Use of end-to-side arterial and venous anastomosis techniques for renal transplantation in two dogs

Heidi Phillips, VMD, DACVS, and Lillian R. Aronson, VMD, DACVS

Case Description—A sexually intact male Old English Sheepdog and a sexually intact female Bull Terrier were evaluated for renal dysplasia and chronic renal failure, respectively.

Clinical Findings—Both dogs were anemic and had high serum concentrations of urea nitrogen and creatinine. Electrolyte abnormalities (calcium and phosphorus) were also evident. The decision was made to pursue renal transplantation, and donor dogs were identified.

Treatment and Outcome—End-to-side anastomosis of the renal artery and vein of each donor’s left kidney to the recipient’s ipsilateral external iliac artery and vein, respectively, was performed. The left caudal abdominal musculature was scarified by making an incision, and nephropexy to that musculature was performed with a simple interrupted pattern of polypropylene sutures. No intraoperative or postoperative complications associated with the vascular anastomoses were encountered. Azotemia, anemia, and electrolyte imbalances resolved after transplantation.

Clinical Relevance—The end-to-side anastomosis technique described here, which is a preferred method in human medicine, was successful, providing an alternative to other renal transplantation techniques in dogs. Additional studies are needed to determine whether any vascular anastomosis technique is preferable for use in dogs requiring renal transplantation. (J Am Vet Med Assoc 2012;240:298–303)

A 3.5-month-old sexually intact male Old English Sheepdog (dog 1) was referred to the medical genetics service of the University of Pennsylvania Matthew J. Ryan Veterinary Hospital for evaluation of renal dysplasia. The referring veterinarian had made the diagnosis on the basis of results of a CBC, serum biochemical evaluation, urinalysis, and abdominal ultrasonography. Historical findings included polyuria and polydipsia, vomiting, and lethargy.

When admitted to the teaching hospital, the dog was in poor body condition (score of 3/9) but well hydrated. Biochemical abnormalities identified by the referring veterinarian included high serum concentrations of urea nitrogen (88 mg/dL; reference limits of referring veterinarian’s laboratory, 6 to 23 mg/dL) and creatinine (5.1 mg/dL; reference limits, 0.5 to 1.6 mg/dL), anemia (Hct, 25.9%; reference limits, 36% to 60%), and isosthenuria (USG, 1.010; reference limits, 1.015 to 1.050). The option for renal transplantation was discussed with the owner. A low-protein diet and sucralfate (17 mg/kg [7.7 mg/lb], PO) were prescribed, and the dog was discharged from the hospital.

Four months later, the dog was returned to the hospital for renal transplantation. No abnormalities were detected during physical examination at admission. Hematologic abnormalities included a normocytic, normochromic, nonregenerative anemia (Hct, 27.1%; range, 40.3% to 60.3%) suggestive of chronic disease.

From the Matthew J. Ryan Veterinary Hospital, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19104. Address correspondence to Dr. Phillips (hphillip@vet.upenn.edu).
A mild amount of aortic regurgitation was observed. A high plasma concentration of parathyroid hormone (25.3 pmol/L; reference limits, 3 to 17 pmol/L) was indicative of renal secondary hyperparathyroidism. Results of coagulation function tests were unremarkable.

Blood typing, DEA matching to the sire and dam, and mixed lymphocyte response testing revealed both parents were compatible candidates for renal donation. Because the dam was younger than the sire, the dam was chosen to be the donor. Serum biochemical evaluation of the dam revealed no abnormalities, but the dog had a history of Lyme disease as diagnosed by means of a screening kit and C6 antibody quantification (522 U/mL; reference limits, 0 to 30 U/mL). Prior to renal donation, the dam had undergone two 4-week treatment sessions with doxycycline (10 mg/kg [4.5 mg/lb], PO, q 24 h). A computed tomographic angiogram revealed the left kidney would be suitable for harvesting; it had 1 renal artery and 1 renal vein of suitable length.1

