Cardiac arrhythmias and conduction defects in systemic sclerosis

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Background: One of potentially fatal effects of systemic sclerosis, cardiac involvement is mostly brought on by collagen fiber deposition in heart, which then results in aberrant conduction.
Aim and objectives: to the frequency of arrhythmias and conduction disturbances and to determine the characteristics and risk factors associated with the occurrence of dysrhythmias in patients with SSc.
Patients and Techniques: 30 studied cases with diffuse or restricted cutaneous scleroderma underwent transthoracic echocardiography, twelve-lead electrocardiogram, & twenty four-hour Holter ECG monitoring.
Results: mean years old of patients had been 58.28 (±14.16 SD) with range (37-81). consistent with the 24-hour Holter monitor findings there were 34 (68%) with relevant arrhythmias and 15 (30%) with atrial fibrillation/flutter. that according to the 12-day ECG patch monitor findings there were 32 (64%) with relevant arrhythmias and 15 (30%) with atrial fibrillation/flutter. the final prevalence of findings was 29 (58%) for relevant arrhythmias and 11 (22%) for atrial fibrillation/flutter.
Conclusion: Patients with systemic sclerosis have an increased risk of conduction and rhythm disorders both at disease onset and over time, compared to nonsystemic sclerosis patients. These findings warrant increased vigilance and screening for electrocardiogram abnormalities in systemic sclerosis patients with pulmonary hypertension.

Keywords: systemic sclerosis, arrhythmias, conduction defects, cardiac involvement, mortality.

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INTRODUCTION

heart may be impacted by autoimmune illness systemic sclerosis, which has variety of organ-specific symptoms. Heart failure, pericardial disease, & rhythm abnormalities are most common cardiac involvements, & they may be asymptomatic or have little symptoms in early stages of disease **(1)**.
It has poor prognosis, & according to European Scleroderma Trials & Research group (EUSTAR) registries, cardiac problems, primarily heart failure & arrhythmias, account for twenty-six percent of SSc studied cases' deaths **(2)**.
Raynaud phenomenon & cardiac microvascular disease both involve repeated bouts of myocardial ischemia & reperfusion that result in contraction band necrosis & fibrotic foci **(3)**. disruption of microcirculation is thought to be followed by

myocardial fibrosis, which is what causes stiffening of ventricular walls. Due to formation of myocardial electrical inhomogeneities, which are key mechanisms of arrhythmogenesis, this results in systolic & diastolic dysfunction **(4)**.
Although cellular & molecular mechanisms that cause fibrosis to manifest are still poorly understood, number of signalling molecules & extracellular components, including TGF beta (transforming growth factor-beta), reactive oxygen species, & endothelin-1, are thought to be implicated **(5)**.
Endothelin-1 promotes fibroblast proliferation & differentiation into myofibroblasts, & when combined with TGF-b, it stimulates release of connective tissue growth factor, which controls collagen synthesis **(6)**. Through increased expression of its receptors, including TGF-b-RI & TGF-b-RII, TGF-b pathway is linked to excessive collagen formation **(7)**.
SSc studied cases regularly experience arrhythmias & conduction abnormalities; according to EUSTAR investigation, they may account for up to six percent of all-cause deaths in SSc studied cases **(8)**.
While bradyarrhythmia & conduction deficiencies are caused by patchy myocardial fibrosis, which appears to affect conduction system, myocardial fibrosis is likely underlying cause of atrial & ventricular tachyarrhythmias **(9)**.
The present study aimed to assess frequency of arrhythmias & conduction disturbances in SSc patients, & to determine features & risk factors related to occurrence of dysrhythmias in studied cases with SSc.

