The Advancements of Feline Renal Allograft Transplantation Techniques and Treatments

Morgan Simon

A Senior Thesis submitted in partial fulfillment
of the requirements for graduation
in the Honors Program
Liberty University
Fall 2018

Acceptance of Senior Honors Thesis

This Senior Honors Thesis is accepted in partial fulfillment of the requirement for graduation from the Honors Program of Liberty University.

_____

Davis McGuirt, D.V.M.
Thesis Chair

_____

Norman Reichenbach, Ph.D.
Committee Member

_____

David Dinsmore, Ph.D.
Committee Member

_____

James H. Nutter, D.A.
Honors Director

_____

Date

Abstract

In recent years, kidney transplants have become a viable treatment option for chronic kidney disease in felines. Chronic kidney disease is the leading disease in geriatric cats with 20% of these geriatric cats being affected. Feline kidney transplantation has been met with many different issues regarding ethics, diagnosis, methods, and complications. There are some individuals that believe kidney transplants should not be done in felines because consent from the feline cannot be obtained. The diagnosis of chronic kidney disease has been on the rise in recent years which may be due to new classification standards. There have been many different methods used to carry out the vascular anastomosis and ureteroneocystostomy. There have been many improvements of these methods to help reduce complications and mortality.

The Advancements of Feline Renal Allograft Transplantation Techniques and Treatments

The first organ transplant was attempted using animal donor and recipients in the early 20th century (Bleedorn, 2008). According to Bleedorn (2008), in recent years organ transplantation has become more common in both humans and animals. Some successfully transplanted organs include corneal, bone marrow, and kidneys. Live donors are preferred over cadavers, but cadaver organs are often used because of the lack of living donors. The first renal transplant was performed at the University of California-Davis School of Veterinary Medicine in 1987 for chronic kidney disease in cats (Bleedorn, 2008). This treatment for felines was not described in literature until 1992 (Budgeon, 2017).

Bleedorn (2008) explained that kidney transplantation is another option besides long-term peritoneal dialysis or hemodialysis. It is also an alternate option to treating end-stage kidney failure. This option is often chosen due to greater survival time and quality of life. The mortality rate in kidney recipients within the first year in one study was found to be 5%. The increased survival time and low mortality rate is due to the development and success of new surgical methods, pre-transplant screening, matching between the recipient and the donor, and immunosuppressive treatments. The average length of time a feline can live after transplantation has not been adequately determined due to loss of contact with the feline owner and/or the research ended before the death of the feline (Bleedorn, 2008).

Kidney transplants have been shown to work in both felines and canines. Bleedorn (2008) explained that kidney transplants have been shown to be much more effective in felines compared to canines. This is mainly due to canines needing a higher

level of immunosuppression to avoid renal allograft rejection. The number of surviving felines has increased with the advancements of surgery techniques and immunosuppressive treatments (Bleedorn, 2008).

Chronic Kidney Disease

According to Bleedorn, chronic kidney disease (CKD) is the most prevalent disease in geriatric cats, with a reported 1.6% to 20% of geriatric cats affected. In cats older than 15 years the occurrence of renal failure increased from 12% to 30% (Bleedorn, 2008). The prevalence also increases as the age of the cat increases even when the cats are under 15 years old (Danielson, 2015). Danielson (2015) explained, that in recent years the prevalence of CKD has increased which may be due to new surveillance and classification systems. It could also be due to the changes in the environment or dietary issues (Danielson, 2015).

One characteristic of CKD is irreversible histological changes due to structural or functional injury of the kidney (Bleedorn, 2008). These changes can be evaluated by preforming a urinalysis, complete blood count, a serum chemistry profile and diagnostic imaging. Bleedorn (2008) explains that by the time kidney dysfunction is found in cats through standard tests it must be assumed that kidney disease is severe, but there are still different levels of severity found in these cats. The progression and severity of the disease is determined by changes in creatinine and blood urea nitrogen electrolyte concentrations, abnormal serum phosphorous concentrations, and packed cell volume (PCV) or hematocrit with decrease in concentration of urine. The inability to properly concentrate urine is associated with a 2/3 loss of functional nephrons. Even in this state, some cats can concentrate their urine. These cats may be in renal failure without

isosthenuria. Isosthenuria is where the excretion of urine does not have a higher or lower concentration than the protein-free plasma. This shows that there has been damage of the renal tubules and medulla (Bleedorn, 2008).

Management of Chronic Kidney Disease

According to Bleedorn (2008), the best management of CKD symptoms is a mixture of diet and drug therapy, because it limits the physiologic and clinical consequences of decreased renal function. The first step of managing chronic kidney disease is identifying what is causing kidney dysfunction. There are different diet recommendations based on the stage of CKD and the feline's specific imbalances. There is a particular balance between keeping appetite, maintaining body weight, and limiting protein intake (Bleedorn, 2008).

In mild to moderate chronic kidney disease the patient must keep adequate caloric intake to prevent malnutrition of protein (Bleedorn, 2008). Bleedorn (2008) suggests restrictions of phosphorus, protein and sodium should start when azotemia remains during the well-hydrated stage of kidney disease. Cats that are polyuric and uremic are more likely to get dehydrated, which can cause progression in renal dysfunction. Because of this, these patients must maintain adequate hydration. A few strategies that promote adequate hydration is the use of drinking fountains, canned food diets, and providing fresh water. If the patient is still not receiving adequate hydration, subcutaneous fluids may be given. This can help the patient receive the proper hydration and increase the quality of life (Bleedorn, 2008).

Complications of Chronic Kidney Disease

In late stages of CKD anemia develops due to less erythropoietin being produced, shorter erythrocyte survival caused by uremic toxins, and bleeding in the gastrointestinal tract (Bleedorn, 2008). This can be corrected by administering recombinant human erythropoietin but must be monitored due to risk of hypertension, polycythemia, and formation of anti-erythropoietin antibodies. The other consequences and causes of renal injury must also be addressed. This includes uremic gastritis, hypercalcemia, hyperphosphatemia, metabolic acidosis, hypokalemia, and hypertension. These consequences must be treated before the individual is considered for a kidney transplantation (Bleedorn, 2008).

The decreased clearance of plasma gastrin causes uremic gastritis. Bleedorn (2008) explains that this can also help determine the severity of CKD and is treated with famotidine. Famotidine is a H_2-receptor blocking agent that can help lessen the severity of gastrointestinal ulceration thus increasing appetite (Bleedorn, 2008).

According to Bleedorn (2008) there are also different imbalances that can negatively impact felines with CKD such as phosphate and calcium. Hyperphosphatemia occurs after a low rate of glomerular filtration. These cats are given oral phosphate binding agents if they cannot keep the normal serum phosphorous concentration with dietary restriction of phosphorous. Calcitriol production may not work properly due to interruption of calcium homeostasis which leads to the development of hyperparathyroidism. Calcitriol supplements may be given but recipients' serum phosphorous and serum parathyroid hormone levels must be monitored to avoid negative effects of toxicosis (Bleedorn, 2008).

Metabolic acidosis aggravates azotemia and can cause more protein catabolism, hypokalemia and muscle wasting (Bleedorn, 2008). Bleedorn (2008) suggests, if metabolic acidosis is severe, alkalization therapy such as oral potassium citrate or sodium bicarbonate should be given. Hypokalemia is found in 20-30% of cats with CKD. This can make kidney disease worse and causes muscle wasting and weakness. Oral potassium gluconate or potassium citrate is used to treat these abnormalities (Bleedorn, 2008).

