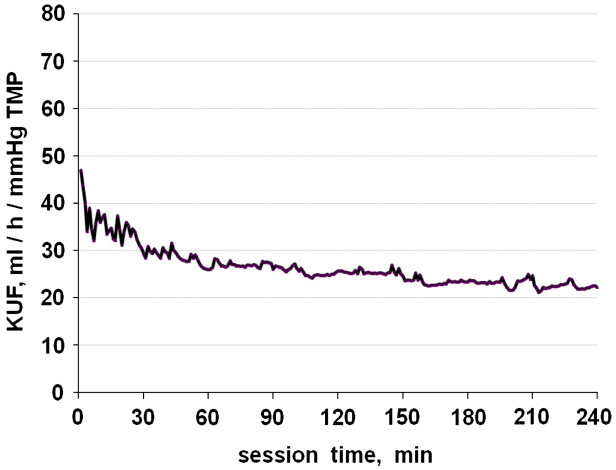

Fig. 1. Mean trend of the in vivo KUF (mL/h/mmHg) during post-dilution HDF in studies [2,3].

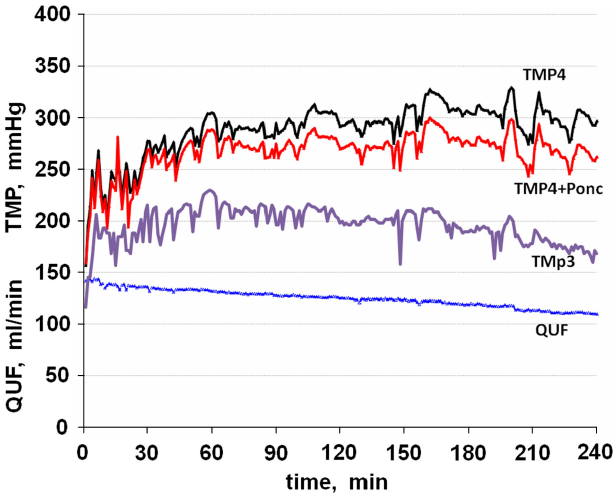

Fig. 2. Mean TMP trend (mmHg) during post-dilution HDF, as calculated with different methods. TMP4, 4-points TMP;TMP4+Ponc, 4-points TMP accounting for oncotic pressure; TMP3, 3-points TMP; QUF (mL/min), ultrafiltration rate.

Another pitfall implicit in the relation described by Ficheux *et al.* may result from the method of TMP calculation. If only three pressure points are known, the fourth one (inlet dialysate pressure) must be inferred or assumed, so introducing great variability related to dialyser characteristics and operational setting. The impact of the fourth point on TMP calculation is highly significant and the error is increased by disregarding the contribution of oncotic pressure (Ponc). In high-efficiency post-HDF, haemoconcentration inside the capillaries may double the protein concentration, and Ponc opposing filtration pressure may achieve values of 80–90 mmHg. Based on the same data as above, we could show that substantial differences arise from the different methods in TMP computation during post-dilution HDF (Figure 2). In conclusion, KUF max seems not to be a reliable index to characterize dialysers or modulate QUF during HDF. In addition, its identification would be cumbersome and its value highly variable between and within patients, as also admitted by the authors.

On the other hand, the authors disregard that efficient feedback systems to modulate QUF have already been implemented and validated experimentally on different HDF systems. Some of them provide continuous measurement and control of four-point TMP and allow maximal QUF to be safely achieved, accounting for effective blood flow, haematocrit changes (blood volume monitoring) and dialyser characteristics. This TMP/QUF feedback adapts QUF to the individual needs automatically and without the intervention of nurses whatever the patient and treatment operational conditions in different HDF modalities [3,5].