MATERIAL AND TECHNIQUES

This had been retrospective cohort research was performed on 40 studied cases who underwent insertion of tunneled hemodialysis catheter through common femoral vein.
research included 50 studied cases who met 2013criteria of American College of Rheumatology/European League Against Rheumatism for diffuse or limited cutaneous systemic sclerosis.
In addition to thorough physical examination & blood tests, studied cases also underwent cardiopulmonary testing that included twelve-lead electrocardiogram, twenty four-hour Holter ECG monitoring, transthoracic Doppler echocardiography, spirometry, standard chest radiograph, &, when deemed necessary, high-resolution computed tomography for the detection of pulmonary fibrosis.
Informed written consent had been found from every studied case to be comprised in this research. research protocol had been accepted by ethics committee.
Demographic and clinical variables were gender, age, disease duration, Associated diseases as hypertension, thyroid dysfunction, Dyslipidemia and anemia, medication used and smoking.
Twelve-lead ECGs had been recorded using Esaote P8000electrocardiograph with ECG amplifier sensitivity of ten mm/mV & speed of twenty-five mm/s. twenty four-hour Holter ECG monitoring was done using different electrocardiograph. traces had been thoroughly examined for any signs of myocardial ischemia, low QRS voltage, prolonged QRS, QTc duration, conduction problems, atrial or ventricular hypertrophy, QRS axis deviations, or supraventricular or ventricular arrhythmias. seven-lead BTL CardioPoint H600 device (BTL Industries, Inc., Greeneville, TN) with2000-Hz sampling frequency & sixteen-bit digital resolution was used to capture twenty four-hour Holter ECGs. existence & features of supraventricular & ventricular arrhythmias (total number of premature contractions, number of isolated premature contractions, number of couplets, triplets, & runs; & for ventricular arrhythmias, number of premature ventricular morphologies), existence of paroxysmal

conduction disturbances, QT, & corrected QT had been all studied parameters. When at least one premature ventricular contraction per hour had been documented using Holter ECG monitoring, ventricular arrhythmias had been deemed to be present. Esaote MyLab X-View 50system (Esaote Europe B.V., Maastricht, Netherlands) & 7.5- to 10-MHz transducer had been used to conduct echocardiographic exams. For each subject, typical image acquisition had been carried out. parameters that had been evaluated included chamber size & wall thickness, left & right ventricle systolic & diastolic function, abnormalities in wall motion, systolic, mean, & diastolic pulmonary arterial pressure, existence of valve disease (stenosis & regurgitations), & pericardial effusion. systolic pulmonary arterial pressure of thirty-five to forty-nine mm Hg had been considered mild pulmonary hypertension, fifty to sixty nine mm Hg to be moderate, & seventy mm Hg or higher to be severe.

Complete blood counts, erythrocyte sedimentation rates, blood urea nitrogen levels, creatinine, electrolytes (Na^+, K^+, Ca^{2+}, Cl^-), glycemia, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, uric acid, coagulation parameters (quick time, international normalised ratio, activated partial thromboplastin time), glutamate-oxal Rheumatoid factor, antinuclear antibodies, immunoglobulin A (IgA), IgG, & IgM levels, as well as complement levels, C3, C4, circulating immune complexes, & anti-topoisomerase I (Scl70) levels had been assessed.

RESULTS

Table (1): Distribution of cases according to demographic data

	Subjects (n = 50)	
Age		
Range.	37 – 81	
Mean ± SD.	58.28 ± 14.16	
Gender	No.	%
Female	41	82.0
Male	9	18.0
BMI, kg/m2		
Range.	17.7 – 36.1	
Mean ± SD.	26.63 ± 4.94	
Comorbidities	No.	%
Smoking	8	16.0
Diabetes Mellitus	2	4.0
Hypertension	19	38.0
Hyperlipidemia	16	32.0
Coronary Artery Disease	9	18.0
Pulmonary Hypertension	5	10.0
Interstitial Lung Disease	5	10.0

This table finds that mean age of cases had been 58.28 (±14.16 SD) with range (37-81) years, between cases there had been 41 (82%) female & 9 (18%) male, the mean BMI was 26.63 (±4.94 SD) with range (17.7-36.1) and according to comorbidities there were 8 (16%) smokers, 2 (4%) with DM, 19 (38%) with HTN, 16 (32%) with hyperlipidemia, 9 (18%) with CAD, 5 (10%) with pulmonary hypertension and 5 (10%) with interstitial lung disease.

