Chronic Inappropriate Sinus Tachycardia in Elderly Females

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Background: The vast majority of reports of inappropriate sinus tachycardia (IST) had included predominantly young females with ages ranging between 15 and 46 years. In contrast, the present study presents the findings in four elderly females (aged 61–71 years) with long-standing symptoms of palpitations, more than 15 years, in whom IST was diagnosed in their 6th or 7th decade.

Methods: Clinical and laboratory examinations including electrocardiograms, echocardiograms, and heart rate variability studies were retrospectively reviewed in four of the nine elderly female patients with long-standing cardiac symptoms. Indices of heart rate variability were compared to four age-matched asymptomatic elderly females with no structural heart disease.

Results: The resting electrocardiograms were normal but one had voltage criteria for left ventricular hypertrophy. All traditional time- and frequency-domain indices were significantly decreased in the symptomatic elderly females as compared to the controls. Echocardiograms showed normal ejection fraction, and in three patients evidence of diastolic dysfunction and mild left ventricular hypertrophy. Blood pressures were elevated, with systolic blood pressure ranging from 170 to 190 and diastolic blood pressure ranging from 94 to 106. Anxiety disorders were diagnosed in all patients.

Conclusions: This study demonstrates that IST can be present in a wide spectrum of patient populations, including elderly populations. It seems that some cases of IST can become chronic if not treated adequately. Apparently, earlier identification and treatment could have improved the quality of life of the patients. Traditional HRV indices may not be valuable to support either a sympathetic or parasympathetic mechanism. Therefore, further studies should consider the potential usefulness of the nonlinear method such as, for example, approximate entropy and detrended fluctuation analysis.

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Inappropriate sinus tachycardia (IST) is an arrhythmia that is being clinically recognized with increasing frequency since late 1990s. This rhythm disorder is characterized by high resting sinus rates of no apparent cause with disproportional increases in heart rate (HR) with minimal physical activity. Reported cases of IST deal predominantly with young females and with symptoms of relatively short-to-intermediate duration.^{1–6} In the present study we report four patients with long-standing symptoms of palpitations, more than 15 years, in whom IST was diagnosed in their 6th or 7th decade. This group

of patients represents a unique subgroup within the IST patient population.

METHODS

Patient Population

The medical records of nine elderly females without structural heart disease and long-standing cardiac symptoms, of at least 15 years, were retrospectively reviewed. Electrocardiographic verification of fast resting sinus rates was possible in four

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patients who constitute the basis of this report. Their ages ranged from 61 to 71 years. Heart rates (HR) were documented by appropriate review of medical records, vital signs, and electrocardiograms for 15–21 years. These patients met the following criteria: (1) mean 24-hour sinus rates ≥ 95 beats/min on Holter in nonmedicated state and in which secondary causes of sinus tachycardia, at the moment of study, were excluded, such as neuroendocrine abnormalities, postural hypotension, hypovolemia, fever, anemia, prescription or illicit drugs; (2) same or similar P wave during the slower and faster sinus rates; (3) increase in sinus rates from supine to upright position ≥ 25 beats/min; (4) exaggerated symptomatic sinus tachycardia by minimal physical or physiological stimuli; (5) relatively rapid increase (over a few seconds) in sinus rates, rather than over 1 or 2 beats as in sinus node reentrant tachycardias or other supraventricular tachycardias; (6) sinus rates ≥ 150 beats/min at, or before, the end of stage 1 of the Bruce protocol; (7) symptoms during the easily provoked sinus tachycardia (documented by the Holter diaries) such as palpitations, dizziness, and presyncope; and (8) electrocardiograms, echocardiograms, and heart rate variability indices. Four age-matched females without structural heart disease served as controls.