According to Bleedorn (2008), 20% of cats get hypertension as a sequela of CKD. Cats with continued elevated systolic blood pressure should be monitored for ocular symptoms of hypertensive retinopathy. This includes retinal hemorrhages, blindness, and retinal detachment. One drug used to control hypertension and decrease the occurrence of ocular lesions is amlodipine which blocks the calcium channels (Bleedorn, 2008).

Multiplicity of Veins and Arteries

Cáceres (2008) explains humans are more likely to have multiple renal veins on the right and multiple renal arteries on the left. Felines have been found to have these same trends in renal veins and arteries. In one study it was found that cats have the greatest risk for multiple right renal veins compared to multiplicity in the left renal vein and both renal arteries (Cáceres, 2008).

In both humans and felines, it is 4 times more common to have multiple renal veins on the right (Cáceres, 2008). This is due to embryologic formation of renal veins. There are three pairs of veins in an embryo. These veins are the supracardinal, subcardinal, and postcardinal. Anastomosis of the subcardinal and supracardinal forms the right renal veins. This includes two primitive veins and makes the renal section of the vena cava. The left subcardinal vein goes through degeneration to make the left renal

vein. Since the left vein is formed from only one primitive vein it is less likely to make multiple renal veins. This can help explain why multiple veins are more common on the right compared to the left (Cáceres, 2008).

According to Cáceres (2008), in some felines there has been the presence of a double vena cava which can also be linked to the embryological development. The embryologic development of the inferior vena cava is very intricate and includes a complex process involving regression, fusion, and growth of the three vein pairs. The double caudal vena cava is formed from both of the supracardinal veins because of the persistence of the veins. Usually, the left vena cava stops at the left renal vein in individuals with this abnormality. It then crosses the aorta anteriorly to connect with the right caudal vena cava. At the hepatic level it then forms only one vein. These felines also typically have short renal veins that may be abnormal (Cáceres, 2008).

Cáceres (2008) points out that multiple renal arteries can also occur during embryonic development. During this development time the embryonic kidneys move up from the pelvic region. During this move the arterial supply changes from the caudal arteries to cranial renal arteries. The cranial arteries originated from the adrenal artery whereas the caudal artery came from iliac arteries. The main renal artery is developed through anastomosis of the aortic branches and degeneration of the secondary cranial branches. If these branches fail to degenerate they can result in multiple, polar, or accessory renal arteries (Cáceres, 2008).

Transplant Consideration

Bleedorn (2008) suggests that feline kidney transplants should be considered in cats with acute, irreversible renal failure, or decompensated chronic kidney disease.

Common pathological conditions that indicate possible transplantation include renal fibrosis, chronic interstitial nephritis, ethylene glycol toxicosis, and polycystic kidneys. Other less common conditions include glomerulonephritis, renal dysplasia, amyloidosis, pyogranulomatous nephritis, pyelonephritis, or nephrosclerosis secondary to drug toxicosis. In one study of cats with CKD considered for transplants, 15% were found to have glomerulonephropathy and 70% had tubulointerstitial nephritis (Bleedorn, 2008).

Outcome Predictions

Schmiedt (2008) explains, there are multiple components that are evaluated by ultrasound that may help predict the outcome of kidney transplantation. These components include echogenicity, corticomedullary demarcation, cortical blood flow, resistive index, and graft size. The resistive index (RI) is a value that describes the time-velocity wave form of the pulsatility of the intrarenal artery. This value may provide some predictions for the outcome of the transplant, but it is controversial. The only cases where RI was found to be high was in Schmiedt's study with grafts that had a thrombosis. The RI did not help with evaluating grafts with ureteral obstruction, DGF, or acute rejection. Graft volume was determined to be a better predictor of graft disease than RI. It was found that the graft volume was larger in grafts with acute rejection and ureteral obstruction (Schmiedt, 2008).

In Schmiedt's (2008) study, there was a positive correlation found between RI and the cyclosporine A concentration. Decreased glomerular filtration rate in acute cyclosporine A toxicity is due to vasoconstriction of the renal arteriole by a thromboxane mediated mechanism. There is also a decrease in renal blood flow due to the increased resistance in the renal vascularity. Acute cyclosporine A toxicity is an increase in the

serum creatinine concentration with an increased level of cyclosporine A in the whole blood concentration. This can be fixed with the decrease in cyclosporine A blood concentration. Schmiedt (2008) shows that RI may help determine the acute toxic impacts of cyclosporine A.

Ethics Associated with Kidney Transplantation

Ethical issues have also been discussed regarding the use of living feline donors. In humans, the use of living donors is accepted for kidney transplants since most of the population has two normal functioning kidneys. Humans are also able to give their verbal and written consent whereas animals cannot. Some people would consider the taking of an organ from a nonconsenting animal donor as animal abuse because it would cause unnecessary pain and suffering. But, since veterinarians never have consent from the animal for any procedures performed on animals and most procedures done for the animal's benefit and their survival, the consent is implied. Consent can also be given by the animal owner.

Another issue that has been raised is what will happen to the animal after it donates its organs. One answer to this question that has been suggested is to find a caring home for these animals after their donations. Many of the transplant programs have responded to this suggestion by required adoption of the donor cat even if the recipient does not have a good outcome (Bleedorn, 2008). According to Yeates (2014), kidney transplantation in animals is currently acceptable in New Zealand, Australia, and the United States. These procedures were allowed in the United Kingdom but were discontinued and under review in 2013 to determine if it was ethical (Yeates, 2014).

At a meeting of the Royal College of Veterinary Surgeons (RCVS) in 2016, the issue of ethics and feline kidney transplants in the UK was discussed (Kidney Transplants in, 2016). At this meeting, they pointed out that there are no major issues with using kidneys from donors that have already been euthanized. Some people would argue that this would be mutilation of an animal, thus it would be illegal to carry out these transplantations even if the donor is no longer living (Kidney Transplants in, 2016). This would also impact transplants from animals to humans since these animals are euthanized before using their organs in humans.

Jerry Davies, who attended the RCVS meeting, wanted there to be a rule that all transplant organs and living tissues must be from nonliving donors. If the donor was not dead, it would be unacceptable to harvest their organs. Other council members did not agree with Davies and mentioned that other procedures such as artificial inseminations, embryo transfers, and blood transfusions would fall under this category of materials taken from a living individual. This means that these procedures would also be illegal by Davies' ideal standards (Kidney Transplants in, 2016).

Pre-transplant Screening

Screening of Recipient Cats

Bleedorn (2008) suggests an extensive list of evaluations that both recipient and donor cats must go through before donating or receiving a kidney. The recipient cats must be examined by evaluating total serum thyroxine concentration, blood type, *Toxoplasma gondii* IgG and IgM titers, thoracic radiography, electrocardiography and echocardiography, FIV and FeLV testing, serum chemistry profile, blood count with differential cell count, abdominal ultra-sonography, urinalysis with aerobic urine culture

and sensitivity treatment, and cyclosporine challenge with repeat urine culture. The cats must also be checked for any other conditions that they may have before kidney transplantation. Some of these conditions include urinary tract infections, neoplasia, diabetes mellitus, cardiac disease, poor body condition, cachexia, uncontrolled hyperthyroidism, FeLV or FIV infection, fractious temperament or noncompliant owners, and any other uncontrolled diseases (Bleedorn, 2008).

