



## Original Research

# Retrospective Analysis of the first 100 Kidney Transplants at the Istanbul Okan University, Health Application and Research Center

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### Abstract

**Objectives:** The renal transplant program of Istanbul Okan University Hospital started in August 2017. Five cadaveric and 95 living donor kidney transplants have been performed for over 16 months. In this study, we aimed to share our experiences regarding kidney transplantation.

**Methods:** In this study, a retrospective analysis of 100 patients who underwent kidney transplantation at the Istanbul Okan University over 16 months, the Health Application and Research Center was carried out. Patients' demographics, creatinine levels of donors and recipients, co-morbid conditions, postoperative complications, features of arterial anastomosis and arterial variations observed on computed tomography angiography of donor-patient were assessed.

**Results:** Mean age of donor patients was  $44.05 \pm 13.76$  (18-71) years. All living donors had computed tomography angiography for assessment of the vascular structure of both kidneys. Accessory right kidney artery was the most dominant vascular variation (16.5%). The primary cause of chronic renal disease was diabetes mellitus (36.4%) and hypertension (15.6%). Mean warm and cold ischemia time was  $1.82 \pm 0.44$  (1-3) and  $40.25 \pm 6.12$  (31-57) minutes, respectively. The most observed postoperative complication was stenosis of ureter anastomosis (4.1%). End-to-end arterial anastomosis between renal and internal iliac arteries was the most preferred anastomosis (57.2%).

**Conclusion:** Increasing kidney transplantation, which is the most appropriate treatment in terms of cost-effectiveness, will be beneficial for patient health and economy of the country.

**Keywords:** Cadaver; donation; donor; Istanbul; kidney; nephrectomy; transplantation.

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End-stage kidney disease is a worldwide health problem that can be defined as a burden, with a prevalence rate of 11-13%.<sup>[1]</sup> Definitive treatment of end-stage kidney disease is kidney transplantation, which provides better clinical outcomes, including overall survival compared to long-term dialysis treatment.<sup>[2, 3]</sup> A one-year graft survival rate of the transplanted kidney is increased to over 90% by the

advances in tissue sampling and immunosuppression.<sup>[4]</sup>

In 2016, 89.823 kidney transplant surgeries were performed worldwide. 40.2% of these transplants were from living donors and 59.8% were from deceased donors.<sup>[5]</sup> Clinical results of living donor kidney transplantation are two times better than deceased donor kidney transplantation.<sup>[1]</sup> Paired kidney exchange transplantation is an al-

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ternative solution for the end-stage renal disease, which might be more preferred in countries having low rates of deceased organ donation and increases the rate of living donor transplants.<sup>[6]</sup>

The renal transplant program of Istanbul Okan University, Health Application and Research Center started in August 2017. Five cadaveric, 95 living donor kidney transplants have been performed over 16 months. The kidney transplant team includes five surgeons,<sup>[5]</sup> five anesthesiologists,<sup>[5]</sup> a nephrologist, a psychiatrist, a cardiologist, an urologic surgeon, a radiologist, an infectious disease specialist, an organ donation coordinator, and two transplant nurses, ten nurses (one donor patient coordinator, one clinical nurse coordinator nurse). During the 16 months, ninety-five living donors and five cadaveric kidney transplants. The donor was relatives in 71 cases (thirteen crossovers, eleven non-relative kidney transplants with an ethical committee approval).

In this study, we aimed to share our experiences regarding kidney transplantation.

## Methods

A retrospective analysis of 100 patients who underwent kidney transplantation between August 2017 and January 2019 at the Istanbul Okan University, Health Application and Research Center was performed. Patient data were obtained from patient files, service follow-up charts, and outpatient follow-up charts. Patients' demographics, creatinine levels of donors and recipients, co-morbid conditions, postoperative complications, features of arterial anastomosis and arterial variations observed on computed tomography angiography of donor-patient were assessed. Hepatitis serology, hypertension, and cardiovascular disease were determined. Mortality and graft loss were also identified.

