ORIGINAL ARTICLE

Prevalence of inappropriate sinus tachycardia and the comparison of the heart rate variability characteristics with propensity score-matched controls

Uygunsuz sinüs taşikardisinin prevalansı ve propensite skor eşleşmeli kontrol grubu ile kalp hızı değişkenliğinin karşılaştırılması

Evrim Şimşek, M.D.,[1] Benay Özbay, M.D.,[1] İnan Mutlu, M.D.,[1] Ecem Gürses, M.D.,[1] Hatice S. Kemal, M.D.,[2] Burcu Yağmur, M.D.,[1] Levent Hürkan Can, M.D.[1]

[1]Department of Cardiology, Ege University Faculty of Medicine, İzmir, Turkey

[2]Department of Cardiology, Near East University Faculty of Medicine, Lefkose, Turkish Republic of Northern Cyprus

ABSTRACT

Objective: Inappropriate sinus tachycardia (IST) is a syndrome characterized by an elevated resting heart rate with distressing symptoms and no secondary cause of sinus tachycardia. This study was conducted to evaluate both the prevalence of IST among symptomatic patients and heart rate variability (HRV) characteristics.

Methods: The records of all consecutive symptomatic patients who had undergone 24-hour Holter monitoring between September 2015 and November 2016 at a single center were retrospectively evaluated. IST was defined as a 24-hour mean heart rate (HR) of ≥90 beats/minute and a resting HR of ≥100 beats/minute in the absence of any secondary cause of sinus tachycardia. All of the study data related to clinical characteristics, symptoms, concomitant diseases, and Holter electrocardiogram parameters were obtained from the electronic hospital records. A propensity age- and sex-matched control group was selected from a non-IST patient cohort.

Results: A total of 1865 consecutive patients were evaluated and 32% were excluded due to an inadequate Holter recording period or insufficient quality, atrial fibrillation episodes, atrioventricular block, or >1% atrial or ventricular extrasystoles. Among 1265 patients with sinus rhythm, 4.98% (n=63) had IST. The IST patients were younger (39.6±17.4 vs. 50.2±17.2 years; p<0.001), and female gender was more prominent (60.3% vs. 43.8%; p=0.009). All of the time and frequency domain parameters of HRV except the low frequency/high frequency ratio were significantly reduced in the IST group compared with the propensity-matched controls.

Conclusion: The IST prevalence among symptomatic patients in sinus rhythm was 4.98%. IST was primarily seen in younger women, and they had diminished time and frequency domain HRV parameters.

ÖZET

Amaç: Uygunsuz sinüs taşikardisi (UST) herhangi bir ikincil neden olmadan artmış istirahat kalp hızı ve rahatsız edici semptomlarla karakterize bir sendromdur. Daha önce çok değerlendirilmemiş özellikle semptomatik hastalarda UST prevalansını ve bu hastalardaki kalp hızı değişkenliğini (HRV) değerlendirmek için mevcut çalışma tasarlanmıştır.

Yöntemler: Eylül 2015 ile Kasım 2016 tarihleri arasında tek bir merkezde 24 saat Holter elektrokardiyografi (EKG) tetkiki yapılan hastalar retrospektif olarak değerlendirildi. UST, ikincil bir neden olmadan 24 saatlik ortalama KH ≥90 vuru/dk. ve istirahat KH ≥100 vuru/dk. olması olarak tanımlandı. Hastaların yaş, cinsiyet gibi bazal karakteristik özellikleri, eşlik eden hastalıkları ve Holter EKG dataları elektronik hasta kayıt dosyalarından alındı. HRV analizi için UST olmayan hasta kohortundan yaş ve cinsiyete göre propensite skor eşleşmeli kontrol grubu oluşturuldu.

Bulgular: Toplam 1865 ardışık hasta değerlendirildi ve hastaların %32'si yetersiz kayıt süresi veya kalitesi, atriyal fibrilasyon atakları, atriyoventriküler blok ve >%1 atriyal veya ventriküler ekstra sistoller nedeniyle dışlandı. Sinüs ritmi olan 1265 hastanın %4.98'inde (63) UST saptandı. UST hastaları daha gençti (39.6±17.4'e karşı 50.2±17.2, p<0.001) ve kadın cinsiyet daha belirgindi (%60.3'e karşı %43.8, p=0.009). UST hasta grubunda propensite eşleşmeli kontrol grubuna göre LF/HF dışındaki tüm zaman ve frekans temelli HRV parametreleri azalmış olarak izlendi.