Bleedorn (2008) suggests that if a cat that has a negative urine culture but has had urinary tract infections they must go through a 2-3 week cyclosporine challenge. A second urine culture must be performed after this period. If the culture is positive the cat is treated for chronic pyelonephritis after which another culture is taken. If this culture comes back positive the cat is eliminated as a recipient for a kidney transplant. Cats with feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV) also cannot receive transplants due to the increased infection risks after immunosuppression treatment (Bleedorn, 2008).

Felines that have serum titers against *Toxoplasma gondii* antibodies may not be infected but should be considered to have a larger risk for getting clinical toxoplasmosis after taking immunosupressive drugs (Bleedorn, 2008). According to Bleedorn (2008), Hyperthyroidism often occurs alongside of CKD and must be treated before transplantation. This is due to hyperthyroidism aggravating CKD and decreasing the rate of glomerular filtration. There are also challenges with anesthesia for felines with end-stage kidney disease due to the abnormal renal physiology and pharmacokinetics. A cardiac evaluation must be conducted because of the risks of anesthesia and shorter lifespan in cats with severe cardiac disease (Bleedorn, 2008).

Bleedorn (2008) suggests that, CKD impacts all the following systems in interrelated and individual ways. These systems include the neurological, endocrine, hematopoietic, cardiovascular, metabolic, immunologic, gastrointestinal, and pulmonary. There are several metabolic derangements that can be present such as uremia, acidemia, anemia, hyperphosphatemia, and hypocalcemia. If a recipient is found to have any of these derangements, they should be treated pre-transplantation if possible. If patients were treated with recombinant human erythropoietin and cannot delay transplantation, the anemic felines are given a blood transfusion to get a PCV >30% before transplantation. Pre-transplant, the patients should also get parenteral fluid diuresis with solutions with balanced electrolytes (Bleedorn, 2008).

Screening of Donor Cats

Bleedorn (2008) points out that donor cats must also go through a similar evaluation process as recipient cats. It is crucial to evaluate the function and anatomy of the urinary tract to determine if it is suitable to use for transplantation. This is performed by computed tomography angiography, abdominal ultrasonography or excretory urography. Cats that are positive for anti-*Toxoplasma gondii* antibodies, FIV or FeLV are not used as donors (Bleedorn, 2008).

Screening of Vascular Anatomy

Cáceres (2008) explains that the evaluation of the donor renal vascular and urogenital anatomy is done pre-operatively to determine any abnormalities. Some of these abnormalities include: abnormal renal parenchyma, renal calculi, and collecting systems. Multiple arteries also pose a major problem due to the requirement of more than one artery anastomosis. This increases the surgery time which also increases ischemia

and anesthesia time. Multiple anastomoses have also been linked with higher risk of bleeding and need for blood transfusions. Longer surgery time also comes with more complications such as graft injuries. These injuries may cause more inflammation, rejection episodes, premature graft loss, and graft immunogenicity (Cáceres, 2008).

According to Cáceres (2008), the most accurate way to pre-operatively scan a human's vascular anatomy is the use of multislice computed tomography (CT). CT technology has >97% accuracy for arteries and 96-100% accuracy for veins in humans. CT scans can also find mineralization of collecting system or cortico-medullary junction, nodular fat necrosis, mesenteric lymphadenopathy, irregular kidneys, accessory renal arteries, double caudal vena cava, and splenomegaly (Cáceres, 2008).

In Cáceres' (2017) study with felines there was a 92% agreement between surgical left renal vascular anatomy and the CT angiography findings. The common disagreement was double renal arteries that were not shown on the CT. This may have occurred due to the close placement of arteries to each other. In humans, CT has a higher agreement rate because of the multislice CT angiography with better resolution and the much larger renal vessels compared to felines (Cáceres, 2017).

Cáceres (2008) mentioned, that accessory renal arteries are not common in felines but can be seen in 25% of human patients. These accessory arteries are often missed in CT angiography due to their small size. This is the biggest disagreement between CT angiography and actual anatomy of a human patient. Multislice CT angiography has become the standard technology to use to screen vascularity before surgery. This is due to the better special resolution, less tube heating, short acquisition time for images, and

ability to view larger image volumes with no decrease in signal-to-noise ratio (Cáceres, 2008).

Budgeon (2017) showed early phase conventional intravenous urogram (IVU) could be used to preoperatively determine the anatomy of vascularity. IVU has a failure rate of about 10% so it is not used as often to check the vascular anatomy compared to CT technology. Budgeon (2017) explained, that all of these evaluations are excluded by some surgeons because of the low occurrence of multiple arteries and extra costs for the screening. These screening options can also miss multiple arteries which makes the cost of doing the screening worthless because the surgeon would not know until the patient is open on the table and the surgery cannot be completed.

Methods Used During Transplantation

General Techniques and Medications

Bleedorn (2008) explains that there are multiple techniques used for ureteral implantation and vascular anastomosis but they all use the same general monitoring and anesthetic procedures. Hemodynamic parameters are ideally monitored by a jugular catheter before, during, and after the procedure. The typical anesthetic and premedication protocol include an opioid, anticholinergic, and an inhalant anesthetic. Which agents are used depends on the pre-transplant evaluation and the anesthesiologist's preference (Bleedorn, 2008).

Bleedorn (2008) explains that broad spectrum antibiotics are given for the duration of the surgery. During microvascular anastomosis, atracurium besylate is administered if needed to keep the muscles relaxed. The systolic blood pressure can be kept at an adequate level by the continuous-rate infusion of dopamine in donor cats prior

to nephrectomy and in recipients post vascular anastomosis. Mannitol can be administered to induce osmotic diuresis, which also helps minimize acute tubular necrosis that is related to temporary ischemia. During the operation, the typical physiological parameters are constantly monitored and, if needed, adjustments to the drugs are made. Electrolytes along with venous or arterial blood gas are monitored occasionally and any imbalances are corrected (Bleedorn, 2008).

Preservation Solutions

Katayama (2014) found that cold phosphate-buffered sucrose (PBS) was a better preservation solution than cold heparinized saline (HS) solution for feline kidney allografts. Sucrose is a good osmotic agent due to its size and its decreased ability to cross the cell membrane. A hyperosmotic solution is used due to the theory that it decreases cellular swelling because it balances the intracellular colloid osmotic pressure. This balancing act helps protect the graft. When using PBS, the serum creatinine levels did not vary shortly after the operation unlike the HS solution. This shows that PBS may prevent injuries such as reperfusion and ischemia (Katayama, 2014).

Vascular Anastomosis

Bleedorn (2008) described the typical vascular anastomosis techniques. A ventral midline celiotomy is used to remove the donor cat's kidney. A dissecting microscope is used to help vascular dissection. Both donor kidneys are evaluated for multiple veins and arteries, and appropriate kidney function for transplantation. The kidney from the donor must have only one supplying artery. Transplantation of the left kidney is ideal due to the longer length of the vascular pedicle. The length of the artery must be at least 0.5 cm to perform the arterial anastomosis. The renal vein is measured in order to make a sterile

template to help create the donor phlebotomy site. Before nephrectomy the whole ureter length is isolated from the urinary bladder to the kidney (Bleedorn, 2008).

