The high prevalence of metabolic syndrome in polymyositis

F.H.C. de Souza, S.K. Shinjo

Rheumatology Division, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil.

Abstract

Objective

Metabolic syndrome (MetS) is a cluster of metabolic abnormalities that are associated with increased cardiovascular diseases (CVD). MetS has been systematically evaluated in all systemic autoimmune rheumatic diseases except for polymyositis (PM). This study aimed to evaluate the frequency of MetS in PM patients and analyse the possible association of MetS with traditional risk factors of CVD and PM-related clinical and laboratory features.

Methods

The present cross-sectional, single-centre study included 35 consecutive PM patients (Bohan and Peter, 1975) and 70 healthy controls. MetS diagnosis was determined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATPIII).

Results

The age, gender and ethnicity distributions between the PM and control groups were comparable (p>0.050). The median PM disease duration was 5 years. Compared with healthy subjects, PM patients had higher prevalence of MetS (45.7% vs. 20.0%, p=0.011). In an additional univariate analysis of PM patients with (n=26) and without (n=19) MetS revealed that patients with this complication were older (56.1±7.8 vs. 44.3±12.8 years; p=0.002) with more cumulative prednisolone doses, higher scores on the health assessment questionnaire and on the physician visual analogue scale (p<0.050). Disease duration was comparable between both groups (p>0.050).

Conclusion

MetS and CVD risks are highly prevalent in PM. Monitoring for and early treatments of modifiable risk factors for CVD in PM patients are necessary.

Key words

cardiovascular diseases, inflammatory myopathies, metabolic syndrome, polymyositis

Fernando H.C. de Souza, MD
Samuel K Shinjo, MD, PhD

Please address correspondence and reprint requests to:
Samuel Katsuyuki Shinjo,
Av. Dr. Arnaldo, 455,
3º andar, sala 3150,
CEP 01246-903,
São Paulo, Brazil.
E-mail: samuel.shinjo@gmail.com

Received on May 28, 2013; accepted in revised form on August 7, 2013.

Competing interests: none declared.

Introduction

Polymyositis (PM) is a rare idiopathic inflammatory myopathy characterised by an insidious weakness of the symmetric proximal muscle that can lead to disability and a poorer quality of life. The annual incidence of polymyositis is 2.2 to 7.7 cases per million individuals (1, 2). PM is twice as common in women as in men, and it primarily affects individuals between the ages of 45 and 55 (1-3).

Metabolic syndrome (MetS) is a cluster of classical cardiovascular risk factors characterised by impaired glucose tolerance, dyslipidaemia, central obesity and arterial hypertension (4-6). MetS affects 27%, 30% and 40% of the Indian, European and United States populations, respectively (6-8), and its presence is a strong predictor of cardiovascular diseases (CVD), diabetes mellitus and stroke (4).

It has been postulated tthat the inflammatory process plays a major role in the development and propagation of CVD, which is associated with the dysregulation of lipid metabolism, as well as conventional risk factors such as arterial hypertension, high body mass index, low physical activity and smoking, which contribute to an increased risk of CVD (8).

Studies have assessed MetS in systemic rheumatoid diseases such as systemic lupus erythematosus (6-8), rheumatoid arthritis (8-11) and Sjögren's syndrome (12). In a recent study, we assessed the high prevalence of MetS in dermatomyositis (13).

Some studies (8, 9, 14, 15) report that a high prevalence of MetS in these autoimmune diseases is a consequence of systemic and chronic inflammation. In systemic lupus erythematosus, for instance, MetS is associated independently with corticosteroid therapy, triglyceride levels, hydroxychloroquine sulfate, high-density lipoprotein-cholesterol (HDL-C) levels, antiphospholipid antibodies and C3 complement serum levels (16, 17). In rheumatoid arthritis, MetS is correlated with inflammatory markers and disease activity (8-11). In Sjögren's syndrome, the MetS components hypertriglyceridaemia and diabetes mellitus are related to a higher prevalence of vasculitis and extraglandular features in the liver and kidney (12). In dermatomyositis, we showed that prior hypertension appears to be a major determinant of the development of MetS, while disease and therapy-related factors do not appear to play a role (13).