Sonuç: Semptomatik sinüs ritmindeki hastalarda UST prevalansı %4.98'dir. Sendrom genç kadınlarda daha fazla görülmektedir ve genel olarak zaman ve frekans temelli HRV parametreleri bozulmuştur.

Received: June 12, 2019 *Accepted:* October 04, 2019

Correspondence: Dr. Evrim Şimşek. Ege Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, İzmir, Turkey.
Tel: +90 232 - 343 43 43 e-mail: drevrimsimsek@gmail.com

Inappropriate sinus tachycardia (IST) is a syndrome characterized by an elevated resting heart rate with disturbing symptoms and no secondary cause of sinus tachycardia. It is generally considered to be a benign condition; however, the symptoms may cause severe limitations to daily life and there is also a risk of developing tachycardiomyopathy.[1,2] There were no standard diagnostic criteria until a recent expert consensus document defined IST as a sinus heart rate (HR) of ≥100 beats/minute (bpm) at rest with a mean 24-hour HR of ≥90 bpm and distressing symptoms.[3]

The data on IST are scarce; most of the current knowledge has been generated from several reports of small case series with varying diagnostic criteria.[4,5] Although the recent expert consensus statement emphasizes symptomatic status as a diagnostic criterion, the only available prevalence data (1.16%) are from a middle-aged, asymptomatic patient population.[6] Moreover, the underlying mechanisms of IST are poorly understood. Elevated intrinsic sinus node automaticity and decreased parasympathetic activity and/or beta-adrenergic hypersensitivity have been suggested among possible etiological factors.[7,8] Heart rate variability (HRV), which reflects neuro-autonomic regulation of the heart, has also been analyzed in only small case-control studies of IST.[6,9,10]

The present study was designed to evaluate the prevalence of IST according to the recently agreed upon diagnostic criteria among patients who had undergone 24-hour Holter monitoring due to their symptoms. Additionally, HRV was assessed as a possible factor underlying IST pathophysiology in comparison with an age- and gender-matched non-IST control group.

METHODS

This cross-sectional study initially included all consecutive, symptomatic patients aged 18-85 years from a single center (Department of Cardiology, Ege University School of Medicine) who had undergone a 24-hour Holter recording during the period between September 2015 and November 2016. Holter recording results and clinical data were obtained from the electronic hospital medical records. In the event that there was more than 1 Holter recording per patient, the first recording was used for analysis. All of the patients were retrospectively evaluated for the presence of IST, defined as a 24-hour mean HR of ≥90 bpm and a resting HR of ≥100 bpm in the absence of a secondary cause of sinus tachycardia. Demographic and clinical information, including age; gender; history of hypertension, diabetes, or coronary artery disease; medication use; ejection fraction; and the primary symptom leading to hospital presentation, were also retrieved from hospital records. Patients whose medical records were not accessible or who did not have sufficient clinical information were excluded. Possible causes of a miscalculation of a mean HR were also excluded. Patients with <20 hours of Holter recording time, atrial fibrillation and/or flutter episodes, pacemaker rhythm, ventricular or atrial ectopic beat burden ≥1% of all beats, and 2nd or 3rd degree atrioventricular block episodes were all excluded (Fig. 1). The electronic medical records of patients with a mean HR of ≥90 bpm were analyzed for secondary causes of tachycardia, such as anemia (hemoglobin <10 g/dL), thyroid pathology (abnormal thyroid-stimulating hormone level), history of heart failure, stroke, infection, and pregnancy. Patients with potential secondary causes of tachycardia were excluded.