The presented study was conducted according to the declaration of Helsinki and the Istanbul Okan University, Ethical Board approved the study protocol (March 13<sup>th</sup> 2019,104).

## Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, first quadrant, third quadrant, frequency, percentage, minimum, maximum) were used when study data were evaluated.

## Results

Mean age of donor patients was  $44.05 \pm 13.76$  (18-71) years. Mean hospitalization time of donor patients were  $3.56 \pm 1.32$  (2-6) days. Preoperative mean creatinine was  $0.78 \pm 0.11$  mg/

dl (0.58-1.18) and mean creatinine was  $1.04 \pm 0.25$  (0.73-1.83) mg/dl six months after donor nephrectomy (Table 1). All living donors had computed tomography angiography for assessment of the vascular structure of both kidneys. Accessory right kidney artery was the most dominant vascular variation (16.5%) (Table 2).

Ninety-four (94%) were the first, five (5%) were the second, and one (1%) was the third transplants. Mean age of recipients was  $43.4 \pm 12.93$  (13-65). The cause of primary renal failure is unknown. The primary cause of the chronic renal disease was diabetes mellitus (5%) and hypertension (15%).

**Table 1.** Demographic features and creatinine levels of donor patients

|   | Mean±SD (Min-Max)       |
|---|-------------------------|
| Age (years)                                     |                         |
| Male (n=47)                                     | 40.2±13.64 (18-70)      |
| Female (n=48)                                   | 47.71±13.13 (18-71)     |
| Height (cm)                                     |                         |
| Male (n=47)                                     | 170.88±8.35 (147-188)   |
| Female (n=48)                                   | 162.38±7.27 (141-180)   |
| Weight (kg)                                     |                         |
| Male (n=47)                                     | 63.0±2.64 (49-103)      |
| Female (n=48)                                   | 73.99±12.1 (47-107)     |
| BMI (kg/m <sup>2</sup> )                        |                         |
| Male (n=47)                                     | 27.12±4.53 (19.7-40.3)  |
| Female (n=48)                                   | 28.94±5.50 (18.6- 40.1) |
| Hospitalization time (days)                     | 3.56±1.32 (2-6)         |
| Preoperative creatinine (mg/dl) (n=95)          | 0.78±0.11 (0.58-1.18)   |
| Postoperative day 1 creatinine (mg/dl) (n=95)   | 1.02±0.30 (0.54-1.69)   |
| Postoperative day 7 creatinine (mg/dl) (n=95)   | 1.19±0.26 (0.75-1.97)   |
| Postoperative day 30 creatinine (mg/dl) (n=95)  | 1.16±0.28 (0.75-1.97)   |
| Postoperative day 180 creatinine (mg/dl) (n=46) | 1.04±0.25 (0.73-1.83)   |

**Table 2.** Computed tomography angiography features of arteries in donor patients

|                          | Female (n=48, %) | Male (n=47, %) |
|--------------------------|------------------|----------------|
| Single left RA*          | 39 (84.8)        | 32 (71.1)      |
| Single right RA*         | 38 (82.6)        | 32 (71.1)      |
| Accessory right RA*      | 6 (13)           | 9 (20)         |
| Accessory left RA*       | 5 (10.8)         | 9 (20)         |
| Accessory left-right RA* | 2 (4.3)          | 4 (8.9)        |
| Polar left RA*           |                  | 1 (2.2)        |
| Polar right RA*          | 1 (2.2)          | 2 (4.4)        |
| Polar left-right RA*     |                  | 1 (2.2)        |

\*RA: Renal artery.

Fifty patients were preemptive. Primary initial replacement therapy was hemodialysis in 43 (43%) patients. Mean hospitalization time of recipient patients were 9.21±4.91 (4-32) days. Preoperative mean creatinine was 6.76±2.85 mg/dl (4.55-11.69) and mean creatinine was 2.46±0.23 (0.77-8.33) mg/dl six months after transplantation (Table 3) (Fig. 1).

