An Experimental Porcine Model of Heterotopic Renal Autotransplantation

A. Faure, C. Maurin, L. Bruzzese, P.H. Rolland, C. Coulange, J. Pype, V. Vidal, G. Magalon, and E. Lechevallier

ABSTRACT

Objective. The aim of the present study was to validate an experimental model of heterotopic renal allotransplantation. Such a model, more relevant to the human situation, has never been previously described.

Materials and Methods. Pietrin pigs (40 to 50 kg) were used in the study. Through a midline incision, the left kidney was removed, washed, and preserved in a standard preservation solution (Celsior, Genzyme, France) for 20 hours at 4°C. Heterotopic autotransplantation was performed into the right iliac fossa onto the external iliac vessels with an end-to-side anastomosis and a nonstented uretero-ureteral anastomosis was performed.

Results. Twenty-five renal allotransplantations were performed over a 5-month time period. Mean operating time progressively decreased and stabilized after 15 procedures (mean ± SD: 78.2 ± 19 minutes and 187.4 ± 18 minutes for left nephrectomy and transplantation, respectively) as morbidity decreased concomitantly. Suturing times for end-to-side anastomosis of the renal artery and vein onto the external iliac artery and vein were 21.9 ± 7 minutes and 34 ± 8 minutes (mean ± SD), respectively. Ten pigs died before the end of the experiment.

Conclusions. We have developed and validated the first nonrodent animal model of heterotopic renal autotransplantation relevant to the human anatomy and physiology. The procedure was easy to learn and safe. This model could be used to teach junior surgeons renal transplantation techniques and could also be used as a model to study ischemia-reperfusion injury in renal transplantation.

KIDNEY transplantation is the referenced treatment for end-stage renal disease.[1] The surgical technique for renal transplantation is now well codified. Learning surgical procedures using animals models is necessary before performing renal transplantation in humans. Moreover, the validation of an animal model close to the human physiology is crucial to study ischemia-reperfuson injury in renal transplantation. Porcine models of kidney autotransplantation have been established, nevertheless, little or no detailed information on the technique and surgical procedures are available.[2–4] The pig model seems to be relevant for learning and training[5], thanks to its similarity to humans, in terms of renal physiology and anatomy. The pig kidney is susceptible to preservation injury; therefore it is a sensitive model to study mechanisms of warm ischemia, cold ischemia, and ischemia reperfusion injury.

This experiment was performed to develop an autotransplantation model of porcine kidney in the iliac fossa, similar to a human kidney transplantation. To establish our animal model, we applied the standard technique of kidney trans-

From the Department of Urology and Kidney Transplantation (A.F., C.M., C.C., E.L.), the Laboratory L2PTV, EA 4264 (L.B., P.H.R., V.V.), and Department of Plastic and Reconstructive Surgery (G.M.), Hôpital La Conception, AHPM, Aix-Marseille University, Marseille, France; and the Air Liquid R&D Medical Gases Group (J.P.), Air Liquide—Claude Delorme Research Center, Jouy-en Josas, France.

Address reprint requests to Alice Faure, Aix-Marseille Univ, APHM, Hôpital La Conception, Department of Urology and Kidney Transplantation, 147 bd baille, 13284 Marseille, France. E-mail: alice.faure@ap-hm.fr

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plantation with anastomosis of the renal vessels to the external iliac vessels combined with uretero-ureteral anastomosis.

The aim of this study was to validate a model for kidney autotransplantation in pigs, relevant to the human situation.

MATERIALS AND METHODS

Animals

Twenty-five pigs (JL Biossin, Aubagne, France, Cheptel n° 13 005094), weighing 40 to 50 kg, were housed in common pens. Pigs were allowed to acclimate to their surroundings for 2 weeks before any operative procedures. They were fed ad libitum on a piglet diet with free access to tap water. All experiments were performed in accordance with the Guidelines of the National Institute of Health. The study protocol was approved by an Animal Care Committee.[6]

Anesthetic Protocol

The anesthetic protocol was identical for both nephrectomy and autotransplantation. Food was withheld for 12 hours before surgery. Each pig received ketamine (30 mg/kg, Virbac, Carros, France), Tiietamine/Zolazepam (1 mg/kg, Virbac), and atropine sulphate (1.5 μg/kg, Renaudin) administered intramuscularly (IM) 30 minutes before induction of anesthesia. General anesthesia was induced with propofol 1 to 2 mg/kg administred intravenously (IV) by means of a 21-gauge (G) butterfly cannula inserted into an externa marginal ear vein. After endotracheal intubation (7 to 8-mm endotracheal tube), anesthesia was maintained with sevoflurane at 2% to 3%. We used the following ventilator settings: tidal volume of 550 to 600 mL, peak inspiratory pressure below 35 cm H_2O with the objective to keep the tidal CO_2 between 35 and 40 mm Hg. We monitored electrocardiogram, oxygen saturation (using a tail probe), and esophagus temperature, and prevented hypothermia by using a Bair Hugger (Arizant Healthcare, USA). Ringer's solution (1.5 L/hours) was administred intravenously during surgery. Anesthesia was maintained postsurgery by a continous drip of sufentanil and pancuronium of bromure. BenzyIpenicIlinate procaine (2 millions UI/10 cc) and colistine sulfate (20 millions UI/mL) were intravenously administered were daily for the first 2 postoperative days.

