Article:
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Supplementary data for:

Abnormal electrophysiological testing associates with future incidental significant arrhythmia in Scleroderma

METHODS

Signal averaged electrocardiogram (ECG) (SAE)

An abnormal SAE was defined as the presence of two of the following criteria: total QRS duration (filtered) ≥114ms, duration of high frequency low amplitude (HFLA) signals less than 40uV ≥39ms, root mean squared (RMS) voltage in terminal 40ms <20uV [1].

Autonomic testing

This was determined using ECG monitoring and performed in the electrophysiology lab before implantation of the implantable loop recorder (ILR). The following parameters were measured, of which normal values are age-related. Autonomic dysfunction was present if two or more of the following four tests were abnormal:

1. Respiratory RR interval variation: The shortest RR interval during inspiration and the longest RR interval during expiration were measured over two minutes. The Expiratory/Inspiratory (E/I) ratio was calculated: mean RRmax (mean)/mean RRmin (mean).
2. Valsalva: measured the shortest RR interval during Valsalva for 15 seconds and longest RR interval within 30s after Valsalva. The longest/shortest RR ratio was then calculated.
3. Maximum/minimum 30:15 ratio: calculated by measuring the longest RR interval between beat 20 and 40, divided by the shortest RR interval between beat 5 and 25 after standing up.
4. Orthostatic dysregulation: The difference in systolic blood pressure (sysBP) was measured from sysBP in the supine position to the lowest sysBP within three minutes of being in the upright position. An abnormal result was a drop of more than 28 mmHg.

RESULTS

Table S1: Baseline 24 hour ECG results in study patients, comparing those developing and not developing significant arrhythmias over the three years.

	All patients (n=19)	Patients developing arrhythmias (n=8)	Patients not developing arrhythmias (n=11)
Abnormal 24 hour ambulatory ECG	8/16 (50)	5/6 (83)	3/10 (30)
Supraventricular tachycardia	2/16 (13)	0/6 (0)	2/10 (20)
Atrial fibrillation	0/16 (0)	0/6 (0)	0/10 (0)
Atrial flutter	0/16 (0)	0/6 (0)	0/10 (0)
Ventricular tachycardia	0/16 (0)	0/6 (0)	0/10 (0)
Couplet	3/16 (19)	3/6 (50)	0/10 (0)
Triplet	1/16 (6)	1/6 (17)	0/10 (0)
Dropped beat	3/16 (19)	2/6 (25)	1/10 (10)
Pause	1/16 (6)	0/6 (0)	1/10 (10)
Bradycardia	0/16 (0)	0/6 (0)	0/10 (0)

Values expressed as n (%)
ECG, electrocardiogram

Table S2: Cardiac serum biomarker and CMR outcomes in study participants with abnormal and normal EP tests at baseline

EP test	Variable	Abnormal EP test	Normal EP test	Mean difference (95% CI)
SAE	**Cardiac serum biomarker**			
	Hs-TnI (ng/l)	257 (223) (n=3)	25 (54) (n=9)	232 (-307.17, 770.35)
	NT-proBNP (ng/l)	180(158) (n=4)	136 (146) (n=9)	44 (-154, 241)
	CK (iu/l)	230 (214) (n=4)	84 (38) (n=8)	146(-190, 483)
	CMR			
	LGE present*	0 (0) (n=2)	3 (50) (n=6)	-
	ECV (%)	27 (4) (n=2)	30 (4) (n=6)	-3 (-10, 4)
	MPR (%)	2.28 (0.20) (n=2)	2.36 (1.47) (n=6)	-0.13 (-2.82, 2.56)
	LVEF (%)	61(3) (n=2)	59 (5) (n=7)	1 (-8, 11)
	LV mass/BSA (g/m^2)	37 (6) (n=2)	46 (14) (n=7)	-9 (-34, 15)
Autonomic testing	**Cardiac serum biomarker**			
	Hs-TnI (ng/l)	194 (185) (n=5)	4 (2) (n=8)	190 (-40, 420)
	NT-proBNP (ng/l)	210 (168) (n=6)	86 (86) (n=8)	125 (-53, 303)
	CK (iu/l)	185 (179) (n=6)	82 (41) (n=7)	103 (-50, 256)
	CMR			
	LGE present*	1 (33) (n=3)	3 (50) (6)	-
	ECV (%)	28 (3) (n=3)	29 (4) (n=6)	-2 (-7, 4)
	MPR (%)	1.75 (0.41) (n=3)	2.56 (1.36) (n=6)	-0.80 (-2.76, 1.15)
	LVEF (%)	61 (8) (n=3)	59 (4) (n=7)	1(-7, 10)
	LV mass/BSA (g/m^2)	39 (6) (n=3)	49(13) (n=7)	-10 (-28, 9)
24 hour ambulatory ECG	**Cardiac serum biomarker**			
	Hs-TnI (ng/l)	119 (174) (n=8)	12 (14) (n=7)	107 (-39, 252)
	NT-proBNP (ng/l)	223 (138) (n=8)	63 (42) (n=8)	164 (47, 281)
	CK (iu/l)	151(178) (n=7)	95 (41) (n=8)	57 (-82, 196)
	CMR			
	LGE present*	1 (25) (n=4)	3 (43) (n=7)	-
	ECV (%)	31 (2) (n=4)	29 (4) (n=7)	1 (-4, 6)

	MPR (%)	1.70 (0.52) (n=4)	2.36 (1.31) (n=7)	-0.66 (-2.24, 0.92)
	LVEF (%)	62 (2) (n=5)	59(4) (n=7)	4 (-3, 1)
	LV mass/BSA (g/m^2)	43(9) (n=5)	45(14) (n=7)	-2 (-18, 1)

Mean (SD) values unless stated otherwise

*n, %

BSA, body surface area; CK, creatine kinase; CI, confidence interval; CMR, cardiovascular magnetic resonance; ECG, electrocardiogram; ECV, extracellular-volume fraction; EP, electrophysiology; Hs-TnI, high-sensitivity troponin; ILR, implantable loop recorder; LGE, late gadolinium enhancement; LV, left ventricular; LVEF, left ventricular ejection fraction; MPR, myocardial perfusion reserve; NT-proBNP, N-terminal pro brain natriuretic peptide; SAE, signal averaged ECG

References

1 Breithardt G. Standards for Analysis of Ventricular Late Potentials Using High-Resolution or Signal-Averaged Electrocardiography - a Statement by a Task-Force Committee of the European-Society of Cardiology, the American-Heart-Association, and the American-College-of-Cardiology. Circulation 1991;83(4):1481-8.