Seventy-four (77.8%) left, twenty-one (22.2%) right donor nephrectomies were performed, and seven of them

(7.36%) were converted from the laparoscopic approach to open approach. In all cases converted to open procedure, the cause was uncontrolled bleeding. Mean warm and cold ischemia time was 1.82±0.44 (1-3) and 40.25±6.12 (31-57) minutes, respectively. Double-J ureteral catheter was placed in 80 patients and mean removal time of the catheter was 27.2±20.1(11-126) days. The most observed postoperative complication was stenosis of ureter anastomosis (4%). End-to-end arterial anastomosis between renal and internal iliac arteries is the most preferred anastomosis (58%) (Table 4). One graft (1%) was lost due to vein anastomosis dehiscence.

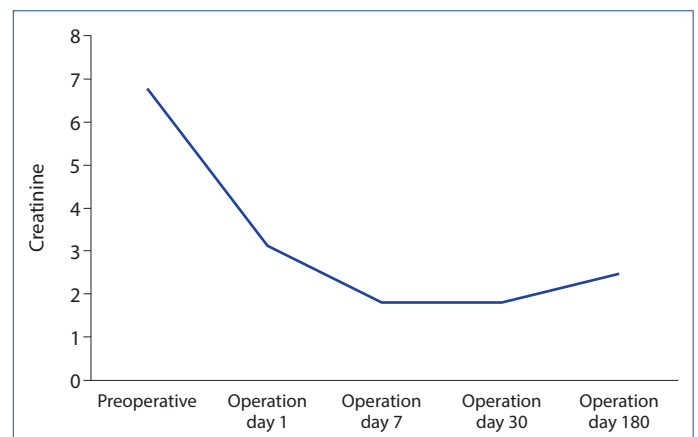
**Table 3.** Demographic features, comorbid conditions and creatinine levels of recipients

|   | n (%)     | Mean±SD (Min-Max)      |
|---|-----------|------------------------|
| Age (years)   | 100 (100) | 43.4±12.93 (13-65)     |
| Height (cm)   | 100 (100) | 168.6±9.58 (141-189)   |
| Weight (kg)   | 100 (100) | 69.57±16.47 (31-104)   |
| BMI* (kg/m <sup>2</sup> )                               | 100 (100) | 24.4± 3.36(19.4- 40.1) |
| Family History of chronic kidney disease                | 13 (13)   |                        |
| Smoker  | 21 (21)   |                        |
| Ex-smoker   | 6 (6)     |                        |
| Hospitalization time (days)                             | 100 (100) | 9.21±4.91 (4-32)       |
| Comorbid conditions                                     |           |                        |
| Diabetes mellitus                                       | 35 (35)   |                        |
| Diabetes mellitus+hypertension                          | 7 (7)     |                        |
| Diabetes mellitus+hypertension+ coronary artery disease | 9 (9)     |                        |
| Hypertension  | 15 (15)   |                        |
| Hypertension+ coronary artery disease                   | 5 (5)     |                        |
| Coronary artery disease+ peripheral vascular disease    | 2 (2)     |                        |
| Amyloidosis   | 4 (4)     |                        |
| Goodpasture's syndrome                                  | 2 (2)     |                        |
| Nephrolithiasis   | 8 (8)     |                        |
| Focal segmental glomerulosclerosis                      | 2 (2)     |                        |
| Systemic lupus erythematosus                            | 1 (1)     |                        |
| Polycystic kidney disease                               | 1 (1)     |                        |
| Preoperative creatinine (mg/dl)                         | 100 (100) | 6.76±2.85 (4.55-11.69) |
| Postoperative day 1 creatinine (mg/dl)                  | 100 (100) | 3.15±1.72 (0.84-9.67)  |
| Postoperative day 7 creatinine (mg/dl)                  | 100 (100) | 1.8±1.64 (0.65-7.94)   |
| Postoperative day 30 creatinine (mg/dl)                 | 100 (100) | 1.76±1.61 (0.6-6.56)   |
| Postoperative day 180 creatinine (mg/dl)                | 49 (49)   | 2.46±0.23 (0.77-8.33)  |
| Previous hemodialysis (months)                          | 46 (46)   | 18.3±22.3 (1-60)       |
| Previous CAPD** (months)                                | 3 (3)     | 4.24±4 (1-7)           |
| Previous blood transfusion (units)                      | 16 (16)   | 3.23±2.12 (1-15)       |

\*BMI: Body mass index; \*\*CAPD: Continuous ambulatory peritoneal dialysis.

