Association of Soluble Fibrinogen-like Protein 2 with the Severity of Coronary Artery Disease

Jing Cheng¹, Yingying Chen², Banglong Xu², Jixiong Wu² and Fei He²

Abstract

Objective The purpose of this study was to investigate the relationship between circulating soluble fibrinogen-like protein 2 (sFGL2) concentrations and the severity of coronary artery disease (CAD) in patients who underwent first-time angiography for suspected CAD.

Methods Serum sFGL2 concentrations were measured in 102 consecutive patients by an enzyme-linked immunosorbent assay (ELISA). The number of circulating CD4⁺CD25⁺CD127low T regulatory cells (Tregs) was determined by flow cytometry and effector cytokines, including transforming growth factor-β1 and interleukin-10 (IL-10), were also evaluated by an ELISA. Associations between sFGL2 and Tregs with angiographic indexes of the severity of CAD (i.e., number of diseased vessels and the modified Gensini score) were estimated.

Results The sFGL2 levels in patients with angiographically confirmed CAD were significantly lower than those in patients with normal coronary arteries (26.95±8.53 vs. 9.88±5.46 ng/mL, p<0.001). Significant correlations were observed between the serum sFGL2 level and number of diseased vessels (r=-0.860, p<0.001) and modified Gensini score (r=-0.833, p<0.001). Using a multivariate analysis, the serum sFGL2 level was independently associated with the presence and severity of CAD.

Conclusion The serum sFGL2 levels are significantly lower in the presence of CAD and correlate with the severity of the disease. Further clinical studies are needed to confirm the use of sFGL2 as a biomarker for the detection and extent of CAD.

Key words: coronary artery disease, Gensini score, T regulatory cell, soluble fibrinogen-like protein 2

Introduction

Inflammation is implicated in the development and rupture of atheromatous plaques, and there is considerable evidence supporting the involvement of CD4⁺CD25⁺ T regulatory cells (Tregs) in this process (1, 2). A previous study demonstrated that naturally occurring CD4⁺CD25⁺ Treg numbers were reduced and functional properties were compromised in patients with acute coronary syndrome (ACS) (2). Animal experiments have also confirmed that upregulated CD4⁺CD25⁺ Tregs can attenuate both early and advanced atherosclerotic lesions (3, 4). Soluble fibrinogen-like protein 2 (sFGL2) belongs to the fibrinogen-related proteins super family and has been demonstrated to be a novel effector mainly secreted by CD4⁺CD25⁺ Tregs (5). The FGL2 gene was originally cloned from cytotoxic T lymphocyte (CTL), and the encoded protein shares 36% homology with the fibrinogen β- and γ-chains and 40% homology with the fibrinogen-related domain (FRED) of tenascin (6-8). To date, two forms of the FGL2 protein have been characterized, the membrane bound FGL2 (mFGL2) and the soluble FGL2. The former form is a 70 kDa molecule that exerts a procoagulative activity (9) and promotes thrombosis (10), generating thrombin directly and playing an important role in innate immunity (6). sFGL2, which has a 50 kDa weight, exhibits immunoregulatory and contradictory properties during tissue injury (11). A recent study has confirmed that

¹School of Nursing, Anhui University of Traditional Chinese Medicine, China and ²Department of Cardiology, Second Affiliated Hospital of Anhui Medical University, China

Received for publication July 10, 2015; Accepted for publication November 19, 2015

Correspondence to Dr. Fei He, coffeelove3344@foxmail.com
sFGL2 is an important molecule of Tregs in its function and development (12), similar to transforming growth factor beta (TGF-β) and interleukin-10 (IL-10) (13). The administration of a neutralizing antibody of sFGL2 inhibited the Treg activity in vitro (14-16). Hence, sFGL2 might play a more critical role in the Treg function. Previous studies have demonstrated the role of TGF-β and IL-10 in atherosclerosis and coronary artery disease (CAD) (17-19). In the present study, therefore, we aimed to investigate the association between serum sFGL2 levels and the severity of CAD as assessed by validated angiographic indexes.

