Original Article

The Impact of Gender Matching Between Donor and Recipient on the Outcome of Kidney Transplant Patients: A Retrospective Study

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ABSTRACT. The influence of donor and recipient gender on patients postkidney transplant (KT) is still controversial, and literature data do not present unanimous conclusions. We were concerned with the gender impact on the outcome of kidney transplantation at the level of acute rejection (AR), graft function represented by serum creatinine level, delayed graft function (DGF), graft survival, and infection rate. The impact of gender matching between donors and recipients was studied in 299 KT recipients performed in the Transplantation Unit, Middle East Institute of Health, Bsalim, Lebanon, between November 1998 and September 2014. The patients were divided into the following groups: Group I (131 patients, male donor to male recipient), Group II (55 patients, male donor to female recipient), Group III (88 patients, female donor to male recipient), and Group IV (25 patients, female donor to female recipient). AR and DGF were not statistically different among the four groups. Moreover, all groups showed excellent graft survival with no statistical difference. Interestingly, human leukocyte antigen AB-DR matching (P < 0.001) and sensitization were statistically different among the four groups (P = 0.05). The number of patients with infections was statistically significantly lower in Group I (35.4%) and Group III (37.5%) (P = 0.35). Most importantly, graft function, represented by serum creatinine, showed a statistically significant difference among the four groups (P <0.004), with Group II (male to female) and Group IV (female to female) showing the best improvement in five-year survival. However, Group III (female to male) had the worst posttransplant graft function. These results revealed that gender impacts graft function, and Group II, male donor to female recipient, had the best 5-year graft function. This emphasizes that gender should be regarded as a determinant for the success of kidney transplantation.

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Introduction

Kidney transplantation (KT) remains the treatment of choice in end-stage renal disease,¹,² however the demand for suitable kidneys is exceeding the supply of available organs, thereby resulting in progressively increased...
need to use both deceased and living organs, older donors, and cross-gender KT. Good improvement has been seen in short-term transplantation outcome, largely due to the introduction of potent immunosuppressive regimens, whereas the long-term graft survival remains suboptimal. This poorer graft function and survival has been attributed to a variety of reasons, including senescence, greater susceptibility to ischemic injury, acute rejection (AR) episodes, and reduced nephron mass in the case of female-to-male transplantation. Although current registry data from the United Network of Organ Sharing report similar graft survival rates for males and females, other reviews on gender differences in kidney transplantation have elicited contradicting results. Recent evidence has demonstrated that the gender of the donor influences several aspects of allograft outcome following kidney and other solid organ transplantation. Short- and long-term outcomes of transplanted organs depend on different donor- and recipient-related factors. Among these, the impact of gender inequality on the outcomes of heart, lung, liver, corneal, and renal transplants has been evaluated in many studies, but with inconclusive results. This was highlighted by the findings that kidney transplants perform better in female than in male recipients, and more specifically, poor graft survival in male recipients transplanted with female kidneys. Compared to males receiving a male kidney and females receiving a female kidney, male recipients receiving a kidney from a female donor had reduced graft survival. Equally important, some reports in the literature have shown that grafts from female donors are more antigenic and more susceptible to both rejection and nephrotoxicity. Moreover, several theories were proposed explaining the poor functional prognosis of female grafts, including protective effect of estrogens, and to the presence of fewer nephrons in female kidneys. The negative influence of female gender on kidney transplants was first reported in 1985 and then confirmed by several studies. It has been suggested that female kidneys perform worse after transplantation as compared with male kidneys, especially when transplanted in a male recipient.

