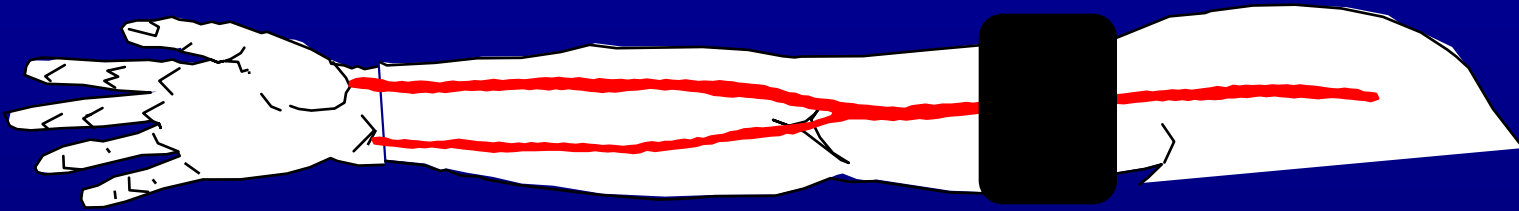


RIPC In Renal Transplantation

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UK**

Human forearm IR-injury model



Normal



Ischaemia (20 mins)



Reperfusion (20 mins)

IR Injury in Renal Transplantation

**IR injury unavoidable consequence
inherent to the process of renal Tx**

**Prolonged ischaemia time is associated
with delayed graft function (*Ojo et al, 1997*)**

**Delayed graft function is associated with
poorer long-term outcome**

RIPC and the kidney

Kidney transplantation provides a good model for exploring the potential of RIPC

Scheduling is convenient, uniform injury, validated endpoint of clinical importance

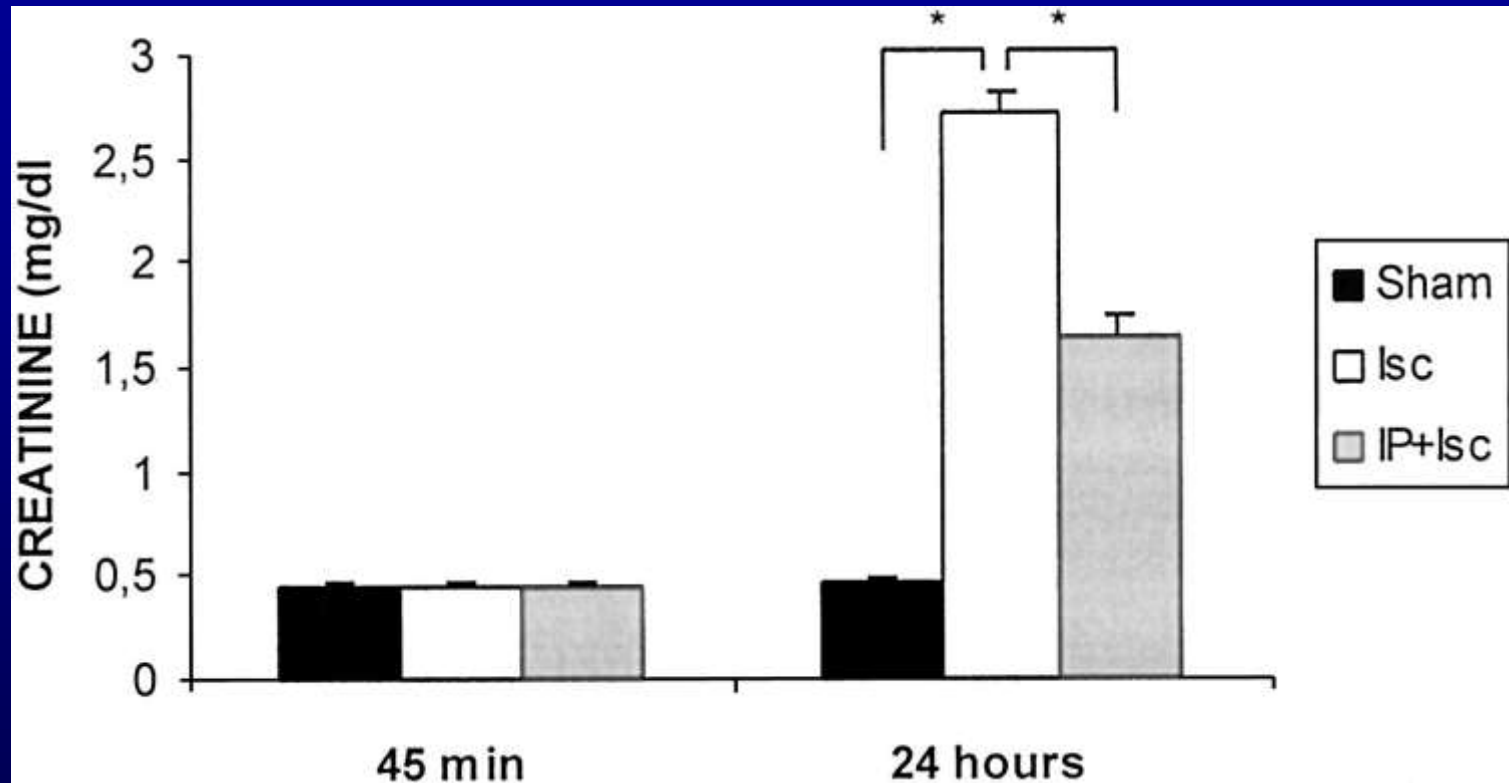
Trials of manageable size fo tractable and fundable