**Table 4.** Surgical features and observed surgical complications of recipient patients

|   | n (%)   | Mean±SD (Min-Max)  |
|---|---------|--------------------|
| Transplantation from living donor                   | 95 (95) |                    |
| Transplantation from a cadaveric donor              | 5 (5)   |                    |
| Warm ischemia time (minute) (n=91)                  |         | 1.82±0.44 (1-3)    |
| Cold ischemia time (minute) (n=91)                  |         | 40.25±6.12 (31-57) |
| Double J catheter removal (day) (n=80)              |         | 27.2±20.1 (11-126) |
| Postoperative complications                         |         |                    |
| Arterial anastomosis dehiscence                     | 1 (1)   |                    |
| Ureter anastomosis leakage                          | 1 (1)   |                    |
| Stenosis of ureter anastomosis                      | 4 (4)   |                    |
| Renal arterial stenosis                             | 1 (1)   |                    |
| Pulmonary embolism                                  | 1 (1)   |                    |
| Severe seroma o the surgical side                   | 1 (1)   |                    |
| Hematoma o the surgical side                        | 1 (1)   |                    |
| Arterial anastomosis                                |         |                    |
| End-to-side (renal artery to external iliac artery) | 42 (42) |                    |
| End-to-end (renal artery to internal iliac artery)  | 58 (58) |                    |
| Anastomosis to vascular graft                       | 1 (1)   |                    |



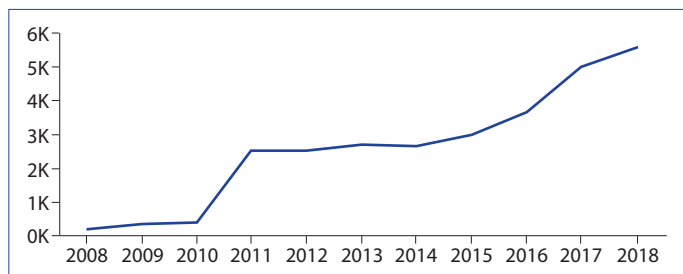
**Figure 1.** Mean creatinine change of recipient over a six-month period.

## Discussion

The first kidney transplant was performed in the world in 1954, while it was first performed in our country in 1975. Since 1975, the number of kidney transplant patients and transplant centers operating in Turkey has increased every year (Fig. 2), and the number of patients suffering from end-stage renal disease also increased.<sup>[4]</sup> In 2018, 76 of 99 organ transplantation centers performed kidney transplantation, 3011 living donors and 859 cadaveric donor kidney transplantations were performed.<sup>[7]</sup>

There is no upper age limit for excluding patient from kidney transplantation. However, the age limit for kidney transplantation, which is generally accepted, ranges between 5-60 years of age and the best result is reported to be between 10-50 years of age.<sup>[8]</sup> Batabyal et al.<sup>[9]</sup> published a systematic review, including fifteen guidelines on kidney transplantation. Majority of guidelines stated that age is not an ineligibility criterion for kidney transplantation. The UK Renal Association guidelines recommended that "age is not a contraindication to transplantation".<sup>[10]</sup> The American Society of Transplantation guidelines also pointed out that "there should be no absolute upper age limit for excluding patients whose overall health and life situation suggest that transplantation will be beneficial".<sup>[11]</sup> In the presented study, the mean age of recipient patients was  $43.4 \pm 12.93$  years and, while the oldest patient was 65 years old, the youngest one was thirteen. Many studies have revealed that kidney transplantation is a safe surgical procedure with a better survival rate compared to hemodialysis for elderly end-stage kidney failure patients.<sup>[12-14]</sup> However, many transplant centers and surgeons are still hesitant to operate elderly patients for kidney transplantation. We think this hesitancy is due to prejudiced opinions because there are no defined absolute criteria for elderly patients.