Five days prior to renal transplantation, the recipient underwent immunosuppressive treatment consisting of microemulsified cyclosporine solution2 at a dosage of 5 mg/kg [2.3 mg/lb], PO, every 12 hours, in accordance with recommendations for achieving a preoperative, whole blood trough concentration of cyclosporine from 300 to 500 ng/dL.3,5 One day prior to transplantation, the cyclosporine concentration was 334 ng/dL. Additionally, enoxaparin sodium3 was administered SC at a dosage of 0.75 mg/kg (0.34 mg/lb), every 24 hours beginning the day before surgery and continuing for 1 week after surgery to prevent thromboembolic complications.5

On the day of renal transplantation, morphine (0.5 mg/kg [0.23 mg/lb], IV) was administered to the donor and recipient dogs, and anesthesia was induced with etomidate (1.3 mg/kg [0.6 mg/lb], IV) and midazolam (0.2 mg/kg [0.09], IV). A surgical plane of anesthesia was maintained by use of isoflurane inhalant and an IV constant rate infusion of morphine at 0.34 mg/kg/h (0.15 mg/lb/h). Mannitol was administered slowly IV to the donor at the time of initial celiotomy (0.25 g/kg [0.11 g/lb]) and again 20 minutes before nephrectomy (1 g/kg [0.45 g/lb]). Cefazolin (22 mg/kg [10 mg/lb]) was administered IV to the recipient 20 minutes before the initial incision and every 2 hours thereafter during surgery. Additionally, methylprednisolone (2 mg/kg [0.9 mg/lb]) was administered IV to the recipient at the start of celiotomy.

A ventral midline celiotomy was performed in both dogs, and the left iliac fossa of the recipient was approached. The left external iliac artery and vein of the recipient were isolated and freed of surrounding connective tissue and adventitia by a combination of blunt and sharp dissection. Pediatric Codman clamps were placed across the external iliac artery and vein. In preparation for end-to-side vascular anastomoses, arteriotomy and venotomy of the external iliac vessels were performed with microvascular scissors to correspond to the widths of the allograft artery and vein, respectively. The iliac vessels were flushed with ice-cold heparinized saline (0.9% NaCl) solution, and sutures of 7-0 polypropylene6 were placed in the cranial and caudal aspects of the iliac arteriotomy site.

Nephrectomy of the donor’s left kidney was performed as described elsewhere.1 The allograft artery was dilated and flushed with 5 to 10 mL of ice-cold heparinized saline solution until venous effluent was evident. The allograft artery was then sutured end-to-side to the recipient’s left external iliac artery, with the surgeon standing on the recipient’s left side, with 7-0 polypropylene in a simple continuous pattern. Afterward, the allograft vein and external iliac vein were approached from the opposite side of the operating table with the surgeon positioned near the venous structures. Two sutures of 6-0 silk7 were then placed in the cranial and caudal aspects of the iliac venotomy and then the cranial and caudal aspects of the allograft vein. The sutures were tied, and the dorsal wall of the venous anastomosis was completed first by use of a back-wall technique wherein the dorsal wall of the vein is sutured within the lumen of the vessel by use of a simple continuous pattern with the silk suture. The ventral wall of the venous anastomosis was completed last by creating a second simple continuous suture line. The arterial and venous clamps were removed, and no significant hemorrhage was observed. Blood flow through the vessels appeared to be excellent, and the allograft was placed in the left iliac fossa.

A ventral midline cystotomy was subsequently performed in the recipient dog. A mosquito hemostat was used to penetrate the apex of the urinary bladder from the lumen and grasp the distal ureter, pulling the ureter from the exterior into the bladder lumen. The bladder was everted, and the distal ureter was trimmed of traumatized tissue and excess fat and spatulated by use of straight microvascular scissors. A mucosal appositional ureteroneocystostomy was performed by use of simple interrupted sutures of 7-0 polypropylene.8 The cystotomy site was closed routinely, and following scarification of the lateral abdominal wall, nephropexy was performed by placement of several simple interrupted sutures of 2-0 polypropylene from the left caudal abdominal musculature to the renal capsule. To prevent intussusception of the small bowel, enteroligation was performed from the duodenal flexure to the ileocolic junction with a simple interrupted pattern of 3-0 polydioxanone.9,10 The native kidneys were left in situ, and no biopsy specimens were obtained. The abdomen was lavaged and suctioned, and routine closure of the cystotomy site was performed.