Abbreviations:

Bpm	*Beats/minute*
ECG	*Electrocardiogram*
HF	*High frequency*
HR	*Heart rate*
HRT	*Heart rate variability*
IST	*Inappropriate sinus tachycardia*
LF	*Low frequency*
NN	*Normal-to-normal intervals between QRS complexes in normal sinus rhythm*
RMSSD	*Square root of the mean squared difference of successive NN intervals*
SDANN	*Standard deviation of the average NN intervals calculated over 5-minute periods*
SDNN	*Standard deviation of all NN intervals*
SR	*Sinus rhythm*
ULF	*Ultra low frequency*
VLF	*Very low frequency*

The clinical characteristics and HRV parameters of patients with IST were evaluated in comparison with a group of non-IST patients (in sinus rhythm [SR] with a mean HR of <90 bpm). There are known age- and gender-dependent alterations in HRV parameters among the healthy population.[11] To evaluate HRV parameters, a 1:1 propensity score-matched control group, also matched for age and gender, was created from the non-IST patients of the study consisting of patients in SR with a mean HR of <90 bpm and without any known secondary pathologies, such as heart failure, thyroid pathology, anemia, acute stroke, or the use of beta blockers or calcium channel blockers. In addition, patients without any secondary cause of

sinus tachycardia and a HR <100 bpm on a resting electrocardiogram (ECG) were also excluded (Fig. 1). The study protocol was approved by the institutional review board (approval number: 18-10.1/6).

24-hour Holter recordings

All of the Holter recordings were analyzed both manually and automatically with NH-301 ECG Holter Analysis software v2.4.5 (Norav Medical, Del Ray, FL, USA) to assess underlying rhythm, mean HR, arrhythmia episodes, and HRV parameters. Both the standard time and frequency domain HRV parameters were evaluated. The HRV parameters of the normal-to-normal interval between QRS complexes in normal sinus rhythm (NN), the standard deviation of NNs (SDNN), the standard deviation of the average NN intervals calculated over 5-minute periods (SDANN), and the square root of the mean squared difference of successive NN intervals (RMSSD) were included. Spectral power components of HRV included the high frequency (HF) band, which captures HR oscillations in the range of 9 to 24 cycles per minute, similar to adult respiratory frequencies (0.15–0.40 Hz); low frequency (LF) oscillations in the range of 3 to 9 cycles per minute (0.04–0.15 Hz); very low frequency (VLF) oscillations in a pattern at frequencies between every 25 seconds and 300 seconds (0.003–0.04 Hz); and ultra low frequency (ULF) oscillations occurring every 5 minutes to once in 24 hours (≤0.003 Hz).[11]

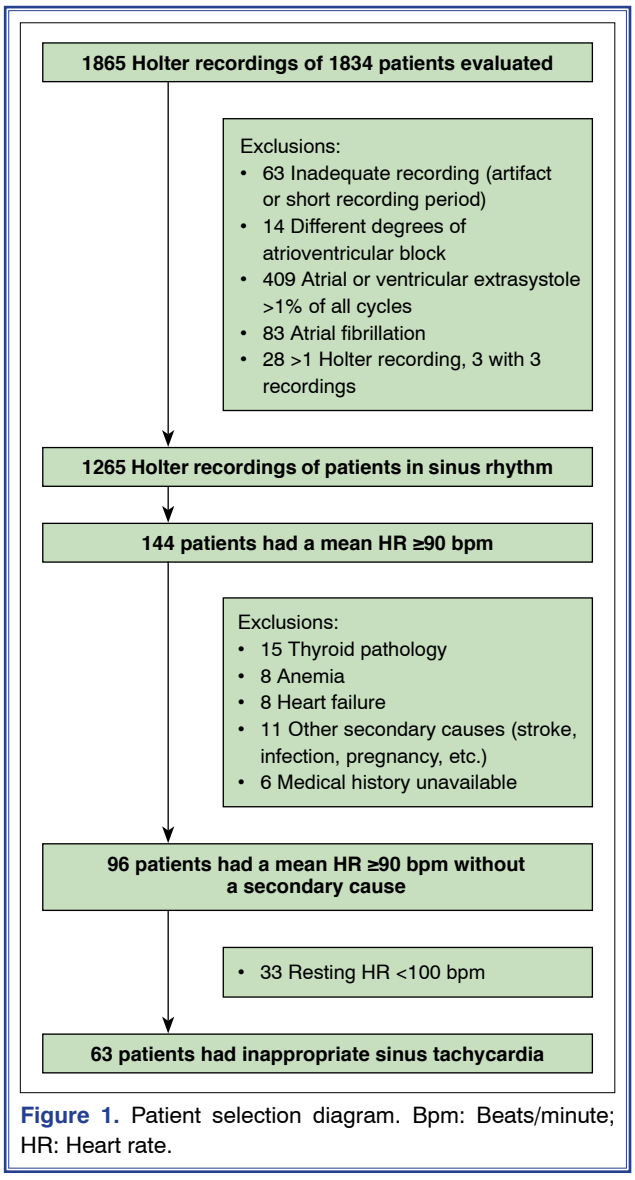

Figure 1. Patient selection diagram. Bpm: Beats/minute; HR: Heart rate.