Accessory arteries of the kidney are the most prevalent and clinically significant vascular variation of kidneys.<sup>[15]</sup> Incompatible with the literature, accessory arteries are the most observed variation of donor kidneys.<sup>[15-17]</sup> The knowledge



**Figure 2.** The increase of kidney transplants in Turkey over a 10-year period (Data obtained from the website of the Turkish Ministry of Health).

of these vascular variations of the kidney is essential for surgeons performing kidney transplantation. Thus, evaluation of these vascular variations before transplant surgery is necessary for operative planning. Computed tomography angiography provides useful information about vascular alterations of the kidney.

Most observed complications of kidney transplant surgery involve renal artery, renal vein, or ureter anastomoses and most of these complications require surgical or radiologic intervention for proper treatment (Table 5).<sup>[18-20]</sup> Our most observed complication was stenosis of uretero-neocystostomy, and three of four complicated cases were treated by a second surgical approach, the interventional radiological approach solved one case. Despite these improvements in outcomes, instances of graft-threatening ureteral obstruction still occur.<sup>[21, 22]</sup> Early stenosis is most often related to perioperative factors, such as a narrow ureterovesical anastomosis, ureteral kinking, or external compression by a lymphocele or hematoma.<sup>[23]</sup> Late stenosis generally occurs due to fibrosis of anastomotic side from chronic ischemia, and polyomavirus BK virus is a known reason for ureter stenosis, reporting a prevalence of 2 to 6%.<sup>[24-28]</sup> Elevated serum creatinine level, which should be discriminated from other causes, alerts the surgeon (Table 6). Ultrasonographic evaluation of the graft usually demonstrates hydronephrosis, which is a useful screening tool, yet the most specific diagnostic method is the percutaneous nephrostogram. Percutaneous balloon dilatation of the obstructed anastomosis by interventional radiology and stent placement may yield good results.<sup>[18]</sup> However, in case of failure, the surgical approach should be preferred.<sup>[19, 20]</sup> Reanastomosis of neoureter for distal strictures or anastomosis of neoureter to native urether may be used to bypass the obstruction side. The most severe observed complication in this series was dehiscence of end-to-side arterial anastomosis between the renal artery and external iliac artery, which was solved by creating a new end-to-side arterial anastomosis via a PTFE vascular graft. The most common cause of vascular anastomosis dehiscence is pseudoaneurysm and hypertension, tissue trauma, weakness of a branch, weakness around valves secondary to absence of circular muscle in the media, atherosclerotic changes, mycotic vasculitis, and dissection of the vein graft is associated risk factors for pseudoaneurysm formation.<sup>[29]</sup> Comorbid conditions of hypertension, coronary artery disease, and surgical trauma were associated risk factors of our case.

Although some doubts sustain on what the best method for kidney artery anastomosis is: end-to-side or end-to-end? Since the use of large Carrel patch obtained from abdominal aorta, creating an end-to-side anastomosis between re-

