCC and similar values of LVEF, but exhibiting neither SVT nor multiple episodes of non-SVT on 24-h Holter monitoring, was studied (non-SVT group; $n = 11$ patients).

Patients with other diseases or conditions potentially interfering with sympathetic innervation, such as diabetes mellitus, artificial ventricular stimulation with a pacemaker, non–sinus node cardiac rhythm, and obstructive coronary artery disease (CAD), were excluded from the study.

Study Design

All patients prospectively underwent an initial clinical evaluation including a 12-lead resting electrocardiogram, a transthoracic echocardiogram for LVEF evaluation, and 24-h Holter monitoring. They subsequently underwent resting myocardial perfusion with ^{99m}Tc-methoxyisobutylisonitrile (^{99m}Tc-MIBI) and myocardial sympathetic innervation scintigraphy with ^{123}I-MIBG, with a 48-h interval between the procedures. Invasive electrophysiologic study was not performed as part of the investigation protocol but was performed when clinically indicated for the investigation of syncope. Programmed ventricular stimulation was done at the apex of the right ventricle, with frequency cycles decreasing from 600 to 450 ms and application of a maximum of 3 extra stimuli during ventricular diastole after 8 beats of ventricular pacing.

The study was approved by the Research Ethics Committee of the University Hospital, Faculty of Medicine of Ribeirão Preto, University of São Paulo, and was conducted according to the precepts of the Declaration of Helsinki. All patients gave written informed consent to participate.

Myocardial Sympathetic Innervation Scintigraphy

All patients were studied after a resting period of at least 1 h and after discontinuation for more than 48 h of medications possibly interfering with sympathetic function such as β-blockers, tricyclic antidepressants, antipsychotic drugs, reserpine, phenylephrine, pseudoephedrine, and calcium channel blockers. Approximately 1 h before the beginning of the study, the patients received 20 mL of a 10% potassium iodide solution by mouth and were injected with 185 MBq of ^{123}I-MIBG through a peripheral vein, followed by a flush with 20 mL of saline solution. The images were acquired at 3 h after the injection of the radiotracer with a double-detector digital γ-camera (DST; Sopha Medical Vision) equipped with high-resolution and low-energy collimators with parallel orifices. SPECT images were acquired with the patient supine, with a semicircumferential orbit (from the right anterior oblique projection to the left posterior oblique projection) in 32 projections, 60 s/projection. The 20% energy window was centered on 159 keV. The acquisition matrix was of 64 × 64 pixels, with a pixel size of 0.6 cm.

Myocardial Perfusion Scintigraphy

All patients underwent myocardial perfusion scintigraphy at rest by injection of 370–740 MBq of ^{99m}Tc-MIBI preceded by sublingual administration of isosorbide dinitrate (5 mg). The SPECT images were acquired at 1 h after the injection of the radiopharmaceutical using the equipment and parameters described, with a 20% energy window centered on 140 keV.

Processing and Analysis of Scintigraphic Images

The tomographic sections of the perfusion and innervation images were analyzed using a dedicated workstation (Vision PowerSation; SMV America) and specific software (Myocardial SPECT; SMV America). The images were aligned to permit the simultaneous visualization of the 3 orthogonal planes (short axis, horizontal long axis, and vertical long axis). The images were analyzed visually by 2 masked experienced observers using a 17-segment left ventricular segmentation model. Segmental ^{123}I-MIBG and ^{99m}Tc-MIBI uptake was assessed by attributing a visual semiquantitative score: 0, normal; 1, mild uptake reduction; 2, moderate uptake reduction; 3, severe uptake reduction; and 4, no uptake.

Summed perfusion and sympathetic innervation scores were calculated for each patient, representing the overall extent or severity of the respective defects. The difference between the summed innervation and perfusion scores was also calculated, corresponding to the estimate of the overall extent or severity of the myocardium with preserved perfusion and reduced sympathetic innervation.