Because there have been no studies that analyse MetS in PM, we herein assess the frequency of MetS in PM patients and analyse the possible association of MetS with the traditional risk factors of CVD and PM-related clinical and laboratory features.

Materials and methods

Study design

The present cross-sectional study was performed at one centre and included 35 consecutive PM patients and 70 healthy control individuals from June 2011 to May 2012. All of the patients met all of the Bohan and Peter criteria (18), and they were recruited from the myopathies unit of our tertiary service. Healthy individuals aged >18 years were included in the study; patients with cancer-associated myositis or overlapping rheumatic diseases, as well as pregnant or lactating women, were excluded. The study was approved by the local ethics committee, and all of the study participants signed an informed consent form.

Patient data

All of the participants underwent a clinical evaluation that included a standardised interview, and all of their medical charts were extensively reviewed. The following data were collected:

a) Demographic data obtained: current age, gender, ethnicity, household income status, waist circumference and body mass index (BMI: weight/height^2 [kg/m^2].
b) Clinical and laboratory data collected: the patient's age at disease onset, the disease duration, as well as the serum levels of creatine kinase, aldolase, alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase, total cholesterol, HDL-C, low-density cholesterol (LDL-C), triglycerides, fasting blood glucose and inflammation

markers [C-protein reactive (CPR, reference value: <5 mg/L) and the erythrocyte sedimentation rate (ESR, reference value: <19 mm/1st hour)].

c) Disease status: The patient's disease status was evaluated through the application of questionnaires and scores such as manual muscle testing (MMT-8) (19), global assessment of the disease by the physician and the patient through the visual analogue scale (VAS), and the health assessment questionnaire (HAQ) (20).
d) Pharmacological therapy: immunosuppressants, corticosteroids, and statins were recorded. When necessary, the patient's charts were reviewed to obtain drug history information.
e) Comorbidities: information on arterial hypertension, dyslipidaemia, type 2 diabetes mellitus, hypothyroidism, myocardium infarction, and ischaemic stroke was collected. Dyslipidaemia was defined as having a plasma total cholesterol >200 mg/dL, an HDL-C <40 mg/dL, an LDL-C >130 mg/dL, triglycerides >150 mg/dL or drug treatment for an elevated LDL or TG (21).
f) Lifestyle: information regarding tobacco use, alcohol use (defined as having up to one drink/day for women and up to two drinks/day for men), sedentary lifestyle (22,23) and food habit alteration was collected.
g) Family history of CVD: myocardial infarction, angina, and sudden death in first-degree relatives before the age of 55 for men and before the age of 65 for women were recorded.

Metabolic syndrome

MetS was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) (24), which requires the presence of three or more of the following five criteria: (a) central obesity (waist >102 cm in men and 88 cm in women); (b) hypertriglyceridaemia >150 mg/dL; (c) low HDL (<40 mg/dL in men and <50 mg/dL in women); (d) high blood pressure (≥130/85 mmHg or use of drugs for high blood pressure); (e) high fasting glucose level (≥110 mg/dL).

Table I. General characteristics of polymyositis patients and controls.