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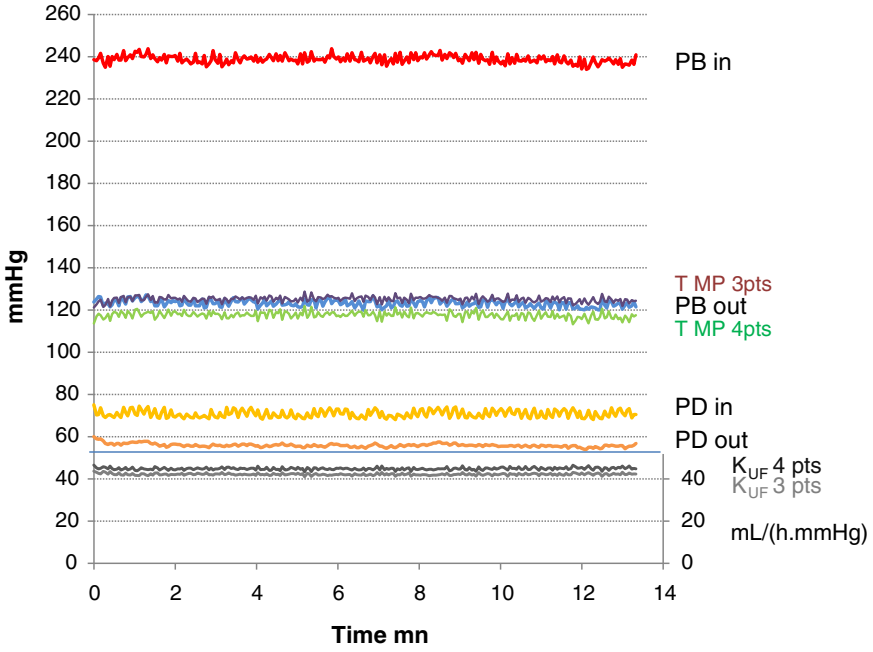
The ultrafiltration coefficient of a dialyser (KUF) is not a fixed value, and it follows a parabolic function: the new concept of KUF max

Sir,

We read with interest the comments on our work recently published in *Nephrology Dialysis Transplantation* and analysed in detail the data provided by Dr L Pedrini. We were aware of his excellent work and we had already quoted some of it in our paper (reference 25 of our manuscript) [1]. The figure provided in his letter presents the evolution over time of the KUF in their system, designed to maintain a constant QUF (ultrafiltration rate, which in that setting was particularly high). This is not related to the behaviour of a haemodiafilter in terms of transmembrane pressure (TMP), QUF and KUF, over a range of QUF or TMP, which represents the characteristics of the dialysis setting at an instant '*t*'. The QUF/TMP (KUF) over a QUF range depicts a parabolic curve. This is a new concept, reported in our study, which also applies to the system described by Dr Pedrini at every time point. There is



	Pbout	Pbin	Pdout	Pdin	TMP 3 pts	TMP 4pts	KUF 3 pts	KUF 4 pts	Qb	Quf
	mmHg	mmHg	mmHg	mmHg	mmHg	mmHg	mL/(h.mmHg)	mL/(h.mmHg)	mL/mn	mL/mn
Mean	123,2	238,9	55,9	70,9	125,1	117,7	42,2	44,9	313,5	88,0
SD	1,7	2,0	0,8	0,8	1,3	1,3	0,5	0,6	0,3	0,2

(TMP4mean-TMP3mean)/TMP3mean = -6,0%

Fig. 1. Recordings of the pressures at dialysate inlet (PD in) and outlet (PD out), as well as at blood inlet (PB in) and outlet (PB out) during a dialysis procedure. The TMP and KUF obtained using three- or four-point measurements are depicted. Note that the difference in pressure between the dialysate inlet and outlet (PD in to PD out) is ~15 mmHg. KUF increases by ~6% when obtained with four-point measurement compared to three-point measurement.

no pitfall in this point and it has simply not been measured (or perhaps reported) previously.

There was concern raised that two factors may be pitfalls in our work: not determining oncotic pressure and not measuring the fourth point of pressure in the dialysate inlet. Oncotic pressure is difficult to measure, and some authors choose to ignore it, some integrate it as a constant and some provide estimates according to different formulae. Other authors may change their approach in different work. Actually, the decline in QUF observed with an estimated oncotic pressure [2] was not observed when oncotic pressure was considered a constant [3]. As commented in our paper, we preferred to assess the global performances of the dialysis system (which integrate all the pressures the dialyser is submitted to and does not require knowing the precise value of its components across the membrane length within the dialyser). Indeed, regardless of the approach used, we understand that oncotic pressure does not impact on the difference in pressure between the dialysate inlet and the dialysate outlet. This difference is a function of the dialysate flow and viscosity as well as the physical characteristics of the system (Poiseuille equation); since viscosity, radius and length do not change in the dialysate side, it exclusively depends on dialysate flow, which is constant in haemodialysis and varies according to the infusion rate in haemodiafiltration.