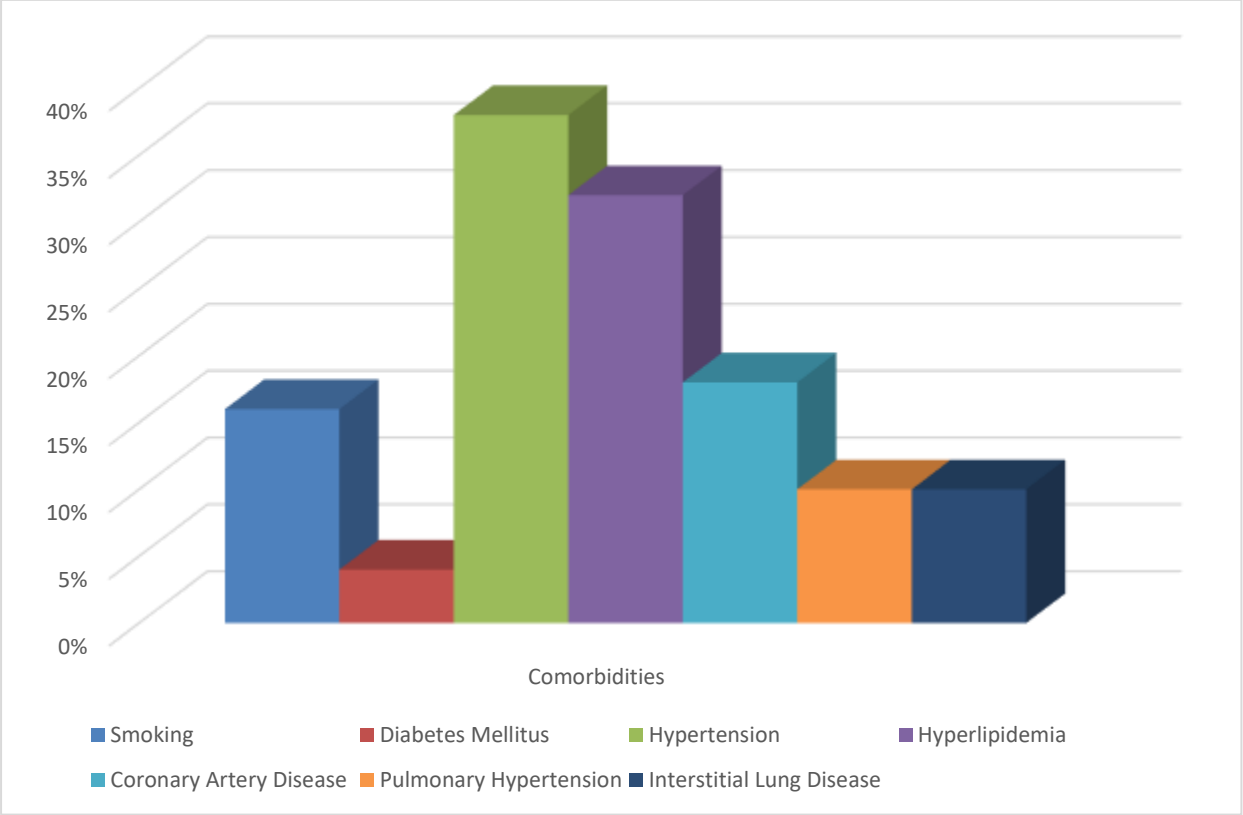

Fig (1): Comorbidities distribution among the studied patients.

Table (2): Distribution of cases according to Indications of ECG monitor

	Subjects (n = 50)	
Indications of ECG monitor	No.	%
Dizziness or near syncope	6	12.0
Ischemic stroke	7	14.0
Palpitation	21	42.0
Syncope	16	32.0

This table shows that according to indications of ECG monitor among the studied cases there were 6 (12%) with dizziness or near syncope, 7 (14%) with ischemic stroke, 21 (42%) with palpitation and 16 (32%) with syncope.