Several mechanisms have been proposed as potential explanations for the effect of gender on renal transplantation, including anatomical and immunological mechanisms. The hyperfiltration hypothesis in human renal transplantation was suggested for the first time by Brenner and Milford, which states that women have smaller kidneys and fewer nephrons than men; hence, the discrepancy between the mass of the grafted kidney and that of the recipient, by inducing nephron overload, could be responsible for the poor long-term outcome of grafts from female donors to male recipients. For instance, several investigations have suggested a graft survival advantage for recipients receiving larger kidneys relative to their body size. Interestingly, females usually have smaller kidneys than males, and it has been hypothesized that the recipient’s metabolic demand exceeds the capacity of the smaller donor kidney, hyperfiltration from nephron underdosing could occur. Larger donor kidney mass in relation to smaller recipient mass diminishes the hyperfiltration injury, and subsequently, immune-mediated rejection. Finally, intrinsic differences in renal physiopathology have been described between men and women; sex hormones may contribute to a different ability to tolerate renal injury. While estrogens have a protective effect, other evidence suggests that testosterone plays a significant role in renal damage. Furthermore, it was shown that alloimmune response mediated by H-Y minor histocompatibility antigens could be associated with AR in gender mismatch investigations of bone marrow, corneal, and kidney transplants. More recently, an analysis from the Collaborative Transplant Study demonstrated that female recipients of male donor kidneys had the worst graft survival after the 1st year and up to 10 years posttransplant. However, other studies have failed to show an influence of donor and recipient gender on graft and patient survival, and this issue is still a matter of debate. Collectively, this suggests that gender
should be considered as criteria in choosing donors and recipients in organ allocation. In this retrospective study, we evaluated the effect of gender disparities between donor and recipient on short- and long-term kidney graft function in 299 kidney transplant recipients.

Methods

Patients and donors

This was a retrospective study conducted between November 1998 and September 2014. Sixteen patients received kidney grafts from deceased donors. The remaining 283 patients received kidneys from living donors after consent from the local and the national ethics committee and the Lebanese Ministry of Health in accordance with the Lebanese rules and regulations. The patients were divided into four groups based on the gender of the donor and recipient: Group I (n = 131; male donor, male recipient), Group II (n = 55; male donor, female recipients), Group III (n = 88; female donor, male recipient), and Group IV (n = 25; female donor, female recipient). Differences in human leukocyte antigen (HLA) AB-DR matching (P < 0.001; Figure 1) and sensitization were compared between the four groups. The study group had other characteristics which were noted: previous transplantation (8/5/6/0), multiple transplantsions (7/3/3/1), multiple pregnancies (0/12/2/5), high panel reactive antibodies score (>20%; 3/3/6/2), and multiple transplantsions and pregnancies (0/3/0/1) in Groups I, II, III, and IV. Three cases of combined multiple transplantsions and previous transplantation were noted in Group I only.

The indications for kidney transplantation (P = NS) included chronic glomerulonephritis (13/7/7/3), chronic pyelonephritis (13/2/6/3), polycystic kidney disease (5/4/12/2), re-transplant (11/5/6/0), focal and segmental glomerulosclerosis (7/4/10/4), arterial hypertension (6/6/5/1), Berger disease (7/2/2/1), interstitial nephritis (4/3/2/1), diabetes mellitus (12/1/3/0), and others, in Group I, II, III, and IV. Recipient body mass index (BMI), donor-to-recipient blood grouping (identical, compatible), and the duration of pretransplant dialysis were comparable among the four groups.

Operation

All transplants were heterotopic and the allografts were placed in the iliac fossa. Vascular anastomoses were performed with the recipient’s external iliac vessels in an end-to-side manner, the vein first and then the artery using prolene 5-0 for the vein and 6-0 for the artery. Vesico-ureteric anastomosis was performed as described by Shanfield. To minimize urological complications, an internal double-J ureteric stent was inserted before ending the uretero-neocystostomy, and then removed six weeks after KT by cystoscopy. A closed drain was left in the operative area before wound closure and removed when the quantity of drain was <50 mL/day. Foley catheters were removed on day 4 after KT and urine culture was routinely obtained.

Peri-operative antibiotic prophylaxis

Intraoperative antibiotic prophylaxis, primarily with intravenous first-generation cephalosporin, or others in case of specific preoperative infections or drug allergies, was instituted for all patients and continued for 24 h thereafter. Intravenous ganciclovir was administered during hospitalization, and the dose was adjusted according to the renal graft function (glomerular filtration rate). Oral valacyclovir or lately valganciclovir was then administered for three months after hospital discharge, or for six-month period in high-risk patients for Cytomegalovirus (CMV) infection, according to antithymocyte globulin Fresenius (ATG-F) extended protocol; for example, multiple AR episodes needing high dose of steroids, or CMV-negative recipient receiving a kidney from a CMV-positive donor. In addition, trimethoprim/sulfamethoxazole was used for one year after the transplant for Pneumocystis jiroveci prophylaxis.