Analysing the figure provided by Pedrini one can observe an increase in the difference between TMP-4 and TMP-3, which we supposed corresponds to the TMP obtained with the three-point measurements and the TMP obtained with the four-point measurements (adding the pressure at the dialysate inlet). This difference reaches values of 130 mmHg towards the end of the haemodiafiltration procedure. Thus, adding the measurement of the pressure at the dialysate inlet would influence TMP by 130 mmHg. Since the hydrostatic pressure on the dialysate side is the mean of the pressures observed at the inlet and at the outlet, respectively, this means that the difference between both would be 260 mmHg. We have measured this difference in studies that were not included in the paper and found that it was of the order of 15 mmHg at a dialysate flow of 500 mL/min, verifying the figures provided by the manufacturer. A drop in the dialysate side of 260 mmHg does not seem plausible (our Figure 1). Therefore, the TMP-3 plotted in the figure provided by Pedrini could not correspond to the measurements at three points that we reported (blood inlet, blood outlet and dialysate outlet) and renders the comparison not plausible and does not illustrate a putative pitfall to the determination of KUF in our system.

Finally, as we reported in our paper, the parabolic function observed with KUF over QUF was also obtained in a

setting where no dialysate was used and only three points were measurable. Obviously, the fourth point could not impact on these observations. We are therefore quite confident in the results that we reported.

We thank Canaud *et al.* for their comments as they provide some hypothesis to explain our findings. Most issues are covered in the previous section. The accuracy of the ultrafiltration pump is certainly not an issue as we have measured the precision of the total ultrafiltration in the dialysis setting and found an error <0.2%, as well as that of the infusion pump in the haemodiafiltration setting, which is <2%. We are sure that the new concept of KUF max, which we understand has provoked some surprises, will be adopted widely.

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Severe crescentic glomerulonephritis linked to an acute Hantaan virus infection?

Sir,

We read with interest the report by Soi Kim *et al.* [1], describing a case of acute crescentic glomerulonephritis (ACGN) with prolonged acute kidney injury (AKI), which the authors link to a concomitant 'hemorrhagic fever with renal syndrome' (HFRS), in this case, an infection with the prototype Korean hantavirus species, *Hantaan virus* (HTNV). Concerning the latter association, however, many questions arise as to its relevance and reliability: (A) The 'other various glomerular diseases reported in hantavirus infections' are in fact a total of 10 patients with membranoproliferative glomerulonephritis (GN), one with membranous GN and one with mesangioproliferative GN, all reported by J. Mustonen and his Finnish coworkers after, and not during, proven acute nephropathia epidemica (NE), i.e. a milder HFRS form with the prototype European hantavirus species, *Puumala virus*. Moreover, and in contrast with the Korean case, all Finnish cases relapsed with a rapidly emerging nephrotic syndrome 1 week to 3 months after complete remission from their acute NE, and appropriate therapy induced again in all, except one case, a complete remission [2]. (B) Oliguria apparently started already from Day 1 on post onset of symptoms (POS), which may be compatible with ACGN, but not at all with HFRS, where oliguria begins mostly at least 1 week POS, in a third phase after a prior fever and hypotensive phase [2–5]. (C) Myalgiae, a chief complaint and a presenting symptom in all Old and New World hantavirus infections, were apparently absent, suggesting an ACGN rather than an HFRS [3,5]. (D) Fever on admission (Day 4 POS) was only 37.3°C, compatible with ACGN but not with HFRS, where fever is between 38 and 41°C during several days [3,5]. (E) Thrombocytopenia, again in all Old and New World hantavirus infections, a cardinal presenting symptom, is not mentioned. Neither are the characteristic marked leukocytosis with a left shift nor the marked inflammatory parameters [2–5]. (F) Only IgG enzyme-linked immunosorbent assay (ELISA) was used for diagnosing a recent HTNV infection. Since IgG antibodies can persist for life, and since Korea is a country highly endemic for HTNV, a positive IgG does not necessarily mean a recent infection, even less so in a 70-year-old patient. In fact, a titer of 1:2048 is unusually high for a very recent infection and should have been confirmed by IgM ELISA and preferably by other molecular-based confirmation tests. The repeated IgG ELISA 3 months POS was higher by one more dilution only (1:4096) and cannot be used as conclusive proof for a recent infection. (G) The renal biopsy showed diffuse endocapillary proliferation, with frequent neutrophil infiltration, both features highly unusual for HFRS, where slight mesangial proliferation is often the only glomerular anomaly, if any [3–10]. Some NE cases might show swelling of the epithelial cells of the Bowman's capsule and/or adhesion of the glomerular tuft to the capsule, but crescent formation has indeed never been reported [2,3]. The most pathognomonic feature for HFRS, rupture of the peritubular capillaries with interstitial microhemorrhages in the outer medulla of the kidney, is lacking [3–5,8]. (H) Immunofluorescence (IF) staining of the glomerulus is often completely negative in HFRS, and if some IgM, IgG or C3 deposits are found indeed, they are considered aspecific, particularly after or during an episode of heavy proteinuria, which in HFRS is always aselective [4–6,8]. Predominant C3 and Ig A deposits are