Materials and Methods

Participants

The study population consisted of 102 consenting patients who underwent first-time coronary angiography for suspected CAD from November 2012 to February 2014 at No. 2 Hospital of Anhui Medical University. Patients with histories of malignant disease, recent myocardial infarctions, unstable angina, major trauma or surgery, renal insufficiency, acute or chronic infectious disease, any kind of immunemediated disease, or recent prescription of statins were excluded from the study. The diagnosis of CAD was confirmed by coronary angiography using a quantitative coronary angiographic system. CAD was defined as significant coronary stenosis with at least one main coronary vessel with ≥50% luminal narrowing. Non-CAD patients were defined as those with no stenosis or <50% diameter narrowing according to the quantitative coronary analysis (QCA) measurement. The study protocol was approved by our ethics committee, and all patients provided their informed consent.

Blood samples preparation

Peripheral blood samples were taken from an antecubital vein after overnight fasting and before angiographic procedures. Blood samples for sFGL2 determination were drawn, centrifuged, and stored at -80°C for subsequent assays. Before coronary angiography, complete blood counts and serum creatinine and serum lipid profiles were determined in all patients. All patients had normal serum creatinine levels and normal white blood cell counts. Total cholesterol, triglycerides, and high-density lipoprotein cholesterol were measured using enzymatic methods after overnight fasting. The low-density lipoprotein cholesterol concentration was calculated using the Friedewald formula.

Determination of circulating CD4+CD25+CD127low Tregs

Peripheral blood mononuclear cells (PBMCs) were isolated from the peripheral blood using a Ficoll gradient as described previously (20). The presence of Tregs was determined by measuring the following markers: PC5-labelled anti-CD4 (BD Biosciences-Pharmingen, San Diego, USA), FITC-labelled anti-CD25 (eBioscience, San Diego, USA) and PE labelled anti-CD127 (BD Biosciences-Pharmingen). Briefly, 5×10^5 fresh PBMCs were incubated with specific antibodies conjugated with fluorochrome (0.42 μg/mL of CD25-APC, 0.33 μg/mL of CD4-FITC and 0.33 μg/mL of CD127-PE) for 30 minutes at 4°C. The cells were then washed using phosphate-buffered saline (PBS), resuspended in Pharmingen Stain Buffer (PSB) and analyzed using a flow cytometer (FACSCalibur, BD Biosciences, San Diego, USA).

Serum levels of sFGL2

The serum sFGL2 concentrations were determined using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Bio Legend, San Diego, USA) according to the manufacturer’s instructions. Briefly, serum samples (30 μL) were added to each well of a plate precoated with anti-human FGL2 antibodies. Following 2-hour incubation at room temperature and four washes with buffer, 100 μL of human FGL2 detection antibody were added to each well for 1-hour incubation at room temperature. The plate was washed again and treated with secondary horseradish peroxidase-conjugated antibodies. After another five washes, 100 μL of substrate solution were then added for a 20-minute incubation in the dark. After the reaction was stopped, the absorbance was measured at 450 nm using an ELISA plate reader. The concentration was determined using a standard curve according to the kit’s instructions.

Measurement of inflammatory cytokines

The levels of cytokines including TGF-β1, IL-10, high sensitivity C-reactive protein (hs-CRP) and IL-10 were analyzed using an ELISA, according to the manufacturer’s protocol (Invitrogen, Rochester, NY, USA). Prior to analyzing the TGF-β1 levels, 100 μL of serum were activated by adding 4 μL of 1 N HCl and incubated at room temperature for 15 minutes and neutralized using 3 μL 1 N NaOH. The activated serum was then diluted 4× with assay buffer and dispensed into 96-well plates which were pre-coated with TGF-β1 antibody, which was followed by the addition of the detection antibody and streptavidin-horseradish peroxidase (HRP) conjugate. Specific binding was visualized after adding the substrate solution. A standard curve (log-log curve fit) was generated using respective recombinant human cytokine and the absolute concentration of the cytokine in the serum was determined from this curve. The detection of IL-10, hs-CRP and IL-10 levels were performed as described above without the serum activation procedure.