Immunosuppressive regimen

Induction therapy was instituted for 97 patients (74.0%) in Group I, 45 patients (81.8%) in Group II, 53 patients (60.2%) in...
Group III, and for 13 patients (88.0%) in Group IV \( (P = 0.002) \). This consisted of anti-CD25 antibody \( (43/16/13/7) \), or as an intraoperative bolus of ATG-F \( (40/17/31/6) \) or extended regimen \( (14/12/9/0) \) in Groups I, II, III, and IV. Maintenance immunosuppression comprised triple therapy in which cyclosporine (N), FK506 (F), or rapamycin (R) was combined with an antimetabolite [mycophenolate mofetil (C) or azathioprine (A), and prednisone (P)]. These consisted of NAP \( (6/2/5/2) \), NCP \( (40/7/31/7) \), FAP \( (0/1/0/0) \), FCP \( (66/40/36/9) \), N/FCP \( (10/3/7/5) \), N/RCP \( (1/0/4/1) \), and F/NCP \( (4/2/1/0) \) given to Groups I, II, III, and IV patients, respectively. One patient in Group I and another in Group IV received quadruple therapy (FRCP), and two patients in Group III received F/NRCP.

**Diagnosis of infections**

Cultures of urine, throat, nose, and peritoneal fluid in peritoneal dialysis patients, and blood in case of hemodialysis (HD) catheter, were obtained before KT. They were all negative. Serology for CMV, herpes simplex virus, herpes zoster, Epstein–Barr virus and toxoplasmosis virus was obtained before transplantation. Cases with active infections were excluded. After KT, blood, urine, and sputum cultures for bacteria and fungi were performed when indicated. The indwelling arterial and central venous monitoring catheters were removed in all patients as early as possible and their tips were cultured. Similarly, intravascular catheters used for HD access were also cultured. Cultures were also taken from other sites (e.g., drains, peritoneal catheters) when patients had persistently elevated leukocyte counts or episodes of fever. Intravascular catheters were considered infected, using the semi-quantitative culture method of Maki technique,\(^46\) if more than 15 organisms were cultured from the tip of the removed catheters regardless of whether fever was present or whether blood cultures were positive. The urine was considered infected if >100,000 organisms/mL were present. Viral infections were diagnosed on the basis of polymerase chain reaction (PCR) in blood, urine, or tissue specimen, or histological proof of tissue invasion. CMV testing was performed only in symptomatic patients, that is, CMV disease or suspicion of CMV syndrome. Detection of BK virus also was requested in case of occurrence of symptoms, or a rise in serum creatinine. In such cases, kidney graft biopsy and urine BK-PCR tests were performed. Specific immunohistochemistry coloration was performed systematically in all kidney graft biopsies. Bronchoscopy and bronchial lavage were performed when a pulmonary infiltrate was present and sputum samples were inadequate. Chest X-rays were taken daily until extubation, and when indicated. All infections occurring during the 1\(^{st}\) year after transplantation were recorded.

**Diagnosis of rejection**

Allograft biopsies were performed when abnormal renal graft function tests occurred, after ruling out surgical complications by appropriate radiological investigations. The histological criteria for AR proposed by the Banff classification were used.\(^47\) AR episodes were treated with a three-day course of bolus steroids. Steroid-resistant rejection was treated by an additional course of ATG-F.

**Statistical Analysis**

Data analysis was conducted using Statistical Package for the Social Sciences software for Windows version 13.0 (SPSS Inc., Chicago, IL, USA). Data were expressed as percentages of total (categorical variables) or as mean ± standard deviation (continuous variables). Student’s \( t \)-test was used to determine differences in means, and Pearson’s Chi-square or Fisher’s exact tests were used to assess inter-group significance. Statistical significance was set at \( P <0.05 \).

**Results**

**Overview**

Table 1 summarizes the patient demographics. Donor age \( (P <0.001) \) and recipient age \( (P = 0.05) \) were significantly different between
the four patients groups. Preemptive transplantation was performed for 18, 6, 14 and 8 patients, in Groups I, II, III, and IV, respectively and showed no significant difference. Furthermore, there was no statistical significance between recipient BMI, donor-to-recipient blood grouping (identical, compatible) and the duration of pretransplant dialysis.

