Systolic Blood Pressure is a Useful Measure in Predicting the Risk of Endothelial Dysfunction in Patients with Rheumatoid Arthritis

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ABSTRACT Whether risk factors exert more-important roles in the development of cardiovascular disease (CVD) with rheumatoid arthritis (RA) is unclear. We investigated traditional and non-traditional risk factors for coronary artery disease (CAD) in relation to endothelial function and ascertained which measure was a better screening strategy for assessing the risk of endothelial dysfunction in patients with RA. Forty-three RA patients were divided into either a normal (n = 29) or an abnormal (n = 14) endothelial function group based on the measurement of flow-mediated vasodilation. Thirty-three CAD patients were recruited from among cardiology clinic outpatients. Traditional (i.e., smoking, drinking, systolic and diastolic blood pressures, and lipid profiles) and non-traditional risk factors (i.e., inflammatory and immune responses, plasma homocysteine, and deficiency of B vitamins) for CVD were recorded or measured. Systolic blood pressure was significantly higher and was associated with abnormal endothelial function in RA patients (n = 20.7, p < 0.01) and CAD patients (n = 20.6, p < 0.01) than RA patients with normal endothelial function after adjusting for various potential confounders. Systolic blood pressure had the highest area under the receiver operating characteristic curve (AUC) (AUC = 0.80, 95% confidence interval, 0.65~0.94) for predicting the risk of endothelial dysfunction. The optimal cutoff value for systolic blood pressure to determine a risk of endothelial dysfunction was 112 mmHg. Systolic blood pressure could be a practical tool to screen for risks of endothelial dysfunction in patients with RA. Patients with RA should try to control their blood pressure in order to reduce the risk of CAD.

Key words: rheumatoid arthritis, endothelial function, coronary artery disease, systolic blood pressure

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease that causes joint destruction and functional disorder. Increased mortality has been observed in patients with RA when compared with control subjects [1]; and cardiovascular disease (CVD) is the
major cause of death in patients with RA [2,3]. Traditional risk factors such as age, gender, hypertension, lipid profiles and diabetes are the most widely recognized risk factors for CVD and have been observed in RA patients [4-6]. Other studies [7-9], however, indicated that traditional risk factors for CVD were independent of RA.

In addition to traditional risk factors, systemic inflammation is known to be involved in all stages of the atherosclerotic process [10]. Systemic inflammation, therefore, may pose another risk for cardiovascular events in patients with RA, and this has been demonstrated in several studies [2-3]. However, Shadick et al. [11] did not support that the hypothesis C-reactive protein (CRP) could significantly predict the risk of RA. Other than inflammatory responses, hyperhomocysteinemia has been demonstrated to be an independent risk factor of CVD [12,13]. The elevation of plasma homocysteine concentration by 5 μmol/L increases the incidence of cardiovascular disease by 60-80% [13]. Since B-vitamins (folate, vitamin B-12 and B-6) play a role in the remethylation and transulfuration reaction of homocysteine metabolism, deficiencies of these B-vitamins may be associated with hyperhomocysteinemia. Increased homocysteine level has been observed in patients with RA due to deficiencies of B-vitamins [14], this raises an interesting question about whether homocysteine status would affect endothelial function in patients with RA.

Impaired endothelial function often initiates and propagates the atherosclerotic process, and represents the early stage of atherosclerosis [10]. Moreover, endothelial dysfunction has been commonly found in patients with RA [15]. Since the cause of increased risk of CVD in patients with RA is still highly controversial and also unclear, and data have not been established the predictor for endothelial function in patients with RA.

The purpose of this study was to investigate traditional and non-traditional risk factors for CVD in relation to the endothelial function; and to ascertain which measure is a better screening strategy for the risk of endothelial dysfunction in patients with RA.

