

Can speckle tracking echocardiography detect subclinical left ventricular dysfunction in patients with primary Sjögren's syndrome?

Sirs,

In Sjögren's syndrome (SS) distinct heart disease is rare (1-4), but pulmonary effusion, pulmonary hypertension and left ventricular diastolic dysfunction are frequent.

It has been found that two-dimensional speckle tracking echocardiography (2-D STE) is more sensitive than conventional echocardiography in detecting sub-clinical ventricular dysfunction in various clinical disorders (5-7).

The aim of this study was to use STE to evaluate left ventricular myocardial function in a cohort of patients with pSS and a normal ejection fraction.

Forty-nine outpatients (7 males and 42 females; mean age 57±6.9 years), who fulfilled the American European Consensus (AECG) for pSS (8) and 49 healthy volunteers matched in terms of the anthropometric characteristics was included in the study. None of the them had smoked cigarettes during the previous ten years.

The study was approved by local Ethics Committee and conducted in accordance with the ethical guidelines of the 1975 Helsinki Declaration, and informed consent was obtained.

The clinical data were determined by means of a standardised clinical interview, and the pSS-related laboratory variables of erythrocyte sedimentation rate, WBC and platelet counts, and C-reactive protein levels were measured using routine methods.

IgM rheumatoid factor (RF), anti-nuclear autoantibody (ANA) levels and antibodies against extractable nuclear antigens (ENAs) including SSA, SSB were also detected. The CV risk profile was assessed by means of standard electrocardiography (ECG), conventional and stress trans-thoracic echocardiography with coronary flow reserve (CFR) measurement, carotid ultrasonography and pulse wave velocity (PWV). Speckle tracking analysis was performed off-line using commercially available QLAB 9 software (Philips Medical System, USA). Two-dimensional images were obtained from the apical 4-chamber view at a high frame rate (70–80 frames/sec), and three cardiac cycles were stored in cine-loop format for off-line analysis in order to assess end-systolic LV longitudinal.

Table I shows the characteristics of the study population. All of the pSS patients showed extra-glandular systemic involvement (30% articular, 22% haematological, 7% cutaneous, 8% constitutional and 4.5% peripheral nerve system involvement) 30 were being treated with hydroxychloroquine (HCQ) 400 mg/day, 11 with azathioprine (AZA) at a mean dose of 150 mg/day (range 50–200 mg), and eight with methotrexate (MTX) at a mean dose of 7.5 mg/weekly. None of the patients showed any signs or symptoms of

Table I. Characteristics of the study population.

| | Primary SS patients (n=49) | Healthy controls (n=49) | p-value |
|---------------------------------|----------------------------|-------------------------|---------|
| No. of females (%) | 42 (85.7%) | 40 (81.6%) | 0.06 |
| Age (years) | 57.5 ± 6.90 | 59.6 ± 2.08 | 0.07 |
| BMI (kg/m ²) | 25.6 ± 3.77 | 23.69 ± 1.12 | 0.07 |
| Systolic blood pressure (mmHg) | 126 ± 17 | 125 ± 12 | 0.08 |
| Diastolic blood pressure (mmHg) | 82 ± 6 | 80 ± 8 | 0.08 |
| Heart rate (bpm) | 65 ± 10 | 68 ± 12 | 0.07 |
| CRP (mg/dL ⁻¹) | 7.36 ± 2.08 | 0.41 ± 0.09 | <0.0001 |
| ESR (mm/h ⁻¹) | 23.33 ± 12.86 | 4.84 ± 0.24 | <0.0001 |
| Disease duration (months) | 77.16 ± 34.68 | | |

Mean values ± standard deviation (SD).

BMI: body mass index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

CV disease, pulmonary involvement such as interstitial lung disease, or any other complication.

Four patients were receiving corticosteroids 2.5 mg/day, and three were receiving 5 mg/day due to joint involvement relapse for 3–5 months; three were receiving nifedipine 30 mg/day because of Raynaud's phenomenon. All of the patients were positive for ANA and/or RF and/or SSA or SSB, and had significantly higher CRP and ESR values than the healthy controls ($p<0.001$ for both); however, there were no significant differences in heart rate, arterial blood pressure, age or BMI (Table I).

The patients' mean LVEF and E/A ratios were respectively 59.11±6.35% and 0.94±0.24, which were not significantly different from those of the controls; however, although within the normal range, their CFR was lower (median 2.7, IQR 2.40–2.90 vs. 3.20, IQR 3.06–3.33; $p<0.0001$).

