ced chronic kidney disease, renal flare or salvage therapy), but with no significant differences. This is also a subgroup analysis, which binds us to be cautious of interpretations. Another subgroup analysis, with the same cautious interpretation[3], emphasizes that patients receiving CYC induction did significantly better with MMF compared to azathioprine (AZT) in maintenance (4.7 vs. 14.5 in relative risk of treatment failure). Along the same lines, though without achieving statistical significance, subjects who received MMF induction also presented better results with MMF than with AZT (relative risk 10.1 vs. 20.1 on treatment failure). On the American Nephrology Congress (November 2011, Philadelphia, USA) Appel GB mentioned, regarding the ALMS study, that "patients who were treated with CYC induction presented less treatment failure on the maintenance phase than patients treated with MMF, independently from the drug received on this second phase". I believe this is the part you mentioned on the Consensus Document. This statement would make us conclude that CYC induction adds an additional benefit regardless the immunosuppressive maintenance option. This a theme to be debated, although it can be subject to future research, and we should examine it with discretion given that it originated from a subgroup analysis.

2. There are few studies on the best immunosuppression in patients with LN and renal clearance (ClCr) <30ml/min, probably because reference studies with CYC excluded patients that presented stage 4 renal failure (RF), except for some involving a patient with creatinine of 4.8mg/dl[4] with not many details and no results subanalysis. Even so, we have relied on the suitability of CYC in patients with severe LN and RF, and thus have been captured in the Consensus Document.

The ALMS study[5] rated with a 4-5 score on the Jadad scale, included a total of 32 patients (8.7%) with ClCr <30ml/min, 20 (10.8%) in the MMF branch and 12 (6.5%) on CYC. In the total group of 370 patients, 122 had scarring on renal biopsy, 66 (35.7%) on the MMF branch and 56 (30%) on the CYC branch. Regardless the data, no differences were found between both groups in the main variable results, which measured the efficacy of immunosuppressive treatment in inducing response. Based on this data, every day more of us begin induction treatment for LN class III-IV-V still with stage 4 RF with MMF and especially if the patients are women in their childbearing years. Besides, this kind of patients are treated with steroid pulses, which will act more rapidly and effectively in reducing the acute inflammation in the renal parenchyma, awaiting the additional benefit and hoping that they would add the non-steroid immunosuppressants.

If we continue to recommend CYC in patients with creatinine >3mg/dl (or with crescents/fibrinoid necrosis on biopsy), I believe that we will be depriving them from the opportunity of treatment with a drug free of gonadal toxicity and preventing the possibility of obtaining evidence with MMF on cases of important reduction of glomerular filtration rate, as long as it is a individualized responsible decision.

Conflict of interest
The authors declare that there is no conflict of interest associated with this manuscript.

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B) BRIEF PAPERS ON RESEARCH AND CLINICAL EXPERIMENTS

On-Line haemodialfiltration versus high flux haemodialysis

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To the Editor:
The influence of convective techniques on the evolution of the dialysed patient's anaemia is controversial when compared with haemodialysis performed with high flux membrane and ultrapure bath. In many studies short-term benefits could not be found.[1] It is possible that the effect of convective technique on anaemia may require a longer development time. To analyse

this hypothesis, we have studied the anaemia evolution in the patients of our unit that have received uninterrupted treatment with posilutional on-line haemodiafiltration (OL-HDF) for at least 18 months.

OL-HDF was implanted in our Chronic Haemodyalisis Unit on July 2009. Between the initial date and March 2012 (date of study closure) a total of 128 patients with chronic kidney disease were treated. Among them, 36 (28%) received OL-HDF and the other 92 were treated exclusively with high-flux haemodialysis technique. we used biocompatible high-flux membranes (ultrafiltration rate >59ml/h/mmHg) and ultrapure dialysis bath on all patients.

Of the 36 patients receiving OL-HDF at some point in the period under review, we selected those who were treated with the convective technique for a minimum of 18 months. 11 patients have been recorded (OL-HDF group). As control group we have considered the 16 patients that at the time of study closure (31 March 2012) had been treated with hemodialysis for the previous 18 months (HD group).

Table 1 shows the data of both groups. Compared with the HD, the OL-HDF group is younger, has a lower proportion of males and more time on dialysis, although the differences did not reach statistical significance in any of these parameters.

Table 2 shows the evolution of the concentration of haemoglobin and the weekly dose of erythropoietin. The haemoglobin concentration remained stable in both groups during the study. Although the HD group started with a lower haemoglobin concentration, there was no statistically significant difference between the two groups at any time during the evolution. In the OL-HDF group, the weekly dose of erythropoietin began to decline after the sixth month of treatment, but the decrease only reached statistical significance at 18 months, when 5 of the 11 patients did not require erythropoietin. In the HD group, erythropoietin dose underwent no significant changes, and could not be removed from any of the patients. When comparing both groups, the difference in the dose of erythropoietin began to be statistically significant after 12 months of treatment with OL-HDF.

The effect of convection on anaemia in our patients was not detected until the sixth month of treatment, when we began to observe a decrease in the need for erythropoietin. When compared to the group of patients treated with hemodialysis, the difference in erythropoietin dose began to reach statistical significance from month 12. These results are similar to those observed in the long term by Peña et al.[2] With shorter periods of evolution it is feasible that the relevant effects on anaemia are impossible to observe.