No postoperative complications were encountered. On day 2, the recipient began immunosuppressive treatment with prednisolone (0.5 mg/kg, PO, q 12 h) and cyclosporine treatment was continued at a dosage to maintain whole blood trough concentrations within reference limits. Treatment with enoxaparin was continued at 0.75 mg/kg, SC, every 24 hours for 3 days. The dose was decreased to 0.3 mg/kg (0.14 mg/lb, q 24 h) for 3 additional days before discontinuation. The recipient dog’s serum concentrations of creatinine (1.3 mg/dL), phosphorus (5.9 mg/dL), and calcium (10.4 mg/dL) returned to within reference limits 2 days after surgery, whereas the SUN concentration remained moderately high throughout hospitalization. The dog was discharged from the hospital 6 days following transplantation.
For the first 8 weeks after surgery, the recipient dog was monitored carefully through weekly physical examinations and assessments of serum creatinine and urea nitrogen concentrations, PCV, blood total solids and glucose concentrations, and USG. Afterward, examinations were performed less frequently. Whole blood cyclosporine trough concentrations were maintained within reference limits for the first 6 months after surgery, and then the dosage was decreased to achieve a trough concentration of 250 to 350 ng/dL for maintenance. The dosage of prednisolone was gradually decreased to 0.23 mg/kg, PO, every 12 hours by 6 months after renal transplantation. By 3 months after surgery, the SUN concentration had decreased to near the upper reference limit.

Allograft function remained stable until 20 months after transplantation, at which time the recipient dog began to have signs of lethargy and inappetence and became hyphopneic (USG, 1.009) with a mature neutrophilia. Abdominal ultrasonography revealed an enlarged, 8.9-cm allograft with pyelectasis of 2.2 cm and proximal ureteral dilatation of 1.5 cm from ureteral obstruction. Additionally, a 3-cm oval mass was detected in the right caudal abdomen and was possibly associated with the colon. No abnormalities of the vascular anastomosis were detected. Serum biochemical evaluation at that time revealed a urea nitrogen concentration of 64 mg/dL and a creatinine concentration of 2.1 mg/dL.

The dog was returned to the teaching hospital for exploratory surgery. Adhesions resulting in partial obstruction of the allograft ureter were identified surrounding the allograft kidney and ureter. The vascular anastomosis appeared patent and unaffected by the adhesions. The ureter was dissected free of the fibrotic tissue. A mass associated with the cecum was removed via typhlectomy; the intestine was closed routinely, and the mass was submitted for histologic evaluation. Although the dog’s azotemia resolved afterward, a septic peritonitis developed, presumably attributable to dehiscence of the right caudal abdomen and was possibly associated with the colon. No abnormalities of the vascular anastomosis were detected. Serum biochemical evaluation at that time revealed a urea nitrogen concentration of 64 mg/dL and a creatinine concentration of 2.1 mg/dL.

Prior medical management of dog 2 included administration of isotonic crystalloid fluids (5 mL/kg/h, IV, as needed), cephalexin (22 mg/kg, PO, q 12 h), doxycycline (10 mg/kg, PO, q 24 h), sulfacetamide (1 g, PO, q 8 h), benazepril (5 mg, PO, q 24 h), aluminum hydroxide (320 mg, PO, q 8 h), famotidine (10 mg, PO, q 12 h), coenzyme Q10 (30 mg, PO, q 24 h), various homeopathic medications, and a prescription renal diet as well as hemodialysis 2 to 3 times weekly.

The dog was admitted to the teaching hospital 2 days following the last hemodialysis treatment. At that time, serum biochemical evaluation revealed high concentrations of urea nitrogen (43 mg/dL), creatinine (8.1 mg/dL), calcium (13.6 mg/dL), and phosphorus (7.5 mg/dL). A CBC revealed persistent normocytic, normochromic, nonregenerative anemia (Hct, 16.1%).

