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MO214 HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS WITH ANCA VASCULITIS

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BACKGROUND AND AIMS: Anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) is a debilitating disease that can have a significant impact on a patient's quality of life. The aim of this study was to assess the longitudinal quality of life amongst those diagnosed with AAV using the EQ-5D instrument, which allows for calculation of quality-adjusted life years (QALYs.)
METHOD: A total of 343 patients with AAV participated in this study, of which 191 (55.7%) were male, resulting in 2746 episodes. The EQ-5D-5L standardised instrument was used to evaluate health-related quality of life in the domains of mobility, self-care, usual activities, pain/discomfort, anxiety/depression and to generate a summary index score. Overall health was also rated using a visual analogue scale (0–100). EQ-5D questionnaires were completed during routine nephrology clinic attendances and through a vasculitis patient support smartphone app. We used a random effects model to control for multiple entries relating to individual patients.
RESULTS: A lower quality of life was seen amongst those with AAV (median index value 0.80, overall population average 0.856). The mean visual analogue scale score was 75.6 ± 17.3 (overall population average 82.8, Fig. 1). Patients' pain and discomfort level (mean 1.95) was most affected while self-care (mean 1.33) was least affected (Fig. 1). An increase in BVAS tightly correlated with a reduction in quality of life. Using the random effects model, the index score was seen to decrease with increasing age with a 2.7% reduction in index score per decade. A 7% reduction in index score was seen during periods of disease activity compared with periods of remission. Patients with end-stage kidney disease requiring dialysis had an 8% reduction in index score. A reduced quality of life was seen following COVID-19 lockdown with a 5% reduction in index score seen. Using a median survival rate of 6.16 years for patients with small vessel vasculitis, we calculated the QALYs for this population as 4.9 years.
CONCLUSION: We have defined for the first time the EQ-5D index value over the full disease course in patients with AAV. Notably, we have identified a reduction in quality of life during periods of disease activity. Other studies have demonstrated a reduction in quality of life during active disease using the AAV–PRO questionnaire and the Medical Outcomes Study Short Form-36. A decrease in work productivity has also been noted. Previously reported mean index values of 0.72 and 0.76 were lower than our observed values, although both are significantly reduced compared with population norms. In conclusion, this research highlights the negative impact of AAV on patients' lives.

MO215 INTRARENAL SINGLE CELL SEQUENCING OF MPO-ANCA ASSOCIATED GLOMERULONEPHRITIS PATIENTS REVEAL NOVEL TARGETABLE TREATMENT OPTIONS

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BACKGROUND AND AIMS: The etiopathogenesis underlying myeloperoxidase anti-neutrophil cytoplasmic antibody-associated glomerulonephritis (MPO-ANCA-GN) remains incompletely understood. Furthermore, there are only limited treatment options and treatment resistance of MPO-ANCA-GN is still a common problem.
METHOD: To identify new targeted treatment options, intrarenal single-cell RNA sequencing (scRNA-seq) was applied to 11 kidney biopsies from MPO-ANCA-GN patients and 2 health kidney tissues to define the transcriptomic landscape at single-cell resolution. Intrarenal scRNAseq was also applied to a pre-clinical mouse model of MPO-ANCA-GN to show that this model of disease can be used to trial new targeted treatments.
RESULTS: We found that kidney endothelial cells in MPO-ANCA-GN patients displayed increased expression of several genes, including *CD9* and *SPARC*, which were closely related to parietal epithelial hyperplasia and crescent formation. NF-κB pathway activation was confirmed in a variety of kidney cells in MPO-ANCA-GN patients. Kidney infiltrating immune cells of MPO-ANCA-GN patients were mainly enriched in inflammatory pathways including TNF signalling, IL-17 signalling and NOD-like receptor signalling. These findings were similar in our pre-clinical mouse model of MPO-ANCA-GN. Furthermore, there was an overexpression of inflammasome-related genes (*AIM2, IFI16*) in MPO-ANCA-GN patients. Treatment resistance was associated with increased infiltration of $CD8^+$ T cells and elevated expression of *SPARC*, *LAMA4*, *IL33* and *CFL1* in mesangial cells when compared with patients who achieved remission after induction therapy.
CONCLUSION: These results offer new insight into the pathogenesis of MPO-ANCA-GN, treatment resistance and identify new therapeutic targets for MPO-ANCA-GN that can be tested in a pre-clinical model of disease.

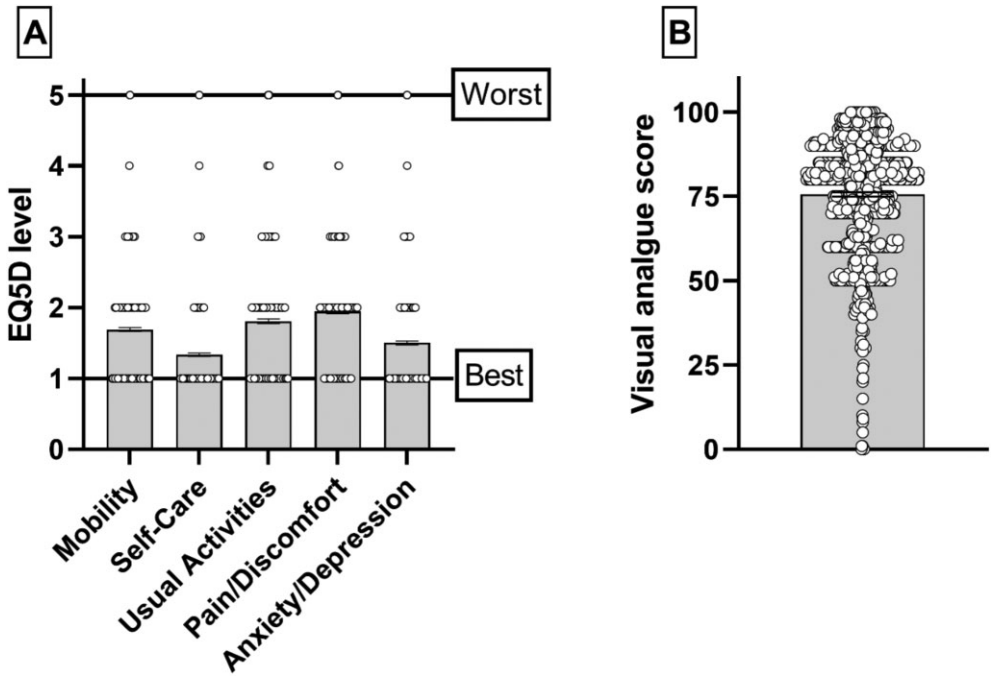

FIGURE 1: (A) Domain-specific EQ5D levels and (B) visual analogue score. Both graphs reflect mean and 95% confidence interval.