Urinary tissue inhibitor metalloproteinase-2(TIMP-2) · IGF-binding protein-7(IGFBP7) predict delayed graft function after kidney transplantation

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BACKGROUND & AIMS

Recently, urinary TIMP-2 and IGFBP-7, markers for G1 cell cycle arrest, have been identified and validated in predicting the development of AKI in critically ill patients. It is unknown, however, whether these two biomarkers could predict the development of delayed graft function (DGF) after kidney transplantation.

SUBJECTS & METHODS

This is a single center, prospective observational study. We enrolled 50 patients who underwent KT (living donor: 5, deceased donor: 45) between August 2013 and December 2015. Urine sample were collected right after the operation. The primary outcome was development of DGF as defined by need for dialysis of more than 1 session within 7 days of KT. .

RESULTS

Nine patients (18%) were diagnosed as DGF. In univariate analysis, kidneys from expanded criteria donors, donor serum creatinine, donor estimated glomerular filtration rate (eGFR), urinary IGFBP-7 and TIMP-2 were significantly different between early graft function (EGF) and DGF. However, in multivariate analysis adjusting for effects of donor eGFR only IGFBP7 x TIMP-2 at 0 hour post transplantation could predict the development of DGF. The receiver operating characteristic curve for prediction of DGF showed an area under the curve of 0.77 (sensitivity 0.77, specificity 0.81) for a cut off value of 1.76.

Figure 1. and Table 3. The receiver operating characteristic analyses for post operation 0-hour urinary IGFBP7, TIMP-2, [TIMP-2]*[IGFBP7].

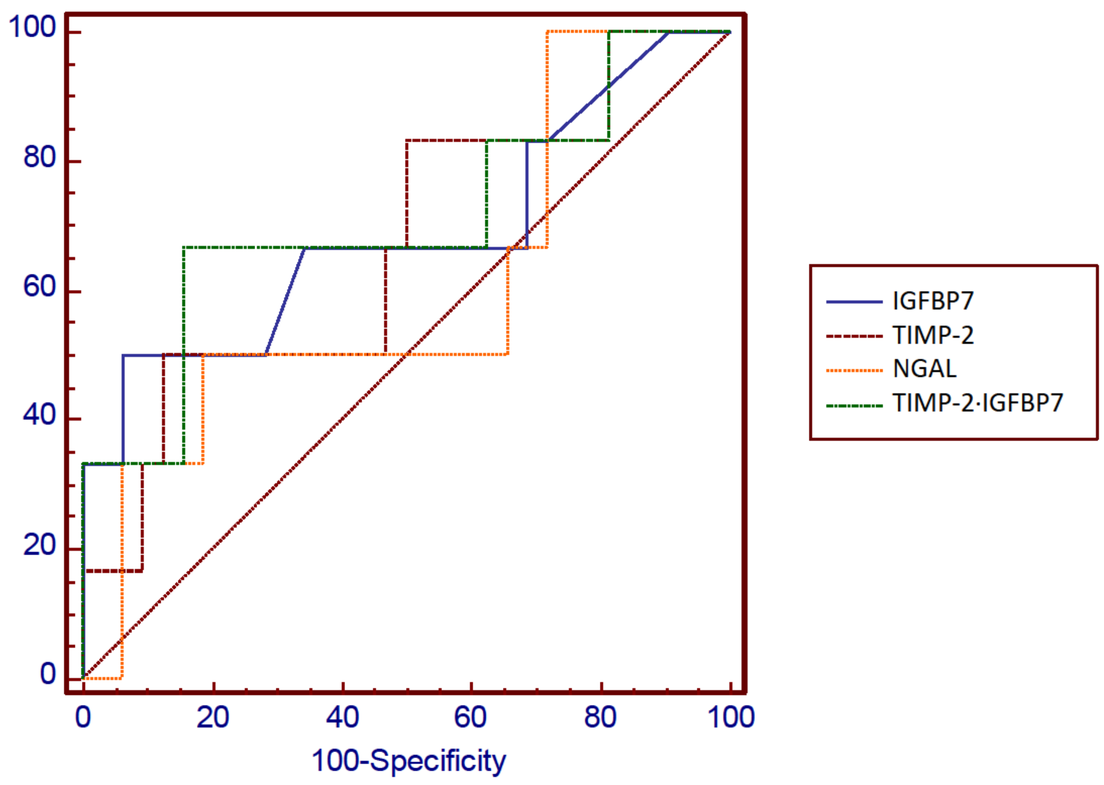

Table 1. Dermographic factor for DGF and EGF

	EGF (38)	DGF (9)	p-value
Age (years)	48.3 ± 11.5	50.4 ± 13.2	0.662
Gender (male)	26 (68%)	7 (77%)	0.503
BMI (kg/m²)	24.2 ± 3.2	21.3 ± 8.1	0.101
Dialysis mode(HD)			
Cause of ESRD			
HTN	7	0	
DM	10	10	
GN	3	1	
unknown	13	3	
HTN	30 (90.9%)	13 (92.9%)	0.999
DM	12 (36.4%)	9 (64.3%)	0.112
Expanded criteria	9 (29%)	10 (71.4%)	0.011
Donor age	48.4 ± 13.6	45.4 ± 13.5	0.571
Donor creatinine	1.39 ± 1.0	2.82 ± 1.8	0.005
Donor eGFR	75.9 ± 37.3	42.8 ± 31.6	0.025
Cold ischemic time	194.3 ± 157.9	245.4 ± 185.1	0.461
Warm ischemic time	26 ± 9.1	42.3 ± 48.5	0.056
HLA mismatch	3 ± 2	2.5 ± 1.6	0.465
1 month SCr (mg/dL)	1.3 ± 0.6	2.91 ± 2.0	< 0.001
IGFBP7	13.6 ± 20.3	231.3 ± 435.2	0.003
TIMP-2	3.5 ± 5.8	16.7 ± 19.5	0.001
NGAL	409.4 ± 284.1	463.1 ± 353.5	0.736
[TIMP-2]·[IGFBP7]	1.16 ± 0.7	2.27 ± 1.2	0.001

Table 2. Multivariate logistic regression analysis for predicting delayed graft function.

	Odds ratio	95% CI	p-value
[TIMP-2]·[IGFBP7]	4.494	1.41-14.36	0.011

CONCLUSION

Our results indicate that urine IGFBP7 x TIMP-2 immediately after transplantation could be an early, predictive biomarker of DGF in kidney transplantation.

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