Nature of Immunosuppression and Risk of Chronic Kidney Disease in HIV-positive Persons

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BACKGROUND

It is well documented that HIV-positive persons are at increased risk of chronic kidney disease (CKD) compared to the general HIV-negative population [1-2].

Likewise, immunosuppression has, in several studies, been independently associated with CKD [3-7] with a relatively low CKD prevalence in HIV-positive persons with preserved immune function [8].

As the exact nature of the association between immunosuppression and CKD is unknown, the objectives of this analysis was to investigate the association between various measures of impaired immune function and CKD in the settings of a large heterogeneous cohort.

METHODS

D:A:D study participants without CKD and with ≥2 Cockcroft Gault (estimated glomerular filtration rate) eGFR measurements after 01-Jan-2004 (baseline) were followed until the earliest of a CKD diagnosis (eGFR<60, confirmed >3 months apart), last eGFR >6 months or 01-Feb-2014. Measures of immunosuppression included baseline, current and nadir CD4 count, 6-months time-taged CD4 count, % of follow-up time (%FU) with CD4 count <200, time-averaged AUC for CD4 count and CD4 count recovery (baseline CD4 count <200 followed by a current CD4 count >200).

Poisson regression models were used to determine the relationship between CKD and each measure of immunosuppression (in separate models) accounting for relevant confounders including demographics, viral hepatitis status, hypertension, diabetes, antiretroviral treatment (ART) and other HIV-related factors.

Akaike Information Criteria (AIC) was used to indicate which measures of immunosuppression were better CKD predictors.

The strongest immunosuppression CKD predictor was tested for interactions with the D:A:D CKD risk score, demographics, ART and HIV-related factors.

RESULTS

Of the 33,144 persons included in analyses 1,588 developed CKD (incidence rate, IR, 7.2 [95%CI 6.8-7.5]/1000 PYFU) during a median 7.2 years FU (IQR 5.0-8.9).

• Those included in analysis were predominantly white (47.6%), male (74.0%) with a baseline median age of 41 years (IQR 35-47) and median CD4 count of 440 (292-626).

Table 1

<table>
<thead>
<tr>
<th>Measure of Immunosuppression</th>
<th>Baseline eGFR &gt;90</th>
<th>Baseline eGFR 60-89</th>
<th>Baseline eGFR 30-59</th>
<th>Baseline eGFR &lt;30</th>
<th>Baseline eGFR &lt;15</th>
<th>Baseline eGFR &lt;9</th>
<th>Baseline eGFR &lt;6</th>
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</thead>
<tbody>
<tr>
<td>Nadir CD4 count &gt;500 vs. &lt;50</td>
<td>0.80 (0.78-0.82)</td>
<td>0.87 (0.84-0.90)</td>
<td>0.83 (0.78-0.88)</td>
<td>0.75 (0.68-0.84)</td>
<td>0.71 (0.58-0.88)</td>
<td>0.66 (0.52-0.84)</td>
<td>0.62 (0.49-0.78)</td>
</tr>
<tr>
<td>% Follow-up with CD4 count &lt; 200</td>
<td>0.80 (0.78-0.82)</td>
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• Although the crude IR of CKD varied for different measures of immunosuppression, the rate was consistently higher with more advanced immunosuppression.

• Multivariately, the strongest CKD predictor was %FU CD4 count <200 (>25% vs. 0%, 1.24 [1.05-1.46]), Table 2.

Figure 2

• The strongest association between CKD and immunosuppression was observed for the nadir CD4 (count >500 vs. <50, IR 0.39 [0.31–0.48]) and %FU CD4 count <200 (>25% vs. 0%, 1.86 [1.62-2.13]).

• These observations support aggressive ART to maintain or restore immune function and thereby reduce the immunosuppression associated increased risk of CKD.

CONCLUSIONS

• The strongest association between CKD and immunosuppression was observed for the relative duration of severe immunosuppression.

• Immunosuppression was of greatest relative importance as a CKD predictor in persons at low estimated CKD risk, whereas more traditional renal risk factors dominated at higher levels of CKD risk.

• On-going analyses are investigating the association between various measure of HIV-viremia and CKD.

These observations support aggressive ART to maintain or restore immune function and thereby reduce the immunosuppression associated increased risk of CKD.

REFERENCES