Budgeon (2017) explains some of the historical techniques used for anastomosis. The original techniques used for these transplantations required ureteral drop-in and end-to-end renal-to-iliac artery anastomoses (Budgeon, 2017). In previous studies, the external iliac vessels were used for anastomosis, but these cats had complications with rear limbs. In more recent articles, the postrenal aorta and vena cava were used during anastomosis (Bleedorn, 2008). Since the first transplants, the procedures have greatly improved. This combined with better patient management has decreased complications and death (Budgeon, 2017).

The common technique now includes anastomosis of the end of the renal artery to the side of the aorta and the end of the vein to the side of the vena cava. This technique is also simpler and faster than the previous technique used. Some complications that are decreased by the current technique include pain, edema, paresis or paralysis, and ipsilateral pelvic limb hypothermia. Even though this procedure decreases these complications it did not change any complications linked to vascular anastomoses. One challenge that can arise is double arteries to the donor's kidneys. Most of the time the left kidney is preferred, but the right will be chosen for transplantation if the left has multiple arteries. Implantation of the right kidney is technically more difficult due to a shorter artery to vein length. The right kidney also lines up better to be transplanted on the right side of the recipient which is not the prepared side of the recipient (Budgeon, 2017).

Bleedorn (2008) illustrates that the area between the caudal mesenteric artery and left renal artery of the recipient cat should be expose and isolated. This is done to prepare

the donor for the graft. The kidney from the donor is not harvested until the vessels in the recipient are ready for implantation. 8-0 to 10-0 nylon is used for the donor's renal artery which is anastomosed end-to-side to the aorta. This is done in a simple interrupted pattern. 7-0 silk is used while the renal vein is anastomosed to the caudal vena cava. This is done with simple continuous sutures and is done in two rows (Bleedorn, 2008).

Carrel Patch Method

In 1905 Alexis Carrel described the carrel patch which is a technique used for vascular anastomoses (Budgeon, 2017). According to Budgeon (2017), this technique is widely used today in vascular surgery. Using a carrel patch in kidney transplantation means that a patch of the aorta centered above the renal artery or arteries is removed. In human kidney transplantation this method is thought to help reimplantation and decreases the risk of thrombus formation. This technique when used in felines would allow the use of a donor kidney that has multiple renal arteries (Budgeon, 2017).

Budgeon (2017) explains that a dorsal recumbency position was given to the donor feline when using the carrel patch method. Then a ventral midline celiotomy is conducted. The pathology of both donor kidneys is examined. Dissection of the perirenal fat is done to expose the renal artery and vein. Next, transection and ligation was performed on the ureter close to the entrance to the bladder or it is resected with the ureteral papilla. Before vessel occlusion all preparations are finished. This is done to limit the occlusion time of the aorta of the donor and warm ischemia time of the graft. A Satinsky clamp was placed tangent to the aorta's long axis to seclude the left kidney arteries without occluding the right renal arteries. The incision on the aorta is done with a specialized scalpel blade and is lateral to the single or multiple renal arteries with a

Vannas scissor. The incision is extended around the single or multiple renal arteries with 1mm of tissue from the base of the vessels. Transection of the renal vein occurs after it is clamped and is done close to the vena cava with standard techniques. After the kidney is removed, CDId sucrose-phosphate preservative is used to flush the vessels and is submerged in the cold solution over ice until the time of graft implantation (Budgeon, 2017).

According to Budgeon (2017), 9-0 nylon is used to close the donor aorta in an overlapping simple continuous pattern. The Satinsky vascular clamp is then taken off the aorta. 4-0 silk is used to ligate the donor's renal vein and the vein is checked for hemorrhaging. The abdomen is closed in a common manner. In the recipient cat, 10-0 braided polyester sutures are used to complete the venous anastomosis in an end-to-side fashion. This is done after the vena cava is partially occluded by using a #7 Sundt slimline temporary aneurysm clip. A Cooley neonatal vascular clamp is used to isolate part of the aorta. A small patch, about the size of the donor patch, is cut out of the aortic wall. 9/0 nylon is used for 2 simple continuous suture patterns to suture the donor patch into the recipient's aorta (Budgeon, 2017).

Budgeon (2017) explains two different techniques were used to implant the ureter in carrel patch method kidney transplantations. In one method, a neouretercystostomy is done, and in the other method there is an implantation of the ureteral papilla extravesicularly. 5-0 polyglactin 910 sutures are used to tact the renal capsule to a fold of the peritoneum. The abdomen is closed using common procedures. The major outcome predictor factor is the length and diameter of the renal artery. The shorter the blood vessels the more complicated the procedure. The smaller the diameter of the renal arteries

increases the risk of inaccurate apposition and thrombosis. Due to these factors larger donor cats are ideal due to larger kidneys and vessels (Budgeon, 2017).

Budgeon (2017) suggested using the carrel patch method when the kidney is found to have multiple arteries at the time of surgery because it makes the kidney usable. The carrel patch method also allows surgeons to pick the left kidney over the right even if there are multiple arteries. The carrel method may be beneficial to use in single artery transplants as well. This is due to graft destruction and thromboembolic events still being major complications of kidney transplants. If there is a gap at the anastomic site within the epithelium there may be exposure to collagen. This may cause a formation of a thrombus. Due to the difficulty of the 90-degree end-to-side anastomosis, the correct positioning of the epithelium may be hard to achieve. The carrel patch method can lower this risk by having the suture line away from the renal artery entrance (Budgeon, 2017).

Theoretically, the reducing of the angle of contact of the aortic wall and vessel tissue can aid endothelial apposition, which decreases the risk of formation of a thrombus (Budgeon, 2017). Some surgeons find placing the carrel patch in the aortic wall technically easier than the end-to-side method. For the carrel patch method to work, the surgeon must realize that the feline aorta is comparatively small, particularly the circumference. This means that the patch must be very small, approximately 1mm around the vessel. Budgeon (2017) recommends making an eclipse shaped incision parallel to the length because it makes closing the aorta simpler. The patch is best removed by microsurgical scissors instead of a scalpel (Budgeon, 2017).

Ureter Removal Techniques

Bleedorn (2008) explains that there have also been multiple techniques used to implant the donor ureter in to the recipient's urinary bladder. One technique uses an extravesicular ureteroneocystostomy. This technique is said to be the fastest fix for mucosal apposition of the donor ureter to the recipient's bladder and renal pelvic dilation. Both of these decrease the occurrence of obstruction postoperatively. A peritoneal-transverse abdominis muscle flap is made, then the renal capsule is connected to the abdominal wall. This prevents kidney torsion on the pedicle (Bleedorn, 2008).

Danielson (2015) explained that the technique used to harvest the kidney along with ureter before 2003 involved the transection and ligation of the distal ureter at the urinary bladder. This is called the ureteral transection (UT) technique. After 2003, this procedure was modified to harvest all of the ureter along with all ureter papilla and a part of the bladder wall. This is called the ureteral papilla harvest (UPH) technique. The UPH technique is not as technically challenging and could lessen the risk of dehiscence, obstruction, and leakage at the neoureterocystostomy site compared to the UT technique (Danielson, 2015).

