25 Years of Kidney Transplantation in Hawaii

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The first kidney transplant in Hawaii was performed in August 1969. In the following 25 years, more than 433 kidney transplants were performed. The most common etiology leading to transplantation was chronic glomerulonephritis. Patient and graft survivals after a kidney transplant have progressively improved, particularly after the introduction of cyclosporine in 1984. The overall one-year patient and graft survival rates now are 96% and 85%, respectively; these results exceed the national averages.

Introduction

The first kidney transplant in Hawaii was performed in August 1969 on a 43–year–old man with a diagnosis of membranous glomerulonephritis. Prior to the transplant, he had been maintained on hemodialysis for 17 months. The early efforts of Drs Livingston Wong, David Hume, Arnold Siemsen, and Herbert Y.H. Chinn brought about this surgical procedure; combined with excellent follow-up care provided by the nephrologists, the quality of life for many patients with end-stage renal disease has improved. The growth and development of this new technology was crucial in Hawaii where geographic isolation might otherwise force many patients to travel to the Mainland for kidney transplantation or to remain on dialysis without surgery.

The objectives of this study were to: 1. Examine St. Francis Medical Center's experience from a historical perspective; 2. Compare the results with available national statistics; 3. Review briefly the indications, techniques, and immunosuppression used in kidney transplantation.

Methods

Between August 1969 and December 1993, a total of 433 kidney transplants were performed at St. Francis Medical Center in Honolulu. The approach to patient care, including recipient and donor selection, timing of the transplant, surgical techniques, immunosuppressive protocols, treatment of rejection, and ancillary care have been similar to those described in detail in the literature.[1,2,3,4,5,6,7] Of these 433 transplants, 405 were available for analysis using the UCLA/United Network of Organ Sharing (UNOS) Scientific Registry.

The UNOS Scientific Registry was created in October 1987 following enactment of legislation contained in the Transplant Act of 1984 and records all kidney transplants performed in the United States. Prior to 1987, kidney transplantation registry data was maintained by Dr Terasaki at the UCLA Tissue Typing Laboratory. This retrospective review used the UNOS Kidney Transplant Registry data base and locally available charts at St. Francis Medical Center.

Because of the number of study patients, data was stratified into historical periods:

1. Era I–August 1969 to December 1983. This is referred to as the pre–cyclosporin A (Pre–CsA) period. Immunosuppression consisted of steroids and azathioprine. A total of 186 transplants were performed during this period.

2. Era II–January 1984 to December 1989. The powerful new drug, cyclosporin A (CsA) was introduced and used on all transplant patients to prevent graft rejection, in addition to steroids and azathioprine. OKT3 also was available to treat acute rejections. A total of 137 transplants were performed during this time period.

3. Era III–January 1990 to December 1992. A total of 89 transplants were performed during this time period. The same immunosuppressive regimen as Era II was used.

4. Era IV–January 1993 to December 1993. A total of 21 transplants were done this past year. The same immunosuppressive regimen as Era II and III was used.

Patient and graft survival rates for each era were calculated by statistical analysis using the Kaplan-Meier method for estimating survival. Graft loss was defined as the earliest return to maintenance dialysis, retransplantation, or death and all causes of death were included in the analysis.

Results

The number of kidney transplants performed each year since the premier transplantation in 1969 and the source of donor

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kidneys are shown (Fig 1). Only living-related donor (LRD) kidney transplants were performed in 1969 and 1970. Most of the donor organs came from cadavers (CAD), with a total of 344 cadaver– versus 88 living–related donor kidneys. The patients' ages ranged from 3.5 years to 70 years and 58% were men and 42% were women. The majority of the patient population was Asian (Table 1). Most of these patients had ABO blood type A and were non-diabetic. Some of the common causes of renal failure for our population are listed (Table 2).

The overall patient survival rates were stratified by era. Prior to 1984, prednisone and azathioprine, or *conventional therapy* were used for immunosuppression. After 1984, CsA was added to the immunosuppressive regimen. The overall patient survival rates have improved with each era (Fig 2). The one-year patient survival now is about 97%.

The overall kidney graft survival rates also were stratified (Fig 3). The one-year kidney graft survival in the pre-CsA era was only 45%; now it exceeds 85%.

Both the patient and kidney graft survival rates were better for patients with a living-related donor (LRD) as compared to a cadaver donor (Fig 4 to 7). The current one-year patient survival with an LRD is 100% versus 97% with a CAD. The current one-year kidney graft survival with an LRD is 100% versus 84% with a CAD.

