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THE IMPACT OF HAEMODIALYSIS INITIATION ON CKD-ASSOCIATED MYELOID CELL DYSREGULATIONSarah Cormican^{1,2}, Serika Diane Naicker¹, Denise Connolly², Gemma Prendergast², M. Conall Denney³, Matthew Dallas Griffin^{1,2}¹National University of Ireland, Galway, REMEDI, School Of Medicine, Galway, Ireland, ²Galway University Hospitals, Saolta University Healthcare Group, Nephrology Services, Galway, Ireland and ³National University of Ireland, Galway, Discipline of Pharmacology, School of Medicine, Galway, Ireland

Background and Aims: Abnormalities of the myeloid immune cell lineages are well described in people with both Chronic Kidney Disease (CKD) and End Stage Renal Disease (ESRD). Increased numbers and proportions of the intermediate (CD14⁺⁺CD16⁺) and nonclassical (CD14⁺CD16⁺) monocyte subsets and increased neutrophil numbers have been reported in both settings. These changes are one aspect of the chronic inflammatory state which exists in people with CKD and ESRD and which contributes to complications including cardiovascular disease and protein-energy malnutrition.

The effects of transition from advanced CKD to dialysis on myeloid cell populations has not been well studied. We investigated these changes by measuring major leucocyte population numbers and monocyte subset numbers and proportions in adults with Stage 5 CKD prior to and after haemodialysis initiation.

Method: Adults with stage 5 CKD and a non-emergent indication for dialysis initiation (in-centre haemodialysis) were recruited after informed consent. Blood samples were collected within the week prior to dialysis initiation and follow-up samples were collected prior to a dialysis session at one week and one month after haemodialysis initiation. Major leucocyte population numbers were determined by two-colour flow cytometric analysis of whole blood on an AccuriTM Flow Cytometer. Peripheral blood mononuclear cells were isolated and stained for multi-colour flow cytometric analysis on a Canto IITM flow cytometer. The absolute number of each monocyte subset/ml blood was calculated based on the above values.

Results: Ten individuals (six male, four female) with a mean age of 78 ± 6.4 years were enrolled and completed all follow-ups. The mean eGFR was 9 ± 1.9 ml/min at the time of haemodialysis initiation.

Total monocyte numbers had not changed after one month of haemodialysis (**Figure 1A**) ($3.6 \times 10^5 \pm 1.6 \times 10^5$ cells/ml) compared to initiation ($5.2 \times 10^5 \pm 3.2 \times 10^5$, $p=0.11$). However, the proportion of nonclassical monocytes was markedly increased after one week of haemodialysis (16.8% (IQR 12.8–21.0%) compared to 11.2% (IQR 9.3–12.3%) at initiation, $p=0.007$) (**Figure 1B**). At one month the proportion of nonclassical monocytes was maintained (17.1% (IQR 14.5–20.5%)) but had not increased further compared to the one week timepoint ($p=0.97$). This proportionate change was not reflected in the absolute nonclassical count. There were no significant changes in the proportion of classical or intermediate monocytes.

Neutrophil numbers were reduced at one month ($3.6 \times 10^6 \pm 1.3 \times 10^6$ cells/ml) compared to initiation ($4.8 \times 10^6 \pm 1.6 \times 10^6$ cells/ml, $p=0.04$) (**Figure 1A**). Total lymphocyte numbers did not change significantly after dialysis initiation.

Conclusion: Haemodialysis initiation is associated with an increase in the proportion of nonclassical monocytes without significant increases in the absolute number of any monocyte subset. A reduction in total neutrophil number also occurs one month after dialysis initiation. It has been previously been shown that progression of CKD results in increasing abnormalities of the myeloid cell lineages. Here we have demonstrated that transition from advanced CKD to haemodialysis results in further modulation of myeloid cell numbers and myeloid cell subset proportions.

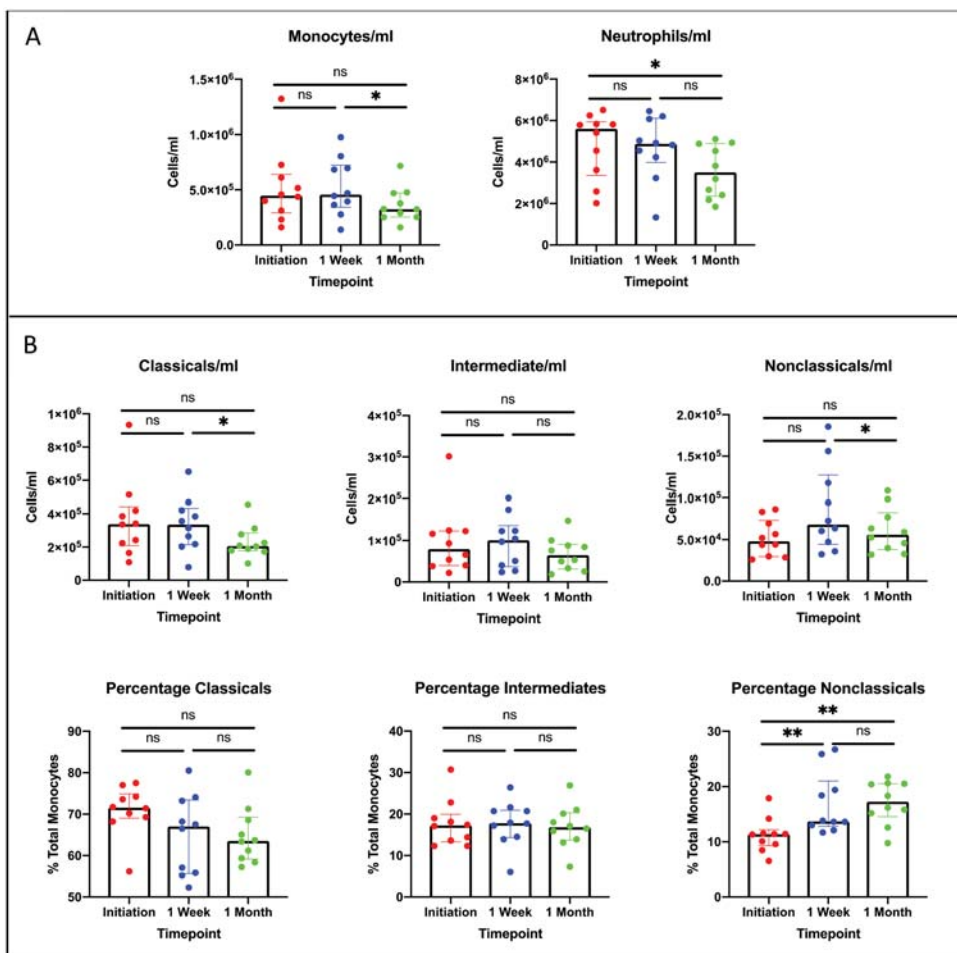


Figure 1: Changes in the number of total monocytes and neutrophils at one week and one month after dialysis initiation (A) and changes in the numbers and proportions of monocyte subsets at one week and one month after dialysis initiation (B)