	Polymyositis (n=35)	Control (n=70)	*p*-value
Current age (years)	49.7 ± 12.2	48.7 ± 9.5	0.699
Age at disease onset (years)	43.3 ± 12.8	–	–
Female	27 (77.1)	54 (77.1)	1.000
White ethnicity	21 (60.0)	43 (61.4)	1.000
Disease duration	5 [3-11]	–	–
Body mass index (kg/m^2)	27.5 [24.3-31.5]	26.0 [23.6-29.0]	0.355
Waist circumference (cm)	96.0 [87.0-106.0]	87.0 [79.0-97.0]	**0.020**
Prednisolone	17 (48.6)	–	–
Prednisolone >20 mg/day	1 (2.9)	–	–
Antimalarial	1 (2.9)	–	–
Acetylsalicylic acid	1 (2.9)	1 (1.4)	0.614
Immunosuppressive	20 (57.2)	–	–
Statin use	0	3 (4.3)	0.549
Family history of CVD	13 (37.1)	4 (5.7)	**<0.001**
Systemic arterial hypertension	16 (45.7)	19 (27.1)	**0.047**
Diabetes mellitus	12 (34.3)	3 (4.3)	**<0.001**
Ischaemic stroke	1 (2.9)	0	0.155
Dyslipidaemia	25 (71.4)	36 (51.4)	**0.025**
Myocardial infarction	1 (2.9)	1 (1.4)	0.614
Hypothyroidism	5 (5.7)	7 (10.0)	0.460
Alcohol consumption	0	1 (2.9)	0.313
Sedentarism	28 (80.0)	48 (68.6)	0.121
Tobacco	5 (14.3)	13 (17.1)	0.708
Fasting blood glucose (mg/dL)	91.0 [78.0-108.0]	81.0 [73.0-89.0]	**0.003**
Triglycerides (mg/dL)	149.0 [70.0-211.0]	99.0 [80.0-123.0]	**0.011**
Total cholesterol (mg/dL)	196.0 [168.0-227.0]	194.0 [174.0-210.0]	0.422
HDL cholesterol (mg/dL)	57.0 [47.0-72.0]	55.0 [48.0-66.0]	0.901
LDL cholesterol (mg/dL)	111.0 [90.0-131.0]	122.0 [90.0-129.0]	0.881
C-reactive protein (mg/L)	3.4 [1.1-7.4]	1.3 [0.7-2.5]	1.000
ESR (mm/1st hour)	12.0 [8.0-31.0]	6.0 [3.0-8.0]	**<0.001**
Metabolic syndrome	16 (45.7)	14 (20.0)	**0.011**

The results are expressed as percentages (%), means ± standard deviation or medians [interquartile].
Immunosuppressive drugs: azathioprine, methotrexate, cyclosporine, mofetil mycophenolate.
CVD: cardiovascular disease; ESR: erythrocyte sedimentation rate; HDL-C, high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

Statistical analysis

The Kolmogorov-Smirnov test was used to evaluate the distribution of each parameter. The demographic and clinical features are expressed as the means and standard deviation (SD) for continuous variables or as frequencies and percentages for categorical variables. The median (25^{th} – 75^{th} percentile) was calculated for continuous variables that were not normally distributed. Comparisons between the patients and the controls and between the patients with and without MetS were performed using Student's *t*-test or the Mann-Whitney test for continuous variables. Pearson's chi-squared test and Fisher's exact test were used to evaluate the categorical variables. The measurements were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). A value of $p<0.050$ was considered significant. All of the analyses were performed using the SPSS 15.0 statistics software (Chicago, USA).

Results

The present cross-sectional study included 35 PM patients and 70 healthy control individuals. The PM patients and the control subjects had a comparable median age ($p=0.699$), female gender frequency ($p=1.000$) and white ethnicity count ($p=1.000$) (Table I). The median disease duration was five years [range: 3–11].

The body mass index was similar between the groups ($p=0.355$), but the waist circumference ($p=0.020$) was higher in the PM patients than in the controls (Table I).

Seventeen (48.6%) PM patients were using prednisolone, and one of these patients was taking more than 20 mg/day. Twenty (57.2%) PM patients were using immunosuppressive drugs, and

one (2.9%) was taking an antimalarial drug. No PM patients were taking statins (Table I).

Higher frequencies of the following CVD risk factors were found more frequently in the patients than in the controls: a family history of premature cardiovascular disease, systemic arterial hypertension, diabetes mellitus and dyslipidaemia (as shown in Table I). However, no differences were observed in the rates of ischaemic stroke, myocardial infarction, hypothyroidism, alcohol consumption, smoking or sedentary lifestyle.

The blood fasting glucose levels, triglyceride levels and ESR were higher in the PM patients compared with the control group (Table I), whereas the CPR, HDL-C, total cholesterol and LDL-C levels were similar between the two groups.

According to the NCEP-ATPIII, MetS was present in 45.7 and 20% of the PM and control groups (p=0.011), respectively.

A further analysis of the PM patients with (n=16) and without MetS (n=19) revealed that the patients with this complication had higher ages (56.1±7.5 *vs*. 44.3±12.8, p=0.002), whereas the gender and ethnicity distributions were comparable between the two groups (Table II).