Coronary angiograms and quantitative analysis

Coronary angiograms were obtained according to standard techniques, and the severity of stenosis was assessed using quantitative coronary angiography as previously described (21). The angiograms and quantitative coronary angiographic analysis were evaluated by 2 experienced interventional cardiologists blinded to the clinical information and were scored according to 2 scoring systems: (1) the
Table 1. Clinical and Angiographic Characteristics of Patients with and without CAD.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total</th>
<th>Non-CAD (n=50)</th>
<th>CAD (n=52)</th>
<th>t/x²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men/Women</td>
<td>51/51</td>
<td>27/23</td>
<td>24/28</td>
<td>0.428</td>
<td>0.553</td>
</tr>
<tr>
<td>Age(years)</td>
<td>60±11</td>
<td>59±12</td>
<td>60±10</td>
<td>-0.629</td>
<td>0.531</td>
</tr>
<tr>
<td>Body mass index(Kg/m²)</td>
<td>24.21±3.99</td>
<td>23.53±3.68</td>
<td>24.86±4.20</td>
<td>-1.698</td>
<td>0.093</td>
</tr>
<tr>
<td>Hypertension</td>
<td>52</td>
<td>27</td>
<td>25</td>
<td>0.358</td>
<td>0.360</td>
</tr>
<tr>
<td>Diabetes</td>
<td>48</td>
<td>22</td>
<td>26</td>
<td>0.368</td>
<td>0.559</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>17</td>
<td>9</td>
<td>8</td>
<td>0.126</td>
<td>0.794</td>
</tr>
<tr>
<td>FPG (mmol/L)</td>
<td>6.24±0.92</td>
<td>6.22±0.88</td>
<td>6.27±0.97</td>
<td>-0.270</td>
<td>0.788</td>
</tr>
<tr>
<td>Triglycerides(mmol/L)</td>
<td>1.66±0.61</td>
<td>1.62±0.47</td>
<td>1.71±0.72</td>
<td>-0.756</td>
<td>0.451</td>
</tr>
<tr>
<td>Cholesterol(mmol/L)</td>
<td>5.13±0.79</td>
<td>5.04±0.80</td>
<td>5.22±0.79</td>
<td>-1.147</td>
<td>0.254</td>
</tr>
<tr>
<td>LDL-C(mmol/L)</td>
<td>3.41±0.77</td>
<td>3.26±0.85</td>
<td>3.56±0.66</td>
<td>-2.022</td>
<td>0.046</td>
</tr>
<tr>
<td>HDL-C(mmol/L)</td>
<td>0.96±0.21</td>
<td>1.05±0.20</td>
<td>0.88±0.18</td>
<td>4.294</td>
<td>0.000</td>
</tr>
<tr>
<td>White blood cell count (&gt;10⁹/L)</td>
<td>6.78±1.30</td>
<td>6.95±1.23</td>
<td>6.62±1.36</td>
<td>1.306</td>
<td>0.087</td>
</tr>
<tr>
<td>Lymphocytes count (&gt;10⁹/L)</td>
<td>1.73±0.41</td>
<td>1.80±0.43</td>
<td>1.66±0.38</td>
<td>1.727</td>
<td>0.087</td>
</tr>
<tr>
<td>Treg (%)</td>
<td>4.74±2.01</td>
<td>6.39±1.16</td>
<td>3.15±1.19</td>
<td>13.931</td>
<td>0.000</td>
</tr>
<tr>
<td>sFGL2(ng/mL)</td>
<td>18.25±11.13</td>
<td>26.95±8.53</td>
<td>9.88±5.46</td>
<td>11.978</td>
<td>0.000</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td></td>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location of stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main coronary artery</td>
<td>8/122</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left anterior descending artery</td>
<td>52/122</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left circumflex coronary artery</td>
<td>25/122</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right coronary artery</td>
<td>23/122</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gensini score</td>
<td>24±21</td>
<td>8±6</td>
<td>39±17</td>
<td>-12.295</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Data are expressed as mean±SD, number (percentage), or median (interquartile range).
HDL: high-density lipoprotein, LDL: low-density lipoprotein

possible scores of this index ranged from 0 to 3 diseased vessels. The criterion for 1-, 2-, or 3-vessel disease was a 50% reduction in the internal diameter of the right, left anterior descending, or left circumflex coronary artery. A 50% reduction in the internal diameter of the left main coronary artery was considered to indicate 2-vessel disease. (2) In the Gensini scoring system, narrowing of the lumen was graded as follows: 1 for 1-25% occlusion; 2 for 26-50% occlusion; 4 for 51-75% occlusion; 8 for 76-90% occlusion; 16 for 91-99% occlusion; and 32 for total occlusion. This score is multiplied by a factor accounting for the importance of the lesion position in the coronary arterial tree, such as 5 for LM, 2.5 for proximal LAD, and 1 for proximal right coronary artery (RCA). The severity of the disease is expressed as the sum of the scores for individual lesions (22).

