that the results in fact confirm the view on the particular sensitivity of peritoneal dialysis (PD) patients for post-transplant diabetes mellitus (PTDM) development. Courivaud et al. noticed that the strongest risk factors for PTDM appearance were older recipient age and higher body mass index (BMI) at transplantation, acknowledging simultaneously that PD patients were significantly younger (P = 0.004) and had a lower BMI (P = 0.07) than haemodialysis (HD) treated counterparts. Considering this fact, a lack of difference in PTDM occurrence between PD and HD patients can be interpreted as the argument for the metabolic disorder making PD patients more vulnerable for PTDM. It is noteworthy that, in our observation, the risk of PTDM in PD patients below the age of 50 years was similar to that in the HD group >=50 years. The important distinctive element between Courivaud et al. and our study was the use of different criteria for diabetes diagnosis. We used the more sensitive current American Diabetic Association criteria, whereas they identified diabetes by the prescription of insulin or oral antidiabetics. This is probably the reason of the low diabetes rate (6.8%) in their study compared to our 22.1% revealed after 6 months. This last figure seems to reflect the real scale of glucose intolerance after renal transplantation [3].

We have also noted that two papers quoted in the letter are in fact not in favour of PD treatment. The main findings of Rodriguez Ayala et al. [4] were the observations that plasma ghrelin drops during the 12-month period of PD and this was significantly linked to increased fat mass and inversely correlated with plasma insulin. Rodriguez Ayala et al. commented in the discussion ‘we find it likely that hyperglycaemia and hyperinsulinaemia, two common findings in PD patients, may also be related to the observed decrease in plasma ghrelin levels during PD’. In turn, Wong et al. [5] did not state that inflammation was less activated in the PD group versus HD. They even noticed significantly higher serum TNF and IL-18 concentrations in PD patients.

In conclusion, the data presented by Courivaud et al. [2] does not undermine the assumption that PD treatment may increase the risk of PTDM development. We obviously agree that further studies are needed to finally solve the issue.

Conflict of interest statement. None declared.

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Beck Depression Inventory and survival in elderly hemodialysis patients

Sir,

We read with great interest the article by Chilcot et al. [1]. They showed that depression, as assessed by the Beck Depression Inventory-II (BDI), is an independent predictor of mortality in patients with end-stage renal disease (ESRD) on dialysis. We wish to state that this conclusion is not necessarily applicable to the fastest growing cohort of ESRD patients—the elderly (>=65 years).

We recently published our findings that show that both the BDI and the 15-item Geriatric Depression Scale are useful tools to screen for depression in the elderly hemodialysis (HD) population (compared to the gold standard psychiatric interview) [2]. Eighty-nine patients were included in this study, aged 73.5 ± 6.2 years, with 39 males, 50 Caucasians and 39 African Americans. In this subsequent study, we followed this same cohort for 5.5 years or until death, transferring out of our HD unit or the end of the study period. Data was available on 76 patients. Forty-five patients died (59.2%). Depression (D), as assessed by BDI score ≥10, was noted in 31 subjects, while 45 subjects had BDI scores <10 no depression (ND). Seventeen patients from the (D) group died within the study period (54.8%) as compared to 28 from the (ND) group (62.2%).

Using Kaplan–Meier survival method, the mean survival was 32.9 ± 3.3 months and 34.5 ± 3.4 months for (D) and (ND) groups, respectively. The median survival time was 41.9 months (95% confidence interval: 22.1–66 months) and 30.2 months (95% confidence interval: 18.9–59.2 months) for the two groups, respectively. None of these parameters showed any difference which was statistically significant.

Several studies have shown that depression, as assessed by BDI, was associated with mortality in patients with ESRD [1,3] and non-ESRD patients [4]. Other studies such as Pinquart and Duberstein’s [5] contradicted these findings and were similar to our findings of poor association between depressive symptoms, as assessed by BDI, and mortality. A potential explanation could be related to the ages of the patients tested. Our study, as well as the meta-analysis by Pinquart and Duberstein, were done (mainly) in the elderly (73.5 ± 6.2 and 64.5 ± 11.6 years, respectively). The preponderance of somatic symptoms in elderly patients with ESRD in our population and with cancer in the other study, as picked up by the multiple somatic items in the BDI, may not be necessarily related.

