Evaluation of renal resistive index in different autoimmune diseases

Sirs,

Renal resistive index (RRI) is a non-invasive method to assess intrarenal vascular resistance and compliance. RRI changes may be detected in different conditions, such as tubulointerstitial nephritis, renovascular hypertension, acute kidney injury and kidney transplantation (1).

Few studies have focused on the RRI modifications in patients affected by autoimmune diseases (ADs). Platt *et al*. observed for the first time an association between RRI changes and histologic parameters in lupus nephritis (LN). The authors demonstrated a significant association between pathological RRI and interstitial nephritis (2). More recently, Conti *et al*. analysed RRI in patients with LN, non-renal SLE and healthy controls, founding a significant correlation between pathologic RRI and class IV LN, suggesting that RRI could be used as marker of severity disease (3). Rosato *et al*. demonstrated that RRI was significantly higher in systemic sclerosis (SSc) patients than healthy controls. RRI showed an inverse correlation with measured glomerular filtrate rate (GFR) (4). Finally, only one study evaluated RRI in anti-phospholipid syndrome (APS), identifying in the activation of mammalian target of rapamycin complex pathways, a possible pathogenic mechanism inducing development of a pathologic RRI (5).

In this study we aimed to evaluate RRI in a large cohort of patients affected by different ADs. Our cohort included 188 consecutive patients affected by 91 SSc, 38 APS, 49 LN, 10 SLE without renal involvement attending to Scleroderma Unit and Lupus Clinic of Sapienza University of Rome.

The presence of urinary tract obstruction, renal artery stenosis, heart failure, infectious disease, diabetes, and hypertension was considered as exclusion criteria.

RRI in all patients (SSc, APS and SLE) was evaluated at the time of enrolment. In LN patients, RRI was evaluated before kidney biopsy for standard of care management. Clinical and laboratory data were collected at the time of RRI assessment. The study was conducted in accordance with the protocol, good clinical practice principles and the Declaration of Helsinki statements.

We evaluated 91 SSc patients [79 F, median age 56 years (CI 52–59)], 38 APS (27 F, median age 43 years, CI 39–51), 49 LN (45 F, median age 38 years, CI 28–49) and 10 SLE without renal involvement (9 F, median age 33, CI 29–41). In the subgroup of SSc, 50 (54.9%) patients were positive for anti-topoisomerase I antibodies, 37 (40.7%) for anticentromere, 2 (2.2%) for RNA polymerase III and 2 (2.2%) patients were negative for specific antibodies.

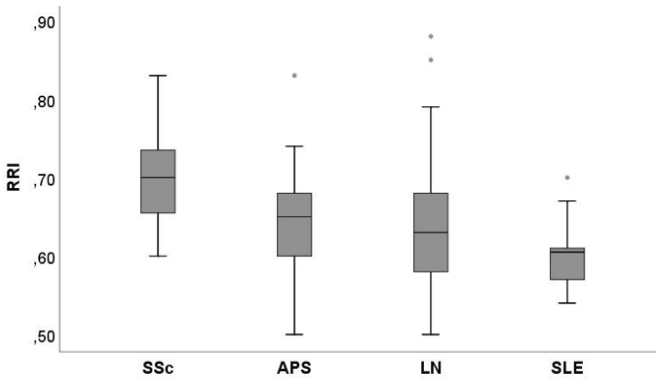

Fig. 1. Median value of renal resistive index (RRI) in systemic sclerosis (SSc), antiphospholipid syndrome (APS), lupus nephritis (LN), systemic lupus erythematous (SLE).

In the study population a median value of estimated GFR (eGFR) was 98 ml/min (CI 80–104). No significant ($p>0.05$) differences of eGFR were observed between LN [92 (67–107)] and other ADs [95 ml/min (90–98)]. The median value of RRI was significantly higher in SSc patients [0.70 (CI 0.68–0.72)] than other ADs: APS 0.65 (CI 0.63–0.67), LN [0.63 (CI 0.61–0.68), $p<0.0001$] and SLE [0.61 (CI 0.57–0.61), $p<0.0001$]. No significant ($p>0.05$) differences of RRI were observed between APS, LN and SLE (Fig. 1). In the subgroup of SSc patients, the mean values of systolic pulmonary arterial pressure (sPAP) and diffusion lung carbon monoxide (DLco) are 30.6±9.3 mmHg and 70.2±16.5 % of predicted, respectively. In the subgroup of SSc we observed a significant positive linear correlation between RRI and sPAP (r= 0.34, $p<0.01$), conversely a negative correlation exists between RRI and DLco (r= -0.27, $p<0.05$).

Renal involvement represents one of the major issues in ADs with different pathogenesis. Scleroderma-associated vasculopathy, characterised by increased renal vascular resistance and endothelial dysfunction, is widely accepted as a condition of SSc-related subclinical renal involvement (6). In SSc patients, increased intrarenal stiffness is due to microvascular damage, narrowing of the arterial lumen, vessel occlusion and impaired angiogenesis (7-8). Conversely, in SLE-related kidney manifestations, renal damage moves from glomerular involvement secondary to immune-complex activation (9). Finally, in APS patients, renal involvement is determined by vascular lesions such as thrombotic microangiopathy, vaso-occlusive lesions, intimal hyperplasia of interlobular arteries.

In our study RRI was higher in SSc patients than other ADs since subclinical renal vasculopathy is the main pathogenic mechanism of all SSc renal manifestations (10).

In SSc patients, RRI is a marker not only of increased intrarenal arterial stiffness, but also of vascular damage of heart (positive correlation between RRI and sPAP) and lung (negative correlation between RRI and DLco). Bruni *et al*. demonstrated that RRI might be used to evaluate renal and extrarenal involvement in SSc and could serve as predictors of mortality (11). In SSc patients, DLco represents a marker of interstitial lung disease and pulmonary vasculopathy. SSc vasculopathy may result in significant morbidity and mortality as in the case of digital ulcers, pulmonary hypertension and interstitial lung disease (12).

In conclusion, RRI represent a marker of renal involvement in ADs with primary vascular damage.

Key message

Renal resistive index is higher in systemic sclerosis than other autoimmune diseases.

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Competing interests: none declared.

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