Statistics

All statistical analyses were performed using the statistical software package SPSS 13.0 (SPSS Inc., Chicago, USA). The independent t-test was used to compare the differences in the immune cells/cytokines levels between CAD and non-CAD patients. A one-way analysis of variance (ANOVA) was adopted to compare the differences in the immune cells/cytokines levels between groups divided by the number of diseased vessels. Spearman’s correlation test was used to assess the correlation between the sFGL2 level and Gensini score, CD4⁺CD25⁺CD127low Tregs, and cardiovascular risk factors. For the multivariate analysis, potential factors identified by univariate analyses were further entered into the multivariate linear regression analysis to determine independent predictors of the serum sFGL2 level and a high Gensini score. A 5% type I error level was used to infer statistical significance. A p level of less than 0.05 was considered to be statistically significant.

Results

Clinical characteristics of CAD and non-CAD patients

The demographic and clinical characteristics of the patients included in this study are tabulated in Table 1. The mean age of the CAD patients was 60±10 years. The mean age of non-CAD patients was 59±12 years. The CAD group had higher low-density cholesterol (3.56±0.66 vs. 3.26±0.85 mmol/L, p=0.046) and lower high-density cholesterol (0.88±0.18 vs. 1.05±0.20 mmol/L, p<0.001) than the non-CAD group. There was no difference between the two groups in other traditional cardiovascular risks, such as age, body mass index, hypertension, diabetes, or triglyceride level.

Comparison of the number of circulating Tregs and serum sFGL2 levels between patients with CAD and non-CAD patients

A previous study demonstrated that the expression of human Treg surface marker CD127 was downregulated on a subset of CD4⁺ T cells in the peripheral blood, which negatively correlated with the suppression function of such
T cells (23). Thus, the combination of CD4, CD25, and CD127 resulted in a highly purified population of Tregs accounting for significantly more cells that previously identified according to other cell surface markers. In the current study, the percentage of CD4^+CD25^+CD127^low Tregs was significantly decreased in CAD patients compared to non-CAD patients (3.15±1.19% vs. 6.39±1.16%, p<0.001, Fig. 1A-C and Table 1). Furthermore, the serum sFGL2 levels in patients with CAD were significantly higher than those in non-CAD patients (26.95±8.53 vs. 9.88±5.46 ng/mL, p<0.001, Fig. 2). In addition, as shown in Table 2, the serum TGF-β1 and IL-10 levels in patients with CAD were significantly lower than those in non-CAD patients while hs-CRP and IL-10 levels in patients with CAD were significantly higher than those in non-CAD patients.

**Comparison of the number of circulating Tregs and serum sFGL2 levels among patients categorized according to the number of diseased vessels**

According to the presence of significant luminal stenosis (defined by stenosis which resulted in more than 50% reduction in the internal diameter of a coronary artery) on coronary angiography, 50 patients were categorized as non-CAD patients, while 52 patients were categorized as having 1-, 2-, or 3-vessel disease (Table 1). We observed that among patients categorized according to the number of diseased vessels, there was a significant difference in the percentage of circulating CD4^+CD25^+CD127^low Tregs (Fig. 1D and Table 3), and an association between the percentage of circulating Tregs and the number of diseased vessels was evident (r=-0.829, p<0.001). Post hoc tests suggested that Tregs of 3- (2.09±0.73%), 2- (3.01±0.56%), and 1-diseased vessel patients (3.61±1.26%) were all significantly decreased compared with that of patients without CAD (6.39±1.16%, p<0.001 for all). In addition, among patients categorized according to the number of diseased vessels, there was a significant difference in the serum sFGL2 levels (Fig. 2 and Table 3), and an association between the number of diseased vessels and the serum sFGL2 levels was also evident (r=-0.860, p<0.001). Post hoc tests suggested that the serum lev-
els of sFGL2 in 3- (4.25±1.51 ng/mL), 2- (6.65±2.30 ng/mL), and 1-diseased vessel patients (13.36±4.68 ng/mL) were all significantly decreased compared with that of patients without CAD (26.95±8.53 ng/mL, p<0.001).