For the analysis of the topographic correlation between the changes in perfusion and innervation, each segment was classified according to the alterations present in the same myocardial segment in each respective image. Segments exhibiting normal or minimally reduced ^{99m}Tc-MIBI uptake (semiquantitative score, 0 or 1) and severe reduction of ^{123}I-MIBG uptake (semiquantitative scores, ≥2) were considered to be mismatch segments—that is, segments with viable myocardium but with sympathetic denervation. Segments showing normal or minimally reduced ^{99m}Tc-MIBI and ^{123}I-MIBG uptake (semiquantitative score, 0 or 1) were considered to be positive-match segments—that is, viable and normally innervated segments. Segments simultaneously exhibiting a significant reduction of ^{99m}Tc-MIBI and ^{123}I-MIBG uptake (semiquantitative scores, ≥2) were considered to be negative-match segments—that is, segments with both reduced viable myocardium and sympathetic denervation. There was no segment with reduced ^{99m}Tc-MIBI uptake (semiquantitative score, ≥2) and normal or minimally reduced ^{123}I-MIBG uptake.

Investigation of CAD

The presence of concomitant CAD was examined only in the 16 patients presenting with precordial chest pain or with 2 or more risk factors for CAD. Thus, CAD was studied in 11 patients (73%) of the SVT group (with coronary angiography in 6 patients and myocardial perfusion scintigraphy under physical or pharmacologic stress in 5) and in 5 patients (33.3%) of the non-SVT group (with coronary angiography in 2 patients and myocardial perfusion scintigraphy in 3).

Significant CAD was defined as substantial myocardial ischemia (stress–rest difference score ≥ 3) or severe coronary obstruc-

tion at angiography (>70% luminal diameter reduction) and was not observed in any of the 16 patients investigated for CAD. In addition, milder CAD (50%–70% luminal diameter reduction) was detected in only 2 patients undergoing coronary angiography (both were from the non-SVT study group), but there was no topographic correlation between the myocardial territory supplied by coronary arteries with mild obstruction and changes in myocardial perfusion.

Statistical Analysis

Quantitative variables are reported as mean ± SD and the categoric variables as frequency or percentage. Normal distribution of the data was assessed by the Kolmogorov–Smirnov test, and the differences between means were determined by the Student *t* test. Data with nongaussian distribution were analyzed by the Mann–Whitney test, and the association between categoric variables was analyzed by the Fisher exact test. The difference in defect scores among the 17 segments was determined by the nonparametric Kruskal–Wallis test, followed by the Dunn posttest. A 2-tailed *P* value of 0.05 was considered to be significant in all analyses.

RESULTS

Table 1 presents the demographic, clinical, electrocardiographic, and echocardiographic characteristics of the patients investigated.

Most SVT episodes (80%) occurred spontaneously, with a morphologic pattern of right bundle-branch block and superior axis (the most common pattern in patients with CCC).

All patients showing SVT were taking amiodarone by the time of their inclusion in this study. However, the patients experiencing spontaneous SVT episodes were previously not taking amiodarone when they exhibited this arrhythmia.

Many of the patients were taking angiotensin-converting enzyme inhibitors. These data reflect the clinical practice of using the angiotensin-converting enzyme inhibitors in patients with CCC with regional wall motion abnormalities to prevent the progression of left ventricular dysfunction.

Changes in Myocardial Perfusion

The prevalence of patients exhibiting perfusion defects at rest was similar for the non-SVT (63%) and SVT groups (86%) ($P = 0.35$, Fisher exact test). Of the 187 segments analyzed in the non-SVT group, 40 (21%) showed perfusion defects, with a mean defect score of 6.9 ± 7.5. These values were similar to those detected in the SVT group, in which 41 of the 255 segments (16%) showed perfusion defects ($P = 0.18$, Fisher exact test), and the mean score for the perfusion defect was 4.4 ± 5.2 ($P = 0.69$, Mann–Whitney test) (Fig. 1).

Regarding the topographic distribution of the perfusion defects, segments in the inferior, posterior–lateral, and apical regions showed 87.5% and 95.1% of all perfusion defects in the non-SVT and SVT groups, respectively.