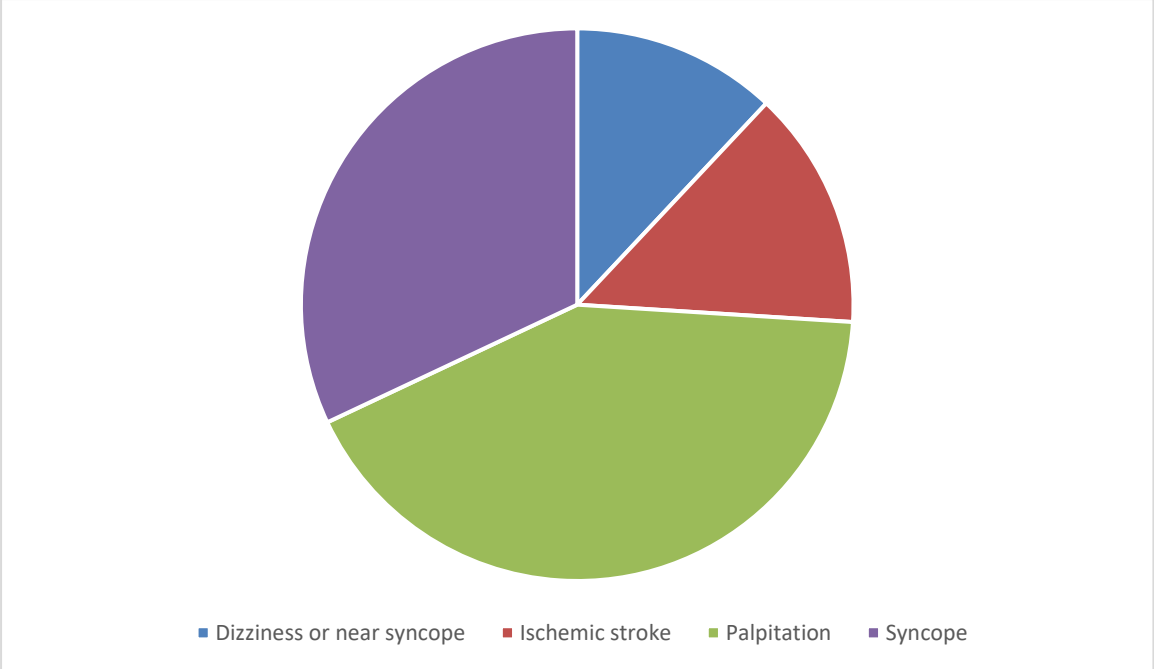

Fig (): Indications of ECG monitor distribution among the studied patients.

Table (3): 24-hour Holter monitor findings among the studied patients

	Subjects (n = 50)	
24-hour Holter monitor	No.	%
Relevant arrhythmias	34	68.0
Atrial fibrillation/flutter	15	30.0

This table shows that according to the 24-hour Holter monitor findings there were 34 (68%) with relevant arrhythmias and 15 (30%) with atrial fibrillation/flutter.

Table (4): 12-day ECG patch monitor findings among the studied patients

	Subjects (n = 50)	
12-day ECG patch monitor	No.	%
Relevant arrhythmias	32	64.0
Atrial fibrillation/flutter	15	30.0

This table shows that according to the 12-day ECG patch monitor findings there were 32 (64%) with relevant arrhythmias and 15 (30%) with atrial fibrillation/flutter.

Table (5): Agreement between24-hour Holter monitor & 12-day ECG patch monitor

		24-hour Holter monitor		**kappa (κ)**
12-day ECG patch	**Relevant arrhythmias**	Positive	Negative	
	Negative	13	3	0.644
	Positive	5	29	
	Atrial fibrillation/flutter			

	Negative	31	4	0.619
	Positive	4	11	

4-hour Holter monitor & 12-day ECG patch monitor showed good substantial agreement regarding lesions classification.

Table (6): Prevalence of relevant arrhythmias & atrial fibrillation/flutter among the studied cases

	Subjects (n = 50)	
	No.	%
Relevant arrhythmias	29	58.0
Atrial fibrillation/flutter	11	22.0

This table shows that the final prevalence of findings was 29 (58%) for relevant arrhythmias and 11 (22%) for atrial fibrillation/flutter.

DISCUSSION

SSc has been linked to electrocardiographic abnormalities, according to various investigations. It is unclear whether electrocardiographic anomalies have been brought on by myocardial participation in SSc, temporary imbalance in oxygen delivery, or some other mechanism **(10).**

In between twenty-five & seventy five percent of SSc studied cases, irregular ECG is found, & it is thought to be reliable predictor of mortality. Arrhythmias can be linked to poor prognosis & account for six percent of all fatal causes in extensive Scleroderma Trials & Research (EUSTAR) database of European League Against Rheumatism (EULAR). thirty-three (twenty six percent) of 128 deaths associated with SSc had been cardiac in nature, with malignant arrhythmias accounting for almost half of them **(11)**.

1 research from250 individuals in Genetics Versus Environment in Scleroderma Outcome Study (GENISOS) cohort reported total of fifty-two deaths, with twenty-nine deaths (55.8percent) being connected to SSc. Only seven variables had been independent predictors of mortality in multivariable Cox model that was used in research, which simultaneously included non-genetic candidate risk factors: BMI, age, FVC, blood pressure, pulmonary fibrosis, anti-centromere antibody, & cardiac arrhythmias [hazard ratio 2.18 (95% CI 1.05, 4.50); P = 0.035 for cardiac arrhythmias] are all significant risk factors **(12)**.