**Correlation between the serum sFGL2 level with Tregs, cytokines, Gensini score, and cardiovascular risk factors**

The modified Gensini score in our study population was significantly higher in CAD patients than non-CAD patients (39±17 vs. 8±6, p<0.001). Post hoc tests suggested that the modified Gensini score of 3- (63.73±7.94), 2- (44.42±9.29), and 1-diseased vessel patients (27.90±10.78) were all significantly higher than that of non-CAD patients (7.57±6.39, p<0.001).

We then analyzed the relationship among the sFGL2 level, Tregs, inflammatory cytokines, the Gensini score and cardiovascular risk factors. As shown in Table 4, we found that the serum sFGL2 level positively correlated with the circulating Treg numbers (r=0.827, p<0.001, Fig. 3A), IL-10 (r=0.615, p<0.001), TGF-β1 (r=0.226, p=0.022), and high-density lipoprotein (HDL)-c (r=0.349, p<0.001), while negatively correlating with the Gensini score (r=-0.836, p<0.001, Fig. 3B), tumor necrosis factor (TNF)-α (r=-0.522, p<0.001), hs-C-reactive protein (CRP) (r=-0.470, p<0.001), and BMI (r=-0.226, p=0.022). In addition, a multivariate linear regression analysis using the stepwise method was performed to further estimate the effects of the serum sFGL2 level with the variables mentioned above in the presence and severity of CAD. The dependent variable was sFGL2 and the regression equation included HDL-c, inflammatory cytokines, BMI, Treg, and Gensini score. As a result, the sFGL2 level was significantly and positively associated with the number of circulating Tregs and negatively associated with the Gensini score (Table 5).

**Discussion**

The present study demonstrated that patients with angiographically confirmed CAD had significantly decreased levels of sFGL2 compared to patients without CAD. Another finding of our study was that the serum sFGL2 concentration significantly and positively correlated with the number of circulating CD4^+CD25^+CD127^- Tregs. Furthermore, a significant and negative correlation was observed between the serum sFGL2 concentration and the modified Gensini index in patients who underwent first-time coronary angiography for suspected CAD.

Atherosclerosis is the main cause of CAD. It is currently appreciated that chronic inflammatory cell-mediated immune responses are involved in the pathogenesis of atherosclerosis (24). Tregs are an anti-inflammatory subset of CD4^+ T cells and a previous study has demonstrated significantly decreased numbers of Tregs in patients with ACS compared with that of patients with stable angina and controls (25). Moreover, another study reported that the ability of Tregs to suppress responder CD4^+CD25^+ T-cell proliferation in ACS patients was significantly attenuated (26). In the current study, we observed that the circulating Treg number, characterized by CD4, CD25, and CD127, was dramatically decreased in CAD patients compared with controls, and an association between the number of circulating Tregs and the number of diseased vessels was revealed. Consistent with our results, another study showed decreased numbers of peripheral blood CD4^+CD25^+CD127^- Tregs in non-ST elevation ACS patients compared with chronic stable angina and chest pain syndrome patients (27). This is consistent with...
what has been described in other conditions with low-grade inflammation, such as obesity, where decreased Treg levels in individuals exhibiting elevated markers of systemic inflammation or impaired glucose tolerance were observed (28). These results suggest that the determination of the number of circulating Tregs using flow cytometry might be a useful indicator of the severity of atherosclerosis.

Previous data have suggested that sFGL2 is an important molecule of the function and development of Tregs, acting similarly to TGF-β and IL-10 (29, 30). Thus, it is not surprising that sFGL2 may be involved in the pathogenesis of CAD. In the present study, the sFGL2 levels were significantly decreased in patients with CAD. We also demonstrated that the serum sFGL2 levels positively correlated with the circulating Treg number and negatively correlated with the severity of coronary stenosis in these patients. However, the mechanism could be complicated and has not been completely elucidated. Previous evidence showed that the proportions of CD8+ T cells were significantly higher in both ACS and stable angina patients compared with controls (31) and highly activated in atherosclerotic plaques (32). It was also reported that sFGL2 can inhibit CD8+ T cell proliferation in a dose-dependent manner and this effect could be blocked by neutralizing antibodies (33, 34). Furthermore, studies have revealed that sFGL2 prevented the maturation of bone marrow-derived dendritic cells (DCs) and markedly reduced the capacity to stimulate T cell proliferation, rather than induce T cell apoptosis (33). Thus, sFGL2 might affect CAD by inhibiting proliferation and attenuating the function of CD8+ T cells. As result of decreased numbers and the impaired function of Tregs in the setting of ACS, this inhibitory effect might occur in patients with CAD due to the reduction in the sFGL2 level.

