Cardiac abnormalities assessed by non-invasive techniques in patients with newly diagnosed idiopathic inflammatory myopathies

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Abstract

Objective

Knowledge of cardiac involvement in idiopathic inflammatory myopathies (IIM) is limited, especially in the early stage of disease. The objective of the present study was to perform a controlled evaluation of cardiac abnormalities in newly diagnosed, untreated patients with idiopathic inflammatory myopathies (IIM) by means of non-invasive techniques.

Methods

Fourteen patients with IIM (8 polymyositis, 4 dermatomyositis, 2 cancer-associated dermatomyositis) and 14 gender- and age- matched healthy control subjects were investigated. Participant assessments included a cardiac questionnaire, cardiac troponin-I (TnI), electrocardiogram (standard 12-lead and 48-h Holter monitoring), echocardiography with tissue Doppler measures, cardiac magnetic resonance (CMR) imaging with T2 mapping and semi-quantitative ^{99m}technetium pyrophosphate (^{99m}Tc-PYP) scintigraphy.

Results

Dyspnoea was present in 8 (57%) of the patients compared to none of the controls ($p<0.01$). Median levels of TnI in patients and controls were 20 ng/L and 6 ng/L, respectively ($p=0.06$). QTc intervals were prolonged in the patient group ($p=0.01$). Two patients had systolic dysfunction, and one diastolic dysfunction. The myocardial ^{99m}Tc-PYP uptake and CMR results differed between patients and controls, albeit not with statistical significance. Overall, cardiac abnormalities were demonstrated in 9 (64%) of the patients versus 2 (14%) of the controls ($p=0.02$).

Conclusion

Cardiac abnormalities assessed by TnI, ECG or imaging modalities were significantly more common in newly diagnosed, treatment naïve patients with IIM compared to healthy control subjects. These abnormalities, although subclinical, may indicate that myocardial involvement is common in patients and calls for larger controlled studies and further investigations of the prognostic implications of this finding.

Key words

idiopathic inflammatory myopathies, subclinical cardiac involvement, echocardiography, cardiac ^{99m}technetium pyrophosphate scintigraphy, cardiac MR, myocarditis

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Introduction

The clinical manifestations of idiopathic inflammatory myopathies (IIM) include skeletal muscle weakness, and often manifestations from other organ systems including the skin, lungs and the heart. Although symptomatic cardiac involvement is a rare event, the increased mortality rate in IIM is predominantly due to cardiac events (1-4). However, prevalence and significance of subclinical cardiac abnormalities in IIM is not known.

Different methods have been applied in search of cardiac involvement in IIM (5, 6). Electrocardiographic (ECG) changes has been reported in up to 85% (7) and echocardiographic (ECHO) abnormalities in up to 65% (8), with diastolic dysfunction as the most prevalent finding (5). In addition, elevated levels of cardiac enzymes have been found (9-11), including cardiac troponin-I (TnI), which is a highly specific marker of myocardial damage (11). Autopsy studies have reported myocarditis in 25-30% of IIM patients, but whether this is the case also in early disease is not known (12, 13). Endomyocardial biopsy is considered to be the gold standard for myocardial involvement in general, though it is an invasive method not without risks for complications. The more recent availability of non-invasive, highly sensitive imaging techniques has enabled detection of subclinical heart abnormalities. Thus, static planar ^{99m}technetium pyrophosphate (^{99m}Tc-PYP) scintigraphy and cardiac magnetic resonance (CMR) are both useful to detect inflammation in skeletal and cardiac muscles (14-17). The aim of this study was to investigate the frequency and type of cardiac abnormalities in unselected newly diagnosed, untreated patients with IIM by applying non-invasive methods including CMR and cardiac ^{99m}Tc-PYP scintigraphy and to compare the results with a gender- and age- matched control population.