In this research we demonstrated that mean age of cases had been 58.28 (±14.16 SD) with range (37-81) years, between cases there had been 41 (82%) female & 9 (18%) male, the mean BMI was 26.63 (±4.94 SD) with range (17.7-36.1) and according to comorbidities there were 8 (16%) smokers, 2 (4%) with DM, 19 (38%) with HTN, 16 (32%) with hyperlipidemia, 9 (18%) with CAD, 5 (10%) with pulmonary hypertension and 5 (10%) with interstitial lung disease.

Kurmann et al. (13) found that in comparison to comparators, studied cases with SSc had lower prevalence of diabetes (three percent vs. twelve percent; P = 0.02) & obesity (twenty one percent vs. thirty nine percent; P = 0.008). There were seventy-eight incident SSc cases in total, with mean age of56 [SD 15.7] years & ninety-one percent female studied cases. Pulmonary hypertension had been more common in SSc patients (eight percent) compared to non-SSc controls (one percent; P = 0.003).

In study to assess cardiac conduction disturbances in rheumatologic disease, **Gerges et al. (14)** found that the mean age was almost fifty years-old and more than two-thirds of the population was female.

In this study we found that according to indications of ECG monitor among the studied cases there were 6 (12%) with dizziness or near syncope, 7 (14%) with ischemic stroke, 21 (42%) with palpitation and 16 (32%) with syncope.

In study to evaluate cardiac dysrhythmias in progressive systemic sclerosis studied cases, **Ferri et al. (15)** found that 31 studied cases (fifty eight percent) had symptoms, with palpitations most prevalent (forty seven percent) & dizziness (also seventeen percent) & precordial discomfort (seventeen percent) next most frequent.

De Luca et al. (16) found that All of the studied cases who were enrolled had symptoms or physical characteristics that suggested heart condition had been present: dyspnea had been present in sixty-eight studied cases (sixty eight percent), & palpitations affected fifty-eight studied cases (fifty eight percent) of the total. Twelve studied cases (17.7percent) had been in NYHA classes III-IV, while most of studied cases with dyspnea (82.3percent) had been in NYHA class II. Only seven studied cases (seven percent) reported history of intermittent & self-limited chest pain; none had history of unexplained pre-syncope or syncope. 14 studied cases (fourteen percent) exhibited low-limb edoema.

Vascular dysfunction, heart systolic & diastolic dysfunction, & conduction system fibrosis are all consequences of immune dysregulation & recurrent ischemia-reperfusion injury in systemic sclerosis. As a result, severe illness is often accompanied by pulmonary arterial hypertension, heart failure, coronary artery disease, & arrhythmias. studied cases frequently complain of syncope, tiredness, & dyspnea **(17)**.

In this study we found that the final prevalence of findings was 29 (58%) for relevant arrhythmias and 11 (22%) for atrial fibrillation/flutter.

Karabay et al. (18) found that Right ventricular hypertrophy, P-wave notching, low QRS voltage, & nonspecific ST-T wave alterations may all be observed as electrocardiographic abnormalities. Most SSc-studied cases experience supraventricular arrhythmias, which have been more prevalent than ventricular tachyarrhythmias.

study by **Roberts et al. (19)** cardiac arrhythmias had been 1 of best predictors of mortality in studied cases with SSc, with HR of 2.18.29 According to EUSTAR database, ECG abnormalities had been linked to six percent of overall fatalities & thirteen percent of SSc-related deaths.

In a study by **Assassi et al. (20)** of The AV node & His bundles had been often involved in the twenty studied cases with SSc who underwent electrophysiological & histopathologic assessment, & SAN fibrosis had existed in forty percent of these studied cases.

Stronati et al. (21) found that sixteen studied cases (ten percent) had supraventricular arrhythmia with new diagnosis (8.7percent had atrial fibrillation, 1.3percent had atrial flutter), & two studied cases (1.2percent) had ventricular tachycardia.

Tzelepis et al. (22) found that examination of the Holter monitoring data revealed that nineteen (or fifty-three percent) of thirty-six individuals had unfavourable test outcomes. 12 studied cases (sixty three percent) experienced early ventricular contractions, two (10.5percent) experienced supraventricular tachycardias, three studied cases (sixteen percent) experienced premature atrial contractions, two (10.5percent) experienced atrial fibrillation, & two (10.5percent) experienced nonsustained ventricular tachycardias. One studied case (five percent) & 2 more

studied cases (10.5percent) both had left bundle branch block & right bundle branch block, respectively.