MATERIALS AND METHODS

Patients

Forty-three RA patients (≥ 18 y) were recruited from the Division of Allergy, Immunology and Rheumatology of Chung Shan Medical University Hospital in Taiwan. Patients were diagnosed with RA according to the 1991 American College of Rheumatology criteria for RA [16]. Clinical measurements, including patients’ visual analog scale, swollen and painful joints counts, disease activity score 28 (DAS 28), rheumatoid factor and disease duration, were assessed by a rheumatologist. Thirty-three CAD patients were recruited from the cardiology clinic of Taichung Veterans General Hospital and were identified by cardiac catheterization as having at least 50% stenosis of one major coronary artery. Patients were excluded if they had any of the following conditions: 1) pregnancy or were lactating; 2) anemia; 3) thrombocytopenia; 4) liver or renal diseases; or 5) cancer. RA patients underwent flow-mediated vasodilation (FMD) 2D imaging measurement of the brachial artery with a high-resolution ultrasound machine (Philips Sonos 5500, Philips, MN, USA) for examination of their endothelial function. They were divided into either the normal (FMD > 10%) or abnormal (FMD ≤ 10%) endothelial function groups based on their FMD measurement. Informed consent was obtained from each subject, and the study protocol was approved by the Institutional Review Board of Chung Shan Medical University Hospital.

Experimental protocol

Patients’ age, gender, smoking and drinking habits, family history and medication uses were recorded. Blood pressure [systolic and diastolic blood pressure (SBP and DBP)] was measured. The hypertension criteria were defined as SBP > 140 mmHg or DBP > 90 mmHg and/or receiving antihypertensive therapy. Fasting venous blood samples were collected. Hematolog-
ical measurements, including serum creatinine, total cholesterol, high and low density lipoprotein cholesterol (HDL-C, LDL-C) and triglycerides, were assessed. Automated high sensitivity CRP (hs-CRP) measurement was performed using particle-enhanced immunonephelometry [17]. Furthermore, erythrocyte sedimentation rate (ESR) was measured. Plasma interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) levels were measured by using an enzyme-linked immunosorbent assay in kit form (Biosource, Camarillo, CA, USA). Plasma pyridoxal 5'-phosphate (PLP) was determined by high performance liquid chromatography (HPLC) as previously described [18], serum folate and vitamin B-12 were analyzed by using standard competitive immunosorbing methods, and plasma homocysteine was measured by HPLC according to the method of Araki and Sako [19].

**Statistical analyses**

Data were analyzed by using SAS statistical software (version 9.1, SAS Institute Inc., Cary, NC). Differences in subjects’ characteristics, and biochemical measurements among the normal and abnormal endothelial function with RA patients and CAD patients were analyzed by using one-way analysis of variance or Kruskal-Wallis one way analysis of variance on ranks. Differences in RA patients’ disease activity assessments between the normal and abnormal endothelial function groups were analyzed by using Student’s t test or Mann-Whiney U test. For categorical response variables, differences among groups were assessed by Chi square or Fisher’s exact test. Multiple linear regression analyses with the three groups as a dependent variable was used to determine the association between traditional and non-traditional risk factors for CVD after adjustment for potential confounders. Adjusted odds ratios (ORs) with 95% confidence intervals (CI) for abnormal endothelial function were calculated from the unconditional logistic regression model. Receiver operating characteristic (ROC) curve analysis was used to measure the predictive performance of endothelial dysfunction of each cardiovascular risk factor based on the area under the curve (AUC); and to calculate the true positive rate (sensitivity) against the false-positive rate (1-specificity) to assess and compare the ability of identifying the risk of endothelial dysfunction. The optimal cut point was defined as the minimal value of $\sqrt{(1 - Specificity) - 0.5} + (Sensitivity - 1)^2$. Statistical results were considered to be significant at $p < 0.05$. Values presented in the text are means ± standard deviation (SD) with the median in parentheses.

**RESULTS**

Forty-three RA patients (5 men, 38 women) participated in this study. Fourteen patients had abnormal endothelial function with a mean FMD value of 7.3 ± 2.8%, while twenty-nine patients had normal endothelial function with a mean FMD value of 18.3 ± 6.4%. RA patients’ age ranged from 33 to 73 years with a mean age of 53.6 ± 8.7 y. The mean DAS 28 was 4.0 ± 1.1 indicating a moderate level of disease activity (3.2 < DAS 28 ≤ 5.1). The duration of RA disease ranged from 0.1 to 7 years with a mean duration of 2.6 years for all RA patients. Thirty-three CAD patients’ age ranged from 41 to 73 years with a mean age of 58.8 ± 8.3 y. There was no significant difference in gender, BMI, smoking and drinking habits between the three groups (Table 1).