Changes in Myocardial Sympathetic Innervation

The prevalence of patients with abnormal ^{123}I-MIBG uptake was high and comparable in both groups (9 patients [81%] in the non-SVT group and 15 [100%] in the SVT groups; $P = 0.17$, Fisher exact test). In contrast, SVT patients presented a greater extent or severity of defects of ^{123}I-MIBG uptake than did the non-SVT patients. In the SVT group, 134 of the 255 analyzed segments (52%) exhibited uptake defects, as opposed to 62 of the 187 segments (33%) analyzed in the non-SVT group ($P < 0.0001$, Fisher exact test). The mean score of ^{123}I-MIBG uptake defects was also higher in the SVT group (22.4 ± 9.5) than in the non-SVT group (10.9 ± 7.8) ($P = 0.007$, Mann–Whitney test) (Fig. 1).

The topographic distribution of ^{123}I-MIBG uptake defects was similar to that of perfusion defects, with a predominance in the inferior, posterior–lateral, and apical walls, which concentrated 87% of abnormal segments in the non-SVT group and 81% in the SVT group.

Topographic Relationship Between Myocardial Perfusion and Innervation Abnormalities

The difference in the summed scores of innervation and perfusion was greater in the SVT group (19.9 ± 7.7) than in the non-SVT group (4.0 ± 5.5) ($P = 0.0002$, Mann–Whitney test) (Fig. 1).

SVT patients had a mismatch in 107 of the 255 segments analyzed (40%), a significantly higher proportion than that detected in non-SVT patients, who had a mismatch in 22 of the 187 segments analyzed (12%) ($P < 0.0001$, Fisher exact test). Thus, the mean number of mismatch segments per patient was significantly higher in the SVT group (7.1 ± 2.0) than in the non-SVT group (2.0 ± 2.2) ($P < 0.0001$, Student *t* test).

In addition, all SVT patients except 1 (93%) had more than 3 segments with mismatch, as opposed to only 2 non-SVT patients (18%). Thus, the presence of more than 3 mismatch segments was strongly associated with the presence of SVT, with 93% sensitivity and 82% specificity ($P = 0.0002$, Fisher exact test).

The topographic distribution of segments exhibiting mismatch was similar to that observed for the innervation and perfusion defects separately—that is, a predominance on the inferior, posterior–lateral, and apical walls, which concentrated 87% of the segments with defect in the non-SVT group and 81% in the SVT group (Fig. 2).

The proportion of segments with positive match (preserved perfusion and innervation) was significantly greater in the non-SVT group (75%) than in the SVT group (50%) ($P < 0.0001$, Fisher exact test). A negative match was seen in 8% of the segments in the SVT group and 13% of the segments in the non-SVT group ($P = 0.62$, Fisher exact test).

DISCUSSION

The present study investigated the presence and extent of myocardial sympathetic denervation in CCC patients without severe ventricular dysfunction (LVEF > 35%) divided into groups with and without SVT. In keeping with previous studies in other groups of CCC patients, the present results

TABLE 1
Demographic, Clinical, and Laboratory Characteristics of Patients Investigated

Characteristic	Non-SVT group (n = 11)	SVT group (n = 15)	P
Demographic			
Age (y)	55 ± 10	61 ± 8	0.09
Male sex (n)	7 (64)	12 (80)	0.40
12-lead electrocardiogram			
Heart rate (bpm)	56 ± 6	55 ± 11	0.83
Right bundle-branch block (n)	6 (54)	10 (67)	0.68
Left anterior hemiblock (n)	6 (54)	7 (47)	1.00
SVT			
Spontaneous (n)	—	12 (80)	—
Induced (n)	—	3 (20)	—
Heart rate (bpm)	—	194 ± 27	—
Hemodynamic instability	—	7 (47)	—
RBBB pattern (n)	—	12 (80)	—
Superior axis (n)	—	10 (67)	—
Echocardiographic characteristics			
LVEF	57 ± 10	51 ± 8	0.14
Left ventricle diastolic diameter (mm)	54 ± 7	54 ± 6	0.94
LVEF > 50% (n)	8 (73)	10 (67)	1.00
Abnormal wall motion (n)	9 (82)	13 (87)	1.00
Ventricular aneurysm (n)	1 (9)	1 (7)	1.00
Holter			
No. of premature ventricular beats in 24 h	1,654 ± 1,801	1,164 ± 2,348	0.57
Multiple non-SVT (n)	—	3 (20)	
SD of all normal RR intervals	134 ± 36	113 ± 37	0.21
Medication			
Amiodarone (n)	4 (36)	15 (100)	<0.05
β-blocker (n)	2 (18)	5 (33)	0.65
Angiotensin-converting enzyme inhibitor (n)	8 (72)	11 (73)	1.00

