

Predominance of large joint active synovitis in Asian patients with established rheumatoid arthritis

Sirs,

Rheumatoid arthritis (RA) typically involves the small joints (1) but large joint involvement (elbows, shoulders, ankles and knees) may occur (2). Considering that large joints are the predominant determinant of physical function (3), we undertook a study to (i) evaluate the presence of residual large joint synovitis in patients with established RA using ultrasound (US) as the reference standard, and (ii) to study the association of large joint synovitis with increased impact of disease/disability.

101 established RA patients (4) with stable disease were assessed for synovitis by US (GE LogicE) in 28 joint areas (2 shoulders; anterior transverse (subdeltoid), posterior glenohumeral, 2 elbows; anterior longitudinal, posterior olecranon, 2 wrists; longitudinal radiocarpal, 10 metacarpalphalangeal (MCP); longitudinal dorsal, 10 proximal interphalangeal (PIP); longitudinal dorsal and 2 knee joints; longitudinal suprapatellar). Presence of B-mode synovitis was followed by PDUS assessment, scored on a validated semi-quantitative scale (0–3) (5–7) (8). Active synovitis was defined as B-mode ≥ 1 with PDUS ≥ 1 . Large joint involvement included shoulders, elbows, or knees while small joint involvement included wrist, MCP or PIP joints. Baseline demographics, disease activity (DAS28), physical function (modified Health Assessment Questionnaire, SF-12 Physical Component Score; PCS) and impact of disease (Rheumatoid Arthritis Impact of Disease; RAID score 0–10) were evaluated. RAID >2.24 was considered by patients to be in an unacceptable disease state (9). Baseline characteristics were compared by chi-square or Mann-Whitney U-test. Logistic/linear regression evaluated the association of large joint disease as predictor of physical function or impact of disease.

44% had large joint active synovitis with a higher proportion of Chinese ($p=0.02$) (Table I). These patients had higher RAID ($p<0.001$), and lower SF12-PCS scores ($p=0.034$).

At the “joint” level, active synovitis was present in 7% ($n=187$) of the 2828 joints. Of the 606 large joints, 16% had PDUS synovitis, compared to just 4% of the 2222 small joints. Active synovitis was present in 21% of shoulders, 20% of elbows and 6% of knees. The wrist was the most common small joint (27%) while the MCP and PIP joints were rarely involved (2% respectively).

Large joint involvement was significantly associated with mHAQ >0.5 (OR=4.55, 95%CI 1.15–18, $p=0.031$), and SF12-PCS (beta=-4.4, $p=0.022$) after adjusting for age and gender. However, the association with mHAQ, although showed a similar trend, did not remain statistically significant after including wrist involvement and ethnicity. SF12-PCS scores remained negatively asso-

Table I. Baseline characteristics according to patients with and without large joint involvement*.

	All patients n=101	Large joint involvement n=44	No large joint involvement n=57	p-value
Age, years [^]	54.3 (48.4, 62.8)	54.9 (46.9, 61.8)	53.8 (48.5, 63.6)	0.959
Female, no (%)	82 (81%)	35 (80%)	47 (83%)	0.711
Chinese, no (%)	73 (72%)	37 (84%)	36 (63%)	0.020
Disease duration, years	5.3 (2.2, 9.4)	4.9 (2.5, 10.1)	5.5 (1.9, 9.2)	0.962
Rheumatoid factor or anti-CCP positive	77 (77%)	35 (80%)	42 (75%)	0.592
TJC	1 (0.3)	2 (0.4)		
SJC	1 (0.2)	2 (0.3)	0 (0.1)	<0.001
PDUS SJC	1 (0.3)	3 (2.5)	0 (0.1)	<0.001
ESR, mm/hr	22 (14, 37)	28 (16.3, 53.3)	23.2 (12.2)	0.021
PDUS-DAS28	3.2 (2.6, 4.2)	3.9 (3.2, 5.2)	2.8 (2.2, 3.4)	<0.001
Wrist involvement on PDUS	39 (39%)	21 (48%)	18 (32%)	0.11
mHAQ	0 (0, 0.12)	0 (0, 0.8)	0 (0, 0.1)	0.057
SF12-PCS	41.9 (35.1, 51.4)	39 (33.5, 50.3)	46.1 (37.9, 51.8)	0.034
SF12-MCS	47.0 (40.6, 55.1)	45.7 (41.1, 53.6)	49 (41.1, 57.7)	0.651
RAID	2.2 (0.9, 4.4)	3.2 (1.4, 5.3)	1.3 (0.5, 2.6)	<0.001
B-mode synovitis score	7 (4, 14.5)	11 (7, 20)	5 (4, 11)	<0.001
PDUS synovitis score	1 (0.4)	5 (2, 8)	0 (0.2)	<0.001
Oral prednisolone	40 (43%)	19 (46%)	21 (38%)	0.422
Prednisolone dose mg/day	5.0 (2.5, 5.0)	5.0 (2.5, 5.0)	5.0 (2.0, 5.0)	0.915
Methotrexate	77 (80%)	32 (78%)	45 (82%)	0.647
Methotrexate dose, mg/week	15 (12.5, 18.8)	17.5 (12.5, 20)	15 (12.5, 20)	0.262
Combination DMARD therapy	67 (66%)	28 (64%)	30 (53%)	0.288

*large joint involvement includes the shoulders, elbows and knees. [^]continuous variables in median (interquartile ranges). TJC: tender joint count; SJC: swollen joint count; PDUS: power Doppler ultrasound; ESR: erythrocyte sedimentation rate; mHAQ: modified health assessment questionnaire; DMARD: disease-modifying anti-rheumatic drug; DAS: disease activity score.

ciated with large joint involvement (beta=-4.1, $p=0.042$). Large joint involvement was associated with being in an unacceptable disease state (RAID >2.24), OR=3.83, 95%CI 1.66–9.86, $p=0.002$, after adjustment for age and gender; and also after further adjusting for ethnicity and wrist involvement (OR=3.95, 95%CI 1.6–9.7, $p=0.003$).

A significant proportion of patients with established RA had active large joint synovitis, associated with a higher impact of disease and physical disability and a greater likelihood of being in an unacceptable disease state. Unlike Tanaka *et al.* (3), we did not see a significant difference in poorer physical function (HAQ) in patients with predominant large joint disease. This may have been explained by the shorter disease duration and the underestimation of disability with mHAQ. However, patients with large joint involvement were associated with poorer SF-12-PCS even after adjusting for wrist involvement. Limitations included unblinded physician and US assessments. In addition, the scanning protocol did not include the ankle and had included more views in the shoulder rather than knees, thus most likely underestimating the level of knee involvement. However, the shoulder, knee and elbow are known to have the largest contribution to physical function (3). Lastly, radiographic damage was not evaluated. Despite this, the results indicate that physicians need to include routine large joint evaluation even with stable RA.

P.P. CHEUNG^{1,2}
Y. GUO¹
M. LAHIRI^{1,2}

¹Yong Loo Lin School of Medicine, National University of Singapore; ²Division of Rheumatology, University Medicine Cluster, National University Hospital, Singapore.

Address correspondence to:

Dr Peter Cheung, MBBS, PhD, FRACP, National University Hospital, 1E Kent Ridge Road, NUHS Tower Block, level 10, 119228 Singapore.

E-mail: peter_cheung@nuhs.edu.sg

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