Materials and methods

Participants

Fourteen consecutive patients with newly diagnosed and untreated IIM (8 polymyositis (PM), 4 dermatomyositis (DM), 2 cancer-associated dermatomyositis (CAM)) referred to rheumatology departments at two different hospitals during an 18-month period were included in the study. Seven patients had probable PM/DM and 7 patients had definite PM/DM according to the criteria of Bohan and Peter (18). Patients with overlap syndromes (another autoimmune rheumatic disease aside from IIM) or sporadic inclusion body myositis (sIBM) were excluded. Fourteen healthy controls matched for gender, age and smoking status with no history of cardiovascular (CV) or rheumatic diseases and who did not receive any medication were included by advertisements. All participants were examined at the same centre (Odense University Hospital) except for the CMR, which was performed at Aarhus University Hospital. The study was approved by the local ethics committee (reference number S-20100022) and all subjects gave written informed consent according to the declaration of Helsinki.

Myositis baseline measures

Core patient data included demographics and disease characteristics. Disease activity was recorded as suggested by International Myositis Assessment and Clinical Studies (IMACS) using physician and patient global assessment of disease activity (10-cm visual analogue scale), the Health Assessment Questionnaire (HAQ), myositis intention-to-treat activity index (MITAX), and by a standardised manual muscle test including 8 muscle groups (MMT-8), which were scored individually from 0 to 10, yielding a maximal score of 80 (19). Blood samples were collected at the local hospital. Serum levels of creatine kinase (CK) and C-reactive protein (CRP) were determined by standard methods. Due to different assays between hospitals, CK values were categorised as normal or increased according to the upper reference limit value at each site. Antinuclear antibodies (ANA) were measured by indirect immunofluorescence using Hep-2 cells (Immuno Concepts N.A., Sacramento, California), myositis specific autoantibodies (MSA; anti-Jo-1/PL-7/PL-12/OJ/EJ/SRP/Mi-2) and myositis associated autoantibodies (MAA; anti-PMScl/Ro-52(SSA)/La(SSB)/U1-

RNP/Ku) by line immunoblot (Euroline kit, Euroimmun, Lübeck, Germany). All patients underwent chest X-ray or high-resolution computed tomography (HR-CT).

Cardiovascular baseline measures

Before examination participants completed a questionnaire concerning medical conditions and current medication (confirmed by medical records), smoking habits and heart symptoms (dyspnoea, palpitations, chest pain and syncope). Dyspnoea was defined according to the New York Heart Association classification (NYHA, I-IV) (20). Chest pain was evaluated according to the following characteristics; 1) substernal chest discomfort of characteristic quality and duration; 2) provoked by exertion or emotional stress; 3) relieved by rest and/or nitrates within minutes (21). Ischemic heart disease (IHD) was defined as a history of hospital admission for acute coronary artery syndrome, percutaneous coronary intervention or coronary artery bypass grafting, or major ischemic alterations on ECG as defined by Minnesota codes 1.1 to 3 (22). Upon examination, weight and height were measured and body mass index (BMI) was calculated. Systolic (S-BP) and diastolic blood pressure (D-BP) were recorded three times after five minutes sitting and an average of the last two values was calculated. Hypertension was defined as S-BP of ≥140 mmHg or D-BP ≥90 mmHg or treatment with an antihypertensive drug (23). Blood samples were analysed for glycosylated haemoglobin (HbA1c) and total cholesterol (TC). Diabetes mellitus was defined as HbA1c ≥48 mmol/mol or current antidiabetic therapy (23). Hypercholesterolemia was defined as TC ≥5.0 mmol/L or use of lipid-lowering therapy (23). Serum levels of TnI were measured by Architect c16000 Assay or Architect i2000SR (both Abbott Diagnostics, Illinois, USA). The Limit of Detection for these assays is 10 ng/L and 1.9 ng/L, respectively.

Electrocardiography

Standard 12-lead ECG and 48-h Holter monitoring (ambulatory ECG) were performed. Data from the Holter monitoring were stored, digitised and downloaded to a local workstation for further analysis (Pathfinder, Ambulatory ECG Analysis System, Corona Vitas, Denmark). Holter data were read by a trained technician and data from ECG and Holter were interpreted by an experienced cardiologist according to standard published criteria (24). Regarding ECG analysis, prolonged conduction intervals were defined as; PQ >200ms, QRS >120ms, QTc >450ms (25-27).