Statistical analyses

Continuous variables were expressed as mean and SD or median and interquartile range if the variable did not have normal distribution, and categorical variables were expressed as numbers with percentages. The groups with and without IST were compared using a t-test or the Mann-Whitney U test for continuous variables, and a chi-square or Fisher's exact test for categorical variables as appropriate. The covariates for the calculation of propensity score were age and gender. IST patients and the propensity score-matched control group were compared using a paired samples t-test or the Wilcoxon signed-rank test for continuous variables according to the distribution of the data, and the McNemar test was used for categorical variables. A p value of <0.05 was considered statistically significant, and the confidence intervals were calculated at a confidence level of 95%. Analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA)

RESULTS

Of the initially enrolled 1834 patients, who had a total of 1865 24-hour Holter recordings, 600 (32.2%) were excluded because they did not fulfil the inclusion criteria (Fig. 1). SR was detected in the Holter recordings of 1265 patients and only 144 (11.3%) had a mean HR of >90 bpm. Ninety-six patients had a mean HR of ≥90 bpm and did not have a secondary cause. The elevated resting HR (>100 bpm) criterion for an IST diagnosis led to the exclusion of 33 patients. In all, 63 patients (4.98% of the patients with SR) were diagnosed as IST.

The mean age of the patients with IST was 39.67±17.36 years and the majority (60.3%) were female. The major symptom was palpitations in all of the IST patients but one, who presented with the complaint of exertional dyspnea. Only a minority (28.6%) of the IST group had a concomitant disease: 28.6% had hypertension and 9.5% had diabetes mellitus. All had a normal level of thyroid stimulating hormone. Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers were used by 20.6% of the IST patients and 6.3% were taking a beta blocker. Only 1 patient was using a dihydropyridine calcium channel blocker. Fifty-five percent of the IST patients had an echocardiogram before or at the time of the Holter recording. All of the patients had a normal left ventricular ejection fraction and none had moderate or severe valve disease. Neither the IST group nor the propensity score-matched control group had a history or physical signs of heart failure.

IST vs. non-IST control group

Table 1 shows a comparison of characteristics of the IST (n=63) and non-IST (n=1121) groups. The IST patients were significantly younger and more than half (54%) were under the age of 35 years. Only 24.2% of the non-IST patients were under the age of 35 years (p<0.001). Female gender was more prominent in the IST patients (60.3% vs 43.6%; p=0.009). HRV time and frequency domain parameters were both significantly reduced in the IST group compared with the non-IST patients, with the exception of the LF/HF ratio.

IST vs. propensity score-matched non-IST control group

The comparison between the IST and the propensity score-matched (for age and gender) non-IST group revealed that the time domain parameters of SDNN, SDANN, and RMSSD were significantly lower in patients with IST. In addition, the IST group had significantly reduced UF, VLF, LF, and HF frequency domain parameter values compared with the non-IST control group. However, there was no significant difference in the LF/HF ratio between the groups (Table 2).

DISCUSSION

The present study revealed that IST is relatively common in symptomatic patients, with a prevalence of 4.98% in a large, retrospectively evaluated population (n=1265) aged 18–85 years. The available literature about IST consists of a few, small, scaled studies generally exploring asymptomatic patients.[4,9,10,12] The only prospective prevalence study, conducted by Still et al.,[6] reported a prevalence of IST of 1.16% in 604 asymptomatic patients (with or without hypertension) aged 40–59 years. The higher prevalence observed in the present study may be due to symptomatic status and the age range of patients included.

