

The Effect of Donor Age on Recipient Kidney Graft Function

Donör Yaşının Alıcı Greft Fonksiyonu Üzerine Etkisi

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ÖZ

Amaç: Son dönem böbrek hastalığı (SDBH) morbidite ve mortalitesi yüksek bir durumdur. Böbrek nakli bu durumun hasta açısından en çok tercih edilen ve en çok fayda sağlayan tedavi yöntemidir. Yaş, transplantasyonun başarısını etkileyebilecek önemli bir faktördür. Bu çalışmada donör yaşının böbrek nakli sonuçları üzerindeki etkisini araştırdık.

Araçlar ve Yöntem: Bu çalışmaya canlı veya kadavradan böbrek nakli yapılmış 101 SDBH olan hasta retrospektif olarak incelendi. Vericilerin yaş, cinsiyet ve vücut kitle indeksi (VKİ) ve alıcıların yaş, cinsiyet, VKİ, hastanede yatış süreleri, tahmini glomerüler filtrasyon hızları (eGFR) ve serum kreatinin ölçümleri kaydedildi. Alıcı serum kreatinin seviyeleri, nakilden sonraki 18 aya kadar aralıklarla kaydedildi.

Bulgular: Donörler yaşlarına göre (<40 yaş (n:42), 40-50 yaş (n:25) ve >50 yaş (n:34)) olmak üzere 3 gruba ayrıldı. Vericinin cinsiyeti, VKİ, canlı/kadavra oranı ve alıcının cinsiyeti, yaşı ve VKİ açısından istatistiksel olarak anlamlı fark saptanmadı (p>0.05). Verici <40 yaş olan alıcıların hastanede kalış süreleri diğer yaş gruplarına göre istatistiksel olarak anlamlı derecede düşüktü (p:0.001) 1. aydan 18. aya kadar donör yaşı arttıkça GFR'de istatistiksel olarak anlamlı azalma ve serum kreatinin değerinde artış gözlemlendi (p<0.05).

Sonuç: Donör yaşı, greft sağkalımı için önemli bir faktördür ve organ dağıtım prosedürlerinde göz önünde bulundurulmalıdır.

Anahtar Kelimeler: donör; greft sağkalımı; yaşlanma

ABSTRACT

Purpose: End-stage renal disease (ESRD) is a highly morbid and mortal condition. Renal transplantation is the most favorable and preferred solution of this disease. Age is an important factor that can effects the success of transplantation. In this study, we investigated the effect of donor age on the outcomes of kidney transplantation.

Materials and Methods: 101 ESRD patients who underwent live or cadaveric kidney transplantation were included and analyzed retrospectively in this study. We reviewed age, sex and body mass index (BMI) of the donors and age, sex, BMI, length of stay, estimated glomerular filtration rate (eGFR) and serum creatinine measurements of the recipients were recorded. Recipient serum creatinine levels were determined at intervals up to 18 months after transplantation.

Results: Donors were divided into 3 groups according to age (<40 years (n:42), 40-50 years (n:25) and >50 years (n:34). There was no statistically significant difference between the groups in terms of donor's gender, BMI, living/cadaveric ratio, and recipient's gender, age, and BMI (p>0.05). Length of hospital stay of recipients whose donor <40 years old were statistically significantly lower compared to other age groups (p:0.001). From the 1st month to the 18th month, a statistically significant decrease in GFR and an increase in serum creatinine were observed as the donor age increased (p<0.05).

Conclusion: Donor age is an important factor for the graft survival and for the allocation procedures it should be kept in mind.

Keywords: ageing; donor; graft survival

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INTRODUCTION

End-stage renal disease (ESRD) is one of the mortal conditions around the world.¹ Hemodialysis is a temporary solution but it is not favorable for the patients' quality of life.¹ Therefore, kidney transplantation is more preferred solution by the ESRD patients and when compared to the hemodialysis.² However, shortage of donated organs is the most important problem for kidney transplantation.^{1,3} It is important to use either living or cadaveric donor organs appropriately to increase the lifespan of transplanted organ and transplant patients.^{1,3}

There are so many factors that influence the outcomes of kidney transplantation which are related to both kidney donors and the receivers such as age, sex, comorbidities, family history, immunity, and genetic factors.^{4,5} In addition, it has been shown that the number of functional units of the donated kidney has a close relationship with graft functions and survival.^{3,6} However, the functional units of the donated kidney decrease with age and the outcomes of the transplantation may worsen due to this effect.^{4,6,7} Therefore, some age-matching strategies were even suggested to improve total graft survival in the literature.^{6,8}

In the present study, we aimed to investigate the effect of donor age on the outcomes of kidney transplantation in our clinic.