Echocardiography

A comprehensive trans-thoracic echocardiography (ECHO) was performed by two experienced cardiologists. All images were stored digitally for subsequent offline analysis, blinded for patient and control data. From the apical 2- and 4-chamber views, left ventricular (LV) volumes and ejection fraction (EF) were estimated. LV filling was determined from assessment of mitral inflow and of diastolic motion of the mitral plane using tissue Doppler imaging (TDI). From the apical 4-chamber view mitral inflow was recorded using pulsed Doppler ECHO with the cursor parallel to the flow and the sample volume at the tip of the mitral leaflets in diastole. From the image peak early (E) flow velocity and E-wave deceleration time were assessed. Pulsed TDI was obtained from the lateral mitral valve annulus, the early diastolic (e') velocity was measured and E/e' ratio was calculated, E/e' >12 was defined as abnormal. All Doppler-derived parameters were measured and averaged from five consecutive beats during expiration. Left atrium (LA) volume was estimated from the apical 4- and 2-chamber views and corrected for body surface area. LV filling was categorised into four distinct filling patterns based on transmitral inflow, E-wave deceleration time and e' velocity (28). Diastolic dysfunction was defined as "e' " ≤10 cm/s and "LA volume / body surface area" ≥34 ml/m^2 (28).

^{99m}Technetium pyrophosphate (^{99m}Tc-PYP) scintigraphy

The scintigraphic imaging was performed 3 h after intravenous injection of 550 Mbq ^{99m}Tc-PYP using a Siemens Symbia T16 SPECT/CT scanner equipped with low-energy high-resolution collimators with a 15% energy window centred around the 140 keV photo peak of ^{99m}Tc. Single photon emission computed tomography (SPECT) of the heart region was acquired with 64 projections, 40 seconds per projection over a 360-degree orbit in a 128x128 matrix. Non-enhanced low dose computed tomographies (CT) of the thorax and heart were acquired for the purpose of attenuation correction and to optimise the visualisation of the cardiac walls. The images were fused with SPECT images.

Prior to patient scans the sensitivity (counts per second/kBq) of the scanner was measured to calculate the conversion factor from counts/voxel to kBq/mL. Iterative reconstruction of SPECT data with scatter, attenuation and resolution recovery (Flash3d) was performed. The reconstructed transaxial slices were post filtered with an 8 mm Gaussian filter. The borders of the left ventricle (LV) were identified visually by an experienced technician. Semi-quantitative measures of LV myocardial ^{99m}Tc-PYP uptake and blood ^{99m}Tc-PYP uptake within the LV were calculated (kBq/mL). Myocardial ^{99m}Tc-PYP uptake was correlated to blood uptake (i.e. which might give a negative, relative myocardial ^{99m}Tc-PYP uptake value) and adjusted to body weight implying that relative values are provided.

Cardiac magnetic resonance

The CMR protocol was performed on a 1.5 T system (Achieva, Philips Healthcare, Best, The Netherlands) using a five channel sense cardiac coil. Scout images were obtained to determine the position and orientation of the LV long axis. A stack of 12 contiguous short-axis slices encompassing the LV from base to apex was acquired during end-expiratory apnea using a retrospective, ECG-triggered Balanced-Steady-State-Free-Precession (B-SSFP) breath-hold cine sequence, dividing the heart cycle temporally into 30 phases. Imaging parameters included the following: repetition time (TR) = 48.6 ms, echo time (TE) = 1.52 ms, flip angle =60°, acquisition matrix =160x154, field of view = 320x320 mm^2, spatial in-plane

Table I. Characteristics of patients with IIM.

Patients characteristics	Total (n=14)
Age, yrs	59.5±18.8
Female, n (%)	8 (57)
Age diagnosis, yrs	59.5±18.8
Diagnosis n (%)	
PM	8 (57)
DM	4 (29)
CAM	2 (14)
Disease duration, median (range), yrs	0.0 (0.0-0.5)
HAQ, VAS 0-10cm	1.20±0.82
MITAX, 0-1	0.42±0.14
MYOACT global-physician, VAS 0-10cm	5.72±2.27
MYOACT global-patient, VAS 0-10cm	7.75±2.36
MMT8 (right), 0-80	69±8
CRP, mg/L	17.3±24.6
>10 mg/L, n (%)	6 (43)
CK, n (%)	
Increased value	12 (86)
Increased value >3 times	10 (71)

Values are expressed as mean ±SD unless otherwise noted. CAM: cancer associated myositis; CK: creatine kinase (relative values according to upper reference value); DM: dermatomyositis; HAQ: health assessment questionnaire; MITAX: myositis intention to treat index; MMT8: manual muscle test of 8 muscles unilaterally; MYOACT global-patient: patient global disease activity assessment; MYOACT global-physician: physician global disease activity assessment; PM: polymyositis.

resolution = 2.0x2.0 mm^2, slice thickness =8 mm. LV volumes were calculated by segmentation of short-axis images. Global functional data included LV end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV) and EF, which were compared to normal values as reported from a previous CMR reference study of LV global function based on age, gender and body surface area (29).

