paper [1] and report by Angelis et al. [2], however, showed that female gender is not a significant risk factor for calciphylaxis, while we did not collect data regarding body mass index. Furthermore, the hypotensive episode is not unusual in the patients on chronic hemodialysis, and warfarin is also commonly prescribed. Based on these facts and very low prevalence rate of calciphylaxis, we consider that some determinant factor, which is required to induce calciphylaxis in addition to known risk factors, is missing. For the prevention and therapy of calciphylaxis, we should search this missing factor in the future studies.

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Adequacy of intermittent renal replacement techniques and survival of ICU patients with acute kidney injury

Skofic et al. [1] reported that outcomes of critically ill patients treated with intermittent high volume predilution on-line haemofiltration were similar to those of patients receiving conventional intermittent haemodialysis (IHD). Surprisingly, renal replacement therapy (RRT) was not managed by a standard protocol, although the study was performed in a single centre after the results of earlier investigations on IHD were published [2, 3]. Thus, the findings may be biased by uncontrolled differences in the performance of RRT. Moreover, there are major concerns about the adequacy of the two modes of RRT.

First, the performance of IHD did not include measurements of prescribed and delivered dialysis dose. There is ample evidence that conventional IHD (4 h sessions, blood flow 250–300 mL/min, dialysate flow rate fixed, mostly every other day) results in underdosing of acute kidney injury (AKI) patients [3]. The performance of IHD by the authors does not comply with recommended IHD dosage in intensive care unit (ICU) patients with urea compartmentation, which can only be obtained by extended or augmented IHD ($K_d/V$ urea of 1.2–1.4 per session, three times per week [2]).

Second, the authors did not characterize fluid (overload) status, another determinant of outcome. Recommendations of restricted ultrafiltration per session (0–500 mL/h, see Appendix) will cause persistent fluid overload and its well-known sequela in the majority of hypervolaemic critically ill patients with anuria and/or parenteral hyperalimentation. Higher ultrafiltration rates per session result—as demonstrated by the authors—in an unacceptably high rate of potentially life-threatening hypotension. The reasons why the authors did not more often perform daily IHD remain obscure, and the number of patients who received one treatment session prior to enrolment is not given.

Third, RRTs were started very late (mean serum creatinine 5.3 mg/dL). Delayed commencement of RRT may be associated with increased morbidity and mortality in critically ill patients [4].

There is a place for adequately performed intermittent RRTs in the treatment of AKI in ICU patients. However, there is a need to individualize the number of sessions of intermittent techniques according to the clinical situation of the patient. If necessary, they should be performed daily.

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Reply

Sir,

We appreciate the opportunity to respond to the letter by Professor Helmut Schiffl who raised several questions and concerns regarding our study [1]. The major concerns were lack of standard protocol and doubt about the adequacy of the two intermittent dialysis modalities performed, i.e. standard haemodialysis (HD) and high-volume predilution on-line haemofiltration (HF).

In our study, dialysis dose was not prescribed and analysed by means of standard parameters (e.g. $K_d/V$ for
urea). Specific individual parameters that determine the dose of HD and HF were dictated by the study protocol, but others were prescribed individually (Appendices 1 and 2 in the article) with respect to temporary individual patient clinical characteristics and treatment goals.

We agree with many other authors that the issues of dialysis dose and of the adequacy parameters are much more complex and should be considered more extensively than just in terms of removal of small solutes (e.g. urea clearance or surrogate markers), which alone cannot fully reflect dialysis efficiency, nor cover the wide-ranging goals of dialysis treatment, especially not in critically ill patients with AKI as part of multi-organ failure (MOF).

Same as in our everyday clinical practice, dialysis parameters determining the dose were not prescribed on the basis of single particular marker solely, but taking into consideration all the main problems in AKI that can and should be controlled by dialysis support (i.e. uremic retention, fluid overload, electrolyte and acid–base disequilibrium). Except for mean daily urea and creatinine concentration, all these measurements and ‘markers of adequate dialysis’ were not analysed. Even so, we believe that according to our clinical practice, the most important aspects of dialysis support were managed adequately, efficiently and in compliance with the current recommendations.

In critically ill patients with AKI, there is presently no consensus on the optimal dialysis dose. Many recent studies proved that in this specific group of patients, more intensive (high-dose) dialysis treatment does not improve the clinical outcomes or provide any additional clinical benefit when compared with the conventional, less-intensive (standard-dose) treatment strategy, regardless of dialysis modality [2–6].

Concerning the frequency/schedule of dialysis procedures, they were certainly prescribed daily whenever necessary (e.g. in anuric and hypervolaemic patients, in haemodynamically unstable patients with low neto ultrafiltration possible, etc.). We strongly agree with the comment that an individual approach to selection of all characteristics of dialysis care is needed.

Pre-treatment values of urea and creatinine in our study indeed suggest that, in our clinical practice, initiation of renal replacement therapy is quite ‘late’ when compared with other studies/practices [3, 4]. However, except for emergency indications, clinical and biochemical parameters pointing to the optimal time to initiate dialysis support in critically ill patients with AKI as part of MOF remain undefined. Moreover, studies did not show better patient outcomes with ‘early’ versus ‘late’ dialysis initiation [2, 7, 8]. On the contrary, in a study by Bagshaw et al. [7], late initiation (when stratified by median creatinine at the time renal replacement therapy was started) was associated with lower mortality.

As a final note, there is currently no evidence that, in critically ill patients with AKI, any particular dialysis modality is superior to others owing to better clinical outcomes. We have demonstrated that, in the hands of experienced practitioners, both HD and HF can be performed safely and effectively also in the most severely ill patients. We believe that individual dialysis treatment, including individual selection of dialysis modality as well as all other dialysis parameters, is the optimal approach to dialysis management of AKI in critically ill patients with MOF that could potentially improve the grave prognosis of these patients.

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The search for perfect biomarkers in acute kidney damage: the case of NGAL, from AKI to acute pyelonephritis: back to the clinic?

Sir,
The paper by Schinostock et al. [1] regards one of the most promising biomarkers introduced into clinical practice, the versatile neutrophil gelatinase-associated lipocalin (NGAL). We are all looking for the perfect biomarker of kidney damage: rapidly tested, allowing a fast, objective and reliable selection of patients at risk for acute complications and needing hospitalization or intensive care. The