The MetS patients also showed a higher body mass index (p=0.027), a larger waist circumference (p=0.015) and higher current systemic arterial hypertension (p=0.002), but did not show these differences prior to the disease (p=0.105). The physician's VAS (p=0.037) and HAQ (p=0.001) were higher in patients with MetS than in patients without MetS in a univariate analysis, whereas the patient's VAS, MMT-8 score, therapy schemes (type and number of immunosuppressants: azathioprine 2-3 mg/kg/day, methotrexate <25 mg/week, cyclosporine 2-3 mg/kg/day, mycophenolate mofetil 2-3 g/day, antimalarial 3-4 mg/kg/day) and non-steroidal anti-inflammatory drugs were not. The current corticosteroid dosage levels were also similar between the two groups except for a higher prevalence of cumulative doses in the MetS group (p=0.038). In addition, a family history of premature CVD, diabetes mellitus, ischaemic stroke, dyslipidaemia, myocardaium infarction, hypothyroidism and sedentary lifestyle were comparable between the two groups (p>0.050).

Table II. Demographics, disease status, comorbidities, clinical features and treatment of polymyositis patients with and without metabolic syndrome.

	MetS (+) (n=16)	MetS (-) (n=19)	p-value
Current age (years)	56.1 ± 7.8	44.3 ± 12.8	**0.002**
Age at disease onset (years)	48.5 ± 10.0	39.5 ± 13.6	0.050
Female	17 (87.5)	10 (68.4)	0.244
White ethnicity	10 (52.6)	11 (68.7)	0.491
Disease duration (years)	5.3 ± 4.9	5.2 ± 5.8	0.925
Body mass index (kg/m^2)	29.9 ± 4.6	25.8 ± 4.3	**0.027**
Waist circumference (cm)	102.5 ± 13.9	89.4 ± 13.4	**0.015**
VAS, patient (cm)	1.2 [0-6.5]	1 [0-2]	0.230
VAS, physician (cm)	2 [0-3]	0 [0-1]	**0.037**
MMT-8	73 [72-80]	80 [76-80]	0.071
HAQ	1.04 [0.43-1.93]	0 [0-0.48]	**0.001**
Prednisolone			
Pulse therapy	2 (12.5)	3 (15.8)	1.000
Currently using	8 (50.0)	9 (47.4)	1.000
>20 mg/day	1 (5.3)	0	0.457
Cumulative dose (g)	23.0 ± 15.8	21.8 ± 10.4	**0.038**
Immunosuppressive			
None	7 (43.8)	9 (47.1)	1.000
One*	7 (43.8)	8 (42.1)	1.000
Two	2 (12.5)	2 (10.5)	1.000
Antimalarial	1 (6.3)	3 (15.8)	0.608
Statins	0	0	1.000
Acetylsalicylic acid	1 (6.3)	0	0.457
Non-steroidal anti-inflammatory	1 (6.3)	0	0.457
Family history of premature CVD	8 (50.0)	5 (26.3)	0.179
Systemic arterial hypertension	12 (75.0)	4 (21.1)	**0.002**
Before disease onset*	6 (37.5)	2 (10.5)	0.105
Diabetes mellitus	7 (43.8)	5 (26.3)	0.311
Before disease onset**	3 (18.8)	1 (5.3)	0.312
Ischaemic stroke	1 (6.3)	0	0.457
Dyslipidaemia	11 (68.8)	14 (73.7)	1.000
Myocardium infarction	1 (6.3)	0	0.457
Hypothyroidism	2 (12.5)	0	0.202
Alcohol consumption	0	0 1.000	
Sedentarism	12 (75.0)	16 (84.2)	0.677
Tobacco	3 (18.8)	2 (10.5)	0.642
Food habit alteration	0	1 (5.3)	1.000

The results are expressed as percentages (%), means ± standard deviation or medians [interquartile].
Immunosuppressive drugs: azathioprine, methotrexate, cyclosporine, mofetil mycophenolate.
CVD: cardiovascular disease; PM: polymyositis; HAQ: health assessment questionnaire; MetS: metabolic syndrome; MMT: manual muscle test; VAS: visual analogue scale.
*Analysed drug by drug; **Before polymyositis symptoms.