The UNOS Scientific Renal Transplant Registry also provided data based on 41,240 renal transplants performed at 237 U.S. transplant centers between October 1987 and November 1992.[8] These national statistics were compared to Hawaii's: The national overall one-year patient and kidney graft survival rates for cadaver transplants were 93% and 73%, respectively; compared to our most recent results of 95% and 85%, respectively.

The UNOS Scientific Renal Transplant Registry also provided a "1991 Report of Center–Specific Graft and Patient Survival Rates".[9] This report was the first attempt to determine center–specific kidney transplant survival rates for all kidney transplant programs in the United States. In this report, UNOS provided graft and patient survival rates for patients who received a kidney transplant from October 1, 1987 to December 31, 1989. The report analyzed 19,990 kidney transplants performed at 219 separate U.S. transplant programs during this time. In this report, our one-year patient survival of 93% and one-year graft survival of 83% were equivalent to or better than the UNOS national averages (Table 3). The results compare very favorably with those of larger centers in California.

In 1993, 21 kidney transplants were performed in Hawaii: 17 patients received cadaveric organs and 4 received organs from living-related donors. All of the patients have survived to date. Twenty of 21 patients currently have functioning grafts for an overall graft survival rate of 95%. Stratifying the data based on organ source reveals that 100% of the LRD grafts are still functioning and 94% of the CAD organs (16/17) are still functioning.

Discussion

Since the first kidney transplant was performed in Hawaii, kidney transplantation has become the treatment of choice for selected patients with end-stage renal failure. As the sole transplant center for Hawaii, St. Francis Medical Center continues to address the needs of patients with end-stage renal disease. In this retrospective review, the lessons learned over the past 25 years have been tremendous. This retrospective analysis will reflect past accomplishments, compare our current results with those of other centers in the country, and offer a glimpse into the future of kidney transplantation for patients in Hawaii.

As the overall patient and graft survival rates have improved over the years, a milestone improvement seems to be that of better immunosuppression. The survival data improved dramatically after 1984 with the introduction of CsA. This new immunosuppressive regimen presumably allowed for a lower incidence of graft loss from rejection. Although not included in our data, during this period other centers have noted a lower incidence of infection from the lower use of nonspecific immunosuppressive drugs such as prednisone and azathioprine.[7] This might help explain our improved one-year patient survival now at 96% and one-year graft survival now at 85%. Although it is not clear in the data, probably other factors contributed to this improvement including the increased experience of the transplant team, improved ancillary support, better intensive care management, and newer antibiotics such as ganciclovir for treatment of severe CMV infections.

The living-related donor kidney transplants continue to do much better than the cadaveric transplants in long-term graft survival. This is true in all other reports because a living-related donor allows for better HLA matching and shorter ischemic times, thereby avoiding preservation injury from acute tubular necrosis (ATN).

Retrospective reviews and comparison reports are important both to show where we have been and where we could be headed in the future. Data from UNOS compiling national statistics and large center reports have been most helpful.[8,9] In the past, our program had been criticized for its geographic isolation and small size, and it was unfairly assumed that our results would not be as good as those of larger centers. However, our one-year patient survival is equivalent to the national average and our one-year kidney graft survival exceeds the national average. As compared to larger programs in California, our results clearly speak for themselves. This should be very reassuring to the people of Hawaii who rely on St. Francis Medical Center exclusively for their transplantation needs.

Briefly, over the past 25 years, both hemodialysis and renal transplantation have advanced to the point where patients with end-stage renal disease can be managed with good long-term success rates. Recent data indicate that patient survival after transplantation is far superior to that of dialysis. In addition, kidney transplantation continues to be a more cost-effective treatment than dialysis. Perhaps more important, quality of life after successful transplantation is markedly better than dialysis. Thus, in 1994 all patients with end-stage renal disease should be considered as transplant candidates. The only absolute contraindications are active infection, active intravenous drug abuse, positive HIV status, and systemic malignancy. Relative contraindications include hepatitis, history of poor compliance

with medications, or advanced systemic diseases. As the technical aspects of renal transplantation have been perfected, patients in either age extreme or more advanced disease processes have been accepted as candidates.

Preoperative evaluation.—An extensive evaluation of all patients referred for transplantation is performed, including a detailed history and physical exam, routine laboratory studies, chest radiograph, electrocardiogram, blood and human leukocyte antigen (HLA) typing and viral serology. Certain candidates might require more extensive preoperative evaluation such as diabetic patients or patients with potential cardiac and/or pulmonary diseases. Patients older than 65 years constitute an increasingly larger group in the population in general and in those requiring dialysis or transplantation in particular. Careful evaluation of this group must be considered. Once a patient has been accepted for kidney transplantation, donor status is evaluated. Living-related donors are preferred because of the improved survival rates, ability to schedule cases electively, and the shortage of cadaver organs. If no living donor is available, patients are then placed on the cadaver donor waiting list.