RBBB pattern = SVT with morphologic pattern of right bundle-branch block; superior axis = SVT axis between −30° and −90° on frontal plane.
Data in parentheses are percentages.

showed a high prevalence of both rest perfusion defects and of regional sympathetic denervation in the 2 patient groups (*5,8–10*). The most relevant and original result was that SVT patients exhibited a greater extent of ^{123}I-MIBG uptake defects in myocardial segments with normal perfusion at rest, suggesting that the occurrence of severe ventricular arrhythmia in CCC may be linked to the presence and amount of viable but sympathetically denervated myocardium.

It is difficult to determine the disease duration in patients with CCC, because its natural history includes a long asymptomatic period despite the presence of significant structural cardiac disease. The time course of myocardial damage progression presents a high interindividual variation in these patients. On the other hand, previous work by our group in CCC patients without severe ventricular arrhythmia showed that the ^{123}I-MIBG defect area increases in parallel to the extent of myocardial damage and regional fibrosis (*8*). Considering these aspects, instead of trying to use the disease duration, the degree of left ventricular dysfunction was employed for the matching between the group with SVT and the group without SVT.

Resting Perfusion Abnormalities

The present results confirm data from previous studies showing a high prevalence of perfusion defects in patients with CCC despite angiographically normal coronary

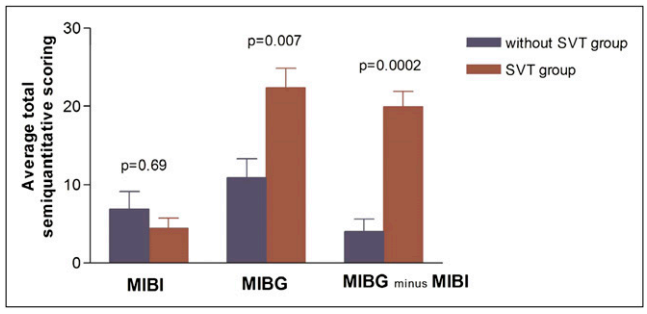

FIGURE 1. Bar graph illustrating results of ^{99m}Tc-MIBI and ^{123}I-MIBG summed scores. There is nonsignificant difference in mean summed resting perfusion score (^{99m}Tc-MIBI) between investigated groups (P = 0.69), despite finding of higher summed score of innervation defects (^{123}I-MIBG) in SVT group than in non-SVT group (P = 0.007). Accordingly, ^{123}I-MIBG minus ^{99m}Tc-MIBI summed scores were also higher in SVT group (P = 0.0002).

