the combination of midodrine and octreotide compared with 10% with SMT, and both the earlier study from Angeli et al. [3] who reported an improvement in renal function in five patients with midodrine doses titrated to achieve an increase in mean arterial blood pressure of 15 mmHg, and the later report from Wong et al. [4] of 10 of 14 responding to treatment. However, none of these positive reports was a large study or a truly randomized prospective study, and as such, there may be an element of publication bias towards reporting positive findings in small case series. Unfortunately, the evidence-based literature in treating patients with HRS-1 is somewhat lacking as pointed out in our review [5], although treatment with vasopressin analogues in combination with SMT would appear to be currently the most promising option.

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Calciphylaxis in end-stage renal disease patients

Sir,

In a recent paper, Hayashi et al. [1] reviewed the cases of calciphylaxis in the Japanese dialysis population. They conducted a survey case–control study to identify the characteristics and risk factors for the development of calciphylaxis in chronic haemodialysis patients in Japan. The study identified warfarin therapy and lower albumin concentration as the strong risk factors for the development of calciphylaxis.

In 2008, our group analysed a series case report [2] of eight calciphylaxis cases diagnosed by skin biopsy in our hospital between January 2001 and December 2006. In our case report, all patients were female, obese, met the established criteria for the cardiometabolic syndrome and all developed hypotensive episodes during haemodialysis sessions. We propose the reduction of blood pressure during haemodialysis treatment that impairs perfusion in the vascular bed of the subcutaneous adipose compartment as a major mechanism for inducing calciphylaxis in our obese patients. Hypotension and subsequent hypoperfusion of subcutaneous adipose tissue (increased in these obese patients) may be responsible for inducing calciphylaxis. Our patients presented lesions proximally in the regions of greatest adiposity which supports our hypothesis [3].

As in Hayashi’s study, our patients also had low serum albumin levels and most of them were undergoing treatment with warfarin. We did not find any association with levels of serum calcium or phosphate levels or parathyroid hormone levels [4] as in Hayashi’s study.

We consider calciphylaxis as a severe complication of obese female patients on haemodialysis. Based on our data, the risk factors for developing calciphylaxis are female gender, obesity associated with type 2 diabetes and anticoagulant therapy with warfarin. In these patients hypotensive episodes during dialysis treatment should be avoided because it may favour a subcutaneous adipose tissue ischaemia and the development of calciphylaxis.

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Reply

Verdalles et al. suggest that the hypotensive episode impairs perfusion in the vascular bed of subcutaneous adipose tissue and results in calciphylaxis. In addition, obesity may deteriorate the tissue hypoperfusion, further. This hypothesis seems very attractive for the etiology of calciphylaxis. In consistent with Verdalles’s report, previous case studies also identified female gender and obesity as risk factors for calciphylaxis as described in Verdalles’s previous report. Our recent
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 hypertensive 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.

Conflict of interest statement. None declared.

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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 ($K_i/V$ 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. $K_i/V$ for