CARDIOLOGIE TUNISIENNE

ARTICLE ORIGINAL

Speckle tracking echocardiography in systemic sclerosis: A useful method for detection of myocardial involvement

Intérêt du strain bidimensionnel dans la détection de l'atteinte myocardique au cours de la sclérodermie systémique

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Résumé

Problématique : La sclérodermie systémique est une atteinte fibrosante multi viscérale. L'atteinte cardiaque est grave et conditionne le pronostic, et peut être sous-estimées par les mesures échographiques classiques. L'imagerie de déformation, en particulier l'échographie 2D Speckle tracking est une nouvelle technique puissante afin d'évaluer l'atteinte myocardique de la maladie dans un stade précoce.

But du travail : Le but de cette étude est d'analyser les atteintes cardiaques au cours de la sclérodermie systémique, en utilisant l'échocardiographie et l'imagerie de déformation (2D Speckle tracking) pour une détection précoce de l'atteinte ventriculaire.

Matériel et Méthodes : Entre mai 2014 et Septembre 2014, 25 patients atteints de sclérodermie systémique et 25 sujets sains ont subi un examen physique, et ont bénéficié d'une échocardiographie au repos et à l'effort afin d'évaluer les anomalies cardiaques et analyser la fonction ventriculaire et les pressions pulmonaires. Pour évaluer la déformation myocardique longitudinale des deux ventricules, une échographie avec Speckle tracking a été pratiquée. Des corrélations ont été analysées entre les mesures échographiques et certaines données biologiques des patients.

Résultats : Les deux groupes étaient comparables en âge et en sexe. Malgré une fonction systolique ventriculaire gauche conservée et comparable (fraction d'éjection ventriculaire gauche 64,58 ± 8,87 VS 68,2 ± 7,41, p = 0,19) les patients avaient des mesures de strain plus effondrées (Strain global longitudinale : -17,42 ± 1,62 VS -19,24 ± 8,85, p <0,0001). Les fonctions systolique et diastolique ventriculaires droites sont atteintes malgré une pression artérielle pulmonaire comparable entre les deux groupes (30,3 ± 14,91 mmHg VS 26,78 ± 4,85 mmHg, p = 0,94). Les valeurs du Strain systolique du ventricule droit étaient significativement plus effondrées par rapport aux témoins. Nous avons objectivé une corrélation entre la dysfonction systolique du ventricule droit et les valeurs de la pression systolique artérielle pulmonaire (R = 0,64). la pression artérielle pulmonaire systolique à l'effort était significative et corrélée avec les valeurs de Brain Natriuretic peptide (R = 0,75).

Conclusion : L'imagerie de déformation par deux 2 dimensions Strain speckle tracking est une méthode fiable pour détecter précocement une atteinte myocardique ventriculaire chez les patients atteints de sclérodermie systémique.

Mots-clés

Sclérodermie systémique, échocardiographie, Atteinte myocardique

Summary

Background: Systemic sclerosis is a multisystem disorder characterized by tissue fibrosis and organ damage. Heart involvement is one of the main factors shortening survival, which may be underestimated by conventional echocardiography measurements. Two-dimensional speckle-tracking echocardiography is a powerful novel modality for the assessment of subclinical myocardial dysfunction.

Aim of the study: The aim of this study is to investigate heart involvement in systemic sclerosis patients, and to determine the usefulness of ventricular longitudinal deformation using the Two-dimensional speckle tracking technology for an early detection of ventricular dysfunction.

Patients and Methods: Between May 2014 and September 2014, 25 patients with systemic sclerosis and 25 healthy subjects underwent echocardiography to assess heart abnormalities and the strain of the two ventricles using two dimensions' speckle tracking echography.

Results: The two groups were age and gender comparable. Despite comparable left ventricle systolic function (Left ventricular ejection fraction 64.58 ± 8.87 VS 68.2 ± 7.41, p=0.19), patients had lower global longitudinal peak systolic strain values than controls (Global longitudinal strain: -17.42 ± 1.62 VS -19.24 ± 8.85, p<0.0001). There was a significant alteration in right ventricular systolic and diastolic function assessed by standard measurement despite a comparable pulmonary artery systolic pressure (30.3 ± 14.91 mmhg VS 26.78 ± 4.85 mmhg, p=0.94). Longitudinal peak systolic strain of the right ventricle was significantly lower in patients compared with controls (p<0.01).

Conclusion: Ventricular deformation analysis by two dimensions' speckle tracking echocardiography is a sensitive method to detect early ventricular impairment in patients with systemic sclerosis, providing a more accurate management of the disease.