Surgical Procedures

All surgical procedures were performed under sterile conditions during normal daylight hours. The external jugular vein was approached through a transverse cervical incision. A single-lumen 16-G catheter was inserted into the vein and tunneled to exit the skin behind the ear for perioperative blood sampling.

A left nephrectomy was performed through a midline laparotomy. The ureter was atraumatically isolated leaving it free from the retroperitoneum. Heparin (350 UI/kg) was intreavenously administered 15 minutes before nephrectomy. The left renal vascular pedicle of the transplant was left as long as possible by freeing the renal artery and vein up to the aorta and the vena cava. The renal artery was ligatured using 2.0 resorbable sutures and the renal vein was clamped at the vena cava with a vascular clamp. The renal artery was immediately cannulated and the removed kidney flushed with 400 mL of Celsior solution (Genzyme France), cooled to 4°C, and infused at an hydrostatic pressure of 100 cm H_2O. The kidney was placed in a sterile organ container and preserved in 400 mL of Celsior solution at 4°C for 20 hours. The distal renal vein was closed using a 7.0 polypropylene running suture. The abdomen was closed and administration of anesthetics stopped. After weaning the animal from the ventilator, it was returned to the pen.

The next day, the same animal was anesthetized as previously described. We performed a right nephrectomy after administering heparin (IV 350 UI/kg). The right ureter was cut close to the renal pelvis to leave it as long as possible to facilitate the anastomosis of the transplant ureter. The left kidney was implanted by anastomosing the renal vein and artery to the external iliac vein and artery, respectively. The external iliac vein was clamped with a Satynski clamp (Surtex Instruments LTD, UK). Next, a longitudinal veinotomy was performed, taking care that the lumen of the iliac vein and the diameter of the renal vein was equal. An end-to-side anastomosis was performed with running sutures using 6.0 polypropylene sutures (Prolene, Ethicon, France; Fig 1). Then, the renal vein was clamped with a bulldog clamp to avoid premature retrograde reperfusion of the graft. An end-to-side anastomosis between the renal transplant artery and the right external iliac artery was performed (Fig 2). During all procedures, the mean arterial pressure was maintained above 100 to 120 mm Hg by administering Gelofusine (B Braun Medical LTD, France) when necessary. Near the end of the arterial anastomosis, 250 mg of Furosemide (Renaudin, France) was infused. We declamped the renal vein and the external iliac artery. The reperfusion of the kidney was noticed. Finally, an end-to-end spatulated uretero-ureteral anastomosis (without double J stent) was performed using a 6.0 polypropylene. The retroperitoneal space was closed with single vicryl sutures, repositioning the peritoneum over the transplanted kidney. The kidney was in a secure position with no possibility of rotation.

Postoperative Course

After weaning the swine from the ventilator, it was set up in cage. Immediately after the transplantation, the pig had free access to food and water. Analgesia was administered until 48 hours (fentanyl patch pasted behind the ear) and electrolyte solution was administered until 36 hours posttransplantation. At 21 days, the animals were anesthetized. The macroscopic aspect of the kidney and anastomoses were evaluated. Next, the pig was sacrificed by an

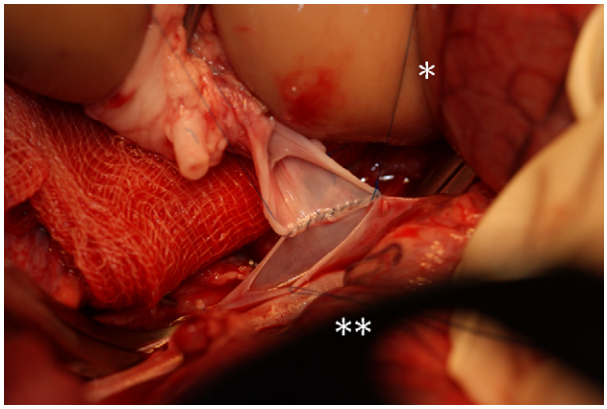

Fig 1. The external iliac vein with a Satynski clamp. An end-to-side anastomosis was performed using a first corner suture (*) and a second suture (**) at the third of the controlateral side with running sutures (6.0 polypropylene).