The traditional and non-traditional risk factors for CVD with all patients are shown in Table 2. RA patients with normal endothelial function had significantly lower SBP than did RA patients with abnormal endothelial function and CAD patients. CAD patients had significantly lower HDL-C and higher LDL-C and triglycerides values than RA patients. The non-traditional risk factors had no significantly difference among three groups. Twenty-eight point six percent ($n=4$) of RA patients with abnormal endothelial function, 10.3% ($n=3$) of RA patients with normal endothelial function and 21.2% ($n=7$) of CAD patients had moderate hyperhomocysteinemia ($\geq 15$ μmol/L).

The association between different groups and of traditional and non-traditional risk factors is shown in Table 3. RA patients with abnormal endothelial function had a significantly higher SBP than RA patients.
### Table 1. Characteristics of all subjects

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>RA patients with normal endothelial function (n = 29)</th>
<th>RA patients with abnormal endothelial function (n = 14)</th>
<th>CAD patients (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>52.0 ± 7.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>56.0 ± 9.6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>58.8 ± 8.3&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sex (Male / Female)</td>
<td>2/27</td>
<td>3/11</td>
<td>10/23</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.2 ± 3.8</td>
<td>25.1 ± 1.9</td>
<td>25.4 ± 3.6</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>6.9 %</td>
<td>7.1 %</td>
<td>18.2 %</td>
</tr>
<tr>
<td>Drinking (%)</td>
<td>6.9 %</td>
<td>0 %</td>
<td>15.2 %</td>
</tr>
<tr>
<td>FMD (%)</td>
<td>18.3 ± 6.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.2 ± 2.9&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-</td>
</tr>
<tr>
<td>Disease duration (y)</td>
<td>2.5 ± 1.7</td>
<td>2.9 ± 1.7</td>
<td>-</td>
</tr>
<tr>
<td>Rheumatoid factor (IU)</td>
<td>25.3 ± 26.2</td>
<td>77.7 ± 119.6</td>
<td>-</td>
</tr>
<tr>
<td>Number of painful joints</td>
<td>7.7 ± 7.2</td>
<td>13.6 ± 21.9</td>
<td>-</td>
</tr>
<tr>
<td>Number of swollen joints</td>
<td>2.3 ± 3.1</td>
<td>7.0 ± 13.7</td>
<td>-</td>
</tr>
<tr>
<td>Disease activity score 28</td>
<td>4.0 ± 1.0</td>
<td>3.9 ± 1.4</td>
<td>-</td>
</tr>
<tr>
<td>Visual analog scale (mm)</td>
<td>49.3 ± 19.6</td>
<td>44.3 ± 15.5</td>
<td>-</td>
</tr>
</tbody>
</table>

<sup>1</sup> Values are means ± standard deviation. RA, Rheumatoid arthritis; CAD, Coronary artery disease. Values with different superscript letters (<sup>a</sup>, <sup>b</sup>) are significantly different within the group; p < 0.05. FMD, flow-mediated dilation.