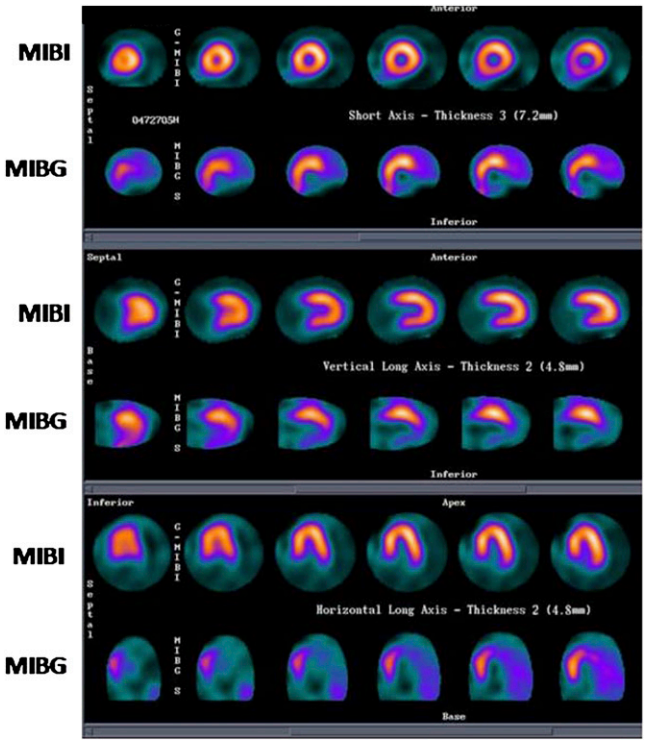

FIGURE 2. Illustrative example of myocardial scintigraphy findings. Images of resting myocardial perfusion scintigraphy (^{99m}Tc-MIBI) and of sympathetic innervation (^{123}I-MIBG) from 63-y-old man with LVEF of 58% who had episodes of spontaneous SVT. Tomographic sections of 3 orthogonal planes are shown: short axis, horizontal long axis, and vertical long axis. Severely impaired ^{123}I-MIBG uptake with normal myocardial perfusion (mismatch) is observed on posterior–lateral, inferior, and apical walls.

arteries (*9*). This study also highlights the fact that the myocardial perfusion disturbances can occur even at early stages of CCC, in patients with preserved global left ventricular function. The predominance of the perfusion derangements on the inferior, posterior–lateral, and apical walls previously reported was also confirmed by the present data (*8–10*).

In this investigation, the extent or severity of perfusion defects was similar in patients with and without SVT and reflected the comparable degree of impairment of left ventricular systolic function observed in the 2 study groups. The notion that perfusion defects observed at rest in the investigated population correspond to regions of myocardial fibrosis is supported by previous studies showing a close topographic correlation between such resting perfusion defects and segmental wall motion impairment in CCC patients (*8,9*). This concept is also corroborated by similar studies in both ischemic and nonischemic dilated cardiomyopathy showing pathologic evidence of fibrosis in regions of rest myocardial perfusion defects (*11*). Finally, in our study, apical aneurysm was observed in both groups, indicating that this structural abnormality, virtually pathognomonic of CCC, is not correlated with the occurrence of SVT, as shown in previous electrophysiologic studies (*5*).

^{123}I-MIBG Uptake Derangements

The present results showing an 81% prevalence of myocardial sympathetic denervation are in agreement with the reported prevalence of 77% in a previous study of patients with CCC. Moreover, in both investigations the sympathetic denervation was predominant in the inferior, posterior–lateral, and apical left ventricular walls (*8*).

Beyond confirmation of the presence of myocardial sympathetic denervation in CCC, the present results show for, to our knowledge, the first time that CCC patients with SVT have significantly larger areas of sympathetic denervation in viable myocardium than patients with a similar degree of myocardial involvement but without severe ventricular arrhythmias. These findings suggest that myocardial sympathetic denervation may be pathophysiologically implicated as a mechanism causing severe ventricular arrhythmia in CCC. Thus, this is the first clinical study reporting on a clinically significant consequence of cardiac autonomic denervation in CCC. Also meaningful is the finding that the topographic location of these viable and denervated segments predominate in the inferior and posterior–lateral left ventricular regions, because these are the areas from which most often the malignant ventricular arrhythmias arise in patients with CCC (*5*).

Our findings in CCC are concordant with other experimental and clinical studies that support the notion that regional myocardial sympathetic denervation is a mechanism for triggering ventricular arrhythmia in several forms of heart disease (*12–14*). Regional cardiac sympathetic denervation documented by ^{123}I-MIBG scintigraphy has been described in several other clinical settings characterized by a high density of ventricular arrhythmias and sudden death, such as arrhythmogenic right ventricular cardiomyopathy, congenital long QT syndrome, Brugada syndrome, and cardiomyopathy of other etiology (*15–17*). Furthermore, additional investigations demonstrated a high prevalence (47%) of defects of ^{123}I-MIBG uptake in patients with a structurally normal heart but who had SVT triggered mainly by physical effort (*18*). Finally, similar results were reported in patients with ventricular tachycardia in the absence of CAD (*19*).