**Main transplantation outcomes**

The main transplantation outcomes are summarized in Table 2. AR occurred in 21 patients in Group I, 10 in Group II, 13 in Group III and three in Group IV (P = NS), and the need for ATG-F rescue therapy were comparable between the four groups with no significant difference. Excellent five-year actuarial patient and graft survival were seen in the four groups. DGF (6/131, 0/55, 2/88, and 2/25) rates were not significantly different between the four patient groups. Comparable hospital stay (days) was also recorded for Group I (11.9 ± 5.4 days), Group II (11.6 ± 3.8 days), Group III (11.1 ± 4.7 days), and Group IV (10.0 ± 3.2) patients with no significant difference. Figure 1 shows the significant differences seen in HLA AB-DR matching (P <0.001) and sensitization among the four groups (P = 0.05).

Table 1. Study demographics of the patients.

| Parameter                | Group I (131) | Group II (55) | Group III (88) | Group IV (25) | P |
|--------------------------|--------------|--------------|---------------|---------------|---|
| Recipient age (years)    | 43.3±14.4    | 41.0±12.7    | 39.7±12.5     | 36.0±13.2     | 0.05 |
| Donor age (years)        | 33.0±9.3     | 33.6±10.0    | 40.5±9.8      | 43.6±11.4     | 0.00 |
| Recipient BMI (kg/m²)    | 25.0±4.1     | 24.8±5.0     | 25.8±4.1      | 22.7±4.8      | NS |
| Blood group              |              |              | NS            |               |     |
| Identical                | 111          | 42           | 69            | 19            |     |
| Compatible               | 20           | 13           | 19            | 6             |     |
| Dialysis                 |              |              | NS            |               |     |
| Pretransplant (months)   | 17.5±23.2    | 18.2±21.6    | 14.5±22.4     | 20.2±30.4     |     |
| Preemptive (patients)    | 18           | 6            | 14            | 8             |     |

BMI: Body mass index.

Table 2. Main outcomes of the study.

| Parameter                | Group I (131) | Group II (55) | Group III (88) | Group IV (25) | P |
|--------------------------|--------------|--------------|---------------|---------------|---|
| AR, n (%)                | 21 (16.2)b   | 10 (18.2)    | 13 (14.8)     | 3 (10)        | NS |
| Need for ATG-F, n (%)    | 6 (28.5)     | 2 (20)       | 3 (21.4)      | 2 (66.7)      | NS |
| Infections               |              |              |               |               |    |
| Patients, n (%)          | 46 (35.4)    | 30 (54.5)    | 33 (37.5)     | 14 (56)       | 0.035 |
| Episodes                 | 76           | 50           | 50            | 20            | NS |
| Hospital stay (days)     |              |              | NS            |               |     |
| Mean±SD                  | 11.9±5.4     | 11.6±3.8     | 11.1±4.7      | 10.0±3.2     |     |
| Range                    | 6–48         | 6–28         | 6–41          | 6–195         |     |
| DGF, n (%)               | 6 (4.6)      | 0 (0.0)      | 2 (2.3)       | 2 (8.0)       | NS |
| GS (%)                   | 93.1         | 96.4         | 89.8          | 96            | NS |
| GS (censored) (%)        | 97.7         | 100          | 95.5          | 100           | NS |
| Death                    | 7            | 2            | 5             | 1             | NS |
| PS (%)                   | 94.6         | 96.4         | 94.3          | 96            | NS |