Danielson (2015) lists the different medications used before, during and after neoureterocystostomy. During this procedure the cats are first given an opioid, usually oxymorphone in a dose of 0.05-0.1 mg/kg intramuscularly (IM). They are also given a benzodiazepine or a phenothiazine. The usual benzodiazepine given is midazolam (0.25-0.5 mg/kg IM) and the typical phenothiazine is acepromazine (0.05-0.1 mg/kg IM). Induction of anesthesia is induced by 10-15 mg/kg of thiopental or 2-6 mg/kg of propofol. Both of these drugs would be given intravenously. Anesthesia is maintained

with the administration of isoflurane. Fluids are given intravenously at 5-10 mL/kg/h during the surgery. 30 minutes before the kidney is harvested, the renal perfusion is increased by administering 0.5 mg/kg of mannitol intravenously and 0.01 mg/kg of acepromazine. Once the kidney is removed, 20 mg/kg of prophylactic antibiotics was given intravenously (Danielson, 2015).

Danielson (2015) explains that the UT method involves dissection of the ureter from the peritoneal attachments. 3-0 or 4-0 silk is used to ligate the ureter. Transection of the ureter occurs approximately 1-2 cm next to the ureterovesicular junction. The UPH technique involves the use of an operating microscope to harvest the whole ureter and 2-3 mm cuff of the bladder wall that surrounds the ureteral papilla. Microdissecting scissors are used to make the circular cut around the ureteral papilla. This is done carefully to avoid injuring the contralateral or ipsilateral ureteral stoma. Two layers of 6-0 polyglactin 910 sutures are used to close the defect in the bladder. After surgery the felines are given opioids for postoperative analgesia. If cats are in the ICU they are given crystalloid fluid therapy at doses of 60-80 mL/kg per day through IV. The surgery time in one study was 55 minutes for the UT technique and 93 minutes for the UPH technique (Danielson, 2015).

Mehl (2005) also explained that there have been a number of techniques used for ureteroneocystostomy in felines. The original technique used was a “drop-in” where the ureter is put into the bladder wall through a small opening and is held in place by only one transmural suture. Complications linked with this technique include granuloma formation at ureterovesicular junction which can cause ureteral obstruction and hemorrage. A mucosal apposition technique reduces inflammatory response and

formation of granulomas. This technique requires eversion of the bladder mucosa and a ventral cystotomy. One issue that may occur is major swelling of the bladder after eversion which can increase the difficulty of suturing the ureteroneocystostomy. These intravesical techniques have been replaced with extravesical ones because they do not need a different cystotomy for access (Mehl 2005).

Mehl (2005) explains the procedure for a intravesical mucosal apposition ureteroneocystostomy. After the ventral cystotomy is performed hemostatic forceps are used to bring the ureter through the bladder's craniodorsal surface. The bladder mucosa is exposed by everting the bladder. After the spatulation of the distal end of the ureter and the ureteral artery bleeding occurred, it was ligated with 6-0 polydioxanone. 8-0 nylon was used to appose the ureteral and bladder mucosa with 6-8 simple interrupted sutures. To ensure openness during the suture placement a 4-0 polypropylene stent was put into the ureteral lumen. This stent was removed before the closure of cystotomy. All of the sutures were made through the full thickness of the ureteral and bladder mucosa. 3-0 polydioxanone was used to close the cystotomy site in a simple continuous pattern. 0.9% NaCl sterile saline solution was injected into the lumen and pressure was applied to check for any leakages (Mehl, 2005).

Mehl (2005) also explained the procedure for an extravesical ureteroneocystostomy. The mucosa of the ventral part of the apex of the urinary bladder was exposed by an incision through the muscularis and submucosa. Spatulation of the distal end of the ureter was performed and an equal size incision was made in the bladder mucosa. The previously mention stent was also used to ensure openness but was placed after two sutures were completed and removed before the last suture. 8-0 nylon was used

to suture the full thickness of the ureter and bladder mucosa. This was done with different sutures in different patients. In some feline patients, a simple continuous pattern was used. In this method, there were two sutures completed between the proximal ureter where it was spatulated and the cranial aspect of the bladder incision. One suture was between the caudal aspect of the bladder incision and the distal ureter. These were both the first knots of two different continuous suture lines. In other felines a simple interrupted suture pattern was used. The sutures were placed in the same locations as the other patients and were cut to make two simple interrupted sutures. Two more of these sutures were done between the ureteral and bladder mucosa. After the completion of suturing, the muscularis and bladder serosa were apposed with a simple interrupted pattern of 4-0 polydioxanone. Sterile saline solution was injected to check for any leaks (Mehl, 2005).

According to Sutherland (2016), about 70% of kidney recipients survive a year after transplantation when using the ureteral papilla implantation method. Eighty-five percent of the felines had fast normalization of the serum creatinine levels. This method is easier to suture because of the larger size and being able to place sutures a few millimeters from the stroma. Since these sutures are not placed in the lumen of the ureter there is a decrease in the risk of granulation formation and obstruction caused by swelling. The fast normalization time may have also been helped by the kidney perfusion with cold sucrose phosphate preservation solution right after it was harvested. The cold preservation has shown to help early graft function and limits the loss of nephrons due to ischemic injury. This method does come with some concerns such as the longer time

required to resect the ureteral papilla and swelling or accidental injury of the contralateral ureteral stoma during the procedure (Sutherland, 2016).

Danielson (2015) explained that there are some potential negative consequences to unilateral nephrectomy such as increased blood pressure and urine protein excretion than pre-nephrectomy. After unilateral nephrectomy there is also a decrease in both effective renal plasma flow and total glomerular filtration rate (GFR). These two decreases are still 50% higher than the pre-nephrectomy function which shows that the remaining kidney has adapted. Even though there are some negative sequelae to unilateral nephrectomy it has not shown to increase the occurrence of end stage kidney disease or survival time of donors (Danielson, 2015).

According to Danielson (2015), there was not a statistical difference between the number of minor complications between these two techniques (UPH and UT). Short-term complications were defined as any complications that occurred during the nephrectomy hospitalization. In the cats receiving the UPH technique some minor short-term complications were transient urine retention, fever, swelling of the incision in the abdominal wall, mild pneumomediastinum, and azotemia. Some of the UT cats have had the following minor short-term complications: seroma of abdominal wall, minor skin dehiscence of incision in abdomen, and viral infection of the upper respiratory tract. There was also no significant difference between long term complications. One minor long-term complication that occurred in UT patients was linked to the urinary tract. One major long-term complication that occurred in one UPH and four UT patients was kidney failure (Danielson, 2015).

Mehl (2005) explained, that the cats with the extravesical-simple continuous sutures had higher serum creatinine concentration and mortality rate. This may be due to the “purse string” effect that occurs with these sutures and causes ureter obstruction. The cats with extravesical-simple interrupted sutures had decreased size in bladder mass, renal pelvic dilation and serum creatinine concentration. These decreases make the simple interrupted sutures the better technique in cats (Mehl, 2005).