In addition to regulating the CD8+ T cell function, sFGL2 might be involved in the pathogenesis and progression of CAD through several other mechanisms. Recent evidence demonstrated that sFGL2 regulates many cellular processes that could play an important role in plaque progression, rupture, or thrombosis. sFGL2 remarkably induced apoptosis of tubular epithelial cells and hepatocytes through upregulating pro-apoptotic genes, including caspase-3, indicating the potential functions of sFGL2 in tissue injury and remodeling (35). Mitogen-activated protein kinases (MAPKs) are key signaling molecules that influence a broad range of cellular processes, such as proliferation, differentiation, migration and apoptosis (36). In addition, a recent study showed that downregulation of sFGL2 decreases phosphorylation of extracellular signal-regulated kinase (ERK) and c-Jun N-terminal kinase (JNK) (37). This suggests that the MAPK pathway may be involved in the downstream signaling of sFGL2. Furthermore, nuclear factor-κB (NF-κB) plays an important role in various biological processes. Many inflammatory genes relevant to the pathogenesis of atherosclerosis are regulated by NF-κB, the activated form of which is present in atherosclerotic plaques (38). NF-κB translocation DCs was significantly reduced in the presence of sFGL2, indicating that sFGL2 influenced the DC-dependent T cell differentiation through a NF-κB signaling pathway (6). Taken together, in addition to Treg per se, its novel effector molecule sFGL2 is also a promising therapeutic target against the inflammatory response during atherosclerosis. Understanding of the link between sFGL2 and the severity of coronary atherosclerosis may help in the treatment of patients with CAD. Therefore, further research on the mechanism of sFGL2 in the development of CAD is warranted.

**Limitations**

There are some limitations associated with our study. First, we conducted a retrospective analysis of a single center cardiac catheterization databank, and thus we were limited by a small study sample size. In addition, because we used angiographic determination to estimate the CAD progression, some of the patients in the non-progression group may actually have some atherosclerotic progression that was not recognized.
Table 5. Multiple Linear Regression Analysis with SFG2L2 as the Dependent Variable.

<table>
<thead>
<tr>
<th>Variables</th>
<th>exp(β)</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treg</td>
<td>2.395</td>
<td>1.433 – 3.337</td>
<td>0.000</td>
</tr>
<tr>
<td>Gensini score</td>
<td>-0.260</td>
<td>-0.351 – -0.169</td>
<td>0.000</td>
</tr>
<tr>
<td>IL-10</td>
<td>0.047</td>
<td>0.070 – 0.528</td>
<td>0.491</td>
</tr>
<tr>
<td>TGF-β</td>
<td>0.055</td>
<td>0.111 – 0.961</td>
<td>0.272</td>
</tr>
<tr>
<td>TNF-α</td>
<td>0.105</td>
<td>0.159 – 0.551</td>
<td>0.114</td>
</tr>
<tr>
<td>Hs-CRP</td>
<td>-0.047</td>
<td>-0.083 – -0.750</td>
<td>0.412</td>
</tr>
<tr>
<td>HDL-c</td>
<td>0.012</td>
<td>0.023 – 0.841</td>
<td>0.822</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.093</td>
<td>-0.187 – -0.965</td>
<td>0.062</td>
</tr>
</tbody>
</table>

Multiple linear regression analysis was performed. The dependent variable was sFGL2. The regression equation included body mass index, HDL-C, Treg, IL-10, TGF-β, TNF-α, Hs-CRP, and Gensini Score.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

The authors thank Dr. Jun Li in the Department of Orthopedics, Second Hospital of Anhui Medical University, for his assistance with the image acquisition.

Jing Cheng and Yingying Chen contributed equally to this work.

References


The Internal Medicine is an Open Access article distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (https://creativecommons.org/licenses/by-nc-nd/4.0/).