De Luca et al. (16) found that 68 studied cases (sixty eight percent) had abnormality on standard ECG; occurrence of ST-T non-specific alterations had been most frequent finding, occurring in thirty-four studied cases (thirty four percent), followed by conduction faults. Particularly, nineteen individuals (nineteen percent) had full or incomplete right bundle branch block. Twelve individuals (twelve percent) experienced supraventricular ectopic beats, & ten studied cases (ten percent) had ventricular ectopic beats.

In research by **Ferri et al. (15)**, 22/53 (forty-two percent) of SSc studied cases had 1 or more aberrant characteristics on their resting ECG. Rhythm disturbances had been seen in thirty percent of studied cases, but when 24-hour Holter ECG monitoring had been done, supraventricular arrhythmias & ventricular arrhythmias had been both discovered in ninety percent of SSc studied cases, with multiform ventricular premature beats being seen in forty percent, pairs of runs of ventricular tachycardia being seen in twenty-eight percent & 1 or more runs of ventricular tachycardia being seen in thirteen percent. Ventricular arrhythmia prevalence & severity did not connect with clinical variations or other clinical symptoms & indicators of illness. While ECG readings had been normal in nearly half of studied cases who had ventricular arrhythmias, studied cases with echocardiographic anomalies had been more likely to have aberrant ventricular arrhythmias. dismal prognosis is commonly accepted for ventricular arrhythmias, especially multiform & repeated ventricular premature beats when they are linked to deteriorated myocardial function. high sensitivity & lesser specificity of Holter ECG can both contribute to increased prevalence of arrhythmias in this research.

multicentre ambulatory ECG research by **Kostis et al. (23)** sixty-seven percent of the 183SSc studied cases exhibited ventricular ectopy, & this anomaly was associated with both total mortality & sudden death. In seven percent & twenty-one percent of studied cases, respectively, episodes of supraventricular tachycardia & ventricular tachycardia had been noted. Even though ventricular arrhythmias happen rather frequently, sudden cardiac death is not extremely common in SSc.

large observational research by **Follansbee et al. (24)** reported sudden cardiac death in Eighteen (five percent) of 391deaths that occurred in 1258SSc studied cases, & individuals with concurrent skeletal & cardiac muscle involvement experienced severe cardiac arrhythmias with poor prognosis substantially more frequently.

In meta-analysis assessing 436consecutive cases, **Follansbee et al. (25)** reported that forty-six percent of studied cases had irregular ECG. irregular ECG had been discovered in ninety-five percent of instances when investigation had been limited to one hundred chosen SSc participants who presented with obvious cardiac abnormalities as determined by thorough cardiopulmonary examination or who passed away from more advanced disease.

Only after thorough & targeted cardiac workup may numerous electrophysiological abnormalities be discovered. **Rokas et al. (26)** SSc studied cases without signs of cardiac involvement or arrhythmias & were evaluated using radionuclide ventriculography, echocardiography, & 24-hour Holter ECG at rest. In fifty-seven percent of studied cases, they discovered 1 or more severe atrioventricular conduction delays, sinus node dysfunctions, or supraventricular or ventricular tachyarrhythmias. abnormal atrial fibres' decreased conduction velocity, variations in resting membrane potential, action potential amplitude, or maximal velocity of action potential upstroke—all of which have been connected to decreased conduction

velocity & abnormal excitability—are likely to be to blame for marked atrial conduction delay. This high incidence in lack of any clinical symptoms or signs on conventional ECG emphasises importance of doing thorough evaluation, even at early stage of disease, long before clinical manifestations of scleroderma heart disease have arisen.

Systemic sclerosis-related pulmonary hypertension compromises left heart filling & ejection by increasing right ventricular strain, elevating end-diastolic pressure, & shifting interventricular septum to left. Reduced cardiac output & hypotension brought on by anaesthesia put coronary perfusion at risk & prolonged right ventricular ischemia. Myocardial ischemia may exacerbate atrioventricular conduction, resulting in total heart block, along with ventricular tachyarrhythmias **(17)**.

CONCLUSION

Comparatively to people without systemic sclerosis, people with the condition are more likely to experience conduction & rhythm problems both at the time of the disease's beginning & later. These results call for enhanced watchfulness & screening for ECG anomalies in individuals with pulmonary hypertension who have systemic sclerosis.

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