URINARY KIDNEY INJURY MOLECULE-1 MONITORING CAN PREDICT ACUTE TUBULAR NECROSIS IN LIVING DONOR RENAL TRANSPLANT RECIPIENT

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Delayed graft function

o Long term outcomes of the allograft depend on early function of the graft

o Delayed Graft Function (DGF) is defined as an early requirement of dialysis within the first week of transplant, decrease in urine output and increase in serum creatinine. It occurs primarily because of acute tubular necrosis and has been reported to be associated with greater incidence of acute rejection and poor graft survival.

o DGF occurs in 3-40% cases of deceased donor and 5-10% of living donor renal allograft recipient.

o After Ischemia, reperfusion leads to increased generation of free reactive oxygen species (superoxide, nitrous oxide, peroxi nitrite) consequently lead expression of Transcription factor NF-kB and c-Jun in endothelial cell.

o These transcription factor induce expression of IL-6, IL-1α, cyclo oxygenase (Cox-2) and ICAM-1, CD40, Heat stable antigen on endothelial cell of renal tubules

o DGF is consequences of renal ischemia injury, an renal injury to tubules that induce recruitment of CD4 and CD8 T cell

o The level of KIM-1 in urine is reported to be associated with degree of extent of tubular damage
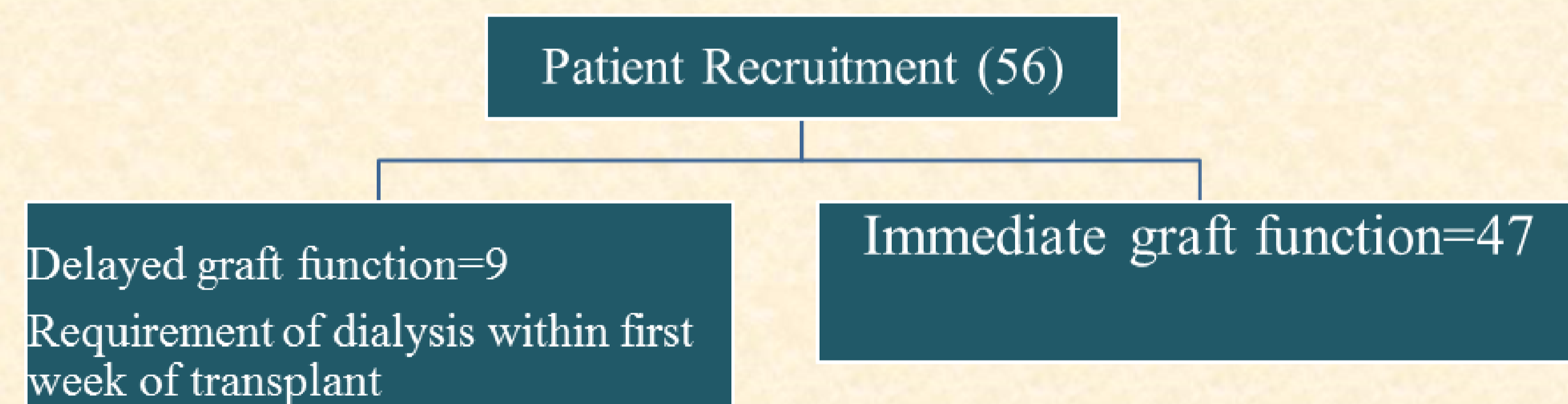
Kidney injury molecule-1 (KIM-1)

✓ A single pass transmembrane glycoprotein
✓ Have Immunoglobulin like and mucine domain in its ecto domain which get cleave and release in urine, thus a sensitive marker

Objectives

➢. To analyze the suitability of uKIM-1 as highly specific, sensitive and early markers of delayed graft dysfunction
➢ To determine a cutoff value of uKIM-1 to predict early and delayed graft dysfunction in live related renal transplant.

Material and method

Patient Recruitment (56)

Delayed graft function=9
Requirement of dialysis within first week of transplant

Immediate graft function=47

Six sample of urine of each patient was collected in sterile urine collection vials at 1,6,12,18, 24 and at 48 hrs. A Sandwich ELISA was performed with urine sample by using R&D system duo set ELISA kit (R&D DY 1750 Minneapolis) for KIM-1.

Results

Patient characteristics

| Characteristic	DGF(Mean±SD)	IGF(Mean±SD)	P value
No. of patient	9	47	
Pt. age	38.0±12.94	39.68±11.86	0.702
Pt. Wt	63.11±7.76	54.31±8.40	0.005
Pt. Height(Cm)	166.33±2.73	165.63±6.33	0.749
Pt. BMI	22.93±2.81	19.74±2.85	0.003
Pt. eGFR	40.35±14.43	65.39±16.91	<0.001
Do. Age	44.00±18.17	47.87±9.29	0.755
Do. GFR	41.89±12.05	45.10±14.84	0.546
Overage seven days TLC	8.88 ±1.06	8.22 ±1.97	0.886
Overage seven days Serum c	2.23 ±0.798	1.37 ±0.44	<0.001
Overage seven days Urine(liter)	5.21 ±1.98	7.29 ±2.19	0.029
Warm ischemia time(Minutes)	15±5.6	15±6.8	NS

Level of uKIM-1 was significantly high in DGF compare to IGF at different hours of transplant