### Table 2. Traditional and non-traditional risk factors for cardiovascular disease in all subjects

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>RA patients with normal endothelial function (n = 29)</th>
<th>RA patients with abnormal endothelial function (n = 14)</th>
<th>CAD patients (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (yes / no) (%)</td>
<td>4/25 (14 %)</td>
<td>4/10 (29 %)</td>
<td>33/0 (100 %)</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>111.8 ± 16.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>132.3 ± 18.5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>134.8 ± 23.2&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>69.0 ± 13.9</td>
<td>79.9 ± 12.0</td>
<td>74.6 ± 14.7</td>
</tr>
<tr>
<td>Lipid profiles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.0 ± 1.2</td>
<td>4.6 ± 0.6</td>
<td>5.2 ± 1.4</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.6 ± 0.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.5 ± 0.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.0 ± 0.3&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>3.1 ± 1.2</td>
<td>2.8 ± 0.5</td>
<td>3.2 ± 1.0</td>
</tr>
<tr>
<td>Total cholesterol/HDL ratio</td>
<td>3.3 ± 1.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.3 ± 1.0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.5 ± 1.9&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>1.2 ± 0.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.0 ± 0.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.3 ± 1.5&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Inflammatory indicators</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hs-CRP (mg/L)</td>
<td>2.1 ± 2.2</td>
<td>4.5 ± 4.7</td>
<td>4.9 ± 7.6</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>19.6 ± 13.8</td>
<td>22.5 ± 10.2</td>
<td>-</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>41.4 ± 3.5</td>
<td>44.0 ± 7.6</td>
<td>-</td>
</tr>
<tr>
<td>TNF-α (pg/mL)</td>
<td>101.1 ± 5.3</td>
<td>104.1 ± 11.3</td>
<td>-</td>
</tr>
<tr>
<td>Plasma PLP (nmol/L)</td>
<td>47.7 ± 52.1</td>
<td>59.7 ± 44.3</td>
<td>37.0 ± 38.0</td>
</tr>
<tr>
<td>Serum folate (nmol/L)</td>
<td>33.2 ± 80.6</td>
<td>37.3 ± 55.1</td>
<td>37.5 ± 26.2</td>
</tr>
<tr>
<td>Serum vitamin B-12 (pmol/L)</td>
<td>446.6 ± 260.3</td>
<td>479.9 ± 209.2</td>
<td>321.3 ± 222.6</td>
</tr>
<tr>
<td>Plasma hcy (μmol/L)</td>
<td>10.3 ± 4.1</td>
<td>12.4 ± 7.5</td>
<td>11.4 ± 5.6</td>
</tr>
</tbody>
</table>

<sup>1</sup> Values are means ± standard deviation. Values with different superscript letters (<sup>a</sup>, <sup>b</sup>) are significantly different within the group; p < 0.05. RA, Rheumatoid arthritis; CAD, Coronary artery disease; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; Hs-CRP, high sensitivity C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; PLP, pyridoxal 5'-phosphate; Hcy, homocysteine.
with normal endothelial function, and CAD patients had significantly positive association with SBP, TC/HDL-C and triglycerides values, whereas negatively associated with HDL-C and plasma PLP concentration than RA patients with normal endothelial function after adjusting age, gender, body mass index and creatinine. However, SBP significantly increased and was associated with abnormal endothelial function RA patients (β = 20.7, *p < 0.01) and CAD patients (β = 20.6, *p < 0.01) than RA patients with normal endothelial function after adjusting for various potential confounders.

To better understand the association of traditional and non-traditional risk factors of CVD with endothelial function, we then calculated the odds ratio from the obtained results using an unconditional logistic regression model (Table 4). Patients with higher SBP and DBP or hs-CRP level exhibited significantly increased the risk of abnormal endothelial function after age and gender were adjusted. When SBP, DBP or hs-CRP level were additionally adjusted, the association of DBP and hs-CRP level with the risk of abnormal endothelial function disappeared; however, higher SBP was still significantly associated with abnormal endothelial function (OR, 1.09; 95% CI, 1.00-1.18).

The ROC curve was performed to compare the predictive performance of various cardiovascular risk factors for the risk of endothelial dysfunction (Fig. 1). Among all cardiovascular risk factors, SBP appeared to have the highest area under the ROC curve to predict the risk of endothelial dysfunction (AUC, 0.80, 95% CI, 0.65-0.94). The best combination of sensitivity and specificity was 93% and 63%, respectively. Therefore, the optimal cut-off value of SBP for predicting endothelial dysfunction was 112 mmHg.

