Combination of area under curve of estimated glomerular filtration rate for 2 years and annual rate change of estimated glomerular filtration rate predicts long-term graft survival in kidney transplants

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Objectives:

Improvement of short term outcomes in kidney transplant (KT) has required clinical trials to evaluate long-term hard outcomes for validation of new therapies. Because of difficulty in conducting clinical trials using hard outcomes, the use of surrogate marker should be considered. We examined the possibility of the combination of area under curve of estimated glomerular filtration rate for 2 years (AUCeGFR2yrs) and % change in estimated glomerular filtration rate (eGFR) between years 1 and 2 after KT as a surrogate marker for long-term graft failure.

Methods:

We studied 1423 kidney transplants performed from 1996 to 2013 at Samsung Medical Center, Korea, including 202 graft losses and 54 deaths. Combination of AUCeGFR2yrs (>1300 ml/min/month vs < 1300 ml/min/month) and % change in eGFR (> 2% vs < 2%) was assessed to determine risk of graft failure using Cox proportional hazard analysis.

Results:

The combination was significantly associated with graft failure (p < 0.0001). Patients with AUCeGFR2yrs < 1300 ml/min/month and % change in eGFR < 2% formed 16.7% of all patients and showed higher graft failure risk (hazard ratio [HR], 3.36; 95% confidence interval [95% CI], 2.52 to 4.48). The Harrell C-index of the combination was 0.65 (95% CI, 0.60 to 0.69), and was internally validated via 5-fold cross-validation (average Harrell C-index, 0.64; 95% CI, 0.60 to 0.68). We also evaluated > 30% decline in eGFR between years 1 and 3 after KT. The incidence of > 30% decline in eGFR was 6.9% of patients. HR of graft failure was 7.18 (95% CI, 5.22 to 9.89) and Harrell C-index was 0.65 (95% CI, 0.63 to 0.66).

Conclusions: We conclude the proposed combination might be useful as a surrogate outcome in KT trials in that it requires shorter surveillance period (2 years) than the known surrogate marker (3 years) while having comparable predictability.