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Association between non-malignant monoclonal gammopathy and risk of adverse outcomes in chronic kidney disease

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Introduction

The presence of non-malignant monoclonal gammopathy (MG) can be causally associated with kidney damage (monoclonal gammopathy of renal significance [MGRS]) and shorter survival. However, the implications of a MG in patients without MGRS or a known plasma cell/B cell lineage disease are uncertain. To address this, we examined the association between MG and risk of end-stage renal failure (ESRF) and death in patients with chronic kidney disease (CKD).

Methods

Data were used from three prospective cohorts of individuals with CKD (not on dialysis or with a kidney transplant). Participants were excluded if they had multiple myeloma or other malignant B cell lymphoproliferative disorder. Baseline serum was tested from participants of the RIISC study (878 participants, recruited 2010-2015 from secondary care, with outcomes up to end 2018) for MG, defined as a monoclonal protein on electrophoresis confirmed by immunofixation or an abnormal free light chain (FLC) ratio with an increased level of the involved light chain. Further, to assess the association between light-chain (LC) MG (an abnormal FLC ratio and an increased level of the involved light chain), data from the RIISC study was amalgamated with data from (i) CRISIS (861 participants, recruited 2002-2010 from secondary care, outcomes up to end of 2017), and (ii) RRID (1739 participants, recruited 2008-2010 from primary care, outcomes up to 2015). Associations with risk of ESRF (defined as the initiation of dialysis or kidney transplantation) were estimated by competing-risks regression (to account for the competing risk of death) and adjusted for age, sex, ethnicity, cause of CKD, MAP, eGFR, and ACR (expressed as a subhazard ratio [SHR] with 95% confidence interval [CI]). The associations with risk of death were estimated by Cox regression and adjusted for age, sex, ethnicity, comorbidities, smoking status, eGFR, and ACR (expressed as a hazard ratio [HR] with 95% CI).

Results

102 (11.6%) of the 878 RIISC participants had MG. During a median follow-up time of 74.0 months there were 324 ESRF events and 202 deaths. The presence of MG was not associated with risk of ESRF (univariable SHR 0.98 [0.69-1.39]; multivariable SHR 0.79 [0.43-1.43]). The presence of MG was associated with a higher risk of death (HR 2.13 [1.49-3.05]), but the significant association was lost in multivariable analysis (HR 1.26 [0.83-1.90]). 55 (1.6%) of the 3478 participants from all three studies had LC-MG. During the median follow-up time of 62.5 months, 564 participants progressed to ESRF and 803 died. LC-MG was not associated with risk of ESRF (univariable SHR 1.05 [0.53-2.08]; multivariable SHR 1.32 [0.63-2.77]). There was a higher risk of death in those with LC-MG (HR 2.53 [1.60-4.00]), but not in the multivariable model (HR 1.42 [0.87-2.35]).

Discussion

The prevalence of monoclonal gammopathy was higher in this CKD cohort than that reported in the general population, but was not independently associated with an increased risk of kidney failure or death.