Original Article

Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in evaluation of the development of polycystic kidney disease

Qing-Quan Liu1, Zhi-Gang He2, Qing Xu1, Wen-Hui Qiu1, Hong-Bing Xiang2, Yong-Man Lv1

Departments of 1Nephrology, 2Anesthesiology and Pain Medicine, Tongji Hospital of Tongji Medical College, Huazhong University of Science & Technology, Wuhan, Hubei, PR China

Received January 20, 2016; Accepted April 18, 2016; Epub June 1, 2016; Published June 15, 2016

Abstract: Background: It is well known that the neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are available markers of systemic inflammation, and increased inflammation is along with progress of chronic kidney disease (CKD). The inflammation is risk factors for increased morbidity and mortality in autosomal dominant polycystic kidney disease (ADPKD). Therefore, we evaluate the association between the NLR and PLR level and unfavorable prognosis in ADPKD patients.

Methods: A total of 65 ADPKD patients with preserved renal function, 50 ADPKD patients with end-stage renal disease (ESRD) need dialysis and 32 healthy volunteers were included. The level of NLR and PLR were recorded in different stages of ADPKD patients, and investigated if NLR and PLR could predict development of ADPKD. We also examined the expression of inflammation marker in renal interstitium of ADPKD patients.

Results: The level of NLR (5.22 ± 2.91 vs 3.38 ± 2.03, P < 0.001) and PLR (203.8 ± 121 vs 152.2 ± 70.9, P < 0.001) were significantly higher in ADPKD patients with dialysis than ADPKD patients without dialysis, and the level of NLR (3.38 ± 2.03 vs 1.42 ± 0.58, P < 0.0001) and PLR (152.2 ± 70.9 vs 92.7 ± 26.9, P < 0.0001) were significantly higher in ADPKD patients without dialysis than in controls. Increased NLR over 4.3 and PLR over 174 were related to increase the events of dialysis. A cutoff value for NLR > 2.65 and PLR > 130.2 could predict development of renal function deficit (RFD) with the sensitivity 74.7%, 66.7% and specificity 96.9%, 96.9%, respectively. In addition, the CD45 staining significantly increased in ADPKD groups.

Conclusions: We conclude that NLR and PLR are significantly higher in ADPKD patients with RFD and increase across worsening CKD stages. Our data suggest that lower NLR and PLR level may be potential and novel preventive and therapeutic options for ADPKD patients.

Keywords: Neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, polycystic kidney disease, chronic kidney disease, prognosis

Introduction

The leading cause of mortality in autosomal dominant polycystic kidney disease (ADPKD) is cardiovascular disease [1, 2]. Menon et al. demonstrated ADPKD patients with higher plasma level of CRP and interleukin (IL)-6, and the levels of inflammation markers were pronounced with worse kidney disease [3]. Although the CRP and IL-6 are recognized inflammation markers, however, detecting of CRP is still not as a routine examination in nephrology clinics worldwide [4]. Higher levels of inflammatory markers were reported to be associated with faster progression of chronic kidney disease (CKD) in patients, while total WBC count has been reported to predict deterioration of the kidney function [5]. Neutrophil to lymphocyte ratio (NLR) can easily be calculated by the ratio of neutrophils to lymphocytes in peripheral blood. NLR was introduced as a novel inexpensive and readily available indicator that reflected the severity and extension of systemic inflammation and atherosclerosis, and predicted adverse clinical outcomes, and estimated survival in cardiac and noncardiac disorders including ESRD [6-8]. In recent years, neutrophilia and relative lymphopenia were shown to be an independent predictor of mortality in patients with post-myocardial infarction heart failure [9]. Moreover, several of studies showed NLR was introduced as a potential
marker to determine inflammation in cardiac and end-stage renal disease (ESRD) [10, 11].

Although Turkmen reported that the ADPKD patients had higher levels of NLR compared with normal group [12], and platelet to lymphocyte ratio (PLR) was reported to be a simple and valuable prognostic marker for acute coronary syndrome in a few studies [13], limited data are available regarding assessment of NLR and PLR in relation to renal diseases, namely in ADPKD patients. The cause-and-effect relationship between ADPKD and NLR, PLR is still no clear. Therefore, the present study was designed to evaluate the NLR and PLR in relation to the progress of ADPKD patients.

