About the manuscript of Nishitani Y *et al.* (*Kidney Int* 2005; 68: 1078–1085)

Kidney International (2006) **69**, 1092. doi:10.1038/sj.ki.5000178

To the Editor: In IgA nephropathy patients, Nishitani *et al.*[1] prospectively tested the association between the number of fibroblast-specific protein 1-positive ($FSP1^+$) fibroblasts in the renal interstitium and incident renal outcomes (i.e. doubling in baseline serum creatinine or end-stage renal disease), and concluded that staining $FSP1^+$ in renal biopsy specimens provides a valuable histologic index of progression.

The study is of interest and well conceived, but there are major statistical problems to clarify to better understand its potential clinical implication:

1. Apparently, the authors did not consider the treatment imbalance (corticosteroid/renin–angiotensin system antagonists) between the study groups ($FSP1^+$ above and below 20%) because no allowance for this potential confounder was made in the multivariate analysis.
2. Over 8 years of follow-up, only 38 out of 142 patients with IgA nephropathy exhibited adverse renal outcomes. Have the authors considered as renal outcome for the Cox analysis in Table 4 the doubling of serum creatinine alone ($n = 24$) or both doubling of serum creatinine and end-stage renal disease ($n = 38$)? In any case, multivariate Cox regression analysis in this study was overtly underpowered, because at least 100 events would have been required to assess the independent prognostic value of the 10 covariates included into the Cox analysis (i.e. one variable every 10 events in the model)[2]. Thus, the small number of events in this study precludes the drawing of firm conclusions, and for this reason, more powerful studies are needed to determine the prognostic value of $FSP1^+$ in IgA nephropathy patients.

1. Nishitani Y, Iwano M, Yamaguchi Y *et al.* Fibroblast-specific protein 1 is a specific prognostic marker for renal survival in patients with IgAN. *Kidney Int* 2005; **68**: 1078–1085.
2. In: Hosmer Jr DW and Lemeshow S (eds). *Applied Survival Analysis: Regression Modeling of Time to Event Data*. Wiley-Inter-science: New York, 1999.

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Response to Parlongo *et al.*

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We thank Drs Parlongo, Tripepi, and Zoccali for their query regarding the statistics in our paper. We feel pretty comfortable with our original analyses based on the biostatistical advice given during their preparation. Technically speaking, all clinical studies never have enough power. The power of a study, however, is usually of concern when no differences are observed – this was not the case in our study.

To answer the new questions asked by our correspondents, in our original report, we performed multivariate analyses for clinical parameters and for histologic parameters separately; therefore, the number of covariates is not 10, but 5. Because of further questions about number of events, we performed two additional Cox analyses with advice from our statistician. First, using two covariates and every possible combination ($FSP1^+$ fibroblasts/HPF versus gender, age, serum creatinine, hypertension, sclerosis, proliferation, fibrosis, or smooth muscle actin). In all analyses, $FSP1^+$ fibroblasts/HPF were higher and a more significant risk factor for progression to renal failure (range of relative risk for >20 $FSP1^+$ fibroblasts/HPF: 8.8–16.1; $P \leqslant 0.0001$). Second, to consider the effect of any treatment imbalance, we performed Cox analyses using three parameters, ($FSP1^+$ fibroblasts/HPF, hypertension, with or without RAS blockers – ACEI, ARBs, or both) and ($FSP1^+$ fibroblasts/HPF, hypertension, with or without corticosteroid). In all cases, the presence of $FSP1^+$ fibroblasts/HPF was still the higher and more significant risk factor.

Our additional data confirm the significance of increasing numbers of $FSP1^+$ fibroblasts/HPF as a prognostic factor of IgA nephropathy, and our findings strongly suggest our conclusions may have predictive value.

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