Possibility of getting tissue for mechanistic studies

Potential to study ischaemic and reperfusion phases of injury

Potential to study early and late windows of protection

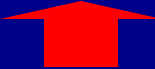
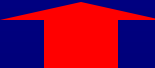

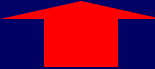
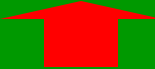
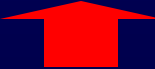
Effect of RIPC induced by liver ischaemia on experimental ischaemia-reperfusion injury of the kidney



Might remote IPC protect the kidney in renal Tx?

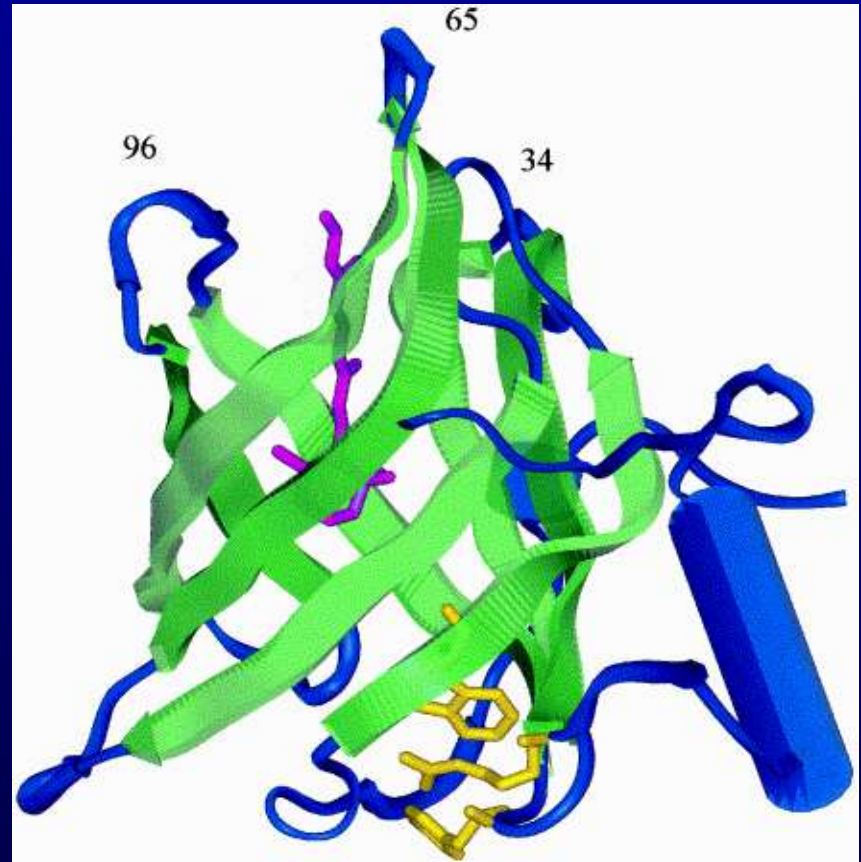


Surrogate markers of renal IR injury

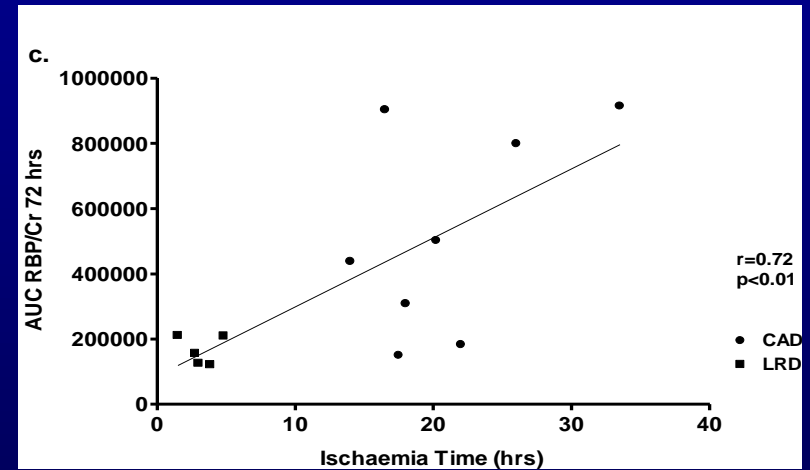
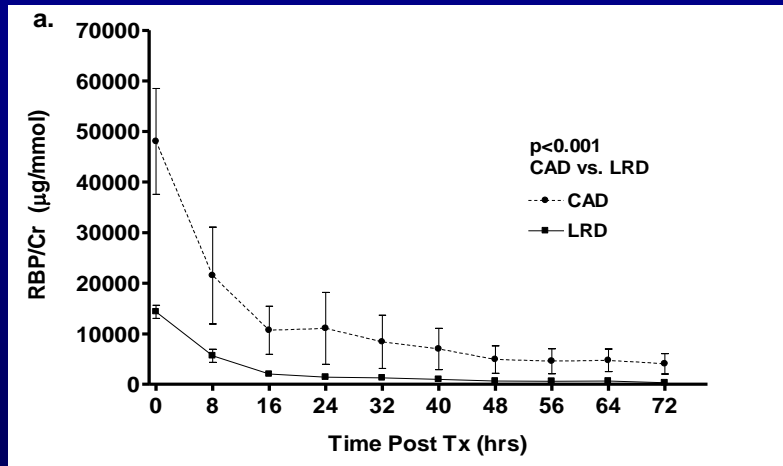
Compound	Measured in Urine?	Measured in Plasma?	Effect of IR injury
TMAO	Yes	Yes	
DMA	Yes	No	
Citrate	Yes	No	
Lactate	Yes	No	
RBP	Yes	No	
β NAG	Yes	No	

Retinol Binding Protein (RBP)

- Low molecular weight protein (MW 21,200 Da).
- 99.9% reabsorbed by the proximal tubule.
- Measured by enzyme-linked immunosorbent assay (ELISA).