**Table 5.** Significant surgical complications after kidney transplants

| Cause                   | Characteristics   | Diagnosis  | Treatment   |
|-------------------------|---|--|---|
| Renal vein thrombosis   | - A sudden drop in urine output<br>- Dark hematuria, tender/swollen graft | Ultrasound with Doppler  | Reexploration for thrombectomy or nephrectomy<br>Reexploration, usually for nephrectomy   |
| Renal artery thrombosis | A sudden drop in urine output, usually no tenderness over graft           | Ultrasound with Doppler  |   |
| Ureter obstruction      | - Elevated creatinine   | - Hydroureter (per ultrasound),<br>- Possible lymphoceles (per ultrasound) | - Percutaneous nephrostogram,<br>- Drainage of any lymphoceles  |
| Urine leak              | - Fever, pain over graft, Fluid leakage from the wound                    | - Renal scan,<br>- Fluid analysis for creatinine (high if urine leak)      | - Drainage of any urinoma, Percutaneous nephrostomy and stenting the ureter<br>- Surgical re-exploration for the early leak or unsuccessful medical treatment   |
| Wound infection         | - Erythema around the wound,<br>- Drainage from the wound                 | - Physical examination<br>- Ultrasound or CT (to rule out deep infection)  | - Wound opening (for superficial infection)<br>- Ultrasound or CT (to rule out deep infection) Drainage (for deep infection with fluid collection)<br>- Drainage (for deep infection with fluid accumulation) |

**Table 6.** Causes of postoperative creatinine level elevation

| Cause                      | Characteristics  | Diagnosis   | Treatment  |
|----------------------------|--|---|--|
| Hypo volemia               | -Decreased central venous pressure<br>-Decrease in urine output<br>-Low blood pressure<br>-Lo hemoglobin (if bleeding exist) | Hemoglobin and central venous pressure analysis                         | Rehydration with appropriate fluids  |
| Vascular thrombosis        | -Sudden drop in urine output<br>-Dark hematuria<br>-Tender, swollen graft  | Doppler Ultrasound of graft   | Thrombectomy by inventional radiological approach or reexploration for thrombectomy/nephrectomy                    |
| Bladder outlet obstruction | -Clots in urinary catheter<br>-Sudden drop in urine output   | -Bladder distention (per physical examination or ultrasound)            | -Irrigation or bladder catheter change   |
| Ureter obstruction         | -Elevated serum creatinine<br>-Possible lymphoceles (per ultrasound)   | -Hydroureter (per ultrasound)<br>-Possible lymphoceles (per ultrasound) | -Percutaneous nephrostogram<br>-Drainage of any lymphoceles  |
| Drug toxicity              | High cyclosporine A or tacrolimus level  | Drug level analysis   | Drug dosage lowering   |
| Acute rejection            | Low drug levels or high panel reactive antibody  | Kidney biopsy   | Bolus steroid or anti lymphocyte treatment<br>Plasmapheresis and intravenous immunoglobulin (if humoral rejection) |
| Delayed graft function     | Low urine output since the transplant<br>Risk factors such as prolonged ischemic time and older donor age                    | Renogram may show a picture consistent with delayed graft function      | Expectant management until function improves   |

nal artery and the external iliac artery is the preferred surgical method in transplantation from deceased donor,<sup>[30]</sup> and if a kidney from a living donor is transplanted, the typical choice is the end-to-end anastomosis between the kidney artery and internal iliac artery at many centers.<sup>[30, 31]</sup> In the presented study, the dominant anastomosis technique is end-to-end anastomosis to internal iliac artery if mobilization of the artery and the length of the transplanted artery are sufficient. We prefer this anastomosis technique so that interventional radiology can interfere more efficiently with a future complication. However, no well-designed prospective studies comparing the results of these two methods are available with long-term follow-up.

## Conclusion

The number of kidney transplants performed in Turkey is continuously increasing over the years, but considering the number of dialysis-dependent patients in our country, we think that the number of transplantations is still far below the number of transplantations needed. The most critical negative issue for our country potential is the cadaveric donation rate is lower than expected. Increasing kidney transplantation, which is the most appropriate treatment in terms of cost-effectiveness, will be beneficial for patient health and economy of the country.

## Disclosures

**Ethics Committee Approval:** The presented study was conducted according to the declaration of Helsinki and the Istanbul Okan University, Ethical Board approved the study protocol (March 13th 2019,104).

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – M.F.F.; Design – M.F.F.; Supervision – A.G.; Materials – T.K., Ac.K., A.İ.F.; Data collection &/or processing – M.F.F.; Analysis and/or interpretation – M.F.F., A.G.; Literature search – Ac.K.; Writing – M.F.F.; Critical review – A.K.

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