Disease activity and left ventricular systolic function in rheumatoid arthritis

We have read with interest the recent paper by Midtbø *et al*.[1] The authors evaluated 119 patients with rheumatoid arthritis (RA), and found that patients with RA active disease (Simplified Disease Activity Index (SDAI) >3.3) compared with those in remission (SDAI<3.3) had lower left ventricular (LV) systolic myocardial function, assessed by stress-corrected mid-wall shortening (scMWS) and global longitudinal strain (GLS).

Data from Midtbø *et al* are in line with our previous work, in which we demonstrated that RA per se is a condition closely related to LV systolic dysfunction (LVSD) assessed by scMWS.[2] Furthermore, similar to other pathophysiological models (systemic hypertension, diabetes mellitus and aortic stenosis), we showed that the LVSD in patients with RA is closely associated with concentric geometry and increased LV mass (LVM),[2] which is inappropriately high in the two-third of them.[3]

However, in a series of 235 patients with RA we did not find any significant relationship between RA disease activity, inflammatory markers and LVSD,[3] though in our patients with active RA the level of disease activity was significantly higher than in the Midtbø's ones (table 1). Similar findings emerged by our analysis performed on 198 patients with RA divided according to the presence/absence of combined circumferential and longitudinal LVSD, defined as the coexistence of impaired scMWS and impaired peak mitral annular systolic velocity S' measured by Tissue Doppler pulsed-wave spectral analysis.[4]

The apparent discrepancy between ours and Midtbø's experiences regarding the relationship between LVSD and RA disease activity could be explained by the large differences in clinical variables existing in the two study populations (table 1). Analysing the pharmacological therapy, in our cohort there was a greater number of patients receiving tumour necrosis factor inhibitors both in the active and remission group, disease modifying antirheumatic drugs (DMARDs), and methotrexate.

The differences between the two study populations are even more relevant focusing on the echocardiographic data. With respect to the Midtbø's study, indeed, our patients had more frequently LV hypertrophy (37% vs 10%), LV concentric geometry (73% vs 8%), higher LV relative wall thickness (0.47 vs 0.36) and worse scMWS (84% vs 98%). Thus, likely due to different selection criteria and differences in the organisation of local health systems, Midtbø's population is prevalently formed by patients with normal LV geometry and systolic function, while the most of our patients have relevant alterations in LV geometry and LVSD. Midtbø *et al* showed little differences in scMWS and GLS (both within the normal range) between patients in active disease and remission, though reaching statistical significance. The presence of the above mentioned great impairment in LV systolic function in our patients could have flattened such little differences in our population.

Table 1 Clinical characteristics of patients with active RA and RA in remission in our and in Midtbø's study

	Cioffi *et al*[3]		Midtbø *et al*[1]		p Value
	Active RA SDAI > 3.3 (n=162)	Remission RA SDAI≤3.3 (n=44)	Active RA SDAI > 3.3 (n=78)	Remission RA SDAI≤3.3 (n=41)	
Age (years)	62.5 (11.3)	58.4 (12.7)	60.7 (11.7)	62.1 (11.2)	NS
Women, n (%)	131 (81)	30 (69)	60 (77)	31 (76)	NS
Body mass index (kg/m^2)	25.7 (4.9)	25.3 (3.6)	25.5 (4.8)	25.6 (4.2)	NS
Current smoking, n (%)	75 (46)	14 (31)	19 (25)	6 (15)	<0.01
Diabetes, n (%)	16 (10)	4 (8)	11 (14)	1 (3)	<0.05
Total serum cholesterol (mmol/L)	5.6 (1.0)	5.5 (1.1)	5.5 (1.2)	6.2 (1.3)	NS
Use of statins, n (%)	52 (32)	8 (19)	15 (19)	3 (7)	<0.01
ESR (mm/hour), median (IQR)	25 (20)	18 (16)	13.5 (8.8–26.3)	10 (6.5–16)	NS
CRP (mg/L), median (IQR)	5.4 (9.0)	2.1 (4.0)	5 (2–11.3)	2 (1.0–3.5)	NS
Systolic blood pressure (mm Hg)	135 (18)	131 (17)	136 (22)	131 (20)	NS
Diastolic blood pressure (mm Hg)	83 (9)	85 (11)	80 (10)	79 (10)	NS
Hypertension, n (%)	91 (56)	15 (35)	47 (60)	14 (0.34)	NS
Medically treated hypertensive patients, n (%)	87 (54)	15 (35)	31 (66)	5 (36)	NS
RA disease duration (years)	16.2 (11.4)	14.3 (11.5)	16.8 (2.1)	17.2 (1.9)	NS
RF positive, n (%)	110 (68)	14 (32)	43 (63)	16 (39)	NS
Anti-CCP positive, n (%)	104 (64)	18 (40)	42 (62)	17 (42)	NS
SDAI score, median (IQR)	13.9 (9.2)	1.5 (1.1)	7.7 (5.1–12.2)	1.8 (1.2–2.3)	<0.001
CDAI score, median (IQR)	13.3 (8.9)	1.3 (1)	6.6 (4.7–10.9)	1.4 (1.0–2.0)	<0.001
DMARDs, n (%)	133 (82)	39 (89)	55 (71)	19 (46)	<0.05
Methotrexate, n (%)	79 (49)	20 (46)	26 (33)	13 (32)	<0.05
TNFi, n (%)	104 (64)	25 (56)	22 (28)	7 (17)	<0.01
Prednisolone, n (%)	107 (66)	15 (33)	24 (31)	12 (29)	<0.01

p Values refer to both active versus active RA and remission versus remission RA patients.
Data are given as mean (SD) unless otherwise stated.
Anti-CCP, anti-cyclic citrullinated peptide; CDAI, clinical disease activity index; CRP, C reactive protein; DMARDs, disease modifying antirheumatic drugs; ESR, erythrocyte sedimentation rate; NS, not significant; RA, rheumatoid arthritis; RF, rheumatoid factor; SDAI, Simplified Disease Activity Index; TNFi, tumour necrosis factor inhibitor.

In conclusion, the relationships between RA disease activity and LV function could be determined by LVM and geometry, degree of LVSD and disease activity itself, so that they should be evaluated in light of these crucial variables.

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