Adipose tissue dysfunction is associated with increased atherosclerotic burden in individuals with or without weight excess
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Introduction: Among obese patients, a group of individuals has been associated with lower risk of cardiovascular complications, considered metabolically healthy obese. Similarly to this phenotype, there is another subgroup with normal body mass index, but with unhealthy metabolic profile, called metabolically unhealthy obese, and characterized by subclinical atherosclerosis (SA) in these individuals. Methods: We included in a cross-sectional study 355 asymptomatic patients, without cardiovascular disease and DM2 that were selected in Medical Sections of Dyslipidemia and Hypertension and Nephrology at the Dante Pazzanese Institute of Cardiology. The presence of SA was evaluated by coronary CT calcium score (CCS) and carotid ultrasound with assessment of intima-media thickness (IMT). Subjects were classified according to body mass index and serum adiponectin levels: Metabolically healthy normal weight, metabolically unhealthy normal weight, metabolically healthy obese and metabolically unhealthy obese. C-reactive protein, leptin, tumor necrosis factor-α and lipoprotein associated phospholipase A2 values were transformed into Z-score and aggregate in their average as a score of Inflammation of Low Degree. Clinical characteristics of the groups were evaluated by analysis of covariance adjusted for age and sex and ordinal logistic regression was used to assess SA. A p < 0.05 was considered significant. Results: Low-grade inflammation score is significantly higher in metabolically unhealthy individuals (β = 0.28, p < 0.001). In ordinal regression model for quartiles of IMT, non-healthy normal weight subjects had an OR of 3.2 compared to metabolically unhealthy normal weight (95% CI: 1.2 to 8.4, p = 0.019), also higher than the risk for metabolically obese group (OR 2.03, 95% CI: 1.04 to 3.97, p = 0.037). In the model of ordinal logistic regression to CCS, metabolically unhealthy normal weight subjects had an OR of 1.58 compared to healthy non-obese, but without statistically significant difference (95% CI: 0.55 to 4.54, p = 0.39). Conclusion: Our data suggest that metabolically unhealthy normal weight patients have a higher risk of subclinical atherosclerosis than metabolically healthy obese patients.

<table>
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<th>Phenotypes</th>
<th>IMT OR</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p</th>
<th>CAC OR</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p</th>
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<tbody>
<tr>
<td>Metabolically healthy obese (128)</td>
<td>2.03</td>
<td>1.04</td>
<td>3.97</td>
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<td>6.82</td>
<td>&lt;0.01</td>
<td>1.77</td>
<td>0.89</td>
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<td>1.21</td>
<td>8.41</td>
<td>0.019</td>
<td>1.58</td>
<td>0.55</td>
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<tr>
<td>Metabolically healthy normal weight (39)</td>
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<td></td>
<td></td>
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<td>1 (ref)</td>
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</table>

Background and Aims: Inflammation plays an important role in the pathogenesis of coronary atherosclerosis. Previous studies have shown that low lymphocyte account (an inflammatory cell) and high platelet levels are associated to worse clinical outcomes in patients with stable coronary disease (CAD). Platelet/lymphocyte ratio (PLR) could be used in clinical setting to analyze both inflammation and coagulation pathways. This study aims to assess the possible use of PLR as a maker of coronary calcification and a marker of CAD severity as well, by comparing this ratio to non-invasive imaging of coronary calcium score (CCS). Methods: Consecutive clinical outpatients were enrolled. Computed tomography CCS was performed to evaluate clinically unapparent CAD. Blood cell account was also obtained from each patient for PLR. After that, gender, age and PLR were compared to CCS progressive levels. A statistical analysis was performed using Chi-squared test, linear regression and logistic regression. Results: CAD patients (n = 136, age 60.0 ± 13.0 yo and 63.2% male) were enrolled and classified in 4 groups according to CCS (Agatston): zero, 1–100, 101–400 and over 400. Data regarding age, gender and PLR are as follows: ECC = 0 (n = 52, 53.1 ± 14.3 yo, 52% male, PLR = 120.1 ± 43.8), ECC 1–100 (n = 35, 61.1 ± 8.6 yo, 55% male, PLR = 117.3 ± 44.8), ECC 101–400 (n = 21, 62.2 ± 9.4 yo, 63% male, PLR = 142.0 ± 61.1) and ECC > 400 (n = 28, 68.8 ± 10.8 yo, 85% male, PLR = 2026 ± 93.6). Chi-squared test using categorical ECC and PLR quartiles showed correlation between these two variables (p = 0.0006). Simple linear regression revealed positive linear relationship between CCS (logarithmic values) and continuous PLR. Although this relationship reached statistical significance, the coefficient of determination (R²) was low (0.15 — weak correlation). Multivariate analysis with logistic regression showed independent influence for gender, age (decades) and PLR in categorized CCS (OR [IC], p value are respectively: 0.33 [0.13; 0.80], p = 0.015; 1.9 [1.3; 2.8], p = 0.0006; 2.03 [1.41–2.9], p = 0.0001). Conclusions: Among CAD patients, there is independent relationship between inflammation (represented by PLR) and severity of CAD (evaluated here by CCS).

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