Keywords

Echocardiography, Left ventricular function, Myocardial strain

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INTRODUCTION

Systemic sclerosis is a clinically heterogeneous generalized disorder affecting the connective tissue of the skin, blood vessel wall, and internal organs such as the heart, gastro-intestinal tract, lungs and kidneys. It is characterized by alterations of the microvasculature, disturbances of the immune system, and by massive deposition of collagen in the connective tissue (1).
Myocardial involvement in systemic sclerosis in reported to be frequent but underestimated and associated with poor prognosis. Thus, the majority of patients are believed to have subclinical primary cardiac involvement (2) which may be underestimated when assessed with conventional measures (3). Recent researches have been focused on echography as a useful tool to detect cardiac abnormalities before symptoms appear. Speckle tracking echocardiography is a novel method for the assessment of global and regional left ventricular myocardial function. It provides valuable insights to myocardial deformation by quantifying strain and torsion. From the clinical perspective, it has already been used for assessing different myocardial and systemic diseases, where it can predict probable sub-clinical cardiac disorder earlier in the course of the disease process when conventional 2D echocardiography appears to be normal (4).
According with these findings, we suppose that the use of 2D speckle tracking echocardiography to assess cardiac involvement in systemic sclerosis could be useful for an early detection of myocardial involvement.

METHODS

Study population
Twenty-five patients with systemic sclerosis according to the American College of Rheumatology classification criteria (24 women, 1 man, mean age 53.64 ± 13.4 years) from our department of internal medicine were included into the study Patients with known coronary heart disease or with ventricular dysfunction were excluded. Moreover, patients affected with diabetes or presenting high blood pressure (hypertension) were excluded. In addition, patients with atrial fibrillation were excluded from the study because of the impossibility of the strain analysis in atrial fibrillation.
Patients were compared with twenty-five healthy subjects from our out patients department of cardiology in the same hospital selected from subjects without medical history of diabetes or hypertension and in sinus rhythm, being investigated for palpitation, and with normal physical examination, laboratory results and echocardiographic findings.
All patients and healthy underwent complete clinical examination (history, Cardio vascular exam, weight, height) and laboratory analysis. All participants provided written consent. The local ethics committee approved the protocol.

Standard echocardiography
Standard echocardiography was performed in the left decubitus position using an ultrasound system (Vivid 9, GE Medical Systems, Horton, Norway) with a 3.4-mhz multi frequency transducer.
Left Ventricle (LV) images were obtained from the parasternal short axis view and 4 chambers axis view. Right Ventricle (RV) images were obtained from the parasternal short axis view. The Left Ventricle Ejection Fraction (LVEF) was calculated according to the modified Simpson's rule using the apical four- and two-chamber views. Measurement of the left and right ventricle, left ventricle end diastolic diameter (LVEDD), left ventricle end systolic diameter (LVESD), intraventricular septum thickness (IVS), posterior wall thickness (PW), left ventricle end diastolic volume (LVEDV) and end systolic volume (LVESV), right ventricle end diastolic diameter (RVEDD) and right ventricle wall thickness were taken as recommended by the European Association of Echocardiography and American Society of Echocardiography. The diameter of the inferior vena cava was measured from subcostal view (5,7).
Real-time 2D ultrasound data from the RV free wall with a frame rate greater than 40 frames per second (fps) were recorded at the apical view for offline 2D strain analysis.

Conventional Doppler echocardiography
Tricuspid valve regurgitation was detected at the apical four-chamber view by color Doppler echocardiography. Trans-mitral diastolic E and A wave velocities were obtained using pulsed-wave Doppler. E/A ratio was calculated for both groups. The E wave deceleration time (EDT) was measured.
Trans-tricuspid retrograde velocities were obtained using continuous wave Doppler. Systolic pulmonary artery pressure was estimated from the peak pressure gradient calculated from three consecutive beats using the modified Bernoulli formula ($\Delta P = 4V2$) and the right atrial pressure derived by the diameter of the inferior vena cava and the collapsibility index.

Tissue Doppler imaging and pulsed-wave TDI
Tissue Doppler Imaging of the RV free wall was performed in the apical four-chamber view at end-expiration. Three consecutive cycles were recorded with a frame rate greater than 150 fps for offline strain analysis. Pulsed TDI was performed to measure systolic and diastolic myocardial velocities at the basal level of the LV lateral wall.