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to depression [5]. We recommend caution with interpreting data related to the association of depression, as assessed by the BDI, and mortality, especially in the elderly.

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

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**Clinical treatment of polycystic kidney disease (APKD): do we need further suggestions from rodents?**

Sir,

The article by Renken et al. [1] recently published in this Journal describes the effects of sirolimus (SRL) in the PCK rat, a model resembling human adult polycystic kidney disease (APKD) in which mTOR inhibitors had never been tested. In this study, oral treatment with SRL (2 mg/kg up to 12 weeks) did not attenuate cyst growth nor the progression of interstitial fibrosis compared to untreated control PCK rats and resulted in an impressive rise in bilirubin concentration [1]. These ‘negative’ data are in line with those recently reported by two large clinical trials on APKD, in which treatment with mammalian target of rapamycin mTOR inhibitors did not substantially affect cyst enlargement nor renal function [2,3].

In preliminary studies on the same rat strain, we have tested two different SRL doses: 0.2 mg/kg/day or 0.15 mg/kg administered 5 days a week (2 days yes/1 day off), both by intraperitoneal route. The higher dosage of the drug (n = 6), commonly used in Han-SPRD rats [4], determined a significant reduction in cyst volume [−34% versus untreated PCK rats (n = 6), P < 0.001] but caused marked hyperbilirubinaemia, a drastic reduction in body weight gain and a significant decrease in renal function compared to control rats. Low-dose SRL-treated rats (n = 6) showed a better body weight gain with respect to the higher dosage (15.4 ± 4 g/week versus 7.57 ± 2.3 of high dose, P < 0.02) and, interestingly, the cystic area remained significantly lower (−32% versus control, P < 0.03), with a significant decrease of total number of cysts and their maximal diameter. This lower dosage and the peculiar administration schedule also preserved both liver and kidney function. Unlike Renken’s study, we also found a significantly depressed activation of phosphorylated mTOR and of S6K protein in treated rats (western blot analysis).

The different outcomes of the two studies certainly reflect varying experimental conditions, like SRL dosage and its administration route, that resulted in different trough levels (1.63 ± 0.25 ng/mL in our study and 0.61 ± 0.06 ng/mL in Renken’s study): this could also explain the lower inhibitory effect on mTOR and S6K protein observed by immunohistochemistry in the latter study. Why Renken’s rat showed hepatic toxicity remains less clear since this side effect was not observed in our animals despite higher trough levels of SRL (different administration schedule, intrinsic hepatic susceptibility?).

Therefore, the same drug may elicit different results on the basis of its dosage, its bioavailability, the length of its administration or the presence of specific genetic patterns; accordingly, the study by Renken et al. should not be considered negative rather ‘not positive’. This could be true in clinical studies, too.

Walz et al. observed a reduction in cyst growth in patients treated with everolimus (24 months), not associated with an improvement in glomerular filtration rate (GFR), but their patients started with a reduced GFR, (averaging 53 mL/min); patients of Serra’s study with a well-preserved renal function (mean GFR: 92 mL/min), conversely, showed no change in cyst volume nor in GFR after SRL treatment, but these latter patients were administered low doses of SRL (averaging 1.5 mg/day per os), only for 18 months. These peculiar methodological aspects might have precluded more favourable results.

Indeed, despite animal studies suggest that treatment with mTOR inhibitors should start very early (i.e. when renal fibrosis and compensatory renal hypertrophy are still absent) and that adequate doses of such drugs must be used, this policy seems unfeasible in clinical practice either for the cost of treatment and the unavoidable occurrence of side effects. Probably, we need further experimental preclinical studies addressed to find out specific associations of SRL with different drugs that may be administered in sequence and with long drug-free periods [5]: we are currently testing new anti-apoptotic agents and cyclic adenosine monophosphate inhibitors. We believe that this is the only way to partially overcome the obvious difficulties of clinical treatment that should be started early but must be safe and affordable in the long term.