Perioperative care.—Current preservation techniques allow kidney storage for up to 72 hours with good success rates. Cold–storage time still is minimized, however, to reduce the incidence of delayed graft function. For this reason, once the cadaver kidney is procured, the recipient is admitted and transplanted as quickly as possible. HLA and blood typing of the donor are performed and preliminary cross matches are done using recipient serum. Once this matching is completed, the kidneys are assigned to the 2 recipients with a negative cross match and the highest number of points according to the allocation system developed by UNOS. This includes the degree of HLA antigen match, length of waiting time, and panel–reactive antibody (PRA). The recipient is admitted to the hospital on an urgent basis; chest radiograph, electrocardiogram, and routine preoperative laboratory tests are performed and a final crossmatch is done. If needed, the recipient is dialyzed prior to surgery. Transplantation occurs within 12 to 24 hours of hospital admission.

Operative procedure.—A central venous pressure monitor is routinely placed in all recipients in order to manage preoperative and postoperative fluids. A Foley catheter is inserted preoperatively and immunosuppressive medications and antibiotics are administered prior to the beginning of the actual surgery. The technical approach to kidney transplantation has remained the same since the procedure was first successfully performed in 1954.

Briefly, a left or right lower-quadrant incision is made and the iliac vessels are dissected free extraperitoneally. The renal artery and vein from the donor kidney are anastamosed to the patient's iliac artery and vein, respectively. Revascularization is performed as quickly as possible to minimize ischemia time to the kidney. Before unclamping the revascularized kidney, the patient is fluid–resuscitated to maintain a systolic blood pressure of 140 mm Hg and central venous pressure to 12 mm Hg.

Table 1 Patient Demographics

Race	Percent
Asian	48.0
White	30.0
Filipino	17.0
Polynesian	4.1
Black	0.6
Hispanic	0.3

ABO Blood Type	Number (Percent)
O	141 (35.0)
A	166 (41.0)
B	64 (16.0)
AB	33 (8.0)
Data Unavailable	2 (0.2)
Total	**405 (100.0)**

Renal Disease	Number (Percent)
Diabetes Mellitis	37 (9.1)
Non-Diabetic	368 (90.9)
Total	**405 (100.0)**

Table 2 Causes of Renal Failure

Primary Diagnosis	Number (Percent)
Chronic Glomerulonephritis	220 (51.3)
Diabetes Mellitus	40 (9.3)
Systemic Lupus	36 (8.4)
Polycystic Kidney	22 (5.1)
Pyelonephritis	5 (1.2)

Table 3 Overall Actual Survival Rates from Oct 1, 1987 to Dec 31,1989

	UNOS	Hawaii	CPMC*	UCSF**
Number of Kidney Transplants with Follow-up	19,588	54	344	521
1-Year Graft Survival (Percent)	80	83	80	77
Number of Kidney Transplants with Follow-up	18,930	54	342	518
1-Year Patient Survival (Percent)	93	93	93	93

* California Pacific Medical Center, San Francisco
** University of California, San Francisco

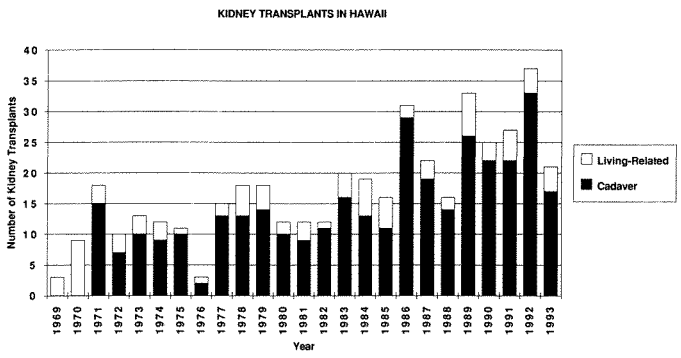

Figure 1.—A breakdown of 433 kidney transplants performed at St. Francis Medical Center by year and donor source.