ATG: Anti-thymocyte globulin, DGF: Delayed graft function, GS: Graft survival, AR: Acute rejection, SD: Standard deviation, PS: Patient survival, GS: Graft survival.
bStudent’s t-test for continuous variables, Fisher’s exact test for categorical variables. cNumber (percent of total), c at 1 year, c5-year actuarial graft survival, c5-year actuarial graft survival death censored, c5-year actuarial patient survival.
Complications
Death occurred in seven patients in Group I, two patients in Group II, five patients in Group III, and one patient in Group IV. The causes of patients’ death are shown in Table 3. Post-transplant infection rate, during the 1st year after transplantation, between the four groups, was as follows: a total of 76 infectious episodes in 46 patients in Group I, 50 infectious episodes in 30 patients in Group II, 50 infectious episodes in 33 patients in Group III, and 20 episodes in 14 patients in Group IV, which translated into 1.65, 1.66, 1.51, and 1.42 episodes/infected patients in the four groups, respectively. This shows no statistical significance except for the number of infected patients, which was statistically significantly lower in Group I (35.4%) and Group III (37.5%; P = 0.35). The majority of the infections were bacterial (64/76, 43/50, 39/50, and 14/20), followed by viral infections in Groups I (9/76), II (6/50), III (8/50), and IV (4/20), respectively. Three cases of fungal infections were detected in Group I, one in Group II, three in Group III, and two in Group IV patients. There were 12 surgical complications in Group I followed by nine in Group III, seven in Group II, and none in Group IV; however, this was not statistically significant. It included renal artery stenosis (3 in Group I and 2 in Group III), ureteral stenosis (3 in Group I, 1 in Group II, and 1 in Group III), lymphocele (1 in Group I and 2 in Group III), hematoma (2 in Group I, 2 in Group II, and 3 in Group III) and ureteral leak (1 in Groups I, II, and III). Other surgical complications occurred in two patients in Group I and three patients in Group II.

Table 3. Causes of death.

| Group I (n=7) | Group II (n=2) | Group III (n=5) | Group IV (n=1) |
|--------------|---------------|----------------|---------------|
| Pneumonia (3 months) | Cardiac surgery (6 months) | Pneumonia (5 months) | Cardiac cause (17 months) |
| Dysrhythmia (7 months) | Cardiac disease (3 years) | Abdominal sepsis (5 months) | |
| MI (11 months) | | Unknown (9 months) | |
| PTLD (13 months) | | Abdominal GIST (30 months) | |
| H1N1 pneumonia (38 months) | | Cardiac cause (55 months) | |
| Leukemia (4 years) | | | |
| Cardiac cause (4 years) | | | |

MI: Myocardial infarction, PTLD: Posttransplant lymphoproliferative disease, GIST: Gastrointestinal stromal tumor.
Table 4. Graft function (serum creatinine, mg/dL).

| Time posttransplant | Group I (131) | Group II (55) | Group III (88) | Group IV (25) |
|---------------------|--------------|--------------|---------------|--------------|
| Upon discharge      | 1.5±0.7      | 1.1±0.4      | 1.4±0.6       | 1.2±0.7      |
| Postdischarge        |              |              |               |              |
| 1 month              | 1.3±0.4      | 1.0±0.2      | 1.6±0.5       | 1.3±0.4      |
| 6 months             | 1.3±0.3      | 0.9±0.2      | 1.3±0.5       | 1.1±0.3      |
| 12 months            | 1.2±0.2      | 0.9±0.2      | 1.4±0.5       | 1.1±0.3      |
| 36 months            | 1.2±0.4      | 0.8±0.2      | 1.4±0.6       | 1.2±0.4      |
| 60 months            | 1.3±0.4      | 0.9±0.5      | 1.5±1.1       | 1.1±0.3      |

Graft function

The graft survival rates (death censored and uncensored) were comparable among the four groups. Graft function, represented by serum creatinine, showed a statistically significant difference among the four groups ($P < 0.004$), with Group II (male to female) and Group IV (female to female) showing the best improvement in five-year graft function as shown in Table 4. Compared to the other groups, Group III (female to male) had the worst graft function at one, three and five years post-transplant.

Metabolic effects

Table 5 summarizes the metabolic profile among the four groups. Pretransplant serum cholesterol level and the incidence of patients having high blood pressure before transplantation were comparable between the four groups and showed no statistical significance. However, pretransplant fasting blood sugar and triglyceride levels were statistically significantly highest in Group I ($P = 0.001$) and lowest in Group IV ($P = 0.013$). Posttransplant hemoglobin levels were lower than pretransplant levels; significant differences existed between the four patient groups regarding pretransplant ($P = 0.023$) and posttransplant ($P = 0.003$) hemoglobin levels. However, no statistical difference existed concerning the need in posttransplant packed red blood cells unit transfusions between the four groups.