Materials and methods

Study population

A total of 115 ADPKD patients [mean (SD) age 50 (10.4) years, 55.7% were females], including 43.5% with end-stage renal disease (ESRD) and 56.5% with preserved renal function, and 32 healthy volunteers [mean (SD) age 47 (9.5) years, 56.3% were females] were included in this cross-sectional study. Exclusion criteria also included acute infections, cancer, steroid use, WBC > 10^3/mm^3, Platelet count < 1000 mL. The study protocol was approved by the Medical Ethics Committee of Huazhong Science and Technology University. Written informed consent was obtained from all subjects included in the study. The diagnosis of ADPKD was defined by the ultrasonographic criteria described by Ravine et al. [14].

Study parameters

Data on patient demographics, BMI (kg/m^2), Systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg in measurements, or being on antihypertensive medications were defined as arterial hypertension, complete blood count, blood biochemistry including uric acid (mg/dL), and lipid parameters including total cholesterol (mg/dL), LDL cholesterol (LDL-c; mg/dL) and triglyceride (mg/dL). ADPKD patients with preserved renal function were classified according to the level of glomerular filtration rate which was estimated according to the Modification of Diet in Renal Disease (MDRD) equation: eGFR (ml·min^{-1}·1.73 m^{-2}) = 186 × plasma Cr (mg/dL)^{-1.154} × age^{-0.203} (× 0.742, if female subjects), where the Cr indicates serum creatinine [15]. The renal function deficit (RFD) was defined as a eGFR ≤ 89 mL/min/1.73 m^2 and classified as follows: eGFR ≥ 90 ml·min^{-1}·1.73 m^{-2} with stage 1; eGFR = 60-89.9 ml·min^{-1}·1.73 m^{-2} with stage 2; eGFR = 30-59.9 ml·min^{-1}·1.73 m^{-2} with stage 3; eGFR = 15-29.9 ml·min^{-1}·1.73 m^{-2} with stage 4; eGFR < 15 ml·min^{-1}·1.73 m^{-2} with stage 5. Patients in stages 2, 3, and 4 were considered as having RFD. Patients in stage 1 were considered as not having renal function deficit [16].

Complete blood count and definition of NLR, PLR

Whole blood cell counts were determined by using automated hematological analyzer Pentra 120 Retic (ABX, Montpellier, France). NLR was calculated as the ratio of the neutrophil and lymphocytes, PLR as the ratio of the platelet and lymphocyte according to the parameters of peripheral blood sample which were obtained at the time of patient's admission and before 24 hours next hemodialysis. ADPKD patients were separated into two groups according to mean value of NLR (group 1: PLR < 4.3, and group 2: NLR ≥ 4.3), or the mean value of PLR (group 1: PLR < 174, and group 2: PLR ≥ 174).

Immunohistochemistry analysis

A total of 6 polycystic kidney tissues from ADPKD patients performed windowing decompression in Tongji Hospital; control tissue was obtained from 6 patients who underwent nephrectomy for renal neoplasms. Paraffin-embedded formalin-fixed tissue was used to perform immunohistochemistry for CD45, which was one of the most abundant molecules expressed on the white blood cell surface. The primary antibody is the Rabbit polyclonal to CD45 (1:100 dilution, Abcam, ab10558). After washing in phosphate-buffered saline, the slides were incubated with goat anti-rabbit IgG antibody conjugated to horseradish peroxidase (DAKO, Tokyo, Japan) for 30 min at room temperature. The signal reaction was visualized with diamino-benzidine, and the slides were then counter-stained with hematoxylin stains.