Analysis of the MR images was performed using the freely available software Segment v.1.9 (http://segment.heiberg.se) (30). T2 values of LV myocardium were measured with a multi slice spin echo sequence, using turbo spin echo (TSE) for read-out of the multi echo sequence (TE = [5; 15; 25; 35] msec). MR images were stored and evaluated by an experienced cardiologist blinded to other information. The T2 values were extracted using OsiriX DICOM viewer. Image quality on each slice was graded 1-4 based on visual interpretation. Slices graded 1 were excluded. The T2 value for each short-axis slice was specified by the mean T2 and standard deviation (SD).

Statistical analysis

Data were presented according to their type, *i.e.* descriptive statistics for continuous variables comprised mean (± SD) and median (range), whereas categorical variables were displayed by means of frequencies and corresponding percentages. Comparisons between patients and healthy controls were carried out using two-sample *t*-test and Wilcoxon rank-sum for continuous normally and non-normally distributed data, respectively. With respect to categorical data, comparisons were made using Chi-square test or Fisher's exact test, depending on the distribution of the data amongst the cells of the respective 2x2 tables. Values of $p<0.05$ were considered significant.

Results

Demographics and disease characteristics

Demographics are summarised in Table I. Median duration of disease symptoms was one year (range 0.1–10.1). The two patients with CAM had cancer of the lung and the oesophagus, respectively. Disease activity was reflected by HAQ, MITAX, physician and patient global activity, MMT8 and levels of CRP and CK. One patient with PM died of aspiration-induced pneumonia within one month following the diagnosis. All, but one patient with pulmonary fibrosis, had normal HR-CT. Five patients were ANA positive (36%). Three patients had MSA; anti-Jo-1 antibody (n=1) and anti-SRP antibody (n=2). MAA were detected in 3 patients; anti-Ro-52 antibody (n=3) and anti-PMScl antibody (n=1).

Cardiovascular measures at time of diagnosis

Measures at time of diagnosis (baseline) are presented in Table II and III. There were no significant differences in traditional CV risk factors between the patients and the controls (age, gender, BMI, smoking habits, hypertension, diabetes and hypercholesterolemia). None of the healthy controls had cardiac symptoms, whereas 8 (57%) of the patients complained of dyspnoea (p=0.002); NYHA II (n=3) and NYHA III (n=5). Three patients had a history of palpitations (p=0.22), but none of angina pectoris or IHD.

Overall, 9 (64%) of the patients had significant cardiac abnormalities based on TnI, ECG, Holter, ECHO or CMR data (Table III), versus two (14%) of the controls (abnormal ECG, see below) (p=0.02). The patients had borderline higher median TnI (20 ng/L) than the controls (6 ng/L) (p=0.06). Four (29%) of the patients had TnI levels >30 ng/L compared to none in the healthy control group (p=0.10). ECG was pathological in 6 patients (43%) (Table III) and in two healthy controls (14%). One patient had atrial fibrillation, while prolonged PQ-, QRS- and QTc-intervals were detected in 3, 1 and 3 patients, respectively. Two of the controls had prolonged PQ or QTc. The patients had longer mean QTc intervals (p=0.01). Holter data showed a higher mean heart rate in patients with IIM compared to healthy control subjects (p=0.05). No further intergroup differences regarding Holter parameters were detected but some patients had a remarkable high number of supraventricular and ventricular extrasystoles.

Cardiac imaging

Data from ECHO, scintigraphy and CMR are shown in Table III and IV. Four patients (29%) had pathological

Table II. Cardiovascular characteristics of patients with IIM compared with age-and sex-matched healthy controls.

