27.2. Screening for multiple myeloma in patients with unexplained AKI

Patients presenting with severe AKI of unknown cause should be screened for monoclonal gammopathy as part of their initial diagnostic workup. The window of opportunity for reversing renal impairment due to cast nephropathy is limited so early diagnosis and prompt treatment is important.

The International Myeloma Working Group (IMWG) recommends screening for monoclonal gammopathy using serum protein electrophoresis (SPE) and sFLC analysis (Chapter 25). This algorithm allows the rapid detection of both FLC and intact immunoglobulin monoclonal proteins. For patients in whom a diagnosis of AL amyloidosis is suspected, the IMWG guidelines recommend a combination of sFLC analysis and immunofixation of serum and urine (sIFE and uIFE) (Section 28.3).

A health economics model has been developed by Cook et al. which compared the IMWG recommended pathway using SPE + sFLC against SPE alone, SPE + urine protein electrophoresis (UPE), and SPE + UPE + serum/urine IFE in parallel. The SPE + sFLC tests were the most cost effective, with cost savings and quality-adjusted life-year (QALY) gains in the diagnostic and treatment stages of the disease.

The recently formed International Kidney and Monoclonal Gammopathy Research Group (IKMGRG) also recommended the use of SPE and sFLC analysis to screen for monoclonal disease in patients presenting with AKI (Figure 27.1). The authors suggested that a concentration of monoclonal sFLCs $\geq 500$ mg/L in patients with AKI, was indicative of tubular interstitial pathology, particularly cast nephropathy. The IMWG recommend the use of a similar sFLC cut-off (defined as a sFLC concentration above a specified range of values [500 - 1500 mg/L]) to identify MM patients with renal impairment that is suggestive of cast nephropathy (Section 25.3.7).

It is of note that the $\geq 500$ mg/L cut-off was based on data generated using Freelite® sFLC assays. In the only study performed so far using the Siemens N Latex FLC assays in the context of AKI, the authors concluded that the IKMGRG recommendations cannot be applied (Chapter 8).

Application of a modified renal reference interval for the $\kappa/\lambda$ sFLC ratio when screening patients with renal impairment may increase the diagnostic specificity with no loss of sensitivity (Section 6.3). Application of the renal reference interval and screening pathways for patients with AKI were reviewed in 2014 by Yadav et al.
**Figures**

**Figure 27.1. Screening algorithm for monoclonal disease in AKI.**

*To exclude the presence of an intact monoclonal immunoglobin, sFLC assays should be combined with SPE. For the assessment of AL amyloidosis and LCDD, urinary assessment is required. ‡Treatment based on high-dose dexamethasone. MGUS: monoclonal gammopathy of undetermined significance. (Reprinted by permission from Macmillan Publishers Ltd: Nature Reviews Nephrology[2] copyright 2011).

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**References**