Table 1. Comparison of IST patients and non-IST patients in sinus rhythm with a mean heart rate of <90 beats/minute

	Non-IST (n=1121)	IST (n=63)	*p*
Age (years)	50.23±17.19	39.67±17.36	<0.001
Age ≤35, n (%)	271 (24.2)	34 (54)	<0.001
Female, n (%)	489 (43.6)	38 (60.3)	0.009
Mean heart rate (bpm)	70.70±8.37	96.69±6.99	<0.001
Standard deviation of all NN intervals (ms)	133.21±44.0	100.05±35.61	<0.001
Standard deviation of the average NN intervals (ms)	118.48±40.97	92.66±37.55	<0.001
RMSSD (ms)	34.16±19.19	23.55±10.87	<0.001
Ultra low frequency (ms^2)	16341.89±11778.94	10358.02±9126.96	<0.001
Very low frequency (ms^2)	2232.10±4661.73	1543.58±4020.12	<0.001
Low frequency (ms^2)	1432.84±3664.24	1347.26±3990.33	0.011
High frequency (ms^2)	576.83±732.57	392.36±417.59	0.007
Low frequency/High frequency	2.70±2.87	2.75±2.19	0.957

IST: Inappropriate sinus tachycardia; NN: Normal-to-normal interval between QRS complexes in normal sinus rhythm; RMSSD: Square root of the mean squared difference of successive NN intervals.

Table 2. Comparison of IST patients and age- and gender-matched propensity score non-IST control group (derived from non-IST patients included in the study)

	Non-IST control (n=63)	IST (n=63)	*p*
Age (years)	39.05±16.83	39.67±17.36	0.891
Female, n (%)	34 (54)	38 (60.3)	0.471
Hypertension, n (%)	11 (17.5)	18 (28.6)	0.230
Diabetes mellitus, n (%)	3 (4.8)	6 (9.5)	0.508
Coronary artery disease, n (%)	2 (3.2)	3 (4.8)	1
ACEI/ARB, n (%)	11 (17.5)	3 (20.6)	0.650
-blocker, n (%)	0 (0)	4 (6.3)	0.119
Calcium channel blocker, n (%)	0 (0)	1 (1.6)	1
Symptoms, n (%)			
Palpitations	56 (88.9)	62 (98.4)	
Exertion dyspnea	3 (4.8)	1 (1.6)	
Syncope	4 (6.3)	0 (0)	
Mean heart rate (bpm)	79.11±7.35	96.69±6.99	<0.001
Standard deviation of all NN intervals (ms)	140.96±38.82	100.05±35.61	<0.001
Standard deviation of the average NN intervals (ms)	126.34±36.09	92.66±37.55	<0.001
RMSSD (ms)	36.09±15.92	23.55±10.87	<0.001
Ultra low frequency (ms^2)	17920.98±9909.04	10358.02±9126.96	<0.001
Very low frequency (ms^2)	2007.17±1206.81	1543.58±4020.12	<0.001
Low frequency (ms^2)	1356.03±1171.06	1347.26±3990.33	0.012
High frequency (ms^2)	654.72±684.61	392.36±417.59	0.025
Low frequency/High frequency	2.45±1.2	2.75±2.19	0.795

ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; IST: Inappropriate sinus tachycardia; NN: Normal-to-normal interval between QRS complexes in normal sinus rhythm; RMSSD: Square root of the mean squared difference of successive NN intervals.

There are some registries in the literature that have reported a prevalence of an increased resting HR (>100 bpm) of 2.1–3.3% in men and 3.2–4.6% in women.[13–15] However, these studies were conducted in very large, asymptomatic populations and based on a resting ECG, not Holter analysis; therefore, the results will likely not represent the true prevalence of IST.

The demographic data of IST patients available in the literature are mostly generated from case reports or case series of young, female patients. Rubinstein et al.[4] studied 22 patients with IST with a mean age of 32.6±9 years. However, IST can also be observed in older patients. The case of a 71-year-old patient with IST has been reported in the literature,[4] and the oldest IST patient in the present study was 76 years old. The reported cases of IST are typically female patients.[16] All of the patients were female in the Rubinstein[4] series of 22 patients and 60.3% of the patients in the current study were female. The reason for female dominance is not clear; however, the high symptom burden of female patients may lead to more hospital admissions and more IST diagnoses.[5] The reason for the lack of gender differences in the Still et al.[6] IST series (57% vs 55%; p: ns) might be due to the inclusion of only asymptomatic patients.