Discussion

Overview

Our results show excellent graft survival and that there was no statistically significant impact of gender on the survival of kidney graft (Table 2). This was consistent with the findings of Vavallo et al among deceased kidney transplantation, and was reminiscent of earlier Korean, Tunisian, and Iranian studies. Precisely, some research reported that donor’s gender did not affect patient or graft survival among female recipients. However, several reports demonstrated that both short- and long-term kidney allograft survival was dependent on the gender of the donor, being

Table 5. Metabolic profile of study patients.

| Parameter                  | Group I (131) | Group II (55) | Group III (88) | Group IV (25) | $P$      |
|----------------------------|--------------|--------------|---------------|--------------|---------|
| Pretransplant glucose (mg/dL) | 99.6±31.6    | 93.4±15.3    | 86.4±22.7     | 85.0±9.8     | 0.001   |
| Pretransplant diabetes, n (%) | 17 (13.1)    | 3 (5.5)      | 5 (5.7)       | 0 (0.0)      | 0.058   |
| Pretransplant hypertension, n (%) | 84 (63.8)   | 28 (50.9)    | 56 (63.6)     | 15 (60.0)    | NS      |
| Pretransplant cholesterol (mg/dL) | 180.3±49.9  | 188.4±51.3   | 181.5±56.1    | 171.2±43.5   | NS      |
| Pretransplant triglyceride (mg/dL) | 201.3±112.8 | 160.5±82.4   | 193.4±109.0   | 143.5±60.8   | 0.013   |
| Pretransplant blood Hb (mg/dL) | 10.5±2.0     | 10.3±1.9     | 10.2±2.4      | 9.0±2.0      | 0.023   |
| Posttransplant blood Hb (mg/dL) | 7.6±1.8      | 6.7±1        | 7.5±1.7       | 6.8±1.6      | 0.003   |
| # Hb blood level*            | 2.9±1.8      | 3.6±2.0      | 2.9±1.8       | 2.5±2.0      | NS      |
| Number of posttransplant units transfusion (patients) | 62 (24)     | 37 (16)      | 41 (21)       | 10 (6)       | NS      |

*Difference between pre- and post-transplant hemoglobin blood levels, Hb: Hemoglobin.
worse when kidneys from female donors were transplanted into male recipients.\textsuperscript{17-19,50} In parallel to this, Ben Hamida reported poor five- and 10-year graft survival rates of male and even female recipients receiving grafts from female donors.\textsuperscript{49} Moreover, Santiago et al showed after a 10-year follow-up period that with regards to graft survival, those from male donors were observed to have longer survival rates as compared to the ones from female donors.\textsuperscript{51} Guo et al found that donor/recipient gender mismatch was associated with significantly worse one-, three-, and five-year graft or patient survival, although gender mismatch had no deleterious effects on DGF in kidney transplantation.\textsuperscript{52} This latter finding goes in parallel with our study findings, in which DGF was not statistically different among genders. Furthermore, Oh et al emphasized that the recipient gender was more important than the donor gender and particularly that the effect of recipient gender on graft function was influenced by the metabolic demands, which were higher in male recipients.\textsuperscript{53} Interestingly, it was shown that female recipients had worse short-term graft survival but the best long-term graft survival.\textsuperscript{54} Moreover, in our analysis, there were no statistically significant differences among the groups with regard to the episodes of AR contrary to Zukowski et al, who showed female recipients of male kidneys to experience a greater risk of early graft loss compared with all other gender combinations.\textsuperscript{55}

Our study showed that gender has a statistically significant impact on graft function (Table 4), which is represented by serum creatinine level (mg/dL). Female recipients were associated with a better graft function for a five-year follow-up period. This was consistent with a previous research where Vavallo et al showed lower serum creatinine level (mg/dL) in male donors to female recipients group as compared with other donor–recipient gender combinations, although this difference lost statistical significance after the 3\textsuperscript{rd}-year posttransplantation.\textsuperscript{58} However, our findings show that female-to-male transplant has the highest level of serum creatinine level after a five-year follow-up period, in which it reached 1.5 ± 1.1 mg/dL, which points toward the poorest graft function in female-to-male kidney transplantation.