Heart Rate Variability

Holter tapes used to study heart rate variability (HRV) were initially analyzed by a nurse practitioner and rescanned by two physicians on two separate occasions using two instruments, first a Zymed (Camarillo, CA) and finally a Marquette software version 002A (Milwaukee, WI).^{5,6} Ectopic beats were less than 25 per patient with artifact time not exceeding 1650 seconds. Recording time of Holter tapes ranged from 23.5 to 24.2 hours. The following time and frequency domain indices were analyzed and compared with those of the four age-matched asymptomatic females without structural heart disease: mean R-R intervals (R-R mean); the standard deviation from the mean of the normal R-R intervals (SDNN); the standard deviation of 5-minute mean standard deviations of R-R intervals (SDANN); percentage of adjacent R-R intervals that differ by > 50 ms (pNN50); root mean square of successive R-R differences (RMSDD). Of the frequency domains, the following indices were compared: low

frequency (LF, 0.04–0.15 Hz) and high frequency (HF, 0.15–0.40 Hz) power [$\ln(\text{ms}^2)$] and high frequency/low frequency ratio (HF/LF). A special software package (Universidad Central de Venezuela, Caracas, Venezuela) was used for statistical analysis. Measurements were performed using paired Student *t*-tests. A *P* value < 0.05 was considered significant.

RESULTS

Physical examination revealed that all four patients had high blood pressure at the time of the diagnosis of IST, with systolic blood pressure ranging from 170 to 190 and diastolic blood pressure from 94 to 106. Review of the medical records for 15–21 years prior to the diagnosis of IST revealed that the patients also had (1) a long-standing history of intermittent palpitations, dizziness and/or presyncope; (2) at least two normal resting electrocardiograms with sinus rates ≥ 95 beats/min; and (3) at least three normal blood pressure readings several years before the diagnosis of IST (Fig. 1, top).

Charts also documented treatment for anxiety disorders on all four patients. None of these patients had any treatment for persistent fast heart rates or for systemic hypertension, the latter was detected within 1–4 years prior to the moment at which the patients were diagnosed with IST.

All time- and frequency-domain indices were significantly lower in the symptomatic patients as compared to the asymptomatic controls. No differences in the low frequency/high frequency ratios were observed, despite the fact that both were significantly lower. This could be attributed to the mathematics of the ratio when expressed as natural logarithms since the quotient reflected a proportional decrease in the numerator and denominator⁷ (see Table 1).

The resting 12-lead electrocardiograms were normal in three patients; the other patient had voltage criteria for left ventricular hypertrophy. Echocardiograms revealed ejection fractions of 50–55%. Whereas one echocardiogram was normal, the remaining three showed the following abnormalities: prolongation of isovolumetric relaxation, reduced rate of rapid filling, and an increase in amplitude of the A wave; interventricular septal thickness of 1.2–1.4 cm and posterior wall thickening 1.1–1.3 cm. These changes can be considered as resulting from systemic hypertension.

BEFORE **AFTER**

Figure 1. Graphs plotting rates (beats/min) versus mean, maximum, and minimal hourly sinus rates in a patient with inappropriate sinus tachycardia. Note decrease in rates after treatment with a beta-blocker (bottom) as compared to before treatment (top).

Table 1. Comparison of Heart Rate Variability Measurements between Symptomatic Elderly Females and Controls

	Controls	Patients	P Value
Mean R-R (ms)	810 ± 45	578 ± 74	<0.005
SDNN (ms)	90 ± 22	55 ± 18	<0.001
SDANN (ms)	81 ± 27	44 ± 20	<0.001
RMSSD (ms)	23 ± 9	11 ± 5	<0.02
pNN50 (%)	6 ± 5	1.9 ± 0.94	<0.02
LFP (ln[ms ²])	6.2 ± 1.3	4 ± 0.92	<0.05
HFP (ln[ms ²])	5.1 ± 1.1	3 ± 0.87	<0.05
LF/HF ratio	1.2	1.3	NS

HFP = high frequency power; ln = natural logarithm; LFP = lower frequency power; ms = milliseconds; pNN50 = percentage of R-R intervals that differ by 50 ms; RMSSD = root mean square of successive R-R differences; SDANN = the SD of 5-minute mean SD of R-R intervals; SDNN = standard deviation of the mean R-R intervals.

