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

Sir,
We read with much interest the article from Ficheux et al. [1] that appeared in advance access in Nephrology Dialysis and Transplantation on 8 September 2010. The paper describes a parabolic relationship between ultrafiltration coefficient (KUF) and ultrafiltration rate (QUF).

The falling KUF with increasing QUF is due to blood protein boundary effects (protein cake effect) and increased resistance to ultrafiltration and is well described in the literature [2].

Our group measured precisely this effect a decade ago in clinical studies using haemodiafiltration (HDF) [3] and showed that the continuous intravenous infusion of hypertonic glucose was able to reduce the decay of KUF [4]. The regulatory authorities recognize this variability of KUF and require its measurement at low QUF to avoid these boundary effects.

The rising KUF with increasing QUF (<60 mL/min) has not been shown in previous studies and is probably an artefact. In order to calculate KUF accurately, values for transmembrane pressure (TMP) and QUF are required. The study did not use an accurate method for measuring TMP. Three pressure transducers were used, whereas four transducers are required for accuracy [5]. TMP is not corrected for oncotic pressure as is required. The study assumed that the actual QUF delivered was the same as set on the machine. The ultrafiltration pump may lose accuracy under increasing load and this could explain the apparently rising KUF.

It is recommended that variations in KUF should be taken into account by the HDF monitor to optimize the treatment. Newer HDF systems such as those designed for mixed HDF already use the technology. They provide real-time continuous measurement of QUF and KUF. TMP is measured using four sensors and corrections are made for effective blood flow, total protein and haematocrit. This information is used to optimize the ultrafiltration rate by adjusting post- and pre-dilutional flow [5].

In conclusion, the only original finding of the paper, that KUF increases with increasing ultrafiltration rate up to 60 mL/min, may be incorrect and requires confirmation by more accurate measurement.

Conflict of interest statement. None declared.

1. Ficheux A, Kerr PG, Brunet P et al. The ultrafiltration coefficient of a dialyser (KUF) is not a fixed value, and it follows a parabolic function: the new concept of KUF max. Nephrol Dial Transplant 2010; doi 10.1093/ndt/gfq510 [epub ahead of print]

doi: 10.1093/ndt/gfq794

Transmembrane pressure, ultrafiltration coefficient and the optimal infusion rate in haemodiafiltration

Sir,
In their work published in NDT in advance access, 8 September 2010 [1], Ficheux et al., based on a parabolic relationship between dialyser ultrafiltration coefficient KUF and ultrafiltration rate QUF (KUF = QUF/TMP; TMP = transmembrane pressure), proposed the concept of KUF max, the highest QUF/TMP ratio (vertex of the parabola), as an index to optimize QUF during post-dilution HDF.

The relationship resulted from an experimental setting, unusual in clinical HDF practice, in which very low QUF...
(20–60 mL/min) were applied in the first part of the session. Here, back-filtration may have affected KUF calculation, as also admitted by the authors. Indeed, an increase in KUF during HDF sessions has never been reported in the literature. Instead, all previous studies demonstrated that KUF rapidly deteriorates just after the start of a HDF session due to the progressive thickening of the secondary membrane protein layer [2, 3].

Our experience, based on several hundred HDF sessions with different infusion modes and high-flux dialysers monitored online with four pressure transducers [3, 4], showed that the highest in vivo KUF always takes place through the intact membrane at the very early start of the session, during which KUF decreases slowly but progressively. This trend is shown in Figure 1, as a mean of the pooled post-dilution HDF session of our studies [3, 4].

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, haemococoncentration 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].

**Conflict of interest statement.** None declared.

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doi: 10.1093/ndt/gfq795
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 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

![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.](http://ndt.oxfordjournals.org/)

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\text{KUF}_{\text{4pts}} = (\text{KUF}_{\text{3pts}} + 6\%)
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\text{KUF}_{\text{3pts}} = \frac{(\text{TMP}_{\text{4pts}} - \text{TMP}_{\text{3pts}}) \times 6\%}{\text{TMP}_{\text{3pts}}}
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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.

Conflict of interest statement. None declared.

doi: 10.1093/ndt/gfq796