2D speckle-tracking strain analysis

For assessment of the longitudinal speckle- tracking strain of the left ventricle, standard 2D ultrasound images at the parasternal mid-ventricular short-axis view (at the level of the papillary muscles) and from the apical long-axis, and two- and four-chamber views with a frame rate between 60 and 80 fps were recorded and stored digitally for off-line analysis (Echopac PC, GE Vingmed, Horton, Norway) as previously described. After manual tracing of endocardial borders, the software automatically traced the region of interest including the entire myocardial wall. In this process, every view of the left ventricle was divided into six segments.

Peak systolic longitudinal strain of the apical two, four-chamber, and long-axis views were calculated averaging the peak systolic strain (PSS) values of the six segments of the corresponding views. Finally, the global longitudinal peak systolic strain PSS of the left ventricle were generated averaging peak systolic values of the three apical views.

B-Mode images of the RV free wall were used to measure 2D strain using speckle-tracking algorithm. 2D strain in the basal, mid and apical segment of the RV free and septal wall was measured. Three beats were stored. The region of interest (ROI) for TDI strain was placed at basal, mid and apical segment of the RV free wall.

Statistics

Statistics were calculated by software (SPSS, Version 10.0, SPSS Inc). All results are presented as mean ± standard deviation (SD). The Mann-Whitney non parametric test was used to compare echocardiographic data from patients and control subjects. Differences were considered statistically significant if the P value was less than 0.05.

RESULTS

Clinical characteristics

Age, gender, body mass index, systolic, and diastolic blood pressure as well as the incidence of cardiovascular risk factors such as diabetes mellitus did not differ significantly between patients and the control group; no patient had hypertension, one is a smoker and no one has diabetic. No patient had a renal or hepatic impairment. (See Table 1 for clinical characteristics of the two groups).

The diffuse form of the disease is the most common, and affects 23 patients. One patient had a CREST syndrome and another was an overlap syndrome. 23 patients have already benefited from specific treatment of scleroderma.

one patients had a higher NYHA stage dyspnea or equal to II. No patient had stage IV dyspnea.

Table 1 : Baseline characteristics; Data are expressed as mean + SD HTN hypertension; BMI body-mass-index

	Patients (N= 25)	Control (N=25)	P 0.37
Age	53.64 ± 13.456	60.8 ± 8.72	0.535
BMI	25.1 ± 5.6	23.8 ± 4.81	0.823
Height Cm	156 ± 6.8	156.4 ± 6.59	0.447
Weight Kg	61.12 ± 13.4	58.4 ± 12.87	0.31
Women	24 (96%)	25 (100%)	0.62
HTN	1 (4%)	0 (0%)	0.07
Tabaco	1 (4%)	0 (0%)	0.3
Diabetes	1 (4%)	0 (0%)	

Standard echocardiographic measures

Systolic and diastolic LV function

Systolic LV function

LVEF is comparable between the two groups with no significant difference (64.5% in patients and 68% for the control group, p = 0.19).No patient or healthy presents left ventricle dysfunction or wall motion disorder.

There is no significant difference in the volume and the surface of the left atrium, left ventricle end-systolic and end-diastolic diameters and end-diastolic and end-systolic volumes as well as posterior wall and interventricular septum thickness. (See Table 2 for echographic measurements of the two groups).

Table 2 : Echography measurement; Data are expressed as mean + SD

	Patients (N= 25)	Control (N=25)	P
LVEF	64.58 ± 8.87	68.2 ± 7.41	0.19
LVEDD (mm)	46.28 ± 5.42	45 ± 5.56	0.36
LVESD (mm)	27.72 ± 4.98	25 ± 5.72	0.15
IVS (mm)	9.36 ± 2.56	8.08 ± 1.65	0.065
PW (mm)	8.80 ± 2.67	7.7 ± 1.30	0.27
LVEDV (ml)	81.00 ± 8.27	86.2 ± 23.03	0.77
LVESV (ml)	32.20 ± 5.88	27.4 ± 9.48	0.01
RV EDD (mm)	25.75 ± 5.94	24.08 ± 3.92	0.58
RV Wall Thickness (mm)	3.79 ± 1.76	4.12 ± 0.88	0.04
E / A ration	1.16 ± 0.4	1.32 ± 0.32	0.06
E/A <1	7 (28 %)	2 (8 %)	0.06
E/A >2	1 (4%)	2 (8 %)	0.55
E/A between 1 et 2	17 (72 %)	21 (84 %)	0.5
EDT (ms)	177.84 ± 68.13	167.04 ± 32.67	0.06

Left ventricle end diastolic diameter (LVEDD), left ventricle end systolic

diameter (LVESD), intraventricular septum thickness (IVS), posterior wall thickness (PW), left ventricle end diastolic volume (LVEDV), left ventricle end systolic volume (LVESV), right ventricle end diastolic diameter (RVEDD), right ventricle wall thickness. E and A: Trans-mitral early diastolic (E) and late diastolic (A) wave velocities. The E wave deceleration time (EDT).

