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Reply

Sir,

We deeply appreciate the interest shown by Drs Keven and Sengul in our article and hope to be able to answer their questions.

(a) There were three living-related kidney donors in patients requiring post-tx IA (one mother, one father and one sister) and five living-related donors in patients not requiring post-tx IA (three mothers, one father and one grandfather). The other 14 kidney donations were living-unrelated donations (13 spouses, 1 good friend). No non-directed donation occurred.

(b) With the exception of the first transplantation, all ensuing procedures were fully covered by the German Health Care System. This also included the costs for immunoadsorptions, rituximab and the hospital stay for patients who eventually could not undergo transplantation.

(c) We estimate the additional costs for an ABO-incompatible transplantation to amount to ~40 000 Euro per successfully transplanted patient.

(d) Drs Keven and Sengul ask why the average time on dialysis before ABO-incompatible transplantation was as long as 44 ± 32 months although there were living donors. This is a very crucial point: until 2004, a substantial number of dialysis patients in Germany could not be transplanted within a justifiable period of time, because waiting time for a cadaveric kidney equalled an average of 6 years and their putative living donor was ABO incompatible. Meanwhile the technique of ABO-incompatible kidney grafting has been adopted at more than 10 centres across Germany and waiting times have decreased considerably within our program (the median time on dialysis of the first 11 patients enrolled in our program was 40.3 months (0–83.1), while time on dialysis for the next 11 patients was only 20.2 months (0-139]). Fortunately, there is also a trend towards slightly shorter waiting times for a cadaveric kidney transplant in Germany in recent years.

(e) Drs Keven and Sengul suggest that median levels, instead of mean levels, should have been used to express estimated GFR after the follow-up period of 17 months. This is a very valid point. The median eGFRs were 52.5 ml/min (28.1–74.5) in patients requiring post-tx IA and 44.8 ml/min (25.1–66.3) in patients without post-tx IA.

(f) We are aware that the kidney function is lower compared to large cohorts of kidney transplant patients, like for example the cited Symphony Study—a study cohort that is hard to compare to this group of patients, since it only included ABO-compatible kidney transplantations.

Although recent reports show very encouraging intermediate term results [1], most data comparing the outcome of ABO-incompatible versus ABO-compatible kidney grafts in the long run document a somewhat poorer long-term graft function for ABO-incompatible grafts [2,3]. The presumed better outcome of ABO-compatible transplantations is the reason why we only recommend and perform ABO-incompatible transplantations if the patient definitely has no ABO-compatible donor.

We are glad to report that since submitting the manuscript 9 months ago, there has been a slight improvement of kidney function in our patients. The median eGFR in patients requiring post-tx IA and not requiring post-tx IA were now 50.2 ml/min (34–64) and 51.3 ml/min (30–77), respectively.

Conflict of interest statement. None declared.

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The neglected role of students in international university rankings

Sir,

We read with great interest the paper by Charon and Wauters on ‘University Ranking’ [1]. The authors mentioned that ‘students need rankings to choose where to study’. But could students also influence the ranking of their universities? The answer is no. Worldwide university rankings have been published since 2003, with an aim to determine the actual standing of higher education institutes of an individual country. Universities are ranked by several indicators: academic quality, research performance, graduate employability and international outlook. Interestingly, no student-oriented criterion has been taken into account in these global classifications. University rankings should not...
be based on academic and research criteria excluding the students’ role. Therefore, we introduce an index for student participation, defined as the number of publications in which students share the authorship, divided by the total number of students of a given university in the preceding year. This could be an additional criterion for university rankings through which the role of students may be further illuminated.

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Editorial Note: Drs Charon and Wauters declined the invitation to reply to this letter.

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Cardiovascular abnormalities in patients with epilepsy receiving renal replacement therapy with dialysis: a true convergence of clinical cardiology, nephrology and neurology

Sir,

We read with great interest a very comprehensive review article entitled ‘Kidney disease in cardiology’ by Professor Charles Herzog [1] published in the January issue of Nephrol Dialysis Transplantation.

