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ADIPOSE TISSUE MASS AND LEAN TISSUE MASS PREDICT MEDIUM-TERM OUTCOME AND PROGNOSIS IN PATIENTS WITH LUPUS NEPHRITIS

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Systemic lupus erythematosus is an autoimmune disease in which chronic inflammation plays an important role in the progression of the disease and its commorbidities. Corticosteroids, an important part in the immunosuppressive therapy regimens used in lupus, also have metabolic effects on remodelling of the adipose tissue and impact on the cardiovascular risk. Not only a site of energy storage or a modulator of the endocrine system, adipose tissue has emerged as an important regulator of multiple important processes including inflammation. Autoimmune diseases are perpetuated by chronic inflammatory responses but the exact etiology of these diseases remains elusive. We included 62 patients in the study, of which 4 men and 58 women, mean age 38,6 years. We assesed their metabolic profile using serum total cholesterol, tryglycerides, CRP, C3, C4, urea, creatinine, total blood proteins, serum albumin and assessing nutritional status using bioimpedance. All patients had biopsy-proven lupus nephritis. We evaluated the patients every month for 1 year. We correlated inflammatory status with lean body mass and adipose tissue mass measured using bioimpedance in a multivariate logistic regression. There was a good correlation between adipose tissue mass and inflammatory status: fat body mass <24% in women (normal) was associated with lower CRP and lower corticoid doses (25 mg/day) p<0.01, and with lower progression of renal failure (GFR declined with 1.9 ml/min/1.73m2), versus in women with >32% of fat mass (obese patients) CRP was higher and prednisone doses were higher (42 mg/day), with loss of GFR 2.4ml/min/1.73m2. In men fat mass <18% was associated with a mean corticoid dose of 15 mg/day, and fat mass between 18 and 25% (normal) with 18 mg/day. On the other hand, malnourished patients had higher CRP values and needed higher doses of prednisone (38 mg/day) and had a higher progression of renal failure that normal patients (reduction of GFR with 2.6 ml/min/1.73m2). Both malnutrition and obesity are associated with higher inflammation and worse prognosis for renal patients. Malnourished patients usually present more aggressive forms of lupus. It is well-known that chronic inflammation rises catabolism and leads to anorexia. Patients that have normal percentage of body fat and lean muscle mass have the best prognosis in the medium- term.

Key words: Lupus nephritis, inflammation, nutritional status, corticotherapy.

INTRODUCTION

Systemic lupus erythematosus is an autoimmune disease in which apoptosis is impaired, there is an overcharge of the phagocytic system, thus resulting in chronic inflammation, altered activity of the antigen-presenting-cells and thus autoimmunity, which can further increase inflammation by secretion of cytokines, and finally tissue fibrosis, in advanced stages of the disease[1-4]. To break this vicious circle, we use immunosuppressive therapies such as corticosteroids – both iv and oral administration, and immunosuppressives of different classes (cyclophosphamide, azathioprine, mycophelonat mofetil, and newer classes such as calcineurin inhibitors – cyclosporine, tacrolimus)[5-7]. One major concern is to balance the benefits and risks of such therapies (infection, malignancy, fertility issues with cyclophosphamide, adverse reactions of corticoids – weight gain, diabetes mellitus, psychosis, iatrogenic Cushing's syndrome etc.)[8,9]. Of these classes of immunosuppressives, corticoids have been used the most, their benefit is very clear, but the important adverse reactions have directed therapeutical options thowards newer classes of immunosuppressive drugs, that should permit lowering of the corticoid dose and should achieve better control of the disease. These medications in themselves impact the metabolic status of the patient. On the other hand, adipose tissue has been proven to be metabolically active and capable of generating inflammatory products and processes[10,11].
Not only a site of energy storage or a modulator of the endocrine system, adipose tissue has emerged as an important regulator of multiple important processes including inflammation[12-14]. Autoimmune diseases are perpetuated by chronic inflammatory responses but the exact etiology of these diseases remains elusive.

Bioimpedance is a method used to determine the nutritional status of patients, based on opposition to the flow of an electric current through the body tissues which can determine total body water, lean mass and adipose tissue mass[15,16].
The purpose of this study was to study the statistical association between adipose tissue mass, lean muscle mass (nutritional status) with the inflammatory status of the patients and with the clinical response to therapy. We analised the association between fat tissue and prednisone dosage used for maintenance therapy.
The aim of these study was: to test the correlation between adipose tissue mass and inflammatory status (CRP levels), to test the correlation between adipose tissue mass and renal function decline (eGFR- MDRD4 equation), to test the correlation between adipose tissue mass and corticoid maintenance dosage.

