Neutrophil-to-lymphocyte ratio (NLR) is an independent predictor of all-cause mortality in patients with end-stage kidney disease on haemodialysis

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Introduction
Neutrophil-to-lymphocyte ratio (NLR) is a surrogate marker of systemic inflammation and has been shown to predict mortality in cancer and cardiovascular disease (CVD). Comparatively little is known about NLR in chronic kidney disease (CKD) and in particular, patients on long-term haemodialysis. We sought to determine the relationship between NLR and overall survival in a group of haemodialysis patients.

Methods
A retrospective analysis was performed of a prospectively acquired database of adults with CKD stage 5, receiving haemodialysis in a single Scottish health board, attending 2006-2017. Start date was date of haemodialysis initiation; end date was date of death or data extraction (10/01/20). NLR was calculated from routine clinically acquired haematology samples on the day of initiation of haemodialysis. Survival analyses were performed to evaluate variables associated with death during follow up as well as cardiovascular (CV) events over the same period. Covariables studied included age, gender, primary renal diagnosis, pre-existing diabetes, pre-existing CVD, first haemodialysis access, serum albumin, haemoglobin, adjusted calcium and phosphate (all assessed on day of haemodialysis initiation).

Results
430 patients were included of whom 59.3% were male and mean age on starting haemodialysis was 63.1 ± 14.1 years. Primary renal diagnoses were similar to national prevalence data. 41.2% had pre-existing diabetes (24.9% with primary renal diagnosis of diabetic nephropathy) and 17.2% had pre-existing ischaemic heart disease or heart failure. Median follow-up was 4.95 (2.3-6.7) years during which time 100 (23.3%) patients underwent renal transplantation and 276 (64.2%) patients died with a median time to death of 2.99 (1.5-4.65) years. Patients who died during follow up were more likely to have diabetes (49.6 vs 26.0% Chi Sq p<0.001) or pre-existing cardiovascular disease (20.7 vs 11.0%, p<0.001). NLR (but not total white cell count) was significantly higher in those who died compared to survivors (7.0 vs 5.5, p=0.03) with cumulatively worse survival across quartile of NLR (Figure 1, Log-Rank p<0.001). NLR was higher in patients with a catheter compared to a fistula as first haemodialysis access (7.6 vs 5.1, p<0.001). On multivariable survival analysis, NLR (hazard ratio [HR] 1.02, 95% confidence interval [CI] 1.00-1.03), initial haemodialysis using a catheter (HR 1.65, 95% CI 1.08-2.52), age (1.06, 95% CI 1.05-1.07) and diabetes (HR 1.6, 95% CI 1.3-2.1) were associated with increased risk of death. There were 94 CV events (21.9% patients) during follow up. Only increased age and diabetes were independently associated with CV events during follow up, with no significant differences in NLR between those with a CV event compared to those without.

Conclusion
In summary, NLR is a novel risk factor which may identify patients at risk of poorer survival in those requiring haemodialysis. It may be associated with dialysis access as a trigger of inflammation.