	Patients (n = 14)	Healthy controls (n = 14)	*p*-value
Age, mean ±SD (yrs)	59.5±18.8	61.0±14.1	0.93*
Female	8 (57)	8 (57)	1.00#
BMI, mean ±SD (kg/m^2)	25.9±5.9	26.0±3.5	0.95*
Smoking			
Present	5 (36)	5 (36)	1.00
Never	9 (64)	9 (64)	1.00
Cardiac symptoms			
Dyspnoea	8 (57)	0	<0.01#
Palpitations	3 (21)	0	0.22#
Chest pain	0	0	1.00#
Syncope	0	0	1.00#
Systolic blood pressure, mean ±SD (mmHg)	138±23	133±14	0.54*
≥140 mmHg	5 (36)	5 (36)	1.00
Diastolic blood pressure, mean ±SD (mmHg)	79±12	81±9	0.59*
≥90 mmHg	4 (29)	3 (21)	1.00#
Total cholesterol, mean ±SD (mmol/L)	5.5±1.1	5.3±1.1	0.65*
≥5 mmol/l	9 (82)	7 (50)	0.21#
HbA1c, mean ±SD (mmol/mol)	38.5±7.4	34.9±4.3	0.12*
≥48 mmol/mol	2 (15)	0	0.22#
Hypertension	8 (57)	6 (43)	0.45†
Diabetes	2 (14)	0	0.21#
Hypercholesterolemia	10 (71)	7 (50)	0.22#
TnI (ng/L), median (range)	20 (0-106)	6 (0-27)	0.06‡
≥30 ng/L	4 (29)	0	0.10#
ECG, mean ±SD			
PQ (ms)	164±33	161±21	0.82*
>200 ms	3 (25)	1 (7)	0.31#
QRS (ms)	97±22	87±10	0.16*
>120 ms	1 (7)	0	0.48#
QTc (ms)	428±21	398±34	0.01*
>450 ms	3 (21)	1 (7)	0.33‡
Holter			
SVE/24 hours, median (range)	19 (0-1558)	14 (2-77)	0.78‡
VE/24 hours, median (range)	31 (1-3901)	6 (0-314)	0.13‡
Heart rate, mean ±SD	78±14	69±7	0.05#
Atrial fibrillation	1 (7)	0	1.00#
Bradyarrhythmia	0	0	1.00
SVT/48 hours	4 (29)	4 (29)	1.00
VT/48 hours	0	0	1.00#

Values are expressed as n (%) unless otherwise noted. BMI: body mass index; HbA1c: glycosylated haemoglobin; SVE: supraventricular extrasystoles; SVT: supraventricular tachyarrhythmia; TnI: cardiac troponin-I; VE: ventricular extrasystoles; VT: ventricular tachyarrhythmia.
*Two-sample *t* test, †Chi-squared test, #Fisher's exact test, ‡Wilcoxon rank-sum test.

ECHO findings (Table III) and none of the controls. The mean BMI-adjusted LA size of the patients and the controls was 30±9 ml/m^2 and 23±8 ml/m^2, respectively (p=0.04). Among patients, one had diastolic dysfunction and two had cor pulmonale. One of the patients with cor pulmonale had lung fibrosis on HR-CT.

In one patient and in one healthy control the contrast-enhanced CT was not conducted and, hence, myocardial ^{99m}Tc-PYP uptake was not calculated. The relative ^{99m}Tc-PYP uptake did not differ significantly between patients and controls but the distributions of the results divided into 5 categories had different patterns (Fig. 1). All of the healthy controls had relative ^{99m}Tc-PYP uptake values within the intervals of 0-12 kBq/mL compared to 6 of the patients (46%). Four patients had relative ^{99m}Tc-PYP uptake <0 kBq/mL (cardiac relative to blood ^{99m}Tc-PYP uptake) and 3 patients had relative ^{99m}Tc-PYP uptake ≥12 kBq/mL.

One patient and two controls declined from having a CMR. T2 measurements failed in 3 patients due to poor image quality. Two patients, but none of the controls, had systolic dysfunction, but no clinical signs of congestive heart failure. On group level, no significant differences of the CMR findings, including median T2 values, median EF values and systolic dysfunction, were detected. Just like the ^{99m}Tc-PYP uptake, the distribution pattern of the mean T2 values differed among the groups (Fig. 2). Ten of the healthy controls (83%) had mean T2 values within the intervals of 65-75 ms compared to 3 of the patients (30%), whereas two patients had mean T2 <65 ms and 5 patients had mean T2 >75 ms, compared to one with mean T2 <65 ms and one with mean T2 >75 ms in the healthy control group, respectively.