Conflict of interest

The authors declare that there is no conflict of interest associated with this manuscript.

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Table 1. Patient data

	OL-HDF Group (n = 11)	HD Group (n = 16)	
Age (years)	67 ± 20	72 ± 14	P = 0.5273
Male/female	4/7	9/7	P = 0.5324
Time in dyalisis (months)	57 ± 32	46 ± 38	P = 0.4247
Diabetic nephropathy	2 (18%)	3 (19%)	
Real arterial flow	360 ± 28	301 ± 28	P = 0.0000
Session duration (h)	3.6 ± 0.2	3.6 ± 0.3	
Replacement value (l)	19.7 ± 2.7	-	

HD: haemodialysis; OL-HDF: *on-line* haemodialfiltration.

Table 2. Anaemia evolution

	OL-HDF Group						
	Basic	3 months	6 months	9 months	12 months	15 months	18 months
Hb g/dl	12 ± 0.8	11.5 ± 0.9	12.2 ± 1.4	12 ± 1.2	12 ± 1.1	11.9 ± 1.4	11.8 ± 1.3
EPO UI/Week	5705 ± 5432	5864 ± 4754	4682 ± 3642	4364 ± 4817	3909 ± 4283	3227 ± 3517	2432 ± 3256[a]

[a] P< 005 as compared to the basic.

	HD Group						
Hb g/dl	11.2 ± 1.5	11.3 ± 0.9	11.7 ± 0.8	11.5 ± 0.8	11.3 ± 1.2	11.1 ± 1	11 ± 0.9
EPO UI/Week	7563 ± 3596	7844 ± 4057	7969 ± 3663	7781 ± 4301	8219 ± 4665[a]	7938 ± 4312[b]	7594 ± 4991[b]

[a] P < 0.05; [b] P < 0.01 compared to group OL- HDF.

EPO: Erythropoietin; Hb: haemoglobine; HD: haemodialysis; OL-HDF:on-line haemodialfiltration.

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Chronic renal failure and peripheral arterial disease

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To the Editor:

It has been well established that both patients with chronic renal failure (CRF) and those with peripheral arterial disease (PAD) have increased the risk of death due to cardiovascular disease. Red blood cell distribution width (RDW) is a marker for mortality in patients with established cardiovascular disease. It has been demonstrated that for every 1% increase in RDW, the risk of death increases by 14%.[1] Increased levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) are also associated with increased cardiovascular mortality and morbidity rates in the general population.[2] With this in mind, we sought to evaluate RDW percentage and NT-proBNP levels in patients with peripheral arterial disease (PAD) with or without CRF.

We performed a cross-sectional observational study involving 40 patients with PAD (all in stage III or IV on the Fontaine scale), with no signs of heart failure. Of these, 17 had CRF and 23 did not, 33 were male and 7 were female, and the mean age was 68.03±11.10. The patients were evaluated upon admission to the vascular surgery department. After signing an informed consent form (study approved by the ethics committee), we compiled clinical, pharmacological, and laboratory values for each patient. NT-proBNP was measured using a solid phase radial partition immunoassay (Acute Care® for Stratus® CS, Siemens). Statistical analyses were performed using SPSS statistical software, version 15.0.

The 40 patients with PAD had the following mean values: body mass index: 26.32±4.71kg/m^2; systolic blood pressure: 133.82±19.10mm Hg; diastolic blood pressure: 75.78±11.30mm Hg; and heart rate: 78.18±10.95bpm. Fifty percent of the patients were active smokers, 82.5% were ex-smokers, 27 were diabetics, and 27 had hypertension. Upon dividing the patients based on the presence or absence of CRF, we found that patients with an MDRD4 score <60ml/min (mean: 41.57±11.38ml/min) were older (73.75±10.84 years vs 63.87±9.51 years; *P*=.007), more prone to hypertension (88.23% vs 57.14%; *P*=.02), and received treatment with beta blockers (52.94% vs 21.74%; *P*=.041) and angiotensin II receptor blockers (ARBs) (35.29% vs 21.74%; *P*=.038) at a greater rate than patients with an MDRD4>60ml/min (81.54±20.90ml/min), with no other differences found in terms of drugs administered. There were also no differences in terms of sex distribution, frequency of diabetes, or tobacco use between these two subgroups. As regards the objectives of our study, we found that patients with CRF had higher levels of NT-proBNP (2561.18±2526.95mg/dl vs. 805.48±1036.02mg/dl; *P*=.01) and a higher RDW percentage (15.54±2.27% vs 14.74±2.11%; *P*=.044) than patients with PAD and without CRF. The percentage of RDW was positively correlated with NT-proBNP levels (r=0.56; *P*=.001).

Based on these results, and despite the small number of patients examined, we could affirm that patients with PAD and CRF have higher levels of biological markers of morbidity/mortality than those with PAD and without CRF, which would imply a greater associated cardiovascular risk and perioperative risk[3] than in patients without CRF.[3] The finding of a positive correlation between RDW and NT-proBNP in these patients could suggest a possible association with cardiorenal syndrome. Further studies with more patients could affirm whether patients with PAD treated with beta blockers or ARBs have a higher rate of CRF.

Conflict of interest

The authors declare that there is no conflict of interest associated with this manuscript.

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