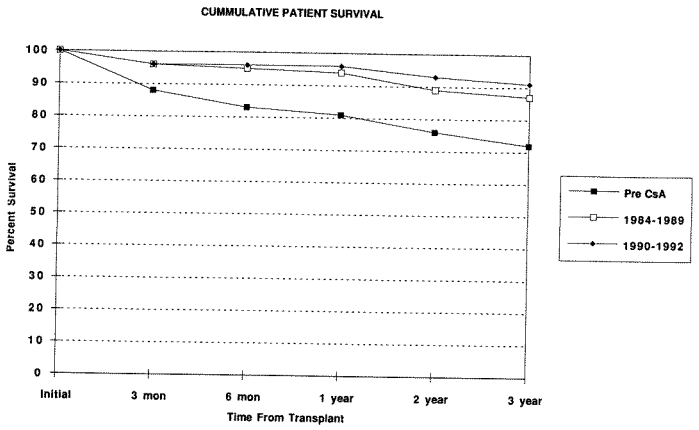

Figure 2.—Overall patient survival rates for recipients of kidney transplants at St. Francis Medical Center. The different eras include Pre CsA (1969 to 1983) and Post CsA (1984 to 1989 and 1990 to 1992).

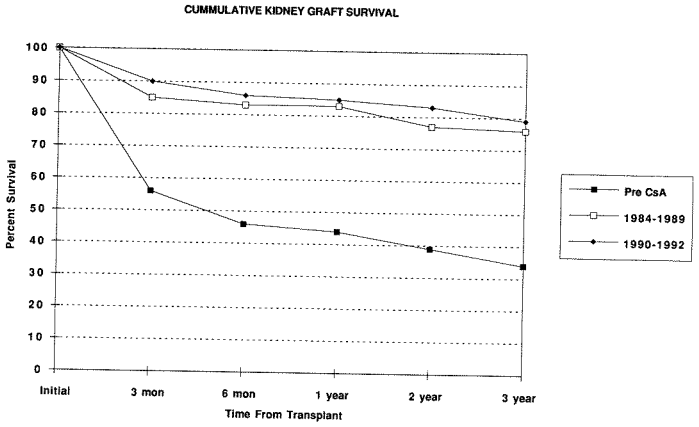

Figure 3.—Overall graft survival rates for recipients of kidney transplants at St. Francis Medical Center.

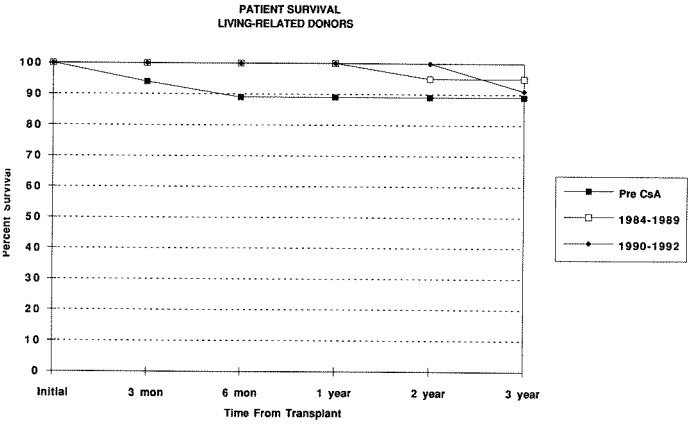

Figure 4.—Patient survival rates for recipients with a living-related donor kidney transplant.

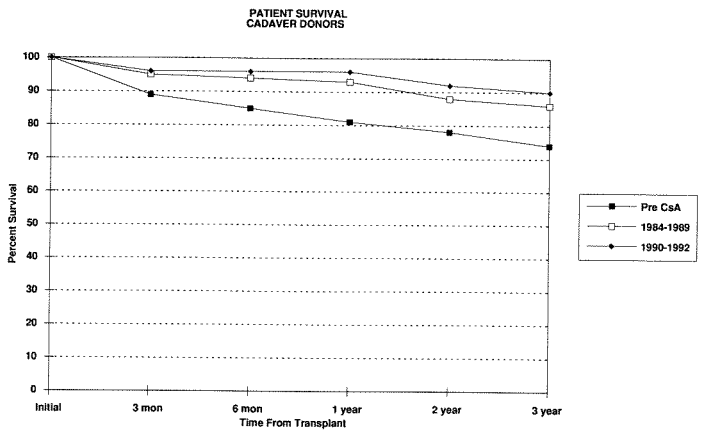

Figure 5.—Patient survival rates for recipients with a cadaver donor kidney.