Discussion

In the present study we compared the occurrence of subclinical cardiac abnormalities in newly diagnosed, untreated patients with IIM to a gender- and age-matched control group without clinical manifest heart disease using non-invasive imaging modalities. We found that subclinical cardiac abnormalities were significantly more common in patients with IIM than in control subjects, indicating that the heart muscle may be affected in patients with IIM.

Dyspnoea was a prominent finding at initial presentation in our patient group (57%). Previous prospective studies have reported frequency rates of dyspnoea between 6% and 46% (7, 8, 31-33). However, in contrast to ours, these patients had been treated with immunosuppressives. Since the frequency of smokers was similar in the two groups and only one of the patients had lung affection by HR-CT, pulmonary comorbidity does not seem to be a likely explanation for dyspnoea in our patient group. Therefore, it seems reasonable to assume that the increased prevalence of dyspnoea in the patient group could be attributed to the heart.

Recently, we have reported substantially increased prevalence of traditional CV risk factors in patients with longstanding PM/DM compared with

Table III. Individual patient characteristics and laboratory and cardiac findings.

Case	Sex	Age (year)	Diagnosis	Cardiac symptoms	CK (U/L)	TnI (ng/L)	ECG	Holter	ECHO/MR	Significant cardiac abnormalities
1	F	40	DM	None	995	10	N	N	N	No
2	F	70	DM	Dyspnoea	968	20	N	SVT	N	No
3	M	63	PM	Dyspnoea	1622	10	AF	AF	CP	Yes
4	F	75	PM	Dyspnoea/palpitations	4737	200	>PQ,QRS	SVT	N	Yes
5	M	62	PM	None	2277	30	>PQ	N	DD, SD*	Yes
6	M	70	PM	Dyspnoea	3298	80	>QTc	N	N	Yes
7	M	52	DM	Palpitations	71	0	N	N	SD*	Yes
8	F	79	PM	None	1740	206	>QTc	SVT	CP	Yes
9	F	24	DM	None	1288	2	N	N	N	No
10	M	74	CAM	Dyspnoea	709	26	>QTc,PQ	N	N	Yes
11	F	76	CAM	Dyspnoea	144	15	N	N	>E/e'	Yes
12	M	57	PM	None	561	0	NA	N	N	No
13	F	66	PM	Dyspnoea/palpitations	6952	35	N	SVT	N	Yes
14	F	21	PM	Dyspnoea	9527	20	N	N	N	No

AF: atrial fibrillation; CAM: cancer associated myositis; CK: creatine kinase (normal <200 U/L); CP: cor pulmonale; DD: diastolic dysfunction; DM: dermatomyositis; E/e': early diastolic transmitral flow/early diastolic tissue velocity index; F: female; M: male; N: normal; NA: non assessed; PM: polymyositis; SD*: systolic dysfunction, measured by MR; SVT: supraventricular tachyarrhythmia; TnI: troponin-I (normal <30 ng/L).

Table IV. Cardiac imaging.

	Patients (n=14)	Healthy controls (n=14)	*p*-value
ECHO			
LA(ml/m^2)	30±9	23±8	0.04*
e´ (cm/s)	10.5±4.1	10.9±1.9	0.70*
E/e´ ratio	7.8±3.6	6.8±2.0	0.42*
Abnormal E/e, n (%)	1 (7)	0	1.00#
Diastolic dysfunction, n (%)	1 (7)	0	1.00#
Cor pulmonale, n (%)	2 (14)	0	0.48#
Valve pathology, n (%)	0	0	1.00#
Scintigraphy			
Relative ^{99m}Tc-PYP uptake (kBq/mL)	5.6±6.1	5.2±2.9	0.83*
MRI			
T2, median (range) (ms)	75 (50-132)	70 (62-81)	0.39‡
LVM index (g/m^2)	74.3±16.0	67.6±12.9	0.26*
- Abnormal LVM index, n (%)	4 (31)	1 (8)	0.45#
LV SDVI (ml/m^2)	67.8±13.6	69.4±13.7	0.78*
- Abnormal LV SDVI, n (%)	2 (15)	1 (8)	1.00#
LV ejection fraction, median (range)	69 (54-74)	65 (61-73)	0.74‡
Systolic dysfunction, n (%)	2 (15)	0	0.48#