Diastolic LV function

The evaluation of diastolic function reveals normal mitral flow in 17 patients while 21 healthy subject had normal mitral flow, with no difference between the two groups. Seven patients have reversal of the E/A ratio and only one patient have restrictive diastolic dysfunction, without significant differences between the two groups. Moreover, there was no differences in the assessment of E wave deceleration time for the two groups. (See Table 2 for echographic measurements of the two groups).

Analysis of right ventricle and systolic pulmonary artery pressure

There was no significant difference in the end-diastolic right ventricle diameter between the two groups (p = 0.58). The mean systolic pulmonary artery pressure derived from the transtricuspid pressure gradient was 30.3 mmHg in the scleroderma group.

Analysis of the ascending aorta:

There was no significant difference in the diameter of the ascending aorta (mean diameter of 27.95 mm for patient group, mean diameter of 28.3 mm for control group, p = 0.38).

Analysis of heart valves:

One patient had first grade aortic regurgitation. No patients had high grade regurgitation that required surgical management.

Analysis of the Inferior Vena Cava and pericardium:

Two patients had moderate pericardial effusion. No abundant pericardial effusion was found. One subject with mild pericardial effusion was found in the control group.

Ventricular longitudinal strain analysis

Left ventricle 2-DimensionsStrain Speckle Tracking (2D-SST) Analysis

The evaluation of 2 Dimensions strain with Speckle Tracking found significant impairment of the left ventricle longitudinal strain with Global Longitudinal LV strain value at -17.42 while the control group did not show significant defect with values of -19.24, p < 0.0001 (Table 3). Myocardial segments with significant myocardial impairment compared to the control group were: basal antero lateral, mid antero septal, mid antero lateral, mid inferior, mid infero septal, apical anterior, apical lateral, apical inferior, and apical septal. The alteration of the deformation is dominant in the apical and mid segments.

Table 3 : Left ventricle Strain in patients and control group; Data are expressed as mean + SD

Global Longitudinal strain	Patients (N=25)	Healthy (N=25)	P
strain	-17.42 ± 1.62	-19.24 ± 8.85	<0.0001
Basal	Basal	Basal	Basal
Basal Anterior	-18.00 ± 3.89	-17.84 ± 4.45	0.79
Basal Antero septal	-18.2 ± 3.39	-20.12 ± 4.95	0.07
Basal Infero septal	-16.08 ± 3.09	-17.4 ± 3.84	0.15
Basal Inferior	-17.32 ± 3.17	-18.64 ± 3.8	0.34
Basal Infero lateral	-14.76 ± 10.68	-17.68 ± 6.36	0.71
Basal Antero lateral	-17.60 ± 4.36	-20.08 ± 4.59	0.02
Median	Median	Median	Median
Mid anterior	-17.32 ± 3.17	-18.64 ± 3.8	0.34
Mid Antero septal	-19.84 ± 2.65	-22.6 ± 4.75	0.007
Mid Infero septal	-19.04 ± 2.26	-20.88 ± 2.48	0.03
Mid inferior	-19.60 ± 2.87	-21.92 ± 3.58	0.02
Mid Infero lateral	-19.04 ± 3.78	-20.44 ± 6.19	0.21
Mid Antero lateral	-18.40 ± 3.34	-21.4 ± 5.25	0.006
Apical	Apical	Apical	Apical
Apical Anterior	-18.56 ± 3.87	-22.8 ± 6.28	0.006
Apical Septal	-20.88 ± 2.31	-21.68 ± 11.40	0.02
Apical Inferior	-20.36 ± 3.21	-22.24 ± 10.38	0.02
Apical Lateral	-19.76 ± 3.07	-22.32 ± 6.50	0.01
Apex	-20.32 ± 2.68	-21.04 ± 10.62	0.06

Right ventricle 2-DimensionsStrain Speckle Tracking Analysis

The study found a significant difference in the septal and the lateral wall with differences in the respective measures (Table 4).

Global RV strain was preserved in control group compared to patients with a (-20.30 ± 5.4 for patient group, -24.97 ± 3.58 for control group, p = 0.0002).