All laboratory results for PM patients with and without MetS were also similar with the exception of higher levels of triglycerides (p=0.002) in patients with MetS.

In a multivariate analysis, we did not find any statistically significant associations between MetS and the previous univariate parameters in PM patients.

Discussion

The literature has mentioned a correlation between MetS and risk factors for premature CVD in systemic rheumatic diseases (8-21, 24) but not in PM. Thus, this is the first study that focuses on MetS in a group of patients with PM. Our results showed a high prevalence of MetS and CVD risk factors in this disease.

We recently showed for the first time that the MetS is highly prevalent in DM, and prior hypertension appears to be a major determinant of its development, whereas disease and therapy-related factors do not appear to play a

Table III. Laboratory findings of polymyositis patients with and without metabolic syndrome.

	MetS (+) (n=16)	MetS (-) (n=19)	*p*-value
Creatine kinase (IU/L)	199.0 [127.0-405.0]	186.0 [103.0-918.0]	0.931
Aldolase (IU/L)	4.9 [3.6-6.8]	6.9 [3.7-9.1]	0.246
Dehydrogenase lactate (IU/L)	436.8 ± 111.5	486.6 ± 140.9	0.623
AST (IU/L)	25.0 [15.0-34.0]	23.0 [16.0-46.0]	0.402
ALT (IU/L)	25.0 [18.0-45.0]	23.0 [19.0-32.0]	0.954
Fasting blood glucose (mg/dL)	97.4 ± 14.7	100.6 ± 71.1	0.850
Triglycerides (mg/dL)	186.0 [148.0-252.0]	110.0 [69.0-145.0]	**0.002**
Total cholesterol (mg/dL)	193.0 [163.0-205.0]	208.0 [168.0-237.0]	0.354
HDL-C (mg/dL)	52.4 ± 13.7	59.2 ± 21.1	0.261
LDL-C (mg/dL)	107.0 [85.0-117.0]	123.0 [99.0-140.0]	0.146
ESR (mm/1st hour)	18.0 [11.0-29.0]	11.0 [8.0-36.0]	0.728
C-reactive protein (mg/L)	3.4 [1.0-10.6]	18.0 [11.0-29.0]	0.728

The results are expressed as means ± standard deviation or medians [interquartile].
ALT: alanine aminotransferase; AST: aspartate aminotransferase; ESR: erythrocyte sedimentation rate; HDL-C, high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; MetS: metabolic syndrome; TG: triglycerides.

role (13). We found a high prevalence of other CVD parameters in DM patients, such as a family history of CVD, dyslipidaemia and defined-diabetes mellitus (13). In the present study, the percentages of these comorbidities remained higher in PM patients compared with controls, leading us to the current discussion of whether these risk factor parameters are common to all idiopathic inflammatory myopathies and are in conjunction with the underlying inflammatory process and a decreased functional capacity.

When PM patients with and without MetS were compared, we observed (in the univariate analysis) a higher age, a higher age at the onset of disease, an increased body mass index, and systemic arterial hypertension prior to the disease and to ESR, which were precisely the same parameters highlighted in DM patients (13).

However, unlike in relation to the DM patients (13), we found increased rates in the physician's HAQ and VAS in those patients that had MetS in this study. The disease activity may be an important factor in this population, which further emphasises the need for early and aggressive treatment for this group of patients.

In the multivariate analysis, we did not find any association between MetS and the previous parameters (age, age at the onset of disease, body mass index, and systemic arterial hypertension prior to the disease and to ESR) with statistical significance in PM patients, whereas in the DM patients, only the prevalence of prior arterial hypertension was increased (13).

In untreated patients with DM, an altered lipid level is a frequent disorder, and CRP is an independent risk factor for CVD characterised by abnormal lipid and lipoprotein patterns that are explained by an increase in TG and a decrease in HDL-C (25). In the present study, TG and ESR were higher in the PM patients compared with the control group. However, we found no differences in the analysis of CPR, HDL-C level, total cholesterol or LDL-C between the groups. This result may suggest a high risk of atherosclerosis in myopathic patients, and increased inflammation may be associated with marked changes in lipid and lipoprotein metabolism.