Values are expressed as mean ±SD unless otherwise noted. E: early diastolic transmitral flow; e´: early diastolic tissue velocity; LA: left atrium; T2: T2-weighted values of left ventricular myocardium; LVM: left ventricular mass index; LV SDVI: left ventricle end-systolic volume index.
*Two-sample t test, #Fisher's exact test, ‡Wilcoxon rank-sum test.

a matched healthy control population (34). Similarly, a study showed a higher frequency of metabolic syndrome in longstanding PM (35). In the present study of newly diagnosed patients with IIM, there were no statistically significant differences in CV risk factors between patients and controls, maybe due to small sample size.

TnI is a highly specific marker of myocardial damage (9-11). We observed a tendency towards higher mean TnI levels in the patient group compared to the control group. Furthermore, 29% of the patients and none of the controls had elevated TnI levels and all these patients had other abnormal cardiac findings. These results are in accordance with previous studies (9, 11, 14, 36). In one retrospective study, TnI was elevated in one of 41 patients in whom the ECHO was abnormal (9). Similarly, expression of elevated TnI in IIM patients with evidence of myocardial damage has been described (11, 14, 36). This supports the role of TnI as a biomarker to alert for cardiac involvement in patients with IIM.

The most frequently reported cardiac abnormalities in patients with IIM are rhythm and conduction disturbances, though the findings are often reported without age and sex matched controls. In a recent series of 58 patients with juvenile dermatomyositis (JDM), 17% had pathological ECG including prolonged PR, QRS and QTc intervals (37). In prospective, uncontrolled studies including adult IIM ECG changes were reported between 7% and 85% (7, 8, 31-33, 38). By comparison, ECG was pathological in 43% of our patients compared to 14% in the matched controls. The mean QTc interval was longer in patients, with three having definite prolongation of the QTc interval. This conduction disturbance may be of major clinical relevance since it is a risk marker of ventricular tachycardia and fibrillation (26).

ECHO revealed a tendency towards dilatation of the left atrium in our patient group, a finding reported in previous studies (7, 33). Only one patient with persistent hypertension had diastolic dysfunction. In contrast, diastolic dysfunction is the most commonly reported abnormality in IIM (7, 8, 30, 34). However, there are few studies on IIM using ECHO techniques like TDI which is considered to be an essential method for assessing diastolic heart function. Two previous studies including TDI

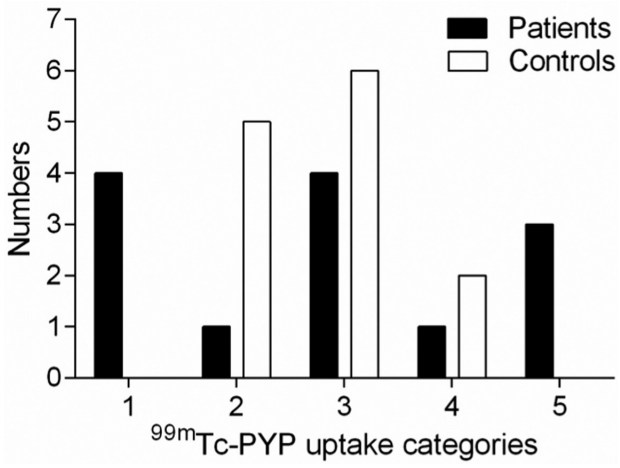

Fig. 1. Distribution pattern of relative myocardial ^{99m}Tc-PYP uptake (kBq/mL) in patients with IIM and in healthy controls.