The results of the STE were significantly different between the two groups, with global longitudinal strain deformation in the apical 4-chamber view (Long. ϵ 4c) being significantly lower in the pSS patients (median 15.28, IQR 12.3–16.2 vs. 19.8, IQR 19.3–20.40; $p<0.0001$).

Right and left pulse wave velocity (PWV) (median 8.8 m/sec, IQR 7.26–10.32 vs. 6.86 m/sec, IQR 6.66–7.10; $p<0.0001$), and right and left coronary IMT (cIMT: median 0.6 mm, IQR 0.5–0.7 vs. 0.53 mm, IQR 0.50–0.60; $p=0.08$) values were all higher in the pSS patients, but the differences in cIMT were not statistically significant.

This study show that LV myocardial longitudinal ϵ , as measured by means of STE, was impaired in our pSS patients in the absence of any clinical evidence of CV disease and when the traditional echocardiographic parameters were still negative, thus suggesting a myocardial alteration (9). We do not have a clear explanation for this finding (10), but these alterations are so small that cannot be clinically detected.

F. ATZENI¹
L. GIANTURCO²
C. COLOMBO²
C. RICCI³
P. SARZI-PUTTINI⁴
M. TURIEL²

¹IRCCS Galeazzi Orthopaedic Institute, Milan, Italy; ²Cardiology Unit, Department of Biomedical Sciences for Health, IRCCS Galeazzi Orthopaedic Institute, Milan, Italy;

³Department of Epidemiology and Preventive Medicine, Faculty of Medicine, Regensburg, Germany; ⁴Rheumatology Unit, L. Sacco University Hospital, Milan, Italy.

Funding: this study was supported by the Rheumatology Unit, L. Sacco University Hospital, Milan, and the Cardiology Unit, Dept. of Biomedical Sciences for Health, IRCCS Galeazzi Orthopaedic Institute, Milan, Italy.

Address correspondence to:

Prof. Maurizio Turiel, MD, FESC,

Director of Cardiology Unit,

Department of Biomedical Sciences,

IRCCS Galeazzi Orthopaedic Institute,

Via R. Galeazzi 4, 20161 Milano, Italy.

E-mail: maurizio.turiel@unimi.it

Competing interests: none declared.

References

1. RAMOS-CASALS M, TZIOUFAS AG, FONT J: Primary Sjögren's syndrome: new clinical and therapeutic concepts. *Ann Rheum Dis* 2005; 64: 347–54.
2. YIXIN W: Sjögren's syndrome with myocarditis. Report of a case. *Chin Med J* 1981; 94: 45–6.
3. TSUJI M, NAKATANI T, NOJIRI T *et al.*: A case of Sjögren's syndrome with valvular diseases. *Jpn Heart J* 1986; 27: 137–43.
4. LEE LA, PICKRELL MB, REICHLIN M: Development of complete heart block in an adult patient with Sjögren's syndrome and anti-Ro/SS-A autoantibodies. *Arthritis Rheum* 1996; 39: 1427–9.
5. MOR-AVI V, LANG RM, BADANO LP *et al.*: Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese society of echocardiography. *J Am Soc Echocardiogr* 2011; 24: 277–313.
6. BANSAL M, CHO GY, CHAN J, LEANO R, HALUSKA BA, MARWICK TH: Feasibility and accuracy of different techniques of two-dimensional speckle based strain and validation with harmonic phase magnetic resonance imaging. *J Am Soc Echocardiogr* 2008; 21: 1318–25.
7. TESKE AJ, DE BOECK BW, MELMAN PG, SIESWERDA GT, DOEVEDANS PA, CRAMER MJ: Echocardiographic quantification of myocardial function using tissue deformation imaging, a guide to image acquisition and analysis using tissue Doppler and speckle tracking. *Cardiovasc Ultrasound* 2007; 5: 27.
8. VITALI C, BOMBARDIERI S, JONSSON R *et al.*: European Study Group on Classification Criteria for Sjögren's Syndrome. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis* 2002; 61: 554–8.
9. SITIA S, TOMASONI L, CICALA S *et al.*: Detection of preclinical impairment of myocardial function in rheumatoid arthritis patients with short disease duration by speckle tracking echocardiography. *Int J Cardiol* 2012; 160: 8–14.
10. BARTOLONI E, BALDINI C, SCHILLACI G *et al.*: Cardiovascular disease risk burden in primary Sjögren's syndrome: results of a population-based multicentre cohort study. *J Intern Med* 2015; 278: 185–92.