**DISCUSSION**

Since cardiovascular morbidity and mortality are frequently observed in RA patients, it is important to prevent or reduce the risk of cardiovascular events before the development of this disease. Endothelial dysfunction has been considered to be the early stage of the development of atherosclerosis. The expression of hs-CRP increases macrophages, which may cause atherosclerotic plaque [20]. Previous studies have indicated that increased CRP level is a good indicator of impaired
endothelial function in RA patients [20,21]. In line with these studies, our study showed that increased hs-CRP level contributed to abnormal endothelial function. However, our results failed to support the implication that inflammatory markers, such as serum hs-CRP, are independently associated with the risk of endothelial dysfunction. Pro-inflammatory cytokines, such as IL-6 and TNF-α, and CRP are involved with the pathogenesis of rheumatoid arthritis [21], and CRP further induces the expression of adhesion molecules on the endothelial surface to promote vascular atherosclerotic damage [22]. However, both the normal and abnormal endothelial function groups in our study had similar values of IL-6 and TNF-α, so these pro-inflammatory cytokines did not seem to be major development of abnormal endothelial function in our patients. In addition, our CRP levels were low when compared to those in some previous studies [21,22], indicating that CRP might not be the key factor to induce expression of adhesion molecules in the vascular wall. On the other hand, our CRP levels were similar to those reported by Chung et al. [7] who also indicated that increased CRP levels were not associated with coronary artery calcification in their RA patients.

Methotrexate (MTX) is an anti-folate widely used in patients with RA, plasma homocysteine concentration might be elevated due to folate deficiency during MTX therapy [14, 23]. Since most of our patients (65%) were taking folic acid supplements while they were under MTX therapy, only 2 RA patients had deficient folate status (< 6.3 nmol/L). This might also explain that plasma homocysteine concentration was not affected by folate status and had no further side effect on endothelial function in this study.

It is likely that traditional risk factors might play more important roles in the development of CVD than inflammatory markers in our RA patients. Among traditional risk factors, increased blood pressure has been
<table>
<thead>
<tr>
<th>Index</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
<th>TC (mmol/L)</th>
<th>HDL-C (mmol/L)</th>
<th>LDL-C (mmol/L)</th>
<th>TC/HDL-C</th>
<th>TG (mmol/L)</th>
<th>Hs-CRP (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC</td>
<td>0.80</td>
<td>0.74</td>
<td>0.59</td>
<td>0.46</td>
<td>0.55</td>
<td>0.56</td>
<td>0.66</td>
<td>0.68</td>
</tr>
<tr>
<td>95% C.I.</td>
<td>0.65-0.94</td>
<td>0.57-0.91</td>
<td>0.39-0.78</td>
<td>0.26-0.67</td>
<td>0.35-0.75</td>
<td>0.36-0.76</td>
<td>0.45-0.86</td>
<td>0.49-0.86</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Index</th>
<th>ESR (mm/h)</th>
<th>IL-6 (pg/mL)</th>
<th>TNF-α (pg/mL)</th>
<th>Hcy (μmol/L)</th>
<th>PLP (nmol/L)</th>
<th>Folate (nmol/L)</th>
<th>Vitamin B-12 (pmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC</td>
<td>0.64</td>
<td>0.67</td>
<td>0.56</td>
<td>0.59</td>
<td>0.45</td>
<td>0.62</td>
<td>0.54</td>
</tr>
<tr>
<td>95% C.I.</td>
<td>0.47-0.82</td>
<td>0.50-0.84</td>
<td>0.395-0.73</td>
<td>0.39-0.79</td>
<td>0.26-0.64</td>
<td>0.43-0.80</td>
<td>0.36-0.72</td>
</tr>
</tbody>
</table>

**Fig. 1** Receiver operating characteristic (ROC) curve of various cardiovascular risk factors in identifying rheumatoid arthritis patients with endothelial dysfunction.