Table 4 : Right ventricle Strain in patients and control group; Data are expressed as mean + SD

	Patients (N=25)	Control (N=25)	p
LATERAL WALL			
Basal Lateral	-21.40 ± 4.59	-28.20 ±7.34	0.0006
Mid Lateral	-21.48 ± 5.41	-31.00 ± 6.48	<0.001
Apical Lateral	-19.28 ± 5.33	-27.04 ± 6.99	<0.001
SEPTAL WALL			
Apical Septal	-15.24 ± 7.39	-20.88 ± 6.57	0.003
Mid Septal	-17.96 ± 3.73	-21.92 ± 4.16	0.002
Basal Septal	-17.68 ± 4.03	-20.52 ± 4.26	0.07
GLOBAL RV STRAIN	-20.30 ± 5.4	-24.97 ± 3.58	0.0002

DISCUSSION

Since cardiac involvement in systemic sclerosis is associated with a poor prognosis, the need for an early detection tool is evident. Myocardial damage appears to be more frequent in patients than clinically suspected (6,14).
Speckle tracking analysis is a relatively new technique and presents many advantages compared with assessment of systolic function based on LVEF; It appears to be an insufficient method because of the complex myocardial motion which is characterized by three-dimensional movements: longitudinal shortening, radial thickening, and circumferential shortening, as well as a twist motion due to the helical nature of the heart muscle (9).
Despite a preserved LVEF, we could demonstrate that global longitudinal systolic strain of the left and the right ventricle derived from 2D speckle-tracking analysis were impaired when compared with a healthy control group.
Several studies found abnormalities in myocardial systolic deformation using Tissue Doppler Imaging in patients suffering from systemic sclerosis with normal LVEF and without left ventricular dilatation.
Thus the Melo et al and Kepez et al (8) found a decreased myocardial deformation assessed by tissue Doppler Imaging with the velocity of the S. But the study with Tissue Doppler Imaging has limitations related to the angle of incidence can vary the results. Moreover, this technique is not suitable to the study of all myocardial segments. These limits are not present in the assessment of myocardial deformation by 2D Strain Speckle Tracking (9).The result of this study confirm those in a comparative study in 100 patients affected with systemic sclerosis without left ventricular systolic dysfunction on standard echocardiographic parameters. Kai Hang Yiu et al (10) found a decrease of -18.2 versus -21.3 SGL for control group; $p < 0.01$. Spethmann et al (3) found the same findings in the analysis of the Strain of the left ventricle in 22 patients with systemic sclerosis. The longitudinal function is predominantly influenced by sub endocardial fibers that are most susceptible to myocardial damage (3). Since the LVEF is mainly dependent on the radial and the circumferential deformation, the LVEF may remain normal despite relevant myocardial damage (11).
Regarding the right ventricle, our study found a significant alteration of the deformation of the myocardial fibers 2D SST predominant on the apical segment, middle and basal of the lateral wall and the middle and apical segments of the septal wall.
To our knowledge, there is currently only one study on the analysis of the lateral wall of the right ventricle 2D SST that would allow us to compare the results of our study (12). Abnormalities of the contractility of the right ventricle affect all segments of the side wall of the right ventricle. The study Moaref et al (13) compared 38 patients with 27 healthy subjects, revealed that strain values were altered in patients and concluded to the usefulness of 2D Strain of the right ventricle to detect early dysfunction right ventricle in patients without pulmonary arterial hypertension.
The reduced regional and global longitudinal deformation detected in our study may also be caused by myocardial fibrosis.
No patients had to be excluded due to poor image quality. This indicates an acceptable feasibility of echocardiographic assessment of LV function by speckle tracking in systemic sclerosis patients.

LIMITATIONS

As a limitation of our study, we mention the low number of subjects and single study nature of the study. In addition, myocardial fibrosis was not assessed by cardiac MRI or myocardial biopsies.
Moreover, no coronary angiography was performed to rule out coronary artery disease as a reason for reduced longitudinal function. However, all patients were asymptomatic in this regard and the pre-test probability was low based on clinical atherosclerotic risk factors, and no significant difference compared with the control could be found.
About ¼ of the patient group had mild valvular heart disease, and 92% of the included patients had already received potentially cardiotoxic disease-modifying agents (azathioprine, methotrexate, or cyclosporine A). Accordingly, we cannot rule out that the reduced longitudinal strain in systemic sclerosis patients was, at least in part, due to valvular heart disease or to the side effects of the medical therapy.

CONCLUSION

In summary, global longitudinal strain measurement derived from STE is reduced in asymptomatic patients with systemic sclerosis having preserved LVEF compared with healthy controls. Ventricular deformation analysis by 2 dimensions' speckle tracking echocardiography appears to be a sensitive method to detect early ventricular impairment in patients with systemic sclerosis, providing a more accurate management of the disease.

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