**Female-to-male match**

Group III (female to male) had the worst graft function at one-, three-, and five years posttransplant. This finding is consistent with a previous research; for instance, Zeier et al documented an inferior graft outcome when kidneys of female donors were transplanted into male recipients as compared with kidneys from male donors regardless of recipient gender.\textsuperscript{17} Furthermore, Zhou et al\textsuperscript{54} concluded that female-to-male kidney transplant showed poor graft survival. In addition, Vereerstraeten et al found after multivariate analysis that female donation to male recipients increased the risk of graft failure by 60\%.\textsuperscript{29} Some hypotheses were proposed to explain why a female kidney allograft functions poorly in a male recipient. These include “nephron underdosing,”\textsuperscript{27} which centers on the fewer nephrons present in female than male kidneys, typically 17\% less,\textsuperscript{22,25,26} which, in turn, increases the workload of individual nephrons. Another possibility is the immunogenicity of female allografts,\textsuperscript{17} and this was consistent with increased incidence of early AR episodes in female kidneys.\textsuperscript{3}

**Male-to-female match**

According to our results, Group II (male to female) had the best kidney graft function, and the investigators speculated that in the context of nephron underdosing, the male-to-female transplant combination has improved graft survival as male kidneys are characteristically larger.\textsuperscript{56} The pathophysiology has been explained by larger kidneys having more glomeruli,\textsuperscript{29} and more glomeruli translate to less susceptibility to progressive renal failure.\textsuperscript{30} As a consequence, in the setting of a larger donor compared to recipient, there is less metabolic demand on the donor graft, thus less hyperfiltration-induced injury.\textsuperscript{53} Precisely, hyperfiltration from nephron underdosing has been hypothesized to initiate pathologic, structural kidney damage to the transplanted
kidney, ultimately resulting in graft dysfunction and failure.\textsuperscript{27}

**Same-sex match**

However, some believe that sex-matching kidney donors and recipients may result in better outcomes in the way that females may not need as many nephrons and could benefit from the less risky female donor kidney.\textsuperscript{40}

**Factors affecting survival in gender mismatch**

1. **Kidney/body weight ratio:** Notably, Giral et al\textsuperscript{57} reported that donors/recipients’ weight incompatibility is an independent predictor of long-term graft survival after kidney transplantation. Precisely, the number of glomeruli per kidney as well as the mean glomerular volume closely correlate with kidney weight and negatively correlate with patient age.\textsuperscript{14} However, Vianello et al\textsuperscript{58} found that an imbalance of the donor and recipient kidney/body weight ratio had no major effect on kidney graft function and survival after four years.

2. **Number/volume of glomeruli:** Information on the number of glomeruli in the two genders is also conflicting: Nyengaard and Bendtsen\textsuperscript{59} McLachlan et al,\textsuperscript{60} and Neugarten et al\textsuperscript{32} found similar numbers of glomeruli in males and females, but larger glomerular volumes.

3. **Immune factors:** They may be indirectly assessed by the number of episodes necessitating antirejection therapy. Indeed, a significantly higher proportion of patients required antirejection treatment by one year after transplantation when kidneys from female donors had been transplanted into male recipients compared with kidneys from male donors transplanted into male recipients. For instance, Vereerstraten et al\textsuperscript{9} saw a higher incidence of AR episodes in male recipients of kidney grafts from female donors.

4. **Hormonal:** Sex hormones influence some endothelial cell indices in the way that androgen exposure increases mononuclear cell adhesion to vascular endothelial cells.\textsuperscript{61} Our results are in contrast with the findings of Meier-Kriesche et al\textsuperscript{62} who found a higher risk of ARs for female recipients but a higher risk of chronic rejection in males. This may be explained by more intense stimulation of the immune system in a high-estrogen environment, as suggested by some experimental and clinical studies.\textsuperscript{63}

**Study limitations**

It was a retrospective, single-center study, with a limited number of patients, with a relatively short-term follow-up. In addition, data about the hormonal levels of the patients were missing.

**Conclusion**

Our study supports the notion that gender does impact graft function, but not survival, and male-to-female kidney transplantation is associated with a better graft function. Despite its limitations, our study recommends inclusion of gender as a key determinant of the success of kidney transplant.

**Conflict of interest:** None declared.

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