Cardiac Denervation in CCC

Several studies have demonstrated an early and intense autonomic cardiac denervation in CCC. The initial observations were derived from necroscopic studies showing extensive parasympathetic neuronal depopulation in the hearts of CCC patients dying from heart failure (*20*). Parasympathetic denervation was also clearly demonstrated by functional studies in humans showing imbalance of autonomic control of the heart rate (*7,21*).

Although these studies are important for documenting cardiac denervation, they present methodologic limitations because they evaluated derangement of autonomic control only over the sinus node, not at the left ventricular myocardium level. Nevertheless, we can speculate that

arrhythmias in CCC may be triggered not only by regional myocardial sympathetic denervation (as demonstrated in this study) but also by parasympathetic denervation.

The sympathetic denervation found at the myocardial level in this investigation is similar to the impairment of adrenergic control of the sinus node as described in previous studies of patients with CCC (*7,22*). However, the mechanisms responsible for sympathetic and parasympathetic denervation in CCC have not been entirely elucidated. Neuronal depopulation caused by intense inflammatory changes induced by the parasite or through adverse immunologic reaction is a likely possibility. Also, microvascular disturbance directly causing myocardial ischemia may lead to the derangement of nerve endings. Finally, circulating antibodies against both cardiac adrenergic and cholinergic receptors have been reported in patients with CCC and may actively participate in the process of myocardial sympathetic denervation (*7*).

Clinical Implications

Arrhythmic sudden death is a frequent complication of CCC, even in patients without serious impairment of left ventricular systolic function (*3,6*). The present results suggest that the investigation of myocardial sympathetic denervation by scintigraphy with ^{123}I-MIBG may be a potentially useful tool for stratification of the risk of severe ventricular arrhythmia and sudden death in this population. However, before being applied in clinical practice, this concept should be validated in a prospective study of a larger number of patients.

Limitations of Study

The presence of CAD was not definitely excluded in all patients. Only those who complained of precordial pain or with more than 2 risk factors for coronary disease were investigated. Seventy-three percent of the patients in the SVT group and 33% of those in the non-SVT group were tested for CAD. However, for the remaining patients, the probability of CAD was low.

We did not perform invasive electrophysiologic studies for mapping the topographic origin of spontaneous SVT. These data could be relevant to further support the participation of denervation in the mechanism of arrhythmia. However, 80% of the patients of the SVT group had spontaneous SVT, with 12-lead electrocardiogram morphology indicating the origin of the tachycardia to be the basal portion of the posterior–lateral left ventricular wall, the same site where the mismatch defects clearly predominated. This particular aspect strongly suggests that the tachycardia was topographically related to a heavily denervated myocardial area.

Gated SPECT images were not acquired in this study. The use of gated SPECT could have provided important information regarding the correlation between perfusion or innervation changes and regional left ventricular function. For instance, the finding of akinesia in segments showing a negative match between perfusion and innervation could have reinforced the interpretation of regional fibrosis.

The absence of attenuation correction is also a technical limitation of this study. In this regard, ^{123}I images are less affected by attenuation artifacts than are ^{99m}Tc images. Therefore, the use of attenuation correction could have removed the attenuation artifacts of the perfusion images in the inferior wall and increased the correlation between perfusion and innervation changes.

The use of septal deconvolution techniques could have improved the image quality of our studies and allowed more accurate defect quantification (*23*). Unfortunately, this processing protocol is not available in our institution. However, it is conceivable that the absence of this technical improvement would similarly affect the image quality of both groups of patients. Thus, we consider that the observed difference in ^{123}I-MIBG defect sizes between the patients with and without SVT should not be attributed to this technical limitation.

CONCLUSION

This investigation showed the quantitative association between regional myocardial sympathetic denervation and the occurrence of severe ventricular arrhythmia in patients with CCC.

These data suggest that cardiac sympathetic denervation may participate in the genesis of malignant ventricular arrhythmia in CCC patients with relatively well preserved left ventricular function and that its detection by ^{123}I-MIBG myocardial scintigraphy may potentially contribute to risk stratification in CCC patients with relatively preserved global left ventricular function.

DISCLOSURE STATEMENT

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