The pathophysiology underlying IST is still unclear. There are several reports suggesting possible mechanisms of impaired neurohormonal modulation, beta-adrenergic hypersensitivity, decreased parasympathetic activity, and/or elevated intrinsic sinus node rate.[7,8] Morillo et al.[17] reported that IST patients had an elevated intrinsic HR and normal sympatho-vagal balance, while Castellanos et al.[10] found a normal intrinsic HR in 6 of 7 IST patients. They also reported abnormal autonomic control of sinus node with diminished increase in HR with atropine and marked slowing with propranolol. In the present study, we evalu-

ated HRV as an indicator of neuro-autonomic balance in order to illuminate its role in the pathophysiology of IST. HRV mostly reflects neuro-autonomic mechanisms, which regulate sinus node pacemaker activity.

The present results also showed that HRV parameters were significantly deteriorated in patients with IST compared with both the non-IST population and the 1:1 propensity-matched non-IST group (Tables 1 and 2). Diminished time domain HRV parameters reflect the lack of a circadian rhythm in IST.[11,18–20] Castellanos et al.[10] studied 10 IST patients and 10 age- and gender-matched controls, and Still et al.[6] evaluated only 7 IST patients. Both studies found that time domain HRV parameters (SDNN, SDANN and RMSSD) were decreased in the IST group . The present study confirmed these results in a larger IST population (n=64) compared with non-IST subjects.

The frequency domain HRV parameters of UF, VLF, and HF are accepted as markers of parasympathetic activity. LF reflects the combined modulation of parasympathetic and sympathetic nervous system and baroreceptor activity of the heart.[11] Our study results demonstrated that IST patients had reduced UF, VLF, LF, and HF parameters compared with both the non-IST population and the propensity score-matched patients (Table 1 and 2). Reduced UF, VLF, and HF parameters in patients with IST probably denote decreased parasympathetic activity. These results are all consistent with the previous small studies of ≤10 IST patients.[6,9,10]

The LF/HF ratio, a measure of relative activity or sympatho-vagal balance, is expected to increase in IST patients. However, LF is also a marker of baroreceptor activity. Leon et al.[12] observed an impaired baroreflex gain in 8 patients with IST, as in the present study. The LF/HF ratio represents a mathematical relationship between the numerator and denominator, regardless of the absolute values, and a decrease in both parameters is a possible explanation of the lack of a significant difference in the LF/HF ratio between IST and control groups.[10] These results reinforce the hypothesis of decreased parasympathetic activity in the pathophysiology of IST.

Limitations

The retrospective nature of the study is the main limitation. However, it constitutes the largest IST patient series to date, with 64 symptomatic patients. Previous series have included a maximum of 25 patients. The evaluation of only symptomatic patients might be accepted a selection bias. However, to the best of our knowledge, by including only symptomatic patients, the present study constitutes the only IST data set consistent with the new IST definition.[3]

Conclusion

The evaluation of a large population of symptomatic patients with new, standardized diagnostic criteria revealed that IST is not as rare as previously reported. The prevalence in this study was 4.98% among symptomatic patients in SR. It is mostly seen in younger women. Both the time and frequency domain HRV parameters are significantly reduced in IST patients, which might indicate a causal disturbance of parasympathetic activity.

Ethics Committee Approval: The study was approved by local clinical research ethics committee (Approval number: 18-10.1/6).

Acknowledgements: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Peer-review: Externally peer-reviewed.

Conflict-of-interest: None.

Authorship contributions: Concept: E.Ş.; Design: E.Ş.; Supervision: E.Ş.; Materials: E.Ş., B.Ö., İ.M., E.G.; Data: E.Ş., B.Ö., İ.M., E.G.; Analysis: E.Ş., B.Ö., H.S.K., B.Y., L.C.; Literature search: E.Ş., H.S.K., B.Y., L.C.; Writing: E.Ş., H.S.K., B.Y., L.C.; Critical revision: E.Ş.

REFERENCES

1. Winum PF, Cayla G, Rubini M, Beck L, Messner-Pellenc P. A case of cardiomyopathy induced by inappropriate sinus tachycardia and cured by ivabradine. Pacing Clin Electrophysiol 2009;32:942–4. [CrossRef]
2. Sağ S, Çoşkun H, Baran İ, Güllülü S, Aydınlar A. Inappropriate sinus tachycardia-induced cardiomyopathy during pregnancy and successful treatment with ivabradine. Anatol J Cardiol 2016;16:212–3. [CrossRef]
3. Sheldon RS, Grubb BP 2nd, Olshansky B, Shen WK, Calkins H, Brignole M, et al. 2015 heart rhythm society expert consensus statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope. Heart Rhythm 2015;12:e41–63. [CrossRef]
4. Rubenstein JC, Freher M, Kadish A, Goldberger JJ. Diurnal heart rate patterns in inappropriate sinus tachycardia. Pacing Clin Electrophysiol 2010;33:911–9. [CrossRef]
5. Pellegrini CN, Scheinman MM. Epidemiology and definition