Statistical analyses

Statistical analyses were carried out using the Statistical Package for Social Sciences for Windows version 16.0 (SPSS, Chicago, IL, USA).
Neutrophil-lymphocyte ratio and polycystic kidney disease

Abnormally distributed variables were expressed as median (range) and normally distributed variables were as mean ± SD. Differences were considered significant when P values were less than 0.05. The normality of distribution of all variables was tested using the Kolmogorov-Smirnov test. Dichotomous variables were compared using the Chi-square test. Statistical differences between parametric data of two groups were analyzed using the Student’s t-test. The Mann Whitney U-test was used to compare nonparametric data. Linear associations between continuous parametric variables were assessed using the Pearson correlation test, while the Spearman correlation test was used to assess the correlation between nonparametric continuous and categorical variables. A receiver operator characteristics curve (ROC curve) analysis was performed to identify the sensitivity and specificity of NLR, PLR cut of value in prediction of RFD.

Results

Demographics, clinical characteristics and laboratory findings in study groups

Demographic and clinical characteristics of patient and control groups were summarized in Table 1. 65 ADPKD patients with preserved renal function without dialysis and 50 ADPKD patients need conventional dialysis. Age, sex, body mass index, uric acid, total cholesterol, HDL cholesterol, and LDL cholesterol were similar between ADPKD patients and healthy subjects.

In patients with ADPKD, incidence of hypertension, neutrophil counts, NLR and PLR were significantly higher, while white blood cell count, lymphocyte count and platelet count were significantly lower compared to that in healthy subjects (Table 1).

Evaluation of the relation between NLR, PLR and dialysis

ADPKD patients without dialysis had a mean NLR of 3.38 ± 2.03, which was significantly lower than the ADPKD patients with dialysis had a mean NLR of 5.22 ± 2.91, both of the NLR significantly higher than normal group (Figure 1A). As far as the PLR, ADPKD patients with dialysis had an obvious high level of PLR (203.8 ± 121 vs 152.2 ± 70.9, P < 0.001), and whether the ADPKD patients with dialysis or not, the level of PLR significantly higher than normal group (Figure 1B). Furthermore, according to the mean of NLR, the ADPKD patients were separated into two groups (group 1: NLR < 4.3, and group 2: NLR ≥ 4.3), there were no statistically significant difference between two

Table 1. Demographics, clinical characteristics and laboratory findings in study groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (n = 32)</th>
<th>ADPKD without dialysis (n = 65)</th>
<th>ADPKD with dialysis (n = 50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47 (22-60)</td>
<td>49.5 (22-72)</td>
<td>51 (23-69)</td>
<td>0.84</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>18/14</td>
<td>35/30</td>
<td>26/24</td>
<td>0.68</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.2 ± 2.5</td>
<td>23.7 ± 2.3</td>
<td>22.5 ± 2.7</td>
<td>0.54</td>
</tr>
<tr>
<td>Hypertension (n)</td>
<td>0</td>
<td>28</td>
<td>27</td>
<td>P &lt; 0.0001</td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
<td>3.8 (2.9-4.5)</td>
<td>4.0 (3.0-4.8)</td>
<td>4.0 (2.8-4.5)</td>
<td>0.75</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>203 (160-250)</td>
<td>207 (169-255)</td>
<td>208 (160-248)</td>
<td>0.35</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>122.0 (95-140)</td>
<td>118.0 (85-142)</td>
<td>115 (84-139)</td>
<td>0.62</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>44.5 (32-58)</td>
<td>44.0 (30-56)</td>
<td>42.7 (29-55)</td>
<td>0.37</td>
</tr>
<tr>
<td>WBC count (10³/mm³)</td>
<td>5.94 ± 1.26</td>
<td>5.16 ± 1.73</td>
<td>5.08 ± 1.56</td>
<td>0.016</td>
</tr>
<tr>
<td>Neutrophil count (10³/mm³)</td>
<td>2.97 ± 0.86</td>
<td>3.43 ± 1.37</td>
<td>3.71 ± 1.40</td>
<td>0.069</td>
</tr>
<tr>
<td>Lymphocyte count (10³/mm³)</td>
<td>2.25 ± 0.60</td>
<td>1.22 ± 0.58</td>
<td>0.87 ± 0.30</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Platelet count (10³/mm³)</td>
<td>198.3 ± 47.9</td>
<td>167.6 ± 78.1</td>
<td>155.2 ± 81.6</td>
<td>0.039</td>
</tr>
<tr>
<td>NLR</td>
<td>1.42 ± 0.58</td>
<td>3.38 ± 2.03</td>
<td>5.22 ± 2.91</td>
<td>P &lt; 0.0001</td>
</tr>
<tr>
<td>PLR</td>
<td>92.7 ± 26.9</td>
<td>152.2 ± 70.9</td>
<td>203.8 ± 121</td>
<td>P &lt; 0.0001</td>
</tr>
</tbody>
</table>