The estimates of area under the ROC curve (AUC) which reflects the overall predictive accuracy and their 95% confidence interval are also shown. SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL, high density lipoprotein-cholesterol; LDL, low density lipoprotein-cholesterol; TG, triglycerides; hs-CRP, high sensitivity C-reactive protein; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; PLP, pyridoxal 5’-phosphate; Hcy, homocysteine.
shown to contribute to the increased risk of CVD in RA patients [4,6, 24,25]. Singh et al. [25] indicated that a mean increase in SBP of 1-5 mmHg was associated with approximately 7,100 - 35,700 additional ischemic heart disease and stroke events based on the data from the Third National Health and Nutrition Examination Survey. SBP rather than DBP has been a strong predictor of cardiovascular risk [26-28]. In the present study, SBP was also associated with abnormal endothelial function. To the best of our knowledge, this might be the first study to employ ROC curve to assess and compare the ability of traditional cardiovascular risk factors in the prediction of endothelial dysfunction in RA patients. Increased SBP (>112 mmHg) seems to be a better predictor of endothelial dysfunction in RA. Since SBP is a simple measurement, it is probably enough to use SBP to screen the risk of endothelial dysfunction for RA patients.

Several reasons for increased blood pressure in RA patients have been raised, including the elevation of CRP level and the use of medication. The mechanism of inflammation in the development of hypertension might be decreasing production of endothelial nitric oxide expression, which affects the rennin-angiotensin system [29,30]. However, we did not observe a relationship between hs-CRP level and blood pressure after other potential cardiovascular risk factors were adjusted, and SBP was actually associated with abnormal endothelial function independently of hs-CRP level in our patients. Arterial stiffness and central blood pressure were not correlated with CRP level in the study by Klocke et al. [24]. The relatively low level of CRP and small sample size could be reasons why we did not observe this association in our study. The medications, such as nonsteroidal anti-inflammatory drugs and corticosteroids, used to treat RA have the side effect of elevating blood pressure [25, 31-33] However, RA patients are less likely to have hypertension if their daily oral glucocorticoid dose (prednisolone) < 7.5 mg [32]. In our study patients took no prednisolone or only a low dose (~5 mg) of prednisolone, and only 18.6% of our patients had hypertension. In addition, the mean blood pressure of patients in the two groups was in the normotensive range. The medication use might not be the main reason for increased blood pressure in RA patients as long as certain classes of medication are carefully used.

The first limitation of this study is the innate property of the cross-sectional design in that the causality between risk factors and abnormal endothelial function could not be established. The second limitation is the small sample size. The lack of correlation of hs-CRP with abnormal endothelial function or blood pressure might be due to this limitation. The third limitation is the short disease duration of these patients who were diagnosed RA less than 10 years. Disease duration may have influenced the inflammatory levels, disease severity and other biochemical markers examined in this study.

In conclusion, RA patients with abnormal endothelial function had significantly higher blood pressure levels than patients with normal endothelial function. Increased SBP (>112 mmHg) was associated with abnormal endothelial function independently of hs-CRP level; and could be a better predictor of endothelial dysfunction for RA patients. Although it may not be a novel suggestion patients with RA should try to control their blood pressure in order to reduce the risk of CVD.

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摘要  心血管疾病已證實為造成類風濕性關節炎病患死亡的主因之一。其可能原因眾多但研究結果卻不一致。本研究目的為探討類風濕性關節炎病患心血管疾病危険因子與其內皮細胞功能的相關性。研究設計以橫斷式進行。由免疫風濕科門診募集 43 位類風濕性關節炎病患，依肱動脈血管擴張程度將病患分為內皮細胞功能正常組（n = 29）及內皮細胞功能異常組（n = 14），並由心臟內科募集 33 位冠狀動脈疾病病患。抽取病患空腹血分析血液生化值、脂質濃度、血清葉酸及維生素 B-12、血漿同半胱胺酸及維生素 B-6、發炎反應。結果顯示內皮細胞功能異常之病患其收縮壓有顯著較高的情形。調整相關因子後，收縮壓為造成病患內皮細胞功能受損之最重要危險因子（β = 20.7, P < 0.01），同時也是預測病患內皮細胞功能受損之最佳指標（AUC = 0.80; 95% CI, 0.65-0.94）。當病患收縮壓高於 112 mmHg 時，其內皮細胞功能受損之風險將會提高。因此建議類風濕性關節炎病患應監控血壓變化，以預防冠狀動脈疾病的發。