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Letters

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Renal impairment resulting from hypothyroidism—or impaired estimated glomerular filtration rate in a patient with hypothyroidsm

Sir,

We read with interest the two cases described by Andrew Connor and Joanne E. Taylor [1].

They summarize the medical literature that the lower cardiac output and renal blood flow is likely to be the predominant mechanism of impaired renal function in hypothyroidism. In the discussion, they also list other possible mechanisms, so that hypothyroidism may increase creatinine release from muscle. This renders creatinine a poor marker of GFR. In case 1 the creatinine kinase (CK) was elevated, as a sign of rhabdomyolysis. We think that in cases with elevated endogenous creatinine, we do not know if there is an impaired renal function or not. Furthermore, we want to highlight some important points, which we have to consider in the treatment of patients with hypothyroidism and rhabdomyolysis.

As often described in patients with hypothyroidism, they may suffer from a polymyositis-like syndrome and an elevated CK may be observed [2–7]. In these cases, there is a high amount of released creatine and therefore higher endogenous creatinine production. In all these cases, eGFR would be wrong and measuring the creatinine clearance rate does not improve the results. Cystatin C, an endogenous marker to estimate the GFR, independent from muscle mass, age and alimentation may be a better parameters in diagnosing impaired renal function in a patient with hypothyroidism. But there are also problems with this measurement in patients with thyroid dysfunction [8–11]. Cystatin C levels are lower in hypothyroidosis and higher in the hyperthyroid state as compared with the euthyroid state. Manetti *et al*. described decreased cystatin C concentrations in 24% of hypothyroid patients [11].

We saw a young patient with hypothyroidism and elevated serum creatinine, normal serum urea, reduced estimated GFR (47 ml/min/1.73 m^2, estimated by MDRD-4; 30 ml/min/1.73 m^2 estimated with a 24-h urine collection) and CK of 4438 U/l. Cystatin C was 0.72 mg/dl, which resulted in a normal GFR of 117 ml/min. We decided to start hormone replacement therapy and to watch closely the pathological parameters. The therapy led to normal laboratory findings for serum creatinine after 6 weeks. Later, we observed a difference in our patient between cystatin C levels in euthyroidism (0.98 mg/l) and in hypothyroidism (0.72 mg/l).

One investigation with radioisotopic filtration markers in patients with hypothyroidism underlines the opinion of A. Connor and J. E. Taylor: Karanikas *et al*. [12] investigated isotopic renal function in severe hypothyroidism and after hormone replacement therapy. They did not find any influence of thyroid hormones on the outcome of 99m-Tc-MAG3-renography. The Cr-EDTA clearance was significantly lower in hypothyroidism. This reflects a normal tubular function and to these authors it seems that the renal haemodynamic changes mainly affect the GFR. If this is right, perhaps in cases of hypothyroidism and mild rhabdomyolysis we have a combination of both high amounts of creatinine and a change in renal haemodynamics. Only inulin clearance may give the answer, if there is really an impaired renal function. Unfortunately, we did not find any case report where the authors use the inulin clearance for estimation of the GFR in a patient with hypothyroidism.

There may be risk factors in patients with hypothyroidism, which lead to renal damage with pathological urine sediment and any other sign for tubular failure, described by Sekine *et al*. [13]: they reported about a patient and cited three other cases with some precipitating factors such as hypotension with myxoedema coma, certain inflammatory reactions of the muscles or, and this is very important, vigorous exercise which may cause massive rhabdomyolysis. In these special cases, high urine and serum myoglobin levels and tubular necrosis can be observed and perhaps dialysis has to be started.