All four patients were treated with 75–150 mg of atenolol daily. This drug normalized the high blood pressure as well as the sinus rates for 19–29 months (Fig. 2).

DISCUSSION

This study demonstrates that IST can be present in a wide spectrum of patient populations, including elderly as well as younger subjects. The observed changes in traditional indices of HRV are similar to those reported in other patient populations with IST. For example, two previous studies^{4,5} reported marked decreased in all time- and frequency-domain indices of HRV as in this article, which have been traditionally considered to be due to abnormally low parasympathetic tone, increased sympathetic tone, and/or rapid heart rates in itself. Although the causes of this arrhythmia have been a source of debate and speculation, several mechanisms acting independently, or most likely in combination, have been postulated. Morillo and coworkers¹ proposed a sinus node abnormality manifested by a higher-than-normal intrinsic sinus rate after autonomic blockade coexisting with a marked sensitivity to isoproterenol and a depressed efferent cardiovagal reflex.

Figure 2. Resting electrocardiograms recorded approximately 20 years before entry into the study (upper left) and in 1997 (lower left). Obtained from an elderly female with inappropriate sinus tachycardia. Dates, sinus rates (beats/min), and blood pressures (mmHg) are shown on the right.

Bauerfiend⁸ et al. had postulated that IST could be due not only to high intrinsic sinus rates but also to high resting sympathetic nerve influences with normal parasympathetic influences, as well as to a predominantly deficient resting parasympathetic influence with normal sympathetic nerve influences.

It is possible for analysis of traditional HRV not to be able to support a primary sympathetic or parasympathetic mechanism. Perhaps nonlinear indices such as approximate entropy and detrended fluctuation analysis may be more useful in this regard.

The present study adds some insight regarding the *natural history* of IST. As previously stated, in most reports patients with IST have been females with ages between 15 and 46 years,^{1,4,5,8} and only one patient was 58 years old.⁸ Symptoms rarely exceed 10 years since only two patients had palpitations for 12 and 15 years prior to being studied.⁷ These findings contrast with those observed

in our patients who were older and had symptoms for more than 15 years. Although the arrhythmia was categorized late in life, it was definitely present in middle age and could even have started when the patients were young (as in most contemporary studies). It is interesting that, while apparently normotensive when young, all four patients with IST developed systemic hypertension after many years of sustained cardiac symptoms of palpitations and documented high resting heart rates. Although a cause-effect relation between chronic IST and systemic hypertension cannot be established based on the results of the present study, it is possible that treatment of their IST could facilitate the treatment of the underlying systemic hypertension.

The occurrence of cardiomegaly has been only anecdotally mentioned in previous reports dealing with IST.³ Although these reports did not specify the type of cardiomegaly, we did not observe dilated cardiomyopathy in our four patients with

chronic IST. However, three of the four elderly females had echocardiographic evidence of mild left ventricular hypertrophy and diastolic dysfunction; therefore, we believe that the tachycardia-induced cardiomyopathy is probably rare in patients with IST as opposed to other types of incessant supraventricular tachycardias.^{9,10} An important factor could be the fact that the former has average and maximal rates that are definitely slower than those of the latter.

The relation of anxiety disorders and IST is even less clear. It is tempting to speculate that the palpitations, dizziness, and presyncope, presumably due to the rapid sinus rates, could have been misinterpreted by the physicians, considered as psychoneurotic symptoms, and treated as such. Likewise, the patients themselves, having been told that they had no organic heart disease, could have self-interpreted the symptoms as psychogenic, consequently somatizing, and thus developing these disorders.

In conclusion, in some cases IST may start at an early age and can become chronic, persisting until later in life if not treated adequately. Thus, treatment should be initiated as early as possible, as soon as the diagnosis is made. This will probably have a significant impact on the quality of life of these patients.

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