MATERIALS and METHODS

This study was conducted in accordance with the Declaration of Helsinki and all patients have given written informed consent. After getting approval from Ankara City Hospital No. 2 Clinical Research Ethics Committee (IRB number: E2-22-2074 Date: 06.07.2022), we retrospectively collected the data of 101 ESRD patients who underwent live or cadaveric kidney transplantation in the Urology department of Ankara City Hospital. Data of age, sex and body mass index (BMI) of the donors and age, sex, BMI, length of stay, estimated glomerular filtration rate (eGFR) and serum creatinine measurements of the recipients were determined. Recipient serum creatinine levels were determined at intervals up to 18 months after transplantation. BMI was calculated by height and weight

measurements and waist circumference. The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) equation.⁹

All living donors underwent laparoscopic transperitoneal donor nephrectomy. The left kidney was the first choice. The donated kidney was placed in the right iliac fossa of the recipient. Vascular anastomosis was performed to the external iliac artery and vein. Ureteroneocystostomy was performed with a double-J ureteral catheter using the antireflux Lich-Gregoir technique. The mean time for ureteral double-j stent removal was 3 weeks.

For the induction treatment, methylprednisolone and basiliximab/anti-thymocyte globulin-ATG were used as immunosuppression in the recipients.

Statistical Analysis

Statistical Package for Social Sciences (SPSS), version 22.0 (SPSS Inc. Chicago, USA) computer package program was used for statistical analysis of the research data. Distribution of data was tested with the Shapiro-Wilk test. In the descriptive statistics section, categorical variables were presented as numbers, percentages. Data are presented as mean±SD. Kruskal–Wallis were used for comparison of data among groups. The relationship between recipient serum creatinine, eGFR and Donor age was evaluated by Spearman's correlation method. $p < 0.05$ was considered statistically significant.

RESULTS

In Table 1, the comparison of donor-recipient characteristics and recipients' graft functions according to donors' age is presented. Donors were divided into 3 groups according to age (<40 years (n:42), 40-50 years (n:25) and >50 years (n:34). There was no statistically significant difference between the groups in terms of donor's gender, BMI, living/cadaveric ratio, and recipient's gender, age, and BMI ($p > 0.05$). Length of hospital stay of recipients whose donor <40 years old were statistically significantly lower compared to other age groups ($p:0.001$). From the 1st month to the 18th month, a statistically significant decrease in GFR and an increase in serum creatinine were observed as the donor age increased

($p < 0.05$) (Table 1).

Table 1. Donor-recipient characteristics and graft functions according to donor age.

| Donor-recipient character | Donor Age | | | p |
|--|------------------|--------------------|------------------|--------|
| | <40 years (N=42) | 40-50 years (N=25) | >50 years (N=34) | |
| Donor | | | | |
| Sex, M/F | 22/19 | 10/14 | 22/12 | 0.22 |
| Age, yr | 29.57±6.71 | 44.28±2.79 | 55.76±4.56 | <0.001 |
| BMI(kg/m ²) | 25.37±3.86 | 25.84±2.33 | 25.65±2.7 | 0.82 |
| Living/cadaveric | 32/10 | 22/3 | 22/12 | 0.12 |
| Recipient | | | | |
| Sex, M/F | 27/15 | 21/4 | 20/14 | 0.1 |
| Age, yr | 42.41±15.63 | 37.58±14.35 | 39.31±12.94 | 0.44 |
| BMI(kg/m ²) | 24.14±4.66 | 23.64±4.65 | 23.06±5.5 | 0.48 |
| Hospital stay, day | 18.2±9.61 | 27.04±17.98 | 27.06±14.44 | 0.001 |
| 1 Months sCreatinine(mg/dL) | 1.19±0.6 | 1.51±1.03 | 1.92±1.5 | 0.001 |
| 1 Months eGFR (ml/min/1.73 m ²) | 79.92±30.86 | 71.58±35.76 | 53.67±24.33 | 0.001 |
| 6 Months sCreatinine(mg/dL) | 1.05±0.3 | 1.47±0.52 | 1.77±1.43 | 0.001 |
| 6 Months eGFR (ml/min/1.73 m ²) | 81.63±24.4 | 64.13±25.84 | 58.75±26.44 | 0.001 |
| 12 Months sCreatinine(mg/dL) | 0.98±0.24 | 1.35±0.37 | 1.92±1.37 | <0.001 |
| 12 Months eGFR (ml/min/1.73 m ²) | 81.41±20.33 | 64.82±15.76 | 50.69±22.59 | <0.001 |
| 18 Months sCreatinine(mg/dL) | 0.99±0.29 | 1.41±0.35 | 1.60±0.55 | 0.001 |
| 18 Months eGFR (ml/min/1.73 m ²) | 81.02±19.67 | 61.42±13.72 | 51.17±15.17 | 0.001 |

BMI: body mass index, eGFR: estimated glomerular filtration rate

Table 2. Spearman's correlation analysis between graft functions and donor age.

| Donor age | Spearman's correlation coefficient | p |
|--|------------------------------------|--------|
| 1 Months sCreatinine(mg/dL) | 0.441 | <0.001 |
| 1 Months eGFR (ml/min/1.73 m ²) | -0.431 | <0.001 |
| 6 Months sCreatinine(mg/dL) | 0.424 | <0.001 |
| 6 Months eGFR (ml/min/1.73 m ²) | -0.474 | <0.001 |
| 12 Months sCreatinine(mg/dL) | 0.572 | <0.001 |
| 12 Months eGFR (ml/min/1.73 m ²) | -0.595 | <0.001 |
| 18 Months sCreatinine(mg/dL) | 0.653 | <0.001 |
| 18 Months eGFR (ml/min/1.73 m ²) | -0.684