A prospective trial correlating clinical outcomes with ADAMTS-13 activity levels will clarify the role of replenishing ADAMTS-13 and/or removing inhibitors in determing TMA response to plasma therapy.

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Endothelial chimerism in association with vascular rejection in patients after kidney transplantation

To the Editor: Cell migration from the host to the transplanted organ results in chimerism in the organ [1]. Chimerism may be detected after gender-mismatched organ transplantation with use of fluorescence in situ hybridization [2]. To verify the endothelial chimerism, we studied kidney grafts with immunohistochemistry for ABO blood-group antigens and in situ hybridization for Y chromosome.

Four male recipients had received living kidney transplants from female donors. The blood type of the recipients was type A in all cases, and that of donors were type O in two cases and type B in two cases. Needle biopsies were performed from 2 to 5 months after kidney transplantation and diagnosed as vascular rejection. Endothelial cells stained with CD34 were positive for Y chromosomes, indicating the presence of recipient-type male cells. These endothelial cells were positively stained for recipient-type blood group A. The patients in the present study have shown that replacement of donor endothelium by recipient cells does occur in vascular rejection after kidney transplantation.

Lagaaij et al [3] have recently reported that grafts in which the endothelial cells are damaged by vascular rejection may incorporate host endothelium as part of the repair process. They speculate that host endothelial cells may be recruited from endothelial stem cells in the circulation. Further studies are required to clarify the mechanism of endothelial chimerism in association with vascular rejection after kidney transplantation.

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Risk factors for late kidney allograft failure

To the Editor: We congratulate Ponticelli et al [1] for an excellent paper regarding the evaluation of risk factors for late kidney allograft failure that recently appeared in *Kidney International.* However, we would like to suggest to the authors to see for the effect of nephron dosing on late allograft failure. Although the authors have evaluated body mass index (BMI) (>25 vs. ≤25) as a risk factor and found no significant effect. This may not have become significant as extreme BMI groups were not considered separately. Meier-Kriesche et al have observed in their study that the relative risk of graft loss death censored and uncensored was more in extremes of BMI compared to other categories. It was evident that of the extreme groups the relative risk of chronic allograft nephropathy (CAN) was significantly more in high BMI group [2]. We have observed in our study and it has been well reported by others that kidneys with insufficient nephron mass for the recipient may be damaged by hyperfiltration injury resulting into proteinuria and CAN [3–5]. Thus we feel that if authors can analyze nephron dosing in addition to other well studied risk factors in this cohort, it would be a significant contribution to the literature.

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Reply from the Authors

We thank Drs. Udgiri, Kashyap, and Minz for their comments and suggestions. However, the data of Meier-Kriesche et al referred to a retrospective analysis of 51,927 renal transplants registered in United States Renal Data System (USRDS). Our data were drawn from a single center experience on quite a smaller number of patients. Only one of our patients had a body mass index (BMI) higher than 36 kg/m^2, which according to Meier-Kriesche, has the highest risk of graft failure. After 14 years, the allograft of this patient is still functioning with a serum creatinine was 2.0 mg/dL. We considered another 14 patients with BMI higher than 30 kg/m^2. Their graft survival probability at 15 years was 92.8%, their median serum creatinine at the last visit was 1.4 mg/dL (0.9 to 2.9 mg/dL), by excluding the only patient who returned to dialysis.

On the other hand, Meier-Kriesche et al interpreted with caution their own data. They pointed out that it was difficult to ascertain whether the poor death-censored graft survival in obese patients was attributable to nephron underdosing or whether it was an obesity-related comorbidity jeopardizing the graft, such as obesity and hypertension. Moreover, they found that also a low BMI increased the risk of late failure. It is difficult to advocate any role for an insufficient nephron mass in the latter patients.

Although the potential role of nephron underdosing in chronic allograft nephropathy (CAN) is intellectually attractive and worth of further investigation, we think that the risk of glomerular hyperfiltration caused by an inadequate nephron mass of the donor is overwhelmed by many other more relevant risk factors.

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Bitter pill it is, but frequent hemodialysis more than thrice weekly may be the answer

To the Editor: The article of Lowrie, Ofsthun and Lazarus [1] interests us as it relates to two of our recent publications [2, 3]. Few will disagree that *under*dialysis is a significant risk factor for death, including small or underweight patients. The survival hazard (RR) depicted in their Figure 1 showed, unlike other body measures, an upturn for body mass index (BMI) >34, and *only* when adjusted. Although not surprising, this finding is new, and provision of more information on patient numbers, case-mix characteristics, and statistical significance between adjusted and unadjusted groups, particularly in the >34 BMI category, would help the readers to better understand the ramifications of this finding.

Figure 3 in the paper of Lowrie, Ofsthun, and Lazarus [1] supports the statement that small and underweight patients are susceptible to underdialysis. However, it should be noted that given the current practice of hemodialysis in the United States, it would be uncommon to find a small or underweight patient receiving lower dose of dialysis; for instance, the frequency of underweight patients with a standard prescription Kt/V of <1.2 was <1% in a recent study [3]. When standard prescription of hemodialysis is applied, dialysis dose, as expressed as Kt/V or urea reduction ratio (URR), is *predictably* higher in small and underweight patients than normal or overweight patients. Thus, it is more common to see underweight patients receiving more dialysis than overweight and obese patients [3]. Despite this information, underweight patients have a higher mortality, and conversely, despite underdialysis, overweight patients tend to have a better survival [3]. The point is that once the patient receives a certain amount of dialysis, the survival is less dependent on dialysis dose delivered per treatment, but more to factors such as nutrition and comorbid conditions.

Thus, the extremely low Kt that is used by Lowrie, Ofsthun, and Lazarus in underweight patients to demonstrate the deleterious effect of underdialysis in such patients is outside the range obtained in regular clinical practice. Therefore, we are concerned that the reported results of the statistical analysis may be based on extrapolation outside the plausible data with a few cases that may exhibit undue influence on the regression. We think