Urine RBP after paediatric renal transplantation



a. Donor

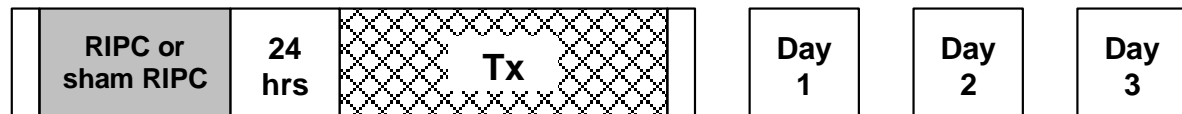


↑
Pre harvest
Blood/Urine

➤ RIPC induced by 3 x (5 min I / 5 min R) of the arm

➤ Operator performing sample analysis was blinded to group allocation

b. Recipient



↑
Pre Tx
Blood/urine

↑ 0 ↑ 8 ↑ 16 ↑ 24 ↑ 32 ↑ 40 ↑ 48 ↑ 56 ↑ 64 ↑ 72

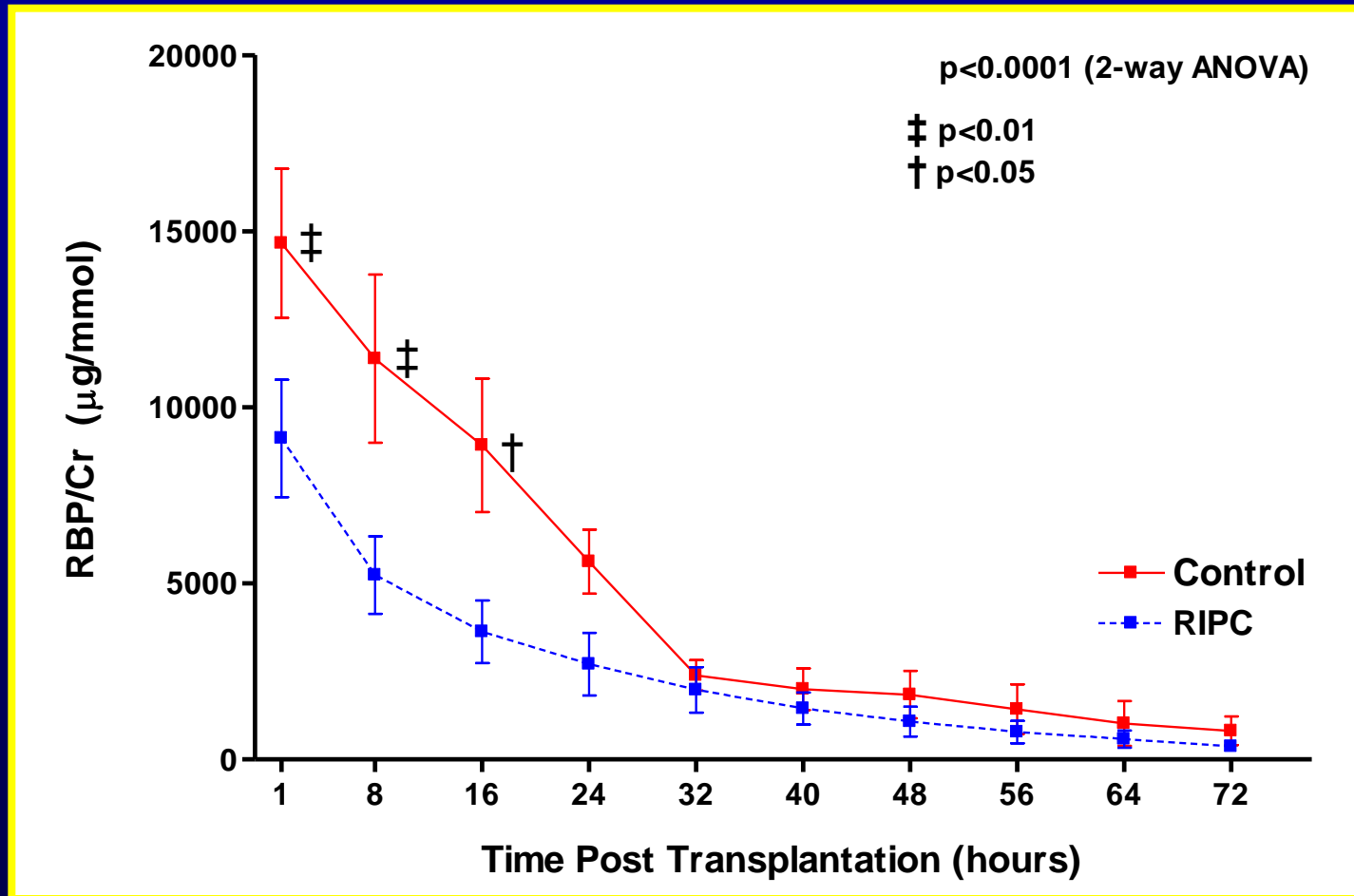


Hours Post Tx

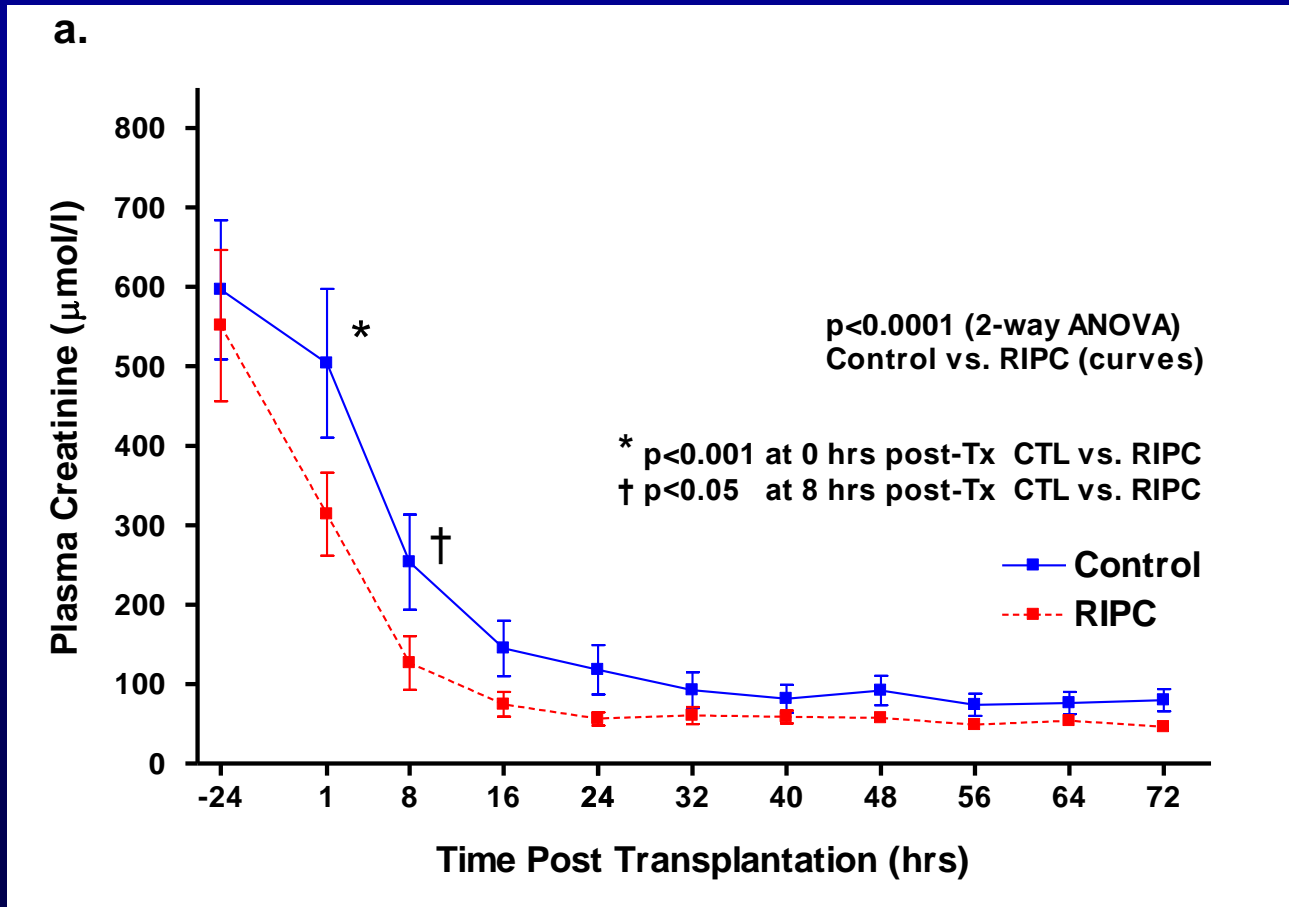
Patient baseline characteristics

	Control (<i>n</i> =11)	RIPC (<i>n</i> =11)
Sex (m/f)	7/4	6/5
Recipient age (years)	10.6 (1.5)	10.0 (1.6)
Donor age (years)	40.7 (2.4)	41.6 (2.4)
Recipient body mass index (kg/m ²)	19.6 (0.8)	20.0 (1.9)
Type of renal disease (congenital/acquired)	10/1	8/3
Pre-transplantation dialysis (on dialysis/total)	7/11	8/11
Native kidney(s) in situ (n/total)	9/11	9/11
Recipient urinary RBP pre-transplantation (µg/mmol of creatinine)	9.9*10 ³ (2.6*10 ³)	9.4*10 ³ (2.1*10 ³)
Donor urinary RBP pre-harvest (µg/mmol of creatinine)	10.8 (1.8)	8.7 (1.5)
Recipient plasma creatinine pre-transplantation (µmol/l)	599 (97)	556 (93)
HLA mismatch	2.6 (0.2)	2.3 (0.3)
Cold ischaemia time (hours)	2.5 (0.5)	2.3 (0.5)