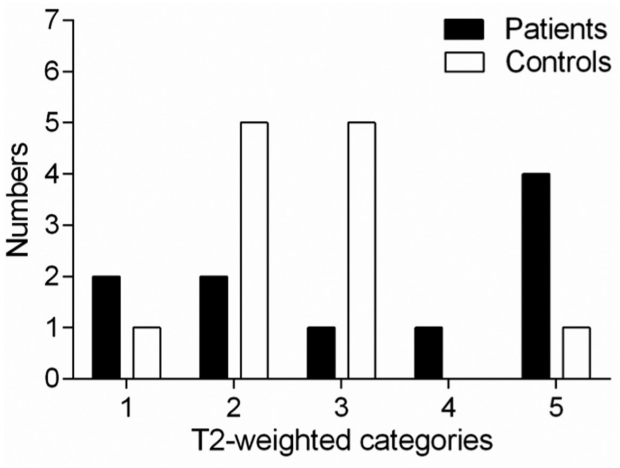

Fig. 2. Distribution pattern of mean T2-weighted values (ms) in patients with IIM and in healthy controls.

noted significantly higher frequency of diastolic dysfunction in patients with PM/DM compared to healthy controls. However, these studies used different criteria for defining diastolic dysfunction (39, 40).

Two of our patients had systolic dysfunction, measured by CMR. A recent study evaluating 20 untreated, newly diagnosed patients with PM/DM, showed one patient with systolic dysfunction by CMR (36). In contrast, EF was within the normal range in 16 patients with PM/DM, in disease remission (16). These studies are of limited size, but the findings may suggest that active disease - and thereby myocardial inflammation - contribute significantly to the systolic dysfunction in IIM.

Endomyocardial biopsy is considered to be the gold-standard for the diagnosis of myocardial inflammation, however, with considerable risk and low sensitivity (41). Semi-quantitative ^{99m}Tc-PYP scintigraphy and CMR quantitative T2 mapping are advanced, sensitive techniques providing a means of non-invasive detection of myocardial inflammation (6, 42). Previous reports on cardiac ^{99m}Tc-PYP uptake in IIM patients with signs of heart affection were based on planar imaging and visual scoring of the ^{99m}Tc-PYP uptake (15, 31, 43) and without control groups. Our use of tomographic images and the addition of CT made it possible to differentiate between the myocardium and the surrounding tissue with high accuracy and to quantify the myocardial ^{99m}Tc-PYP uptake, which is a novel approach compared to previous reports in IIM. Similarly, previous studies have noted abnormal CMR findings consistent with myocarditis in patients with PM or DM, who had signs of heart involvement (14, 36, 44). Even in IIM patients without any clinical or laboratory evidence of myocardial involvement, abnormal CMR was reported (16). The ^{99m}Tc-PYP myocardial uptake and T2-weighted values from CMR did not differ significantly between our patients and controls. However, a majority of the patients had either lower or higher values than the control group, with higher values indicating inflammation. A possible explanation for the lower values in some patients might be prolonged subclinical myocardial inflammation causing myocardial fibrosis, which is evident in autopsy reports of IIM patients (12, 13).

There are limitations of our study to be considered. Some of the differences of the cardiac findings between groups did not reach statistical significance, which is likely due to the small sample size, especially regarding the CMR data. Furthermore, it would be desirable to evaluate potential correlations between disease characteristics and cardiac measurements. However, our sample size was considered too small with risk of type II error. Even though our findings are discrete, they may have prognostic impact, considering the increased mortality rate due to cardiac events in patients with IIM. Whether the present findings reflect myocardial inflammation related to IIM or other pathologies remains to be elucidated. Our data from CMR and ^{99m}Tc-PYP scintigraphy point to inflammation as the primary explanation. As further support for this notion, myocarditis has been shown to occur in up to 30% of patients with IIM at autopsy (12, 13). Additionally, the TnI levels of the patients with raised values decreased after immunosuppressive treatment. We did not perform coronary angiography or myocardial stress test to exclude IHD as responsible for the observed cardiac abnormalities. However, none of our patients had angina or a history of IHD, which makes underlying IHD less likely.

Conclusion

Subclinical cardiac abnormalities detected by non-invasive techniques were significantly more prevalent in patients with newly diagnosed IIM than in matched controls. In particular, conduction abnormalities were common. Pathogenetically, the ^{99m}Tc-PYP scintigraphy and CMR findings point to underlying myocardial inflammation

as a significant source to heart abnormalities in IIM. Even though the study is small, our results of approximately two thirds of the patients having signs of subclinical heart involvement call for further studies of the prognostic implications of these findings.

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