Sr. No	uKIM-1	DGF(Mean±SD)	IGF(Mean+SD)	P Value
1	<0.5 hrs	53.66±37.47	17.14±48.12	0.036
2	6hrs	194.11±53.34	143.24±50.72	0.008
3	12hrs	426.11±115.07	194.24±66.42	<0.001
4	18hrs	520.22±120.09	252.05±76.33	<0.001
5	24hrs	674.77±318	316.6±89.23	<0.001
6	48hrs	652.66±207.4	336.21±123.4	<0.001

uKIM-1 at 18 hrs of transplant is the best predictor for delayed graft function

No	Time after transplant	Area Under curve	Specificity %	Sensitivity %	Predictive cutoff value (pg/ml)	P value
1	<0.5 Hrs of transplant	0.882	77.8	85.1	20	<0.001
2	6 Hrs of transplant	0.762	88.9	57.4	146	0.013
3	12hrs of transplant	0.960	88.9	87.2	278	<0.001
4	18 hrs of transplant	0.953	88.9	91.5	347	<0.001
5	24 hrs of transplant	0.924	88.9	76.6	390	<0.001
6	48 hrs of transplant	0.895	88.9	57.4	345	<0.001

Receiver operating curve (AUC-ROC) for uKIM-1 to predict the delayed graft function.
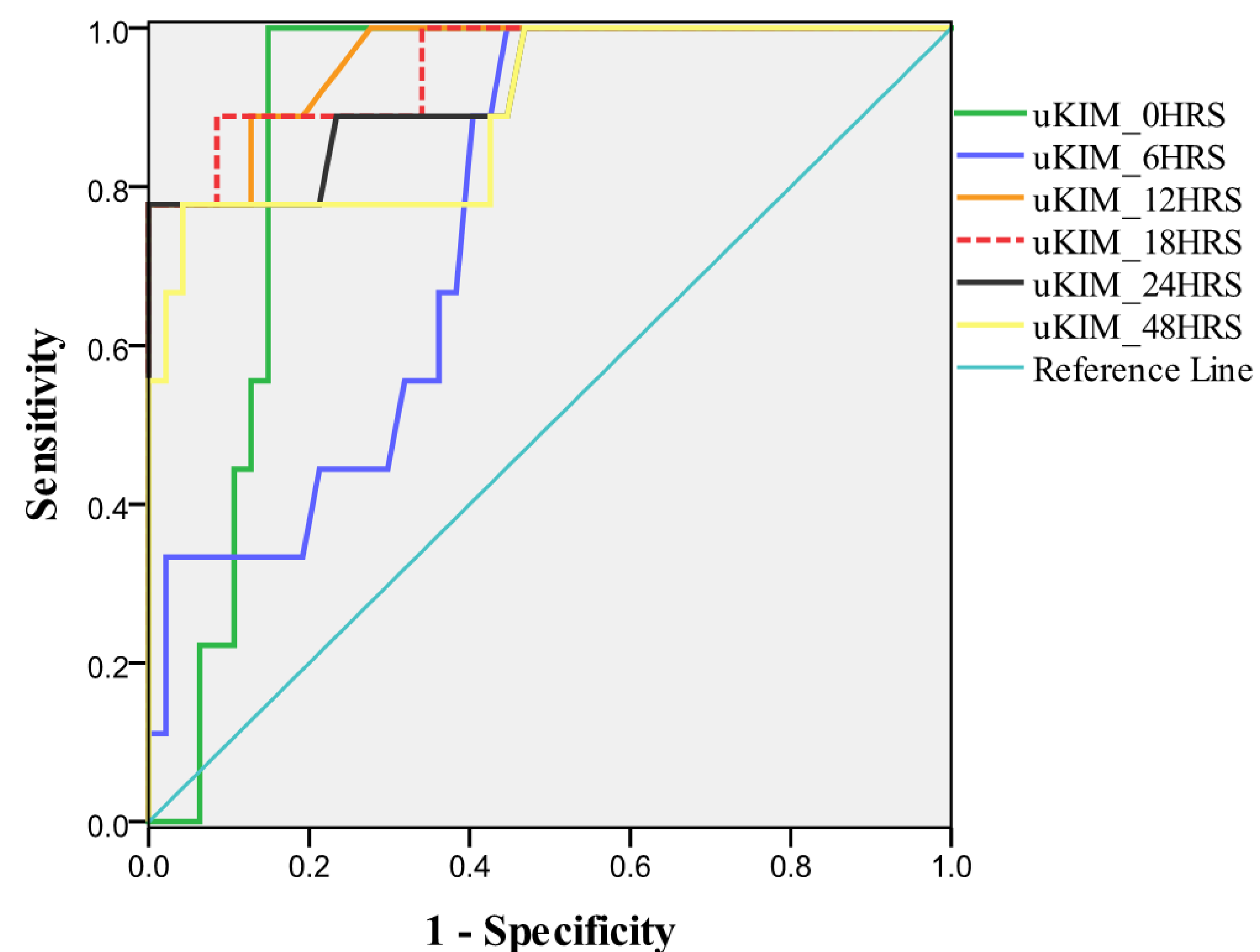
Conclusions

1. uKIM-1 is highly sensitive and specific marker for delayed graft function in living donor renal transplant recipient

2. uKIM-1 at 18 hrs is the best predictor of DGF

3. The cut off value for uKIM-1 to predict IGF and DGF is 347pg/ml in live related renal transplant recipient

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