Immunosuppressive Treatments

According to Bleedorn (2008), early kidney allograft transplants were successful technically but eventually rejected. The survival length of these allografts increased after the invention of immunosuppressive drugs in the 1960’s. The development of these immunosuppressive drugs was the most important advancement in transplantation procedures. These drugs allow transplantation from unrelated individuals because they help prevent rejection of the foreign tissues. The rejection of foreign tissue is due to T-cell mediated recognition of the important histocompatibility complex proteins on a cell’s surface and the peptides they present. Acute rejection occurs in 5 to 8 days when transplanting kidneys from histoincompatible, unrelated donors. The recipient must stay on immunosuppressive drugs for the rest of their life span to prevent rejection of the foreign tissue (Bleedorn, 2008).

Cyclosporine was one of these drugs that changed the survival time due to the selective inhibition of the T lymphocytes, which is the main type of cells that cause kidney allograft rejection (Bleedorn, 2008). Katayama (2012) explained that cyclosporine is isolated from *Tolypocladium inflatum* which is a fungus and a cyclic polypeptide. This molecule is lipophilic and has immunosuppressive qualities. Cyclosporine inhibits the

production of interleukin(IL)-2 which signals activation and proliferation of T-cells. This causes suppression of various cytokine's secondary synthesis (Katayama, 2012).

According to Bleedorn (2008), a combination of prednisone and microemulsified cyclosporine is typically used for immunosuppression treatment. Some transplant locations suggest starting cyclosporine 2 weeks before transplantation, so the serum trough levels are good at the time of the transplant. This helps avoid the start of the host vs. graft immune response. Prednisone (0.25 mg/kg) is also given to the patient pre-transplantation. Cyclosporine is given every 12-24 hours in 3 to 5 mg/kg doses to get 500ng/mL whole blood trough concentration for the first month after surgery. After this time, it is decreased to be 150-250 ng/mL for the duration of their life. This dose is given every 12 hours for the first month after surgery and then only once a day after that (Bleedorn, 2008).

According to McAnulty (1999) some drugs that could lower cyclosporine elimination and increase the cyclosporine concentration in the blood are antibiotics, antifungals, corticosteroids, calcium channel blockers, and antiemetics. Absorption of cyclosporine occurs in the small intestine and is excreted in bile after being metabolized in the liver. Intestinal P-450 oxidases metabolize cyclosporine in the intestines before it is absorbed. Hepatic cytochrome P-450_IIIA microsomal enzymes mediate the metabolism of cyclosporine in the blood (McAnulty, 1999).

According to Bleedorn (2008), there are a few different agents that can alter the metabolism of cyclosporine. Katayama (2012) found that ketoconazole (Kcz) can be given to recipients to lower the dosage of cyclosporine. Ketoconazole lowers the metabolism of cyclosporine by inhibiting P-450 IIIA microsomal enzyme competitively

(McAnulty, 1999). This shows that the metabolism of cyclosporine may be mediated by the inhibition of P-glycoprotein (P-gp) and cytochrome P450 3A (CYP3A) which cyclosporine is a substrate of (Katayama, 2012). But, Kcz has some negative side effects like hepatotoxicity. If this occurs, the treatment with Kcz must be discontinued which can cause acute allograft rejection (Katayama, 2012). Treatment with Kcz also requires another pill, which can increase the difficulty administering treatment to the feline.

Katayama (2012) also found that Clarithromycin (CLM) is less toxic and can also inhibit P-gp and CYP3A. CLM significantly raised the oral bioavailability of cyclosporine. When given cyclosporine and CLM the dosage to prevent acute allograft rejection was reduced from 2 times a day to once a day (Katayama, 2012).

Bleedorn (2008) explained that more issues have been found with canine kidney transplantation due to higher levels of immunosuppression needed to avoid rejection of the graft. In canines the rejection of transplants is frequent and severe. Triple-drug immunosuppressive treatments with cyclosporine, azathioprine, and prednisolone have been used in canines but still show little success (Bleedorn, 2008).

Monitoring After Transplantation

Monitoring Recipients

Bleedorn (2008) suggests taking blood pressure often during the first 12-24 hours due to the possibility of severe postoperative hypertension. Esophagostomy or gastrostomy tubes are used to give supplemental nutrition until patients start eating and drinking on their own. Serum creatinine concentration, trough whole blood cyclosporine concentration, PCV, and total plasma protein concentrations are evaluated every 24 hours. To evaluate the specific gravity of urine and the amount of urine in 24-hours, all

the urine is collected. After 3 to 5 days all hemodynamic parameters and renal functions should be back to normal. Graft rejection should be considered if the patient produces isothernuric urine, anorectic, experiences continued increase in concentration of serum creatinine, or depression. The urinary tract should be examined by ultrasonography to evaluate renal graft perfusion and possibly identify hydroureter or hydronephrosis. If a patient has these conditions, it may be a stricture issue where the ureter was implanted instead of rejection of the transplant. Surgical fixes may be needed to fix this condition and not just a change in medication like some other conditions (Bleedorn, 2008).

Bleedorn (2008) explains that an esophageal or gastric feeding tube can be used for nutrition support postoperatively. After transplantation, the patients are not handled and kept stress free. Any unbalances of acid-base or electrolytes are monitored and corrected (Bleedorn, 2008).

Bleedorn (2008) suggests discharging recipient cats when the function of the graft is acceptable and there is stability of the blood cyclosporine concentrations. Graft function is considered acceptable if there is enough nutritional intake, good attitude, less serum creatinine concentration, and the ability to concentrate urine. Weekly evaluations need to be conducted for at least 4 weeks after discharge. At these appointments PVC, body weight, serum creatinine concentration, whole blood cyclosporine concentration, and total solid concentration must be determined. Urine cultures, complete blood count, cyclosporine concentration, urinalysis, and serum chemistry profile must be evaluated multiple times a year after the first 4 weeks post-surgery. These recheck appointments should be every 2-3 months for the first year after surgery, and every 3-4 months there

after. Any cats that are showing signs of illness should be rechecked more often (Bleedorn, 2008).

Due to the lowered immune system of transplant recipients, they must be strictly indoor pets (Bleedorn, 2008). According to Bleedorn (2008), these cats should still be vaccinated and treated for parasites regularly. When vaccinating these felines, their vaccines should be recombinant or subunit vaccines with killed or inactive viruses rather than attenuated or modified-live vaccines (Bleedorn, 2008).

Monitoring Donors

Bleedorn (2008) points out that there are no specific monitoring needs for the donor cats after surgery. Before the donor cat is released, the serum creatinine concentration will be checked. There are also few long-term risks linked with kidney donation. They do not recommend regular rechecks, but a baseline urine specific gravity and serum creatinine concentration should be taken 1 to 2 months after surgery with yearly rechecks (Bleedorn, 2008).

Complications After Transplants

Kidney Rejection

Kinns (2010) explains that some indications of acute kidney rejection that are found with sonography technology are the resistive indices, echogenicity, and renal size. It may be possible to better detect acute rejection and chronic allograft nephropathy by using contrast-enhanced sonography to find any differences that occur in perfusion in the donated kidney. This method of monitoring perfusion is also less invasive and does not require anesthesia or radiation like magnetic resonance imaging, contrast-enhanced CT, and quantitative renal scintigraphy methods. Two technologies that provide better images

than the traditional doppler ultrasounds are contrast-enhanced power doppler ultrasounds and contrast-enhanced harmonic ultrasounds. Most clinics have the ability to do contrast-enhanced power doppler ultrasounds but lack the specific software to do contrast-enhanced harmonic ultrasound (Kinns, 2010).

