The increased incidence of malignancy in renal allograft recipients has been well documented; renal tumours are reportedly more than twice as common in this group than in the general population [1]. Whilst most renal malignancies arise in native kidneys, a small but significant proportion arise within transplanted kidneys. In a retrospective series of 10 997 renal transplant patients, 16 recipients (0.145%) developed allograft tumours, all of which were renal cell carcinomas [2]. Results from the Cincinnati Transplant Tumour Registry report a higher incidence of 0.32% in 7596 kidney recipients [3]. Whilst most renal allograft tumours present within the first 7–10 years following transplantation, there are a few reports of late tumour presentation [2,4–6]. The longest published interval prior to this case, to our knowledge, is 21 years [6]. Here we report the development of an allograft tumour after 27 years. We believe this represents the longest reported interval between transplantation and tumour presentation, to date. The increased risk of malignancy, late presentation and aggressive course following allograft tumour development has prompted a recent call for lifelong ultrasound screening of renal allografts [7]. This case reinforces the view that if screening is to occur, it will be required for the life of the graft or at least until it is removed.

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ACE genotype and long-term graft survival after renal transplantation

Sir,

Slowinski et al. [1] report that the angiotensin-converting enzyme (ACE) (I/D) recipient genotype has no impact on the occurrence of renal graft dysfunction in 405 Caucasian kidney graft recipients.

In their discussion they refer to the Lancet review by Colhoun et al. [2] on the problems of reporting genetic association studies in disorders with complex outcomes and underline the importance of the publication of negative results in order to avoid publication bias.

Surprisingly, however, they do not cite my group’s paper on 435 kidney recipients that showed the D allele of the recipient ACE genotype to be associated with an increased risk for graft loss in high-risk patients, i.e. a 2.5-fold increased risk in subjects with a creatinine clearance of <50 ml/min at 1 year after transplantation and a 3-fold increased risk in subjects with proteinuria of >0.5 g/24 h. Donor genotype had no effect on the risk for graft loss [3].

Renal function loss is doubtless a complex trait. To unravel the role of possible genetic factors involved, proper understanding of the multifactorial nature of renal function loss is required. Our paper illustrates that it would be naïve to study genetic risk factors as isolated entities and that integration of genetic data with the available knowledge on pathophysiology and on phenotypic risk factors would be more likely to generate relevant insights into the role of genetic factors in renal damage. The authors are apparently aware of this, as they mention the possible importance of epigenetic interaction with factors determining RAAS activity, without, however, identifying such interactions in their study. Studies from my group have consistently identified sodium intake—a main determinant of RAAS activity—as a factor that modifies the impact of the D allele on the renal phenotype in different settings, namely proteinuric patients [4], healthy volunteers [5] and uncomplicated diabetics [6]. Unfortunately, data on sodium status are lacking in almost any clinical study on ACE genotype. For proper interpretation of data from association studies, every effort should be made to obtain data on the factors that can interact with the candidate gene and to take into account their effect. Proper consideration of such interacting factors, in particular if these are modifiable factors such as sodium intake, not only will allow more insights to be obtained from the study, but may also lead the way to intervention in genetically conferred renal risk.

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