Neutrophil gelatinase-associated lipocalin in a pig model of kidney autotransplantation

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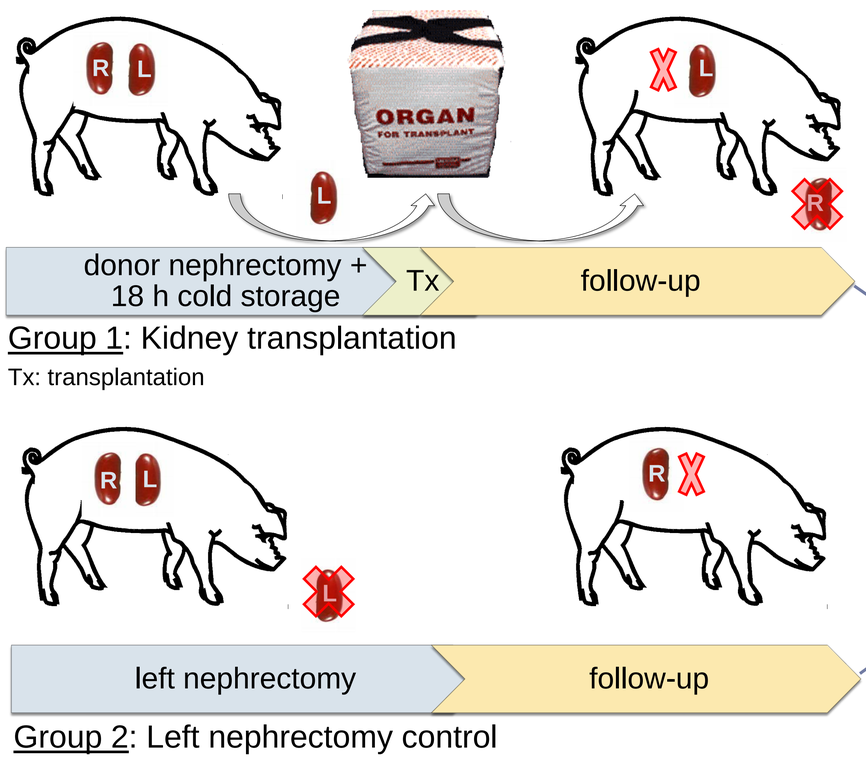
BACKGROUND & RESEARCH QUESTION

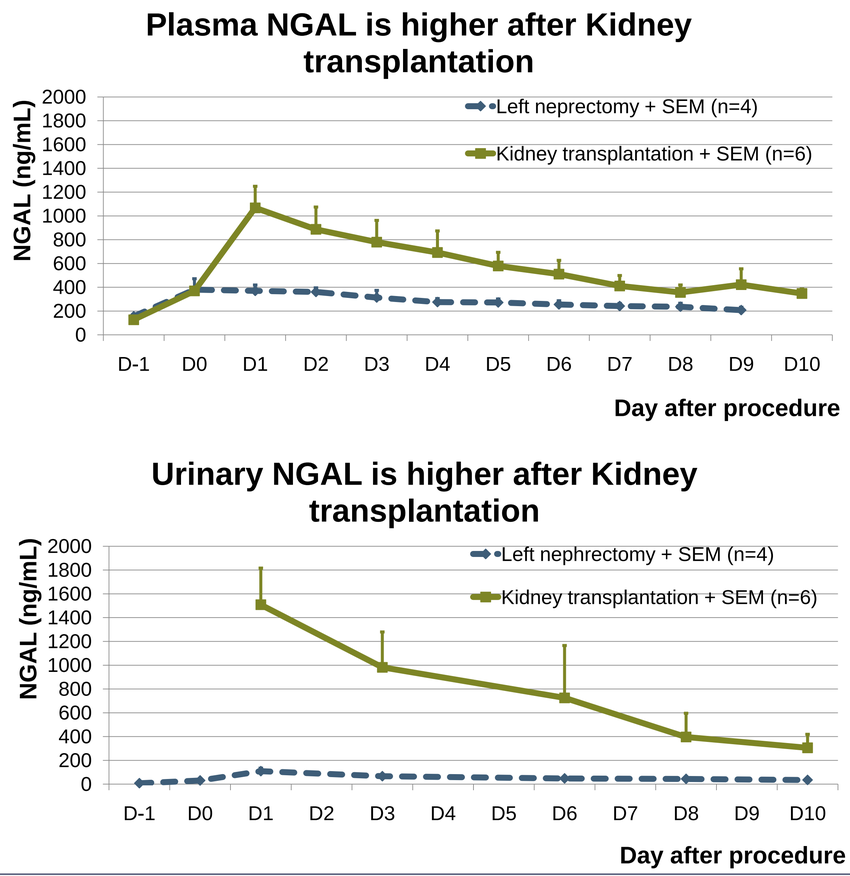
- Kidney grafts are exposed to ischemia-reperfusion injury (IRI)
- IRI leads to acute tubular necrosis and impaired graft function
- Neutrophil gelatinase-associated lipocalin (NGAL) : new biomarker for acute kidney injury

Can plasma and urinary NGAL be used as biomarker for acute tubular injury and impaired graft function in a relevant pig kidney autotransplant model?

METHODS

- Female pigs underwent randomization to :
  (cross-breed between Great Yorkshire/Large White and Dutch Landrace)
  - Group 1 : Kidney transplantation & right nephrectomy (n=6)
  - Group 2 : Left nephrectomy control (n=4)
- 10 day follow-up (D10) : plasma and urine sampling
- Measurement of :
  - **Plasma creatinine, creatinine clearance** to assess kidney function
  - **NGAL**: new Pig NGAL ELISA assay (KIT 044, BioPorto Diagnostics)
- Data presented as mean [range], Mann-Whitney U test used (Statistica 9)





RESULTS

- **Kidney function** after transplantation was impaired compared to controls
  - Plasma creatinine
    - increased after kidney transplantation
      0.9 mg/dL [0.7-1.0] at day D -1 to a peak at D2 (9.0 mg/dL [4.5-14.6])
      declined slowly to 1.8 mg/dL [1.4-2.4] at D10
    - remained stable after left nephrectomy
      0.8 mg/dL [0.7-1.0] at D -1; 1.3 mg/dl [1.0-1.6] at D1
  - Creatinine clearance remained lower after transplantation
    69 mL/min [37-99] *vs.* 123 mL/min [94-148] (p=0.02)
- **Plasma & urinary NGAL** were significantly higher in transplanted pigs
  - Peak plasma NGAL at D1 higher compared to controls
    887 ng/mL [475-1748] *vs.* 361 ng/mL [270-422] (p=0.01)
  - Plasma NGAL remained elevated after transplantation (p<0.05)
  - Initial urinary NGAL levels in the transplanted animals were higher
    1509 ng/mL [645-2796] *vs* 109 ng/mL [61-159] (p=0.01)
  - Urinary NGAL gradually decreased but remained higher after kidney transplantation (p<0.05)

CONCLUSION

- **For the first time we have shown that plasma and urinary NGAL increased significantly after kidney transplantation in pigs**
- **NGAL increase after kidney transplantation could be related to IRI and acute tubular injury**
- **NGAL is a promising marker that could prove to be of application to both medical research and pharmacological toxicology studies**

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