Danielson (2015) hypothesized that an increase in kidney failure in donor cats could be due to 50% decrease in functional renal parenchyma, and can make the cat more vulnerable to interstitial nephritis, toxic insult, infectious damage, and normal age-linked nephron loss that would not be detected in cats with two kidneys. Another cause of increased kidney failure is obstructive ureterolithiasis in cats with only one ureter rather than two ureters (Danielson, 2015). For felines the most common antirejection therapy for kidney rejection is methylprednisolone sodium succinate. Some treatment centers also give intravenous cyclosporine (Bleedorn, 2008).

Post-Transplant Malignant Neoplasia

The high rates of post-transplant malignant neoplasias (PTMN) in transplant recipients emphasizes the need for careful thorough monitoring (Wormser, 2016). Durham (2014) found that there is a difference between the time of transplantation and diagnosis of lymphoma for cats and humans. In humans, the majority of people that develop lymphoma will be diagnosed within the first 12 months following transplantation. Whereas in cats, the median time of diagnosis is 617 days after transplantation (Durham, 2014).

Durham (2014) explained that in human transplant recipients one of the most significant post-transplant complication is transplant linked malignancies. Transplant recipients may have a lower mortality rate in recent years, but they have a 3-4 times

higher rate of neoplasms than the control population. In humans and cats, one of the most common PTMNs is lymphoma. Lymphoma is included in a large spectrum of post-transplant lymphoproliferative disorders (PTLDs). These PTLDs include heterogenous clusters of lymphoid proliferations that are abnormal and usually B-cells. These disorders include reactive polyclonal hyperplasia to aggressive non-Hodgkin's lymphoma. In humans, 90% of PTLDs are Epstein-Barr virus (EBV) linked to an improperly working immune system caused by the immunosuppressive treatment that is used to avoid rejection of grafts. Other PTMNs diagnosed in felines are poorly differentiated hepatic tumor, hepatic neuroendocrine carcinoma, fibrosarcoma, meningioma, malignant melanoma, nasal adenocarcinoma, renal sarcoma and carcinoma, and adrenocortical carcinoma. The difference in Durham's (2014) experiment and control group for lymphoma was significant. The transplant recipients had a 6.7 times higher risk of developing lymphoma than the control population (Durham, 2014).

According to Durham (2014), EBV invades naïve B-cells and changes the differentiation process in the cells to be a memory phenotype. This virus can be latent within the nonactive memory B-cells. During this time, only a small part of the EBV's genes are expressed which makes it difficult for the host's immune system to locate and destroy the infected cells. The B cells that show viral proteins, particularly surface proteins like LMP-1 and those that go through neoplastic transformation are susceptible to T-cell-mediated destruction. In people or cats with immunosuppression there is not as much surveillance done by T-cells which allows for larger numbers of the EBV changed B-lymphocytes to survive (Durham, 2014).

According to Schmiedt (2009) there is not a clear link between PTMNs and cyclosporine concentrations, but cyclosporine could still influence the development of PTMNs. The increased occurrence of PTMNs could be influenced by the treatment with cyclosporine. There are four ways that it is thought that cyclosporine might increase the occurrence of PTMNs. First, the immunosuppression of this drug can cause the recrudescence of some oncogenic viruses. Second, this drug causes T-cell apoptosis which decreases the neoplastic cell clearance and immunosurveillance. Third, it can encourage the presence of DNA mutation, and can have a lower ability to fix these mutations. Fourth, there is a direct impact on the phenotype of cells from the cyclosporine which makes them more invasive and causes other malignant characteristics (Schmiedt, 2009).

Delayed Graft Function

Delayed graft function (DGF) is a risk factor for mortality in humans after transplantation (Katayama, 2014). Katayama (2014) defined DGF in humans as the need to have dialysis in the first 7 days post-transplantation. In animals, there is not as precise a definition due to the short length of time the kidney allograft is preserved. A common DGF cause in felines is swelling that can occur at the anastomosis site which may cause ureteral obstruction (Katayama, 2014). According to Mehl (2006), in cats both ureteral obstruction and ischemic injury can lead to delayed graft function. Lowering the occurrence of ischemic injury can help prevent delayed graft function in felines.

Post-transplant Infections

Lo (2012) mentioned two different studies that have found the post-transplant infection rate to be fairly high in felines. The rate of infection was 25% in one study and

36.7% in another. The first major cause of mortality within the first year after transplantation is acute or chronic rejection. The second leading cause is infections. Infections post-operatively are higher in felines compared to the 14% that occur in human transplant recipients. The common infections that occur in cats are broken into categories. 53% percent of infections were bacterial, 28% were viral, 13% were fungal, and 6.4% were protozoal (Lo, 2012).

Bleedorn (2008) explains that there are some long-term complications that may occur such as the increased risk for infection. This is due to immunosuppressive drugs. Various types of infections can occur and require extreme treatment. Another common complication is urinary tract infections. One serious complication that can occur is the reactivation of chronic respiratory viral infections. When treating these infections special consideration should be taken for nephrotoxic drugs and the impact of the drugs on the half-life of cyclosporine (Bleedorn, 2008).

Hypophosphatemia

Paster (2009) observed that 19-93% of human renal transplant recipients will have hypophosphatemia. This usually occurs shortly after the operation, but can still happen 10 years after the transplant. Hypophosphatemia has been linked with secondary hemolysis, osteodystrophy, pathologic fracture, and decreased phosphorous reabsorption in the renal tubules. Some possible causes of hypophosphatemia include glucocorticoid administration, deficiency of vitamin D, secondary hyperparathyroidism, and disruption of phosphate absorption hormone regulators. Thirty-seven percent of cats had hypophosphatemia with most cases occurring within the first 35 days after transplantation. Some other sequelae to hypophosphatemia include impairment of the

neuromuscular, central nervous system, liver function, and the function of white blood cells. There can also be a loss of bicarbonate and glucose in the renal tubules, lower platelet function and compromised myocardial contractility, that can be reversed (Paster, 2009).

Paster (2009) also found that another sequela of hypophosphatemia is hemolytic anemia. Individuals with this condition have been found to have hyperparathyroidism, anorexia periods with "refeeding syndrome", usage of phosphate-binding antacids, hepatic lipidosis, and diabetic ketoacidosis. The most common treatment for cats with hypophosphatemia is a diet change. This change moves these cats from a phosphorus restricted diet to a maintenance diet. They were also given sodium phosphate orally. Intravenous (IV) treatment is only used in severe cases, because it is linked with kidney failure, hypocalcemia, and tissue dystrophic mineralization (Paster, 2009).

Other Complications

Bleedorn (2008) lists other immediate complications that occur postoperatively are hypertension and neurological signs. The occurrence of neurologic complications has decreased with the better management of hypertension. In feline transplant recipients, 21% of them have central nervous system disorders after surgery. Eighty-eight percent of these cats have had seizures (Bleedorn, 2008).

Toxoplasmosis has been found to be an uncommon sequela that may occur if the transplanted kidney was from a healthy donor that was latently infected. Toxoplasmosis was reactivated in the recipient due to immunosuppression (Bleedorn, 2008). Transplant recipients are also more at risk for diabetes mellitus which increases the risk of infection

even more. The recipients are also more likely to develop neoplasia. The most common is lymphoproliferative neoplasms (Bleedorn, 2008).