Results of all infectious disease screening of dog 2 were negative except for borreliosis testing: a positive antibody titer (1:100 dilution) against *B burgdorferi* was detected. A C6 test to quantify the antibody against *B burgdorferi* was performed, and the result was < 10 U/mL, suggesting a convalescent concentration. Abdominal ultrasonography revealed morphological changes that were similar in both kidneys. The kidneys were of unremarkable size (left, 5.85 cm in length; right, 6.2 cm in length); however, the cortex of each kidney was diffusely hypechoic and thickened, and the medullae were diminished in size. No other abnormalities were noted. Results of thoracic and abdominal radiography were unremarkable. The recipient dog’s urine protein-to-creatinine ratio was high at 1.5 (reference limit < 0.5). Echocardiographic evaluation revealed mild dysplasia of the mitral, pulmonic, and aortic valves with minimal mitral regurgitation. The myocardium of the left ventricle was mildly hypechoic, and 2 ventricular premature contractions of left bundle branch block were evident during ECG evaluation. The changes to the myocardium were believed to be due to uremia or renal-related hypertension.

The dog’s female littermate was judged a compatible donor on the basis of blood typing, DEA matching, and mixed lymphocyte response testing. Computed tomographic evaluation of the littermate’s kidneys revealed the left kidney had 1 renal artery and 1 renal vein of sufficient length suitable for donor nephrectomy. No abnormalities of either kidney were noted on angiographic evaluation, and the donor’s urine protein-to-creatinine ratio was within reference limits. Additional donor screening was performed as for dog 1, and the sibling donor lacked signs of congenital or inherited nephropathy. Therefore, no contraindications to donation were found.

Two days prior to renal transplantation, dog 2 began to undergo cyclosporine immunosuppressive treatment at a dosage of 5 mg/kg, PO, every 12 hours. Enoxaparin sodium was administered SC at a dosage of 0.75 mg/kg, every 24 hours, beginning the day before surgery. A cyclosporine concentration of 211 ng/dL was measured the morning of surgery, and the dose was adjusted to achieve a whole blood trough concentration within reference limits.

Preanesthetic management was similar to that reported for dog 1. Anesthesia was induced with fentanyl (0.024 µg/kg [0.011 µg/lb], IV), propofol (0.6 mg/kg...
[0.27 mg/lb], IV), and midazolam (0.5 mg/kg, IV) and maintained with isoflurane inhalant and a constant rate infusion of fentanyl (2 mL/h, IV). Mannitol was administered to the donor by use of the same protocol used for donor for dog 1. Celazolin and methylprednisolone were administered to the recipient in a manner similar to that for dog 1.

With the exception of the inclusion of ovariohysterectomy to the surgeries performed in the donor and recipient, the donor nephrectomy and recipient cystotomy, nephropexy, and enteroplication were performed as described for dog 1. A wedge biopsy of the native kidneys was not performed given that the severity of histopathologic renal changes did not allow a definitive diagnosis to be made from the original biopsy specimen submissions.

By 2 days after surgery, serum concentrations of urea nitrogen, creatinine, phosphorus, and calcium had decreased to within reference limits. Enoxaparin treatment was continued at 0.75 mg/kg, SC, every 24 hours for 3 days and was decreased to 0.3 mg/kg, every 24 hours for 3 additional days before discontinuation altogether. No postoperative complications were encountered. Dog 2 was discharged from the hospital 6 days after surgery and monitored as described for dog 1.

Following hospital discharge, dog 2's serum biochemical values remained within reference limits, and there were no signs of renal insufficiency or problems with the vascular anastomosis. However, 4 months after renal transplantation, the dog was evaluated by the referring veterinarian for multifocal, red, raised, well-circumscribed cutaneous lesions affecting the lateral thorax, ventral abdomen, and neck. Aerobic and anaerobic bacterial culture of fluid extravasating from the masses yielded moderate growth of *Nocardia* spp, which were susceptible to amoxicillin-clavulanic acid. Treatment was initiated with amoxicillin-clavulanic acid (13.75 mg/kg [6.25 mg/lb], PO, q 12 h). Although the cutaneous lesions initially responded to treatment, they recurred 10 months postoperatively. The cutaneous lesions were excised with a cadaveric donor's renal artery and so-called ‘Carrel patch’ of aorta and vena cava can read

Anastomosis performed by use of the patching method involves dissection of an organ’s vessel together with a patch from the vessel of origin. The patch is cut so that the mouth of the extirpated vessel is situated in the center of the patch. Dissection with such a patch lends itself well to end-to-side anastomosis and is the technique of choice for surgeons performing cadaveric human renal transplantation. This is because a so-called ‘Carrel patch’ of aorta and vena cava can readily be excised with a cadaveric donor’s renal artery and vein, respectively. The advantage to the patch technique is that a clot formed along the suture line of the anastomosis would not disturb the circulation of the renal artery.