MATHERIALS AND METHODS

We included 62 patients in the study, of which 4 men and 58 women, mean age 38,6 years (figure 1).
We assesed their metabolic profile using serum total cholesterol, tryglycerides, CRP, C3, C4, urea, creatinine, total blood proteins, serum albumin and assessing nutritional status using bioimpedance.
All patients had biopsy-proven lupus nephritis, and had different lupus nephritis classes (figure 2). Most of the patients had lupus nephritis class IV, followed by class V, association of class V +IV, and third place classes V +III. We evaluated the patients every month for 1 year - for weight, and every 3 months for the biochemical parameters. Patients who had more imortant disease were monitored monthly and received iv Methylprednisolone 1g/day for 3 conssecutive days. We correlated inflammatory status with lean body mass and adipose tissue mass measured using bioimpedance in a multivariate logistic regression.

RESULTS AND DISCUSSIONS

There was a good correlation between adipose tissue mass and inflammatory status: fat body mass <24% in women (normal) was associated with lower CRP and lower corticoid doses (mean dose 25 mg/day) $p<0.01$, and with lower progression of renal failure (GFR declined with 1.9 ml/min/1.73m^2), versus in women with >32% of fat mass (obese patients) CRP was higher and prednisone doses were higher (mean dose 42 mg/day), with loss of GFR 2.4ml/min/1.73m^2.
In men fat mass <18% was associated with a mean corticoid dose of 15 mg/day, and fat mass between 18 and 25% (normal) with 18 mg/day. On the other hand, malnourished patients had higher CRP values and needed higher doses of prednisone (mean dose 38 mg/day) and had a higher progression of renal failure that normal patients (reduction of GFR with 2.6 ml/min/1.73m^2).

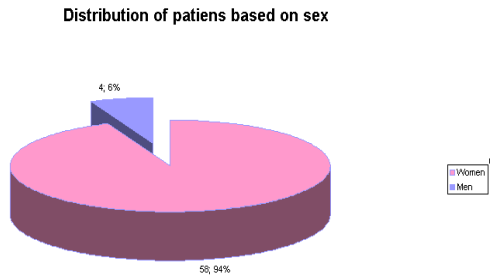

Figure 1 Distribution of patients based on sex.

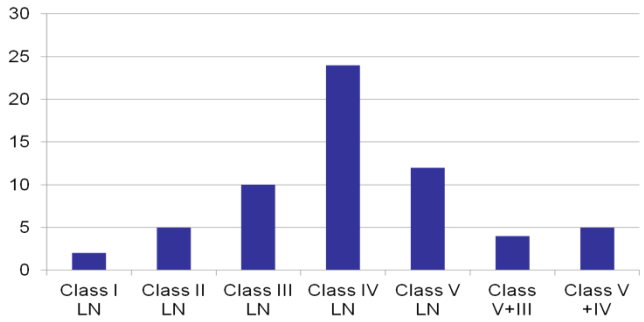

Figure 2 Distribution of patients base don the histopathological classes of lupus nephritis.

There was a good correlation between body –mass index and fat tissue mass in the bioimpedance method. (figure 3). We measured nutritional status of the patients by bioimpedance once every 3 months, and monthly by measuring the body-mass index.

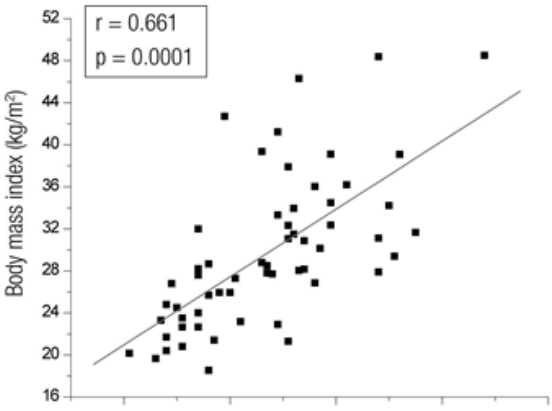

Figure 3 Correlation between fat mass and body-mass index.

In normal weight patients (fat mass >18% and <24%), the mean corticoid dosage used was 25.66 g/day (figure 4).