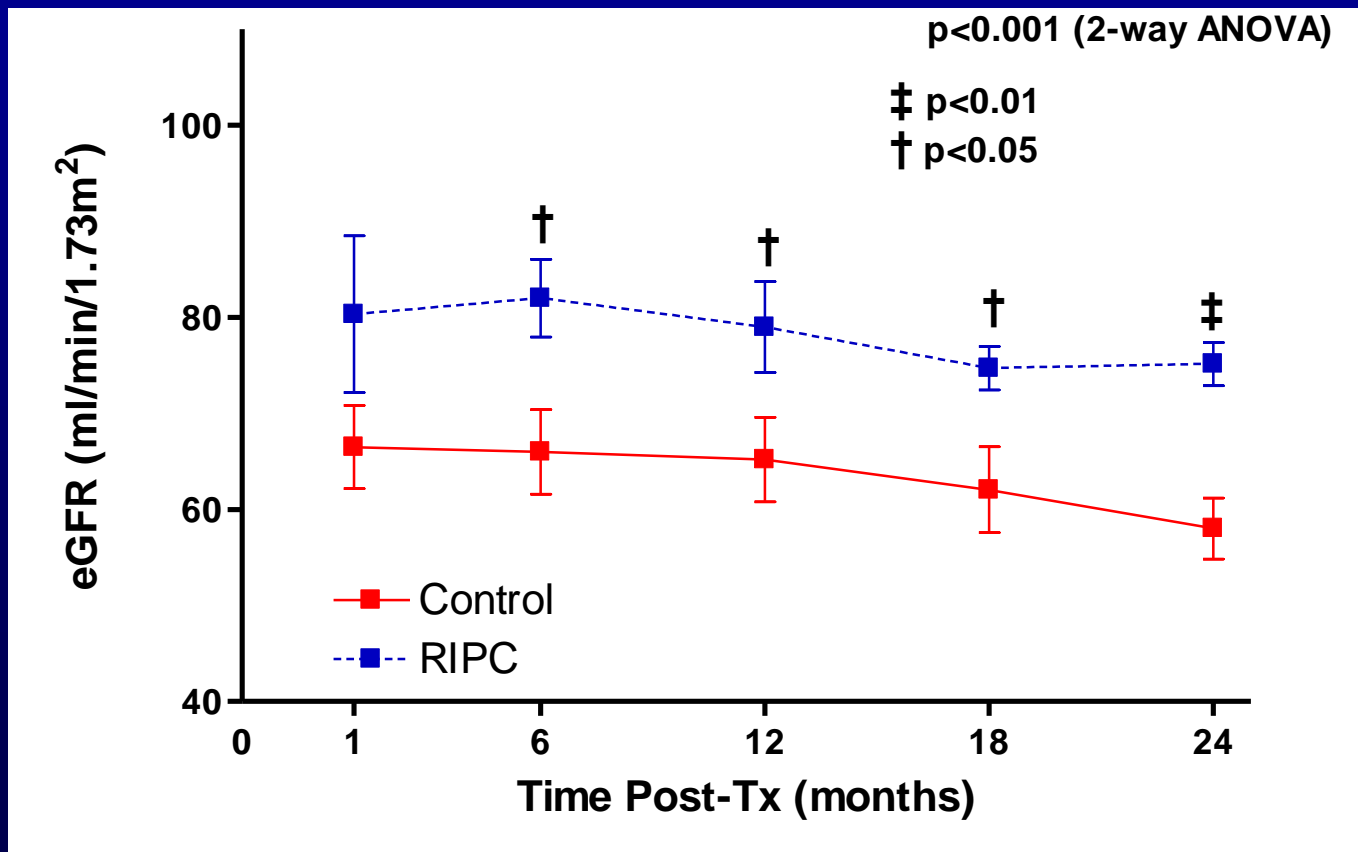
Effect of RIPC on proximal tubular function following living-related renal transplantation



Effect of RIPC on plasma creatinine post transplantation



Effect of RIPC on long-term graft function post transplantation



CONCLUSIONS

- Need larger trials to define the treatment effect robustly
- Kidney transplantation is an attractive model to validate RIPC and demonstrate a useful clinical effect
- Can be done in a trial that is of manageable size

2 STUDY FLOW CHART