René Küss first described placement of the human renal allograft into the recipient’s contralateral iliac fossa with anastomosis of the kidney to the iliac vessels. This technique involved use of the internal iliac artery for an end-to-end anastomosis with the renal artery and the common iliac vein for end-to-side anastomosis with the renal vein. The internal iliac artery was chosen because its diameter closely approximates that of the allograft renal artery while also avoids cross clamping of the external iliac arterial axis and possible risk of limb ischemia. Charles Dubost, however, reportedly preferred implanting the renal artery onto the external iliac artery in end-to-side fashion.

Experimental bilateral and retroperitoneal auto-transplantation of canine kidneys was first described by Holden and Murray. In the retroperitoneal experiments, the ureters of 13 dogs were left intact and the left kidney was autotransplanted from the abdomen to the ipsilateral iliac fossa. Both the renal artery and the renal vein were Anastomosed to the external iliac artery and vein, respectively, in end-to-side fashion without a Carrel patch. Three dogs developed thrombosis resulting in infarction of the kidney. Six dogs survived 3 weeks or longer following surgery. Allotransplantation of the kidney was then performed in 18 dogs in 2 sets of experiments by use of the same vascular anastomosis technique. Although the kidneys failed to remain viable beyond 3 weeks after implantation, kidney anoxia may have been excessive in the autotransplantation group, and variability in flushing of the allotransplants and heparinization of the allotransplants and blood in the recipients may have resulted in damage to these organs. Because no allograft recipient underwent immunosuppressive treatment, the diffuse thrombosis later detected in the transplanted kidneys may have been related to organ rejection, poor anastomotic technique, or another variable.

In 1966, Saltzstein et al attempted to prolong viability of canine allograft kidneys by isolated perfusion of the organs with a low–molecular-weight dextran solution containing heparin. To accomplish administration of the perfusate, catheters were inserted into the femoral vessels and iliac vessels following end-to-side anastomosis of the renal artery and vein to the external iliac artery and vein.

Most recently, Wang et al described immunosuppression with a combination of a novel triptolide and tacrolimus in a renal transplant allograft model that involved DEA-mismatched Beagles. End-to-side anas-
tomes of the donor renal artery to the recipient’s external iliac artery and of the donor renal vein to the recipient’s external iliac vein were performed. The right donor kidney was placed in the recipient’s ipsilateral right iliac fossa, in a manner similar to the technique described in our report. All kidney grafts were reportedly adequately perfused after revascularization, had usual color, and produced urine immediately. No complications associated with the anastomoses were observed. Additional applications of the end-to-side technique reported in the human literature involve ipsilateral placement in double renal transplantation, successful engraftment of kidneys with multiple renal arteries, and other situations involving vascular disease or anomalies.16–21

In contrast, reports of experimental and clinical renal transplantation in dogs describe the use of a technique similar to that described by Kuss,10 except that the renal artery is anastomosed to the external, not the internal, iliac artery in an end-to-end fashion.23,24 The reason for this adaptation is not clear, but it is largely accepted that the collateral circulation of the pelvic limb in dogs allows for sacrifice of the external iliac arterial axis without complication.23 This is not the situation in cats. Indeed, studies24–25 have shown that 12% to 62% of cats undergoing arterial end-to-end anastomosis of the renal artery to the external iliac artery have 1 or more complications, including ipsilateral pelvic limb pain, lameness, limb hypothermia, edema, lameness, neuropraxia, paresis, or paralysis.