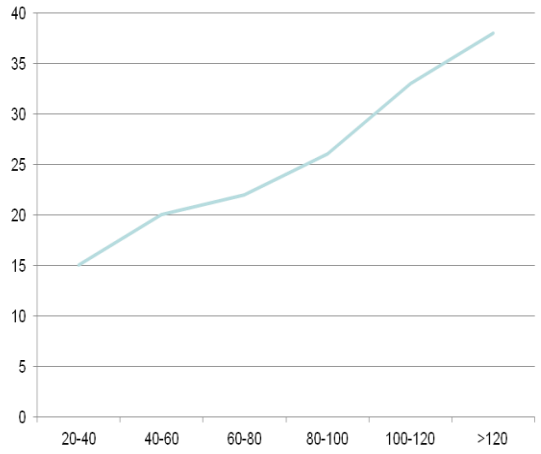

Figure 4 Correlation between inflammation and corticoid dosage in normal weight patients. (vertical values – prednisone dosage in mg/day, horizontally ESR – erythrocyte sedimentation rate in mm/h).

In obese patients, there was also a good correlation between inflammation and corticoid dosage (figure 5), the medium dosage used was 42 mg/day. In the obese patient group we included patients with >32% fat mass in bioimpedance.

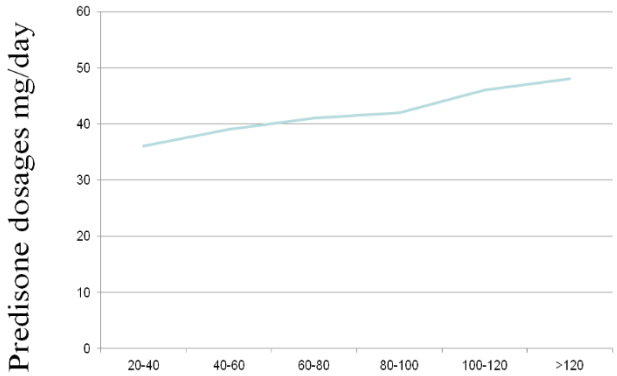

Figure 5 Correlation between inflammation and corticoid dosage in obese patients. (vertical values – prednisone dosage in mg/day, horizontally ESR – erythrocyte sedimentation rate in mm/h).

Malnourished patients (<18% fat mass) had the highest inflammatory markers, and needed the highest doses of corticoids (figure 6). The medium dosage of prednisone used was 38.16 mg/day.
We obtained these conclusions based of a single-center experience. Malnourished and obese patients needed higher doses of corticosteroids than normal weight patients. One possible explanation was that malnourished patients had more aggressive and active disease, and their nutritional status was a result of the activity and more advanced stage of the disease. On the other hand, obese patients also had high inflammatory markers, but in a lower range than malnourised patients.

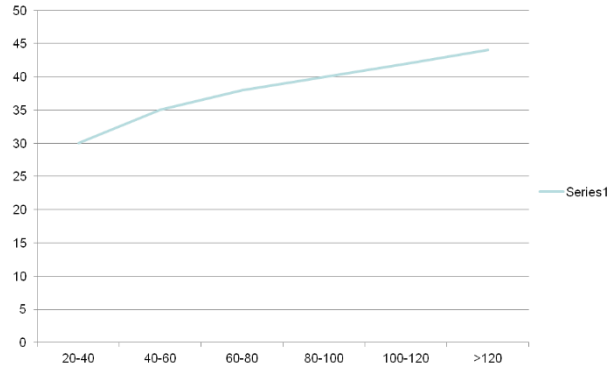

Figure 6 Correlation between inflammation and corticoid dosage used in malnourished patients. (vertical values – prednisone dosage in mg/day, horizontally ESR – erythrocyte sedimentation rate in mm/h).

The limitations of the study include: single-center study, relatively small study population, bioimpedance measurements made at different day times for different patients. The method-related limitations include hydration status of the patients - dehydration is a recognized factor affecting BIA measurements as it causes an increase in the body's electrical resistance, (5 kg underestimation of fat-free mass = an overestimation of body fat)[6,7]. Body fat measurements are lower if measurements are taken shortly after consumption of a meal, causing a variation between highest and lowest readings of body fat percentage taken throughout the day of up to 4.2% of body fat. Moderate exercise before BIA measurements lead to an overestimation of fat-free mass and an underestimation of body fat percentage due to reduced impedance (moderate intensity exercise for 90–120 minutes before BIA =12 kg overestimation of fat-free mass), this last point was controlled, since patients were mostly inpatients who had a static programme while being admitted.

CONCLUSIONS

There was a good correlation between adipose tissue mass and inflammatory status. Normal weight patients had the best prognosis and response to therapy.
Malnourished patients needed higher doses of corticoids that obese patients. New data is needed to assess how other immunosuppressive drugs influence the metabolic status of patients, and how nutritional status is related to the response in other therapeutic classes of drugs.

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