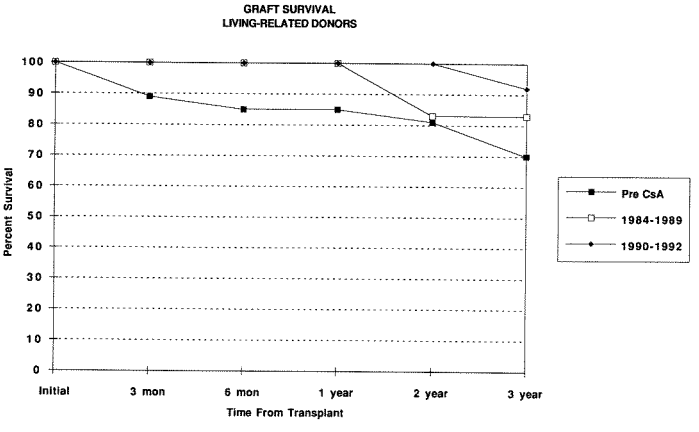

Figure 6.—Graft survival rates for recipients of a living-related donor kidney transplant.

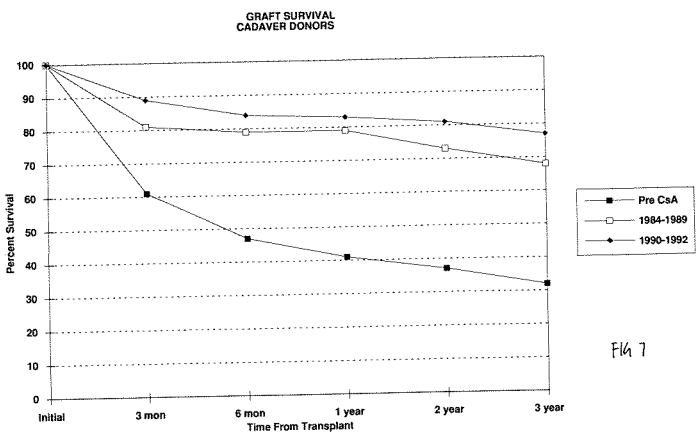

Figure 7.—Graft survival rates for recipients of a cadaver kidney transplant.

Furosemide (Lasix) and mannitol are administered as needed. The ureter is then implanted into the bladder via one of several techniques including the posterior Leadbetter-Politano or the Litch technique.

Postoperative care.—All patients require support in the intensive care unit during the first 24 to 48 hours. Most patients are extubated immediately after completion of the procedure, the fluid and electrolyte status are carefully monitored, and the hourly urine output is recorded and replaced cc for cc during the first 24 to 48 hours. After the first 24 hours, volume replacement is gradually decreased until maintenance replacement levels are reached. Patients with delayed graft function require special attention. Inadequate fluid resuscitation can result in acute tubular necrosis (ATN); overly aggressive fluid replacement can result in pulmonary edema or congestive heart failure.

Medications.—Standard postoperative medications include immunosuppression; the current regimen includes prednisone, azathioprine (Imuran) and CsA in all patients. In addition, OKT3 or ATGAM immunotherapy can be used in cadaver recipients with delayed graft function. These drugs are standard and have been described elsewhere. Other standard medications include H2 blockers and trimethoprim-sulfamethoxazole (Bactrim) to prevent *pneumocystis carinii* and to decrease the incidence of urinary tract infection. Prophylactic antibiotics, CMV prophylaxis and occasionally fluconazol for fungal prophylaxis are used for postoperative care.

Early complications.—Delayed graft function from a preservation injury, ATN, or rejection can occur. A rapid diagnosis using ultrasound or renal scan needs to be done to rule out any technical problems. General complications might occur as with all other surgical procedures. Wound complication such as hematoma, seromas, and infections are of significant concern since these patients are immunosuppressed. Wound complication rates are less than 2%. The most devastating early postoperative complication is bleeding or thrombosis which can present with a sudden onset of anuria. Urologic complications including ureter disruption, urinary leaks and distal ureter stenosis with obstruction can be seen. And as in all organ transplants, acute rejection can occur at any time within the first 3 to 6 months. Chronic rejection and recurrence of original kidney disease also can occur. A kidney biopsy is frequently required to define the cause of a late rise in the serum creatinine level and to direct treatment as needed.

Conclusions

Kidney transplantation has evolved into a treatment of choice for selected patients with end-stage renal disease. With improvements in patient management, HLA matching, and immunosuppressive protocols, the future of renal transplantation will include high risk groups such as the very young or the elderly. It is imperative that all patients with end-stage renal disease be given the option of kidney transplantation. As will be discussed later in this issue of the *Journal*, organ donation remains the major obstacle in kidney and solid organ transplantation. In Hawaii, there are more than 100 patients awaiting kidney transplant. All health professionals can make a difference by selecting and referring appropriate recipients and referring appropriate donors. This *gift of life* must be available to the people of Hawaii.

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