of inappropriate sinus tachycardia. J Interv Card Electrophysiol 2016;46:29–32. [CrossRef]
6. Still AM, Raatikainen P, Ylitalo A, Kauma H, Ikäheimo M, Antero Kesäniemi Y, et al. Prevalence, characteristics and natural course of inappropriate sinus tachycardia. Europace 2005;7:104–12. [CrossRef]
7. Olshansky B, Sullivan RM. Inappropriate sinus tachycardia. J Am Coll Cardiol 2013;61:793–801. [CrossRef]
8. Peyrol M, Lévy S. Clinical presentation of inappropriate sinus tachycardia and differential diagnosis. J Interv Card Electrophysiol 2016;46:33–41. [CrossRef]
9. Lopera G, Castellanos A, Moleiro F, Huikuri HV, Myerburg RJ. inappropriate sinus tachycardia in elderly females. Ann Noninvasive Electrocardiol 2003;8:139–43. [CrossRef]
10. Castellanos A, Moleiro F, Chakko S, Acosta H, Huikuri H, Mitrani RD, et al. Heart rate variability in inappropriate sinus tachycardia. Am J Cardiol 1998;82:531–4. [CrossRef]
11. [No authors listed]. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation 1996;93:1043–65.
12. Leon H, Guzman JC, Kuusela T, Dillenburg R, Kamath M, Morillo CA. Impaired baroreflex gain in patients with inappropriate sinus tachycardia. J Cardiovasc Electrophysiol 2005;16:64–8. [CrossRef]
13. Sharashova E, Wilsgaard T, Mathiesen EB, Løchen ML, Njølstad I, Brenn T. Resting heart rate predicts incident myocardial infarction, atrial fibrillation, ischaemic stroke and death in the general population: the Tromso Study. J Epidemiol Community Health 2016;70:902–9. [CrossRef]
14. Pfister R, Michels G, Sharp SJ, Luben R, Wareham NJ, Khaw KT. Resting heart rate and incident heart failure in apparently healthy men and women in the EPIC-Norfolk study. Eur J Heart Fail 2012;14:1163–70. [CrossRef]
15. Benetos A, Rudnichi A, Thomas F, Safar M, Guize L. Influence of heart rate on mortality in a French population: role of age, gender, and blood pressure. Hypertension 1999;33:44–52. [CrossRef]
16. Diker E, Canbay A, Celebi ÖÖ, Aydoğdu S. Migration of the breakthrough: the advantage of noncontact mapping in targeting inappropriate sinus tachycardia. Turk Kardiyol Dern Ars. 2010;38:355–8.
17. Morillo CA, Klein GJ, Thakur RK, Li H, Zardini M, Yee R. Mechanism of 'inappropriate' sinus tachycardia. Role of sympathovagal balance. Circulation 1994;90:873–7. [CrossRef]
18. Nolan J, Batin PD, Andrews R, Lindsay SJ, Brooksby P, Mullen M, et al. Prospective study of heart rate variability and mortality in chronic heart failure: results of the United Kingdom heart failure evaluation and assessment of risk trial (UK-heart). Circulation 1998;98:1510–6. [CrossRef]
19. Frey B, Heinz G, Binder T, Wutte M, Schneider B, Schmidinger H, et al. Diurnal variation of ventricular response to atrial fibrillation in patients with advanced heart failure. Am Heart J. 1995;129:58–65. [CrossRef]
20. Kleiger RE, Stein PK, Bigger JT Jr. Heart rate variability: measurement and clinical utility. Ann Noninvasive Electrocardiol 2005;10:88–101. [CrossRef]

Keywords: Epidemiology; heart rate variability; Holter electrocardiogram; inappropriate sinus tachycardia.

Anahtar sözcükler: Epidemiyoloji; kalp hızı değişkenliği; Holter elektrokardiyografi; uygunsuz sinüs taşikardisi.