Epilepsy is the most common serious neurological condition. Approximately 50 million people worldwide have epilepsy [2]. In the United States each year, ~100 000 new cases of epilepsy are diagnosed [3,4]. In the UK between 1 in 140 and 1 in 200 people (at least 300 000 people) are currently being treated for epilepsy [5]. Epidemiological studies suggest that between 70 and 80% of people developing epilepsy will go into remission, while the remaining patients continue to have seizures and are refractory to treatment with the currently available therapies [6,7]. The most common risk factors for epilepsy are cerebrovascular diseases, brain tumours, alcohol, traumatic head injuries, malformations of cortical development, genetic inheritance and infections of the central nervous system [8]. In resource-poor countries, endemic infections, such as malaria and neurocysticercosis, seem to be major risk factors [9]. Moreover, the risk of death for a person with epilepsy increases 2- to 3-fold when compared with the risk for the general population [10,11]. Information concerning risk factors for premature death in epilepsy is conflicting, but potential risk factors include age and gender, seizure type and epilepsy syndrome, duration of epilepsy, severity of epilepsy, and congenital neurological deficits and learning disabilities [10]. Additionally, the underlying pathophysiology of premature death in epilepsy is unknown; however, it is very probable that cardiac arrhythmia plays a potential role. In this way, Rugg-Gunn and colleagues, using implantable loop recorders, demonstrated that some patients with refractory partial epilepsy may have potentially life-threatening cardiac arrhythmias [12]. Moreover, it has been established that repetitive seizures can alter the regulation of cardiac activity by the autonomic nervous system (ANS), and ANS dysregulation is thought to be associated with higher morbidity and mortality in patients with epilepsy [13]. From an experimental point of view, a recent study by our group evaluated the heart rate, in vivo (ECG) and isolated ex vivo preparation (Langendorf preparation), of rats with epilepsy [14]. The results showed differences in the mean heart rate in vivo, but surprisingly, no differences in the heart rate could be observed in the isolated ex vivo situation, suggesting a central nervous system modulation on the heart, which could result in cardiac death in epilepsy [14].

In accordance with this reasoning, we postulated the following question: is there a possible relation between epilepsy, renal dysfunction and cardiovascular abnormalities?

Cardiac disease is the major cause of death in patients with end-stage renal disease (ESRD), accounting for ~43% of all deaths [15,16]. In dialysis patients, ~20% of cardiac deaths are attributed to acute myocardial infarction, a catastrophic clinical event in this group of patients [15,17]. In parallel, an estimated incidence of seizure of ~10% in patients with chronic renal failure has been reported [18]. In addition, Plum and Posner [19] also noted that convulsions occurred in one-third of patients with ESRD and was frequently a preterminal event. The seizures in this series were usually generalized tonic–clonic type; however, the mechanism of reduced seizure threshold in renal failure is still unknown. Haemodialysis-associated seizure (HAS) is a common complication of haemodialysis [20]. HAS occurs in 7–50% of children with ESRD, and their seizures are usually reported as generalized tonic–clonic seizures [21]. Risk factors for HAS include young age, prior history of seizures, malignant hypertension, microvascular diseases, uremic encephalopathy and cardiomyopathy. Moreover, induced brain-water disequilibrium, hypocalcaemia, uremic toxins, the use of acetate in the dialysate, intracranial haemorrhage due to systemic heparinization, treatment with recombinant erythropoietin, homodynamic and metabolic defects, and drugs such as penicillin and theophylline are also considered responsible for HAS [21,22,23]. If all these data are taken together, information on the management of seizures in renal failure should be disseminated among professionals treating systemic diseases. In the mean time, there is an urgent need for a large-scale, prospective, international, community-based study of cardiovascular abnormalities in patients with epilepsy receiving renal replacement therapy with dialysis to explore more closely the risk factors so that preventive strategies can be planned.

Finally, we express our congratulations to Professor Herzog for the stimulating review [1] and we are totally in agreement with his conclusion that with regard to kidney