

Reply. Kastritis E. et al. Reversibility of renal failure in newly diagnosed multiple myeloma patients treated with high dose dexamethasone containing regimes and the impact of novel agents. Haematologica 2007; 92:546-9

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The authors of this brief publication report on newly diagnosed myeloma patients with renal failure. They define the renal failure as serum creatinine ≥ 2 mg/dL. The reason for this definition is to exclude patients with mild renal impairment that can be easily corrected with hydration. The authors however did not calculate the creatinine clearance, thereby overestimating the renal function. Serum creatinine levels are not only dependent from renal function but also from the muscle mass. In our own study in multiple myeloma patients with different stages of renal insufficiency we included 40 patients with creatinine clearance from 8-138 mL/min (clearance ≥ 80 mL/min n=10; 79-50 mL/min n=11; 30-49 mL/min n=10; <30 mL/min n=9) only 18 patients had serum creatinine levels > 1.3 mg/dL (normal range) and only 9 >2.0 mg/dL, respectively (Figure 1).¹ To minimize the error the creatinine clearance has been calculated as a mean from 3 methods: creatinine clearance with 24 hour collected urine, MDRD-formula² and Cockcroft and Gault formula.³ The age of the patients ranged from 41-83 years (mean 67.4 ± 9.9 years). Included were patients with biopsy proven kidney disease from multiple myeloma but also patients with reduced kidney function due to nephroangiosclerosis or other renal disease. Because of the wide spectrum of renal diseases associated with multiple myeloma and their different prognosis,⁴ the definition of elevated serum creatinine for renal involvement in multiple myeloma is more than questionable. Patients with cast nephropathy (CN) had a worse prognosis than patients with interstitial nephritis or nephrocalcinosis, whereas patients with light chain deposit disease (LCDD) or AL-amyloidosis (ALA) had an intermediate prognosis regarding their kidney function. Without kidney biopsy it is impossible to distinguish between this different kidney disease. We could show that patients with high free light chain excretion in the urine had predominantly cast nephropathy (*unpublished data*). In our study about free light chain excretion (FLC_{urine}) in urine in patients with biopsy proven CN had FLC_{urine} of 329.5 ± 334.5 mg/dL, patients with LCDD 17.4 ± 21.6 mg/dL and patients with ALA 7.5 ± 10.0 mg/dL respectively ($p < 0.05$). In a series of 35 patients patients with monoclonal light chain disease, who underwent a kidney biopsy cast nephropathy was diagnosed in 13 patients, LCDD in 3 patients and AL-amyloidosis in 8 patients. Eleven patients had other renal involvement such as nephrocalcinosis or interstitial nephritis, which were easily treatable with corticosteroids and bisphosphonates.⁵ Only about one third of our patients had cast nephropathy with unfavorable prognosis. Knudsen *et al.* also describe that the reversibility of renal failure was more frequently observed in patients

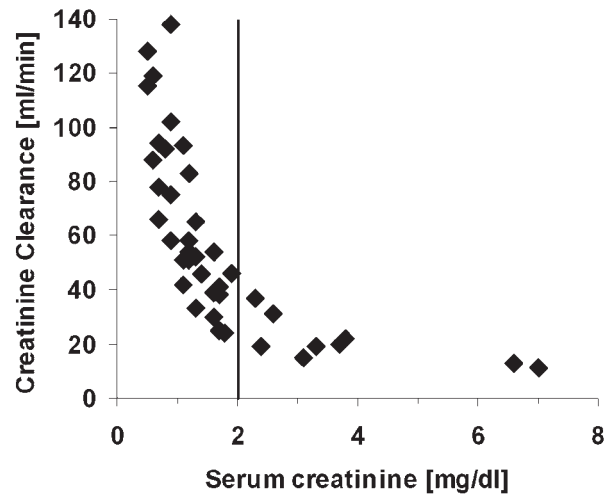


Figure 1. Serum creatinine levels are plotted with the according calculated creatinine clearance. The creatinine clearance was calculated as the mean value of three different methods to calculate the creatinine clearance (collecting urine-method, MDRD-method, Cockcroft & Gault-method).

with moderate renal failure, hypercalcaemia and low Bence-Jones protein excretion.⁶ The observation of the authors that patients with light chain myeloma or Bence-Jones proteinuria had a lower probability of recovery of the renal failure is in accordance with this.

We strongly argue against a comparison of recovery of the two groups of patients without knowing the type of renal disease, as was done in this paper. Furthermore we find it confusing, that the median survival of the patients with renal impairment is not different whether the renal function reversed or not. The conclusion of these data would be that it makes no difference, whether the renal failure would be treated or not. This is in contrast to the findings of Knudsen *et al.*⁶ in a study with 775 myeloma patients, who stated that renal failure in multiple myeloma is reversible in about half of the cases, and reversibility of renal failure improves long-term survival. In an other study it could be demonstrated that the transplant related mortality after stem cell transplantation is 0% in patients with normal renal function, 1% in patients with initial renal failure, who recovered completely before stem cell transplantation and 17% in patients with renal failure, defined as creatinine clearance < 60 mL/min.⁷ Patients with multiple myeloma may have different type of renal involvement, therefore studies dealing with the treatment of renal function in these patients should always clarify the type of renal involvement by biopsy.

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