Compared with other systemic rheumatic diseases, MetS prevalence in PM was higher than that found in systemic lupus erythematosus populations (16.0–29.4%) (6-8) but comparable to that found in rheumatoid arthritis and DM studies (19–42%) (8, 11, 13, 26). Particularly in rheumatoid arthritis, the MetS prevalence ranges from 9.7% to 30.8% according to ethnicity and can contribute also to carotid artery intima-media thickness and carotid artery plaque (25).

The pathogenesis underlying the clustering of CVD risk factors in MetS remains unclear. Although insulin resistance has a central role, genetic predisposition (instead of disease activity), drug treatment (such as corticosteroid therapy), as well as obesity and inflammation, may be involved (27, 28) and should be considered to treatment (24). Moreover, the lipid profile may be influenced by weight, body mass index or antimalarial drugs or statins. Similarly, the exposure of PM patients to corticosteroid therapy is associated with MetS (27, 28). In the present study, there was a significant difference in cumulative prednisolone doses between the PM patients with and without MetS.

PM must be regarded as a condition associated with CVD risk factors. This risk must be due to both an increased prevalence of traditional risk factors and the inflammatory burden as happen in others systemic autoimmune diseases (24). In the present study we had relatively few CVD events, such as stroke and myocardial infarction. Nevertheless, such events require longer observation periods in cohort study before they can be observed in a large sample.

There are some limitations to the present study. First, we had a small sample size which could limit the strength of the results. Second, we selected our patients with PM based on the Bohan and Peter criteria (18) which show poor specificity (29). Third, we analysed patients with chronic defined diseases, and not patients at onset diseases and without glucocorticoid / immunosuppressive therapy naïve; although, in general, PM can increase CVD risk factors, lifestyle and drug therapies can also contribute to the increase of risk factors and must be considered in medical practice. Fourth, we used the NCEP-ATP-III definition for its easy applicability to clinical practice because it does not require insulin and microalbuminuria assessments or the oral glucose tolerance test that is required for the diagnostic criteria suggested by the World Health Organisation.

In summary, our data confirm an increased frequency of MetS and a higher prevalence of CVD risk factors in PM patients. Thus, monitoring and early treatment of modifiable risk

factors for CVD (for example: dyslipidaemia, systemic arterial hypertension, high fasting blood glucose) should be achieved. Furthermore, the management of these patients according to international guidelines, with early control of the disease activity status or systemic inflammatory condition, with the lowest dose for the shortest period possible of corticosteroid use, is necessary to decrease possible CVD morbidity and subsequently mortality amongst PM patients.