ADPKD, autosomal dominant polycystic kidney disease; BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio. Differences assessed by Chi-square test for categorical variables, and by Kruskal-Wallis test. Statistically significant if P < 0.05.
Neutrophil-lymphocyte ratio and polycystic kidney disease


groups in terms of hypertension, uric acid, triglyceride, total cholesterol and Platelet count. However, ADPKD patients with NLR ≥ 4.3 had significantly higher WBC count, neutrophil count, PLR (130 ± 54.3 vs 256.1 ± 135.1, P < 0.0001), especially the incidence rate of dialysis (37.9% vs 59.2%, P = 0.024) when compared to patients with NLR < 4.3, while the lymphocyte count was lower (Table 2). As well, the ADPKD patients were separated into PLR < 174 and PLR ≥ 174, except the same of characteristics, however, patients with PLR ≥ 174 had higher neutrophil count, platelet count, NLR (3.15 ± 1.76 vs 5.71 ± 2.79, P < 0.0001), but the lymphocyte count was lower compared with patients with PLR < 174, and the incidence rate of dialysis had no significant difference (44.4% vs 51.1%, P = 0.49) (Table 2).

Table 2. Demographic, clinic and laboratory features of ADPKD patients according to NLR and PLR groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All ADPKD (n = 115)</th>
<th>NLR &lt; 4.3 (n = 66)</th>
<th>NLR ≥ 4.3 (n = 49)</th>
<th>P value</th>
<th>PLR &lt; 174 (n = 65)</th>
<th>PLR ≥ 174 (n = 50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50 (22-72)</td>
<td>48.5 (22-72)</td>
<td>52 (25-67)</td>
<td>0.43</td>
<td>50.5 (22-72)</td>
<td>50 (25-64)</td>
<td>0.25</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>64/51</td>
<td>36/30</td>
<td>28/21</td>
<td>0.78</td>
<td>32/33</td>
<td>26/24</td>
<td>0.77</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.7 ± 3.5</td>
<td>23.8 ± 4.3</td>
<td>21.5 ± 2.0</td>
<td>0.57</td>
<td>22.3 ± 4.5</td>
<td>20.8 ± 3.9</td>
<td>0.32</td>
</tr>
<tr>
<td>Hypertension (n)</td>
<td>55</td>
<td>30</td>
<td>25</td>
<td>0.55</td>
<td>27</td>
<td>28</td>
<td>0.085</td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
<td>4.0 (2.8-4.8)</td>
<td>3.9 (2.8-4.6)</td>
<td>4.1 (2.9-4.8)</td>
<td>0.39</td>
<td>3.8 (2.8-4.7)</td>
<td>4.1 (2.8-4.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>207.3 (160-255)</td>
<td>207 (169-255)</td>
<td>208 (160-248)</td>
<td>0.35</td>
<td>209 (160-239)</td>
<td>310 (165-255)</td>
<td>0.15</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>123 (84-142)</td>
<td>118 (85-142)</td>
<td>115 (84-139)</td>
<td>0.62</td>
<td>120 (87-142)</td>
<td>114 (84-140)</td>
<td>0.33</td>
</tr>
<tr>
<td>WBC count (10³/mm³)</td>
<td>5.3 ± 2.0</td>
<td>4.9 ± 2.9</td>
<td>6.0 ± 2.4</td>
<td>0.019</td>
<td>5.05 ± 1.59</td>
<td>5.42 ± 1.90</td>
<td>0.49</td>
</tr>
<tr>
<td>Neutrophil count (10³/mm³)</td>
<td>3.6 ± 1.4</td>
<td>3.1 ± 1.1</td>
<td>4.7 ± 2.1</td>
<td>&lt; 0.0001</td>
<td>3.31 ± 1.20</td>
<td>4.07 ± 1.70</td>
<td>0.04</td>
</tr>
<tr>
<td>Lymphocyte count (10³/mm³)</td>
<td>1.1 ± 0.5</td>
<td>1.3 ± 0.4</td>
<td>0.68 ± 0.22</td>
<td>&lt; 0.0001</td>
<td>1.23 ± 0.52</td>
<td>0.79 ± 0.33</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Platelet count (10³/mm³)</td>
<td>160.3 ± 78.8</td>
<td>157.9 ± 76.6</td>
<td>164.2 ± 83.1</td>
<td>0.85</td>
<td>133.3 ± 58.1</td>
<td>201.3 ± 89</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>PLR/NLR</td>
<td>179.2 ± 112.4</td>
<td>130 ± 54.3</td>
<td>256.1 ± 135.1</td>
<td>&lt; 0.0001</td>
<td>3.15 ± 1.76</td>
<td>5.71 ± 2.79</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>ADPKD with dialysis</td>
<td>43.5%</td>
<td>37.9%</td>
<td>59.2%</td>
<td>0.024</td>
<td>44.4%</td>
<td>51.1%</td>
<td>0.49</td>
</tr>
</tbody>
</table>