Kidney Biopsies

After transplantation, one of the feline recipient's dead kidneys is biopsied. This is done for prognostic and diagnostic reasons (Bleedorn, 2008). De Cock (2004) argues that a standard way to interpret kidney allographs is needed. This is particularly important for clinical trials of anti-rejection treatments. In 1991, the first meeting to discuss the need for human kidney rejection classification was held in Banff, Canada. At this meeting they created the first classification guideline called the Banff '91. Since this meeting there have been many updates to the classification guidelines. The Banff '97 separates all kidney allograft biopsies in to five different categories: normal, anti-body mediated rejection, borderline changes, acute or active rejection, and sclerosing or chronic allograft nephropathy (De Cock, 2004).

De Cock (2004) argues that these human rejection classifications can also be used in felines. The kidney samples are taken from one of the removed kidneys from the feline transplant recipient. This sample had to contain at least one artery and 20 glomeruli. The sample was given a score depending on the state of the glomeruli, tubules, vessels, interstitium, and the parenchymal components. These scores correlate with one of the five categories of biopsies. The classification of the recipient feline's original kidney determined what treatments the feline should receive to prevent rejection of the donor kidney (De Cock, 2004).

Conclusion

Due to the high rate of complications, the potential benefits must outweigh the potential cost for kidney transplants to be considered as a viable treatment option for felines. The rejection and complication rates have decreased with the development and improvement of outcome predictions, pre-transplantation screening, surgical methods, immunosuppression, and post-transplant monitoring procedures. All of these improvements have increased the average survival time after transplantation. To determine if a feline is a good candidate for either donation or transplantation many evaluations and prescreening must be done to predict the outcome. The surgical procedures have changed drastically in the last twenty years to lower the rate of complications and make the surgery more efficient. The development of immunosuppression drugs was the biggest breakthrough in preventing kidney allograft rejection episodes. The more extensive post-transplant monitoring protocols have helped to find post-transplant complications in a timely manner to better prevent rejection and improve the quality of life of the recipient. Overall, kidney transplants in felines is a beneficial treatment to chronic kidney disease and late-stage kidney failure.

References

Bleedorn, J., & Pressler, B. (2008). Screening and medical management of feline kidney transplant candidates: Hundreds of cats with failing kidneys have successfully recovered after undergoing this life-saving procedure. Find out how to determine whether some of your feline patients would make good candidates and how to monitor transplant recipients long-term. *Veterinary Medicine*, *103*(2), 92+.

Budgeon, C., Hardie, R. J., & McAnulty, J. F. (2017). A Carrel patch technique for renal transplants in cats. *Veterinary Surgery*, *46*(8), 1139-1144. doi: 10.1111/vsu.12705

Cáceres, A. V., Zwingenberger, A. L., Aronson, L. R., & Mai, W. (2008). Characterization of normal feline renal vascular anatomy with dual-phase ct angiography. *Veterinary Radiology & Ultrasound*, *49*(4), 350-356.

Danielson, K. C., Hardie, R. J. and McAnulty, J. F. (2015). Outcome of donor cats after unilateral nephrectomy as part of a clinical kidney transplant program. *Veterinary Surgery*, *44*, 914–919. doi:10.1111/vsu.12362

De Cock, H. E. V., Kyles, A. E., Griffey, S. M., Bernsteen, L., & Gregory, C. R. (2004). Histopathologic findings and classifications of feline renal transplants. *Veterinary Pathology*, *41*(3), 244-256.

Durham, A. C., Mariano, A. D., Holmes, E. S., & Aronson, L. (2014). Characterization of post transplantation lymphoma in feline renal transplant recipients. *Journal of Comparative Pathology*, *150*(2-3), 162-168.

Katayama, M., Nishijima, N., Okamura, Y., Katayama, R., Yamashita, T., Kamishina, H., & Uzuka, Y. (2012). Interaction of clarithromycin with cyclosporine in cats: Pharmacokinetic study and case report. *Journal of Feline Medicine and Surgery*, *14*(4), 257-261.

Katayama, M., Okamura, Y., Shimamura, S., Katayama, R., & Kamishina, H. (2014). Influence of phosphate-buffered sucrose on early graft function in feline renal autotransplantation. *Research in Veterinary Science*, *97*(2), 409-411.

Kidney transplants in cats: RCVS considers its guidance. (2016). *The Veterinary Record*, *178*(14), 332.

Kinns, J., Aronson, L., Hauptman, J., & Seiler, G. (2010). Contrast-enhanced ultrasound of the feline kidney. *Veterinary Radiology & Ultrasound*, *51*(2), 168-172.

Lo, A. J., Goldschmidt, M. H., & Aronson, L. R. (2012). Osteomyelitis of the coxofemoral joint due to mycobacterium species in a feline renal transplant recipient. *Journal of Feline Medicine and Surgery*, *14*(12), 919-923.

McAnulty, J. F., & Lensmeyer, G. L. (1999). The effects of ketoconazole on the pharmacokinetics of cyclosporine a in cats. *Veterinary Surgery*, *28*(6), 448-455.

Mehl, M. L., Kyles, A. E., Pollard, R., Jackson, J., Kass, P. H., Griffey, S. M., & Gregory, C. R. (2005). Comparison of 3 techniques for ureteroneocystostomy in cats. *Veterinary Surgery*, *34*(2), 114-119.

Mehl, M. L., Kyles, A. E., Reimer, S. B., Pollard, R. E., Nyland, T., Kass, P. H., Griffey, S. M., & Gregory, C. R. (2006). Evaluation of the effects of ischemic injury and

ureteral obstruction on delayed graft function in cats after renal autotransplantation. *Veterinary Surgery*, *35*(4), 341-346.

Paster, E. R., Mehl, M. L., Kass, P. H., & Gegory, C. R. (2009). Hypophosphatemia in cats after renal transplantation. *Veterinary Surgery*, *38*(8), 983-989.

Schmiedt, C. W., Delaney, F. A., & McAnulty, J. F. (2008). Ultrasonographic determination of resistive index and graft size for evaluating clinical feline renal allografts. *Veterinary Radiology & Ultrasound*, *49*(1), 73-80.

Schmiedt, C. W., Grimes, J. A., Holzman, G., & McAnulty, J. F. (2009). Incidence and risk factors for development of malignant neoplasia after feline renal transplantation and cyclosporine-based immunosuppression. *Veterinary & Comparative Oncology*, *7*(1), 45-53.

Sutherland, B. J., McAnulty, J. F. and Hardie, R. J. (2016). Ureteral papilla implantation as a technique for neoureterocystostomy in cats undergoing renal transplantation: 30 cases. *Veterinary Surgery*, *45*, 443–449. doi:10.1111/vsu.12476

Wormser, C., Mariano, A., Holmes, E. S., Aronson, L. R., & Volk, S. W. (2016). Post-transplant malignant neoplasia associated with cyclosporine-based immunotherapy: Prevalence, risk factors and survival in feline renal transplant recipients. *Veterinary & Comparative Oncology*, *14*(4), 126-134.

Yeates, J. W. (2014). Ethical considerations in feline renal transplantation. *Veterinary Journal*, *202*(3), 405-407.