References

1. DIMACHKIE MM, BAROHN RJ: Idiopathic inflammatory myopathies. *Front Neurol Neurosci* 2009; 26: 126-46.
2. PRIETO S, GRAU JM: The geoepidemiology of autoimmune muscle disease. *Autoimmun Rev* 2010; 9: A330-4.
3. GAUBITZ M: Epidemiology of connective tissue disorders. *Rheumatology* (Oxford) 2006; 45 (Suppl. 3): iii3-4.
4. REAVEN GM: Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes* 1988; 37: 1595-607.
5. GRUNDY SM: Metabolic syndrome pandemic. *Arterioscler Thromb Vasc Biol* 2008; 28: 629-36.
6. CAMERON AJ, SHAW JE, ZIMMET PZ: The metabolic syndrome: Prevalence in worldwide populations. *Endocrinol Metab Clin North Am* 2004; 33: 351-75.
7. ISOMAA B, ALMGREN P, TUOMI T *et al*.: Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001; 24: 683-9.
8. FORD ES, GILES WH, MOKDAD AH: Increasing prevalence of the metabolic syndrome among U.S. adults. *Diabetes Care* 2004; 27: 2444-9.
9. CHUNG CP, OESER A, SOLUS JF *et al*.: Prevalence of the metabolic syndrome is increased in rheumatoid arthritis and is associated with coronary atherosclerosis. *Atherosclerosis* 2008; 196: 756-63.
10. GRUNDY SM, CLEEMAN JI, DANIELS SR *et al*.: Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005; 112: 2735-52.
11. TOMS TE, PANOULAS VF, JOHN H, DOUGLAS KM, KITAS GD: Methotrexate therapy associates with reduced prevalence of the metabolic syndrome in rheumatoid arthritis patients over the age of 60- more than just an anti-inflammatory effect? A cross sectional study. *Arthritis Res Ther* 2009; 11: R110.
12. DESSEIN PH, STANWIX AE, JOFFE BI: Insulin resistance and impaired beta cell function in rheumatoid arthritis. *Arthritis Rheum* 2006; 54: 2765-75.
13. DE MORAES MT, DE SOUZA FHC, DE BARROS TBM, SHINJO SK: An analysis of metabolic syndrome in adult dermatomyositis with a focus on cardiovascular disease. *Arthritis Care Res* 2013; 65: 793-9.
14. CHEN YJ, WU CY, SHEN JL, CHU SY, CHEN CK, CHANG YT *et al*.: Psoriasis independently associated with hyperleptinemia contributing to metabolic syndrome. *Arch Dermatol* 2008; 144: 1571-5.
15. MANZI S, SELZER F, SUTTON-TYRRELL K *et al*.: Prevalence and risk factors of carotid plaque in women with systemic lupus erythematosus. *Arthritis Rheum* 1999; 42: 51-60.
16. SABIO J, ZAMORA-PASADAS M, JIMÉNEZ-JÁIMEZ J *et al*.: Metabolic syndrome in patients with systemic lupus erythematosus from Southern Spain. *Lupus* 2008; 17: 849-959.
17. ESDAILE JM, ABRAHAMOWICZ M, GRODZICKY T *et al*.: Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. *Arthritis Rheum* 2001, 44: 2331-7.
18. BOHAN A, PETER JB: Polymyositis and dermatomyositis (first of two parts). *N Engl J Med* 1975; 292: 344-7.
19. LEGG AT, MERRIL JB: Physical therapy in infantile paralysis. *In*: *Principles and Practice of Physical Therapy*. Hagerstown: Mock Pemberton and Coulter; 1932.
20. BRUCE B, FRIES JF: The Stanford Health Assessment Questionnaire: dimensions and practical applications. *Health Qual Life Outcomes* 2003; 1: 20.
21. Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection and treatment of high blood cholesterol in adults (adult treatment Panel III). *JAMA* 2001; 285: 2486-97.
22. CRAIG CL, MARSHALL AL, SJOSTROM M *et al*.: International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003; 35: 1381-95.
23. MATSUDO SM, ARAÚJO T, MATSUDO VR *et al*.: Questionário internacional de atividade física (IPAC): estudo de validade e reprodutibilidade no Brasil. *Rev Bras At Física & Saúde* 2001; 6: 5-18.
24. PETERS MJ, SYMMONS DP, MCCAREY D *et al*.: EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. *Ann Rheum Dis* 2010; 69: 325-31.
25. WANG H, TANG J, CHEN X, LI F, LUO J: Lipid profiles in untreated patients with dermatomyositis. *J Eur Acad Dermatol Venereol* 2013; 27: 175-9.
26. DESSEIN PH, NORTON GR, JOFFE BI, ABDOOL-CARRIM AT, WOODWISS AJ, SOLOMON A: Metabolic cardiovascular risk burden and atherosclerosis in African black and Caucasian women with rheumatoid artrhtiis: a cross-sectional study. *Clin Exp Rheumatol* 2013; 31: 53-61.
27. WESTHOVENS R, NIJS J, TAELMAN V, DEQUEKER J: Body composition in rheumatoid arthritis. *Br J Rheumatol* 1997; 36: 444-8.
28. KONTUNEN P, VUOLTEENAHO K, NIEMINEN R *et al*.: Resistin is linked to inflammation, and leptin to metabolic syndrome, in women with inflammatory arthritis. *Scand J Rheumatol* 2011; 40: 256-62.
29. LINKLATER H, PIPITONE N, ROSE MR *et al*.: Classifying idiopathic inflammatory myopathies: comparing the performance of six existing criteria. *Clin Exp Rheumatol* 2013; 31:767-9.