ADPKD, autosomal dominant polycystic kidney disease; BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio. Differences assessed by Chi-square test for categorical variables, and by Kruskal-Wallis test. Statistically significant if P < 0.05.
Neutrophil-lymphocyte ratio and polycystic kidney disease

In order to explore the relationship between NLR, PLR and different RFD stages, and eliminate the effects of dialysis on blood parameters, we only analyzed the stage 1, 2, 3, 4. Notably, we found NLR, PLR significantly increased across worsening CKD stages, the NLR and PLR of stage 2, 3, 4 significantly increased compared with control group and stage 1, and there was no significant difference between whether NLR or PLR of stage 1 and control group (P > 0.05) (Figure 2). Therefore, we can draw a conclusion that the level of NLR and PLR were trend to increase when ADPKD patients developed RFD stage.

**Correlation analysis**

In the bivariate correlation analysis, NLR, PLR were positively correlated with blood urea nitrogen (BUN) (r = 0.34, P = 0.0005, r = 0.26, P = 0.01, respectively), but were negatively with albumin (r = -0.36, P = 0.032, r = -0.41, P = 0.04, respectively) and the NLR was negatively with hemoglobin (r = -0.2, P = 0.05), however, PLR had no correlation with hemoglobin (r = -0.04, P = 0.7) (Table 3).

**Receiver operator characteristics analysis**

A receiver operator characteristics curve analysis showed that the plot of the NLR and PLR levels yielded significant specificity and sensitivity for predicting the risk of RFD events in patients with ADPKD. When an ROC analysis was completed for the relationship between NLR and RFD events in patients with ADPKD, the results were AUC: 0.96, P < 0.0001; cut-off value 2.65, confidence interval 83.8%-99.1%. A cutoff value for NLR of 2.65 could predict development of RFD events with 74.7% sensitivity and 96.9% specificity (Figure 3A), and analyzed for the relationship between PLR and RFD events in patients with ADPKD, the results

![Figure 2](image-url)

Figure 2. A. """"Control vs ADPKD-CS, Control vs ADPKD-DS, Control vs ADPKD-RFS, """"""""P < 0.0001, respectively. """"ADPKD-normal vs ADPKD-CS, P < 0.05; """"ADPKD-normal vs ADPKD-DS, P < 0.01; """"ADPKD-normal vs ADPKD-RFS, P < 0.0001. """"ADPKD-Ds vs ADPKD-RFS, P < 0.05. B. """"""""Control vs ADPKD-normal, Control vs ADPKD-CS, Control vs ADPKD-DS, """"""""P < 0.01, respectively. """"""""Control vs ADPKD-RFS, P < 0.0001. """"ADPKD-normal vs ADPKD-CS, ADPKD-normal vs ADPKD-RFS, P < 0.05, respectively. """"ADPKD-Ds vs ADPKD-RFS, P < 0.05. ADPKD, autosomal dominant polycystic kidney disease; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; ADPKD-CS, autosomal dominant polycystic kidney disease- compensated stage; ADPKD-DS, autosomal dominant polycystic kidney disease- decompensated period; ADPKD-RFS, autosomal dominant polycystic kidney disease- renal failure stage.

