Insulin resistance varies across connective tissue diseases patients: comparison between rheumatoid arthritis, systemic lupus erythematosus and systemic sclerosis

Sirs,

I read with the interest paper of Sánchez-Pérez *et al*. on insulin resistance (IR) in systemic lupus erythematosus patients (1). It is well known that IR is not restricted to SLE patients but should be recognised as all connective tissue disease related phenomenon. To address this I tried to assess whether IR differs across patients with various types of connective tissue diseases (CTD), rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and systemic sclerosis (SSc). The patients with SLE, RA and SSc recruited to the study were atherosclerosis-free. Patients on statins therapy as well as receiving corticosteroids in doses higher that 10 mg of prednisone (or equivalent) were excluded from the study. The HOMAβ, HOMA-IR and Quicki indexes were calculated as previously reported in literature (2-4). The following inflammatory parameter were assessed: ESR, C-reactive protein, inteleukin-6 (IL-6) and tumour necrosis factor α (TNF-α). All patients underwent ultrasound examination and intima media thickness (IMT) was measured (5).

Statistical analyses were performed with the use of STATISTICA 10. PL software. Student t-test was used for continuous variables and a Mann-Whitney U-test for non-continuous variables. Data were presented as mean ± SD or a median and interquartile range as appropriate. A *p*-value less than 0.05 was considered statistically significant.

SLE patients were characterised with higher HOMAβ than patients with RA and SSc. I failed to show any differences regarding Quicki and HOMA-IR. Among inflammatory parameters studied, ESR and C- reactive protein were numerically higher in RA patients, IL-6 higher in SSc and TNF in SLE, however statistical differences between groups have not been observed (Table I).

The results of the study supported observation of Sanchez-Perez *et al*. on insulin resistance in SLE patients, but also showed that IR vary between various types of CTDs. To address the potential mechanism at partially responsible for this phenomenon it may be speculated that in the course of SLE formation of anti-beta cell antibodies may be observed (6-8). Contrariwise I failed to prove the role of inflammatory processes in IR as the inflammatory parameters studied did not differ significantly between groups. Although the role of proinflammatory cytokines in IR was well established (9), inflammatory state observed in CTDs may contribute to ameliorate differences, thus masking influence of inflammation on IR in this specific group of patients. It may be only speculated that difference between SLE and other group of patients may be also caused by steroids intake. Although the dose of steroids were arbitrary reduced to 10 mg/day almost 100% of SLE patients were on steroids as compared to 27% patients with RA and 20% patients with SSc.

In the study I failed to show any correlations between parameter studied, that may be largely due to small group of participants that may directly reduce statistical power of calculation. Another limitation of the study is the cross-sectional study design; the influence of disease specific influence upon the parameters studied cannot thus be excluded. To overcome this large cohorts of patients with various types of CTDs, further studies should be performed to confirm this first observation.

Table I. Patients' characteristics.

Parameter	Systemic lupus erythematosus (n=15)	Rheumatoid arthritis (n=15)	Systemic sclerosis (n=15)	Significance
Age (years)	36.0 ± 10	48.0 ± 15.0	51.1 ± 14.5	
Female/male	14/1	10/5	12/3	
Disease duration (months)	47 ± 45	66 ± 63	7.0 ± 6.0	
Disease activity	SLEDAI = 6.31 ± 2.91	DAS28 = 4.51 ±1.21	mRSS + 7.1 ± 4.8	
Steroid intake	n=14 (96%)	n=4 (27%)	n=3 (20%)	
BMI (kg/m^2)	21.1 ± 2.8	22.2 ± 4.9	23.9 ± 3.6	ns
ESR (mm/h)	27 ± 19	37 ± 22	22 ± 10	ns
hs-CRP (mg/L)	1.45 (0.48/3.69)	2.56 (1.08/9.34)	3.09 (0.45/4.11)	ns
Interleukin-6 (pg/mL)	14.9 (9.2/29.9)	29.9 (7.2/62.7)	18.2 (12.5/25.2)	ns
TNF (pg/mL	47.3 ± 22.3	32.9 ± 19.4	32.5 ± 34.7	ns
Glucose (mg/dL)	81.73 ± 0,2	88.76 ± 18.47	84.99 ± 9.36	ns
Insulin (mIU/L)	1.31 ± 0.2	1.18 ± 0.26	1.16 ± 0.23	ns
HOMA-IR	3.58 (2.58/5.56)	3.5 (2.14/4.02	3.2 (2.09/3.73	ns
HOMAβ	404.7 (253.4/477.7)*	157.5 (120.4/262.3)	238.9 (192.8/324.8)	p<0.05
Quicki	0.52 ± 0.06	0.55 ± 0.09	0.56 ± 0.08	ns
cIMT (mm)	0.64 ± 0.16	0.67 ± 0.11	0.75 ± 0.20	ns

*Statistically significant as compared to patients with RA and SSc, respectively.
Data presented as mean ± standard deviation or median with interquartile range.
mRSS: modified Rodnan skin score; BMI: body mass index; ESR: erythrocyte sedimentation rate; hs-CRP: high sensitivity C reactive protein; TNF-α: tumour necrosis factor-α; HOMA: homeostasis model assessment; QUICKI: quantitative insulin sensitivity index; cIMT: carotid intima media thickness.

P.J. KOTYLA, *MD, PhD*

Department of Internal Medicine and Rheumatology, Medical Faculty in Katowice, Medical University of Silesia, Katowice, Poland.

Please address correspondence to:
Dr P.J. Kotyla,
Department of Internal Medicine and Rheumatology, Medical Faculty in Katowice, Medical University of Silesia, Katowice, Poland.

E-mail: pkotyla@sum.edu.pl

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References

1. SANCHEZ-PEREZ H, TEJERA-SEGURA B, DE VERA-GONZALEZ A *et al*.: Insulin resistance in systemic lupus erythematosus patients: contributing factors and relationship with subclinical atherosclerosis. *Clin Exp Rheumatol* 2017; 35: 885-92.
2. MATTHEWS DR, HOSKER JP, RUDENSKI AS, NAYLOR BA, TREACHER DF, TURNER RC: Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; 28: 412-9.
3. MOHN A, MARCOVECCHIO M, CHIARELLI F: Validity of HOMA-IR as index of insulin resistance in obesity. *J Pediatr* 2006; 148: 565-6; author reply 6.
4. KATZ A, NAMBI SS, MATHER K *et al*.: Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J Clin Endocrinol Metab* 2000; 85: 2402-10.
5. STEIN JH, KORCARZ CE, HURST RT *et al*.: Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. Endorsed by the Society for Vascular Medicine. *J Am Soc Echocardiogr* 2008; 21: 93-111; quiz 89-90.
6. BAIRD JS, JOHNSON JL, ELLIOTT-MILLS D, OPAS LM: Systemic lupus erythematosus with acanthosis nigricans, hyperpigmentation, and insulin receptor antibody. *Lupus* 1997; 6: 275-8.
7. GEHI A, WEBB A, NOLTE M, DAVIS J JR: Treatment of systemic lupus erythematosus-associated type B insulin resistance syndrome with cyclophosphamide and mycophenolate mofetil. *Arthritis Rheum* 2003; 48: 1067-70.
8. TARDELLA L, ROSSETTI L, DE PIRRO R *et al*.: Circulating anti-insulin receptor antibodies in a patient suffering from lupus nephritis and hypoinsulinemic hypoglycaemia. *J Clin Lab Immunol* 1983; 12: 159-65.
9. TILG H, MOSCHEN AR: Inflammatory mechanisms in the regulation of insulin resistance. *Mol Med* 2008; 14: 222-31.