In the human renal transplantation literature, there is little evidence to support the exclusive use of 1 particular anastomotic technique. Renal arterial end-to-side anastomosis to the external iliac artery has been compared with end-to-end anastomosis to the internal iliac artery in several reports.26–29 Advocates for the end-to-side technique cite evidence that there is a 3-fold greater risk of anastomotic stenosis with an end-to-end than with an end-to-side anastomosis,30 and the disparity in luminal diameters is minimized when the end-to-side technique is used.29–31

Advocates for the use of the end-to-end anastomotic technique in human transplant recipients express concern that complications may develop when the external iliac artery is used for end-to-side anastomosis. Vascular complications have been reported such as early obstruction with a thrombus, late stenosis or fibrotic reaction, and the so-called steal phenomenon (a physiologic mechanism by which blood flow to the graft could become inadequate, causing ischemia during ambulation or intense physical effort).23,28,32 However, 1 study28 found no difference in the incidence of complications when either end-to-side or end-to-end anastomotic techniques were used.

All else being equal, when performing the end-to-end anastomotic technique, it is conventional to place a left-sided donor kidney in the recipient’s right iliac fossa and vice versa.33 This orientation reportedly allows for easier corrective surgery for any ureteral complications in human patients and allows for easier access to the iliac vessels for performance of the end-to-end anastomosis.23,33,34 It has been argued that the converse may be the situation when the end-to-side anastomosis to the external iliac artery is performed, and placement of the allograft in the ipsilateral fossa, as was done in the dogs of the present report, has been favored in human recipients.32

Canine renal allograft transplantation is a challenge to the veterinary surgeon. Historically, surgical techniques for canine renal-systemic vascular anastomoses involved the use of one of several anastomotic techniques, with anastomosis of the renal vessels to the contralateral common, external, or internal iliac artery and vein or the abdominal aorta and vena cava. These techniques allowed for successful mechanical transplantation of the kidney. To our knowledge, there has been no study in which renal allograft anastomotic techniques or renal placement sites (contralateral or ipsilateral iliac fossa) have been compared. Consequently, conclusions cannot be drawn as to whether one technique is superior to another at this time. The dogs in the present study underwent end-to-side anastomosis of the renal allograft artery and vein to the external iliac artery and vein, and the left donor kidney was placed in the ipsilateral left iliac fossa of the recipient. These dogs developed no apparent complications related to the anastomosis. Additional studies would be required to determine whether any of the complications regarding anastomotic technique or placement of the allograft that have been reported for humans and cats are relevant for dogs. Advancements in immunosuppressive protocols and postoperative management of canine transplant recipients are needed to prolong longevity in these patients and allow for long-term critical assessment of transplantation technique and success.

References


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dPolypropylene suture, Ethicon Inc, San Lorenzo, Puerto Rico.

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fPolydioxanone suture, Ethicon Inc, Guaynabo, Puerto Rico.

gNormosol-R, Hospira Inc, Lake Forest, Ill.
Refractive states of eyes and associations between ametropia and age, breed, and axial globe length in domestic cats

Kricket A. Konrade et al

Objective—To determine the refractive states of eyes in domestic cats and to evaluate correlations between refractive error and age, breed, and axial globe measurements.

Animals—89 healthy ophthalmologically normal domestic cats.

Procedures—The refractive state of 196 eyes (2 eyes/cat) was determined by use of streak retinoscopy. Cats were considered ametropic when the mean refractive state was ≥ ± 0.5 diopter (D). Amplitude-mode ultrasonography was used to determine axial globe length, anterior chamber length, and vitreous chamber depth.

Results—Mean ± SD refractive state of all eyes was −0.78 ± 1.37 D. Mean refractive error of cats changed significantly as a function of age. Mean refractive state of kittens (≤ 4 months old) was −2.45 ± 1.57 D, and mean refractive state of adult cats (> 1 year old) was −0.39 ± 0.85 D. Mean axial globe length, anterior chamber length, and vitreous chamber depth were 19.75 ± 1.59 mm, 4.86 ± 0.86 mm, and 7.92 ± 0.86 mm, respectively.

Conclusions and Clinical Relevance—Correlations were detected between age and breed and between age and refractive states of feline eyes. Mean refractive error changed significantly as a function of age, and kittens had greater negative refractive error than did adult cats. Domestic shorthair cats were significantly more likely to be myopic than were domestic mediumhair or domestic longhair cats. Domestic cats should be included in the animals in which myopia can be detected at a young age, with a likelihood of progression to emmetropia as cats mature. (Am J Vet Res 2012;73:278–283)