We agree with A. Connor and J. E. Taylor that patients with renal impairment of unknown cause have thyroid function tests undertaken as part of routine investigation. Also, we have to look for signs of rhabdomyolysis. Taking these points into account, as described above, we can decide to start hormone replacement therapy and to watch closely the pathological parameters in patients with hypothyroidism, rhabdomyolysis and elevated serum creatinine as the only evidence for an impaired renal function. The hormonal therapy will lead to normal laboratory findings for serum creatinine after some weeks. In cases with hypothyroidism and myalgia, patients have to avoid muscle training or vigorous exercise. There is an increased risk to develop massive rhabdomyolysis and renal damage. If the renal haemodynamic changes mainly affect the GFR in patients with hypothyroidism, we have to take these into account in the therapy. For instance, COX-inhibitors to treat myalgia should be avoided. Inhibition of COX-mediated prostaglandin synthesis by NSAIDs can promote further reduction in renal haemodynamics and increase the risk for acute renal failure.

Editorial Note: Dr Connor *et al*. had no further comments on this letter.

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End-stage renal disease (ESRD) contributes to the increasing prevalence of herpes zoster

Sir,

Varicella-zoster virus (VZV) causes two clinically distinct diseases: varicella (chickenpox) and herpes zoster (HZ; shingles). The lifetime cumulative incidence is ∼10–20% of the population [1]. The incidence rates progressively increase with age, presumably owing to decline in the VZV-specific cell-mediated immunity [2]. Age is the most important risk factor for the development of HZ; however, immunocompromised patients such as transplant recipients, patients receiving selective immunomodulatory therapy and HIV-infected patients have an increased risk of VZV reactivation [3,4]. Further, immunosuppressed individuals with HZ exhibit a significantly higher rate of complications (e.g. dissemination of the disease and ocular involvement) [5].

Table 1. The number of patients per group and their gender, classified according to their CKD stage

	Number of patients (male/female)			
CKD stage	Average age	With HZ	Without HZ	Total
1–3	73.78	0/2	38/41	81
4 and 5	74.21	3/1	22/13	39
5D (ESRD)	72.89	4/4	26/21	55
		7/7	86/75	175

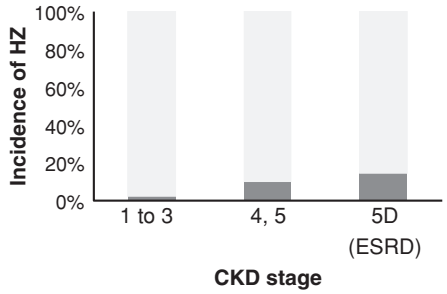

Fig. 1. The graph shows the incidence (%) of HZ in patients classified by chronic kidney disease (CKD) stage.

Patients who have end-stage renal disease (ESRD) with uraemia exhibit an impaired host immune response. The reported immunological abnormalities in ESRD patients include decreased phagocytic function of granulocytes and monocytes/macrophages, defective antigen presentation by monocytes/macrophages, reduced antibody production by B lymphocytes and impaired T-cell-mediated immunity [6]. Physicians working in dialysis facilities generally presume that ESRD contributes to the increase in the prevalence of HZ. Despite this presumption, the morbidity of HZ in ESRD has not been previously reported.

This retrospective study includes information on all septuagenarian patients who visited the outpatient clinic of the nephrology division and dialysis centre affiliated to our university. A total of 220 patients were followed up for at least 3 years within the last 3.5 years. Of these 220 patients, 45 were excluded from this study because they exhibited one or more already identified risk factors for HZ (e.g. corticosteroid and/or immunomodulatory therapies, carcinomas and autoimmune disorders). Potential patients were identified by searching the diagnostic and billing codes of hospital records. If HZ was confirmed in a patient, the medical records were reviewed to verify that the case of HZ was indeed a new one. Our results revealed that the incidence of HZ increased with the progression in the stages of chronic kidney disease (CKD) (Table 1, Figure 1). In fact, the incidence rate of HZ was 84.8 per 1000 person-years in our outpatients undergoing haemodialysis or continuous ambulatory peritoneal dialysis. However, in patients with CKD stage 1, 2 or 3, the incidence rate (8.2 per 1000 person-years) was as low as that in septuagenarian HZ patients without kidney disease [5]. Diabetic nephropathy is the most important cause of ESRD that requires renal replacement therapy. Diabetes as well as CKD is a risk factor for some infectious diseases because these conditions result in a compromised immune system. However, the incidence of HZ and diabetes was not found to be significantly