**Table 3. Bivariate correlation analysis of NLR and PLR to other parameters**

<table>
<thead>
<tr>
<th>Variable</th>
<th>NLR</th>
<th></th>
<th>PLR</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.07</td>
<td>0.48</td>
<td>-0.31</td>
<td>0.0026</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>-0.36</td>
<td>0.032</td>
<td>-0.41</td>
<td>0.04</td>
</tr>
<tr>
<td>Hb (g/L)</td>
<td>-0.2</td>
<td>0.05</td>
<td>-0.04</td>
<td>0.70</td>
</tr>
<tr>
<td>BUN (μmol/L)</td>
<td>0.34</td>
<td>0.0005</td>
<td>0.26</td>
<td>0.01</td>
</tr>
<tr>
<td>Total C (mmol/L)</td>
<td>0.28</td>
<td>0.31</td>
<td>0.25</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Spearman correlation analysis; r correlation coefficient; NLR, Neutrophil-to-lymphocyte ratio; PLR, Platelet-to-lymphocyte ratio; Total C = Total cholesterol, Hb, Hemoglobin. BUN, blood urea nitrogen.

**Relationship between NLR, PLR and different RFD stages**

A cutoff value for PLR of 2.65 could predict development of RFD events with 74.7% sensitivity and 96.9% specificity (Figure 3A), and analyzed for the relationship between PLR and RFD events in patients with ADPKD, the results...
Neutrophil-lymphocyte ratio and polycystic kidney disease

were AUC: 0.82, P < 0.0001; cut-off value 130.2, confidence interval 78.6%-85.8%. A cut-off value for PLR of 130.2 could predict development of RFD events with 66.7% sensitivity and 96.9% specificity (Figure 3B).

**Immunohistochemical analysis**

Furthermore, we analyzed the inflammatory characteristic of ADPKD tissue by immunohistochemical means. CD45 known as leucocyte common antigen (LCA), which was one of inflammatory cell markers [17]. We found that the ADPKD patients with CD45 positive cells were obviously higher than the control group (6.4 ± 2.8 vs 56.6 ± 20.6, P = 0.0079) (Figure 4).

**Discussion**

In the present study, we found that the level of neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) in ADPKD patients...
were related to poor prognosis. The main findings of this study were: (1) NLR and PLR were significantly increased in the ADPKD patients with dialysis or not; (2) NLR and PLR significantly increased across worsening RFD stages 2-4; (3) NLR and PLR could predict the occurrence of RFD events, and showed a significant positive correlation with blood urea nitrogen, while a significant negative with albumin; (4) the inflammatory cell marker CD45 significantly expressed on the ADPKD capsule wall tissue.

Several studies found that the level of NLR or PLR was increased in patients with chronic kidney disease or end-stage renal disease (ESRD) [11, 18, 19]. However, whether the level of NLR was boosted in ADPKD patients, it was remain controversy at present. Turkmen et al. [12] reported that the ADPKD patients had higher levels of NLR than healthy group, but Gul et al. revealed that the NLR level had no significant differences compared with healthy volunteers [20]. We found higher NLR levels in ADPKD patients than that in controls which were in conformity with the Turkmen study corresponding data [19], and our also found that the PLR level also increased in ADPKD patients as compared with control. Especially, both NLR and PLR were steadily increased whatever the ADPKD patients without dialysis or with dialysis, and the ADPKD patients with dialysis had higher NLR and PLR than without dialysis patients, which agreement with the corresponding data in the literature [19].

The most important finding of this study was that NLR ≥ 4.3 was associated with a 1.5-fold increased risk of dialysis, and when PLR ≥ 174, the rate of dialysis increased significantly. Previous studies had shown NLR and PLR utility in predicting unfavorable progression and prognosis [21]. Furthermore, previous studies had been suggested that higher levels of inflammatory markers were associated with faster progression of chronic kidney disease (CKD) in patients [5, 22, 23]. Thereby, NLR may be considered as a marker for evaluating the systemic inflammation [24].

This study indicated that white blood cell count, absolute neutrophil count and NLR, PLR were significantly higher, but absolute lymphocyte count and absolute platelet count were significantly lower in patients with ADPKD compared to healthy subjects. These data were in accordance with previous reports suggesting increased inflammatory markers in ADPKD [3, 12, 25]. It is known that lymphocytopenia is a common finding in chronic inflammatory conditions and lymphocyte count reduction may be an early marker of physiologic stress and systemic inflammation response [26]. Moreover, we found the NLR, PLR level of ADPKD patients with RFD were significant higher than healthy objects and ADPKD patients with normal glomerular filtration rate, and even ADPKD patients with CKD stage 4 had higher NLR, PLR level than the CKD stage 3. Menon et al. [3] showed that ADPKD eGFR of 25 to 60 group had higher levels of C-reactive protein and IL-6 than controls, normotensive ADPKD with eGFR of > 60, and hypertensive ADPKD with eGFR of > 60. Inflammation was evident early in ADPKD even with preserved kidney function [3, 27].

The NLR and PLR have emerged as simple, inexpensive and useful markers of inflammation related to various renal diseases, inflammatory and cardiovascular [11, 19, 28]. Previous studies have demonstrated that an association between the NLR and PLR and worsening renal function in diabetic patients or hypertensive patients [21, 29, 30]. In the present study, we found that ADPKD patients with NLR values greater than 2.65 were found to be associated with renal function deficit with a higher sensitivity and specificity (74.7%, 96.9%, respectively), and ADPKD patients with PLR values greater than 130.2 were more feasible to predict renal function deficit (66.7%, 96.9%, respectively).

In addition, we found CD45-positive was abundant in the renal interstitium of ADPKD patients, which were significantly higher than the normal renal tissue. Previous studies have shown that macrophages and other inflammatory cells constitute the interstitial infiltrates in human and animal models of polycystic kidney diseases. Karihaloo et al. [31] showed that higher number of F4/80+ CD45+ CD11c- macrophages presented in mice model of polycystic kidney disease (PKD). Recent studies in animal models demonstrated that the chronic interstitial inflammation in PKD contributed to cyst development and renal impairment [32]. Ibrahim et al. [33] found that CD45-positive lymphocytes were dense in cyst of human with ADPKD. Several studies indicated that macrophages migrated to cystic areas and contribute...
to promote cyst cell proliferation, cyst growth, and fibrosis [34, 35]. Therefore, interruption macrophages and other inflammatory cells of homing and proliferative signals could alleviate the disadvantageous progression of the ADPKD.

The present study has several limitations. First, this study has a retrospective cross-sectional design with a single-center data. Due to the retrospective retrieval of the patient data, we could not execute the statistical significance concerning the correlation NLR, PLR and others inflammatory markers (i.e., erythrocyte sedimentation rate, IL-6 and C-reactive protein). Second, the cross-sectional design made it impossible to establish any causes and effect relationships. Third, using NLR, PLR in a single preoperative blood sample does not allow for assessing the stability of this variable over time. Finally, the cyst tissue from ADPKD patients is relatively small, which limits us to analyze the correlation between the inflammatory score and clinical parameters. Nevertheless, despite these certain limitations, given the paucity of the solid information available on this area, our findings represent a valuable contribution to the literature.

In conclusion, this study demonstrated that NLR and PLR were significantly higher in ADPKD patients with renal insufficiency, and we found that NLR and PLR significantly increased across worsening CKD stages. Higher level of NLR, PLR was easier to develop hemodialysis. The positive inflammatory markers in cyst tissue from ADPKD patients significantly increased compare to healthy adults. Herein, as NLR, PLR are readily available in routine blood count analysis, they may be used as a cost-effective predictor association with ADPKD poor progression. Our data suggested that lower NLR and PLR level in circulation, might be potential and novel preventive and therapeutic options for patients with ADPKD.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Yong-Man Lv, Department of Nephrology, Tongji Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan 430030, PR China. Tel: 0086-15827327879; Fax: 0086-27-83662853; E-mail: lv Yongman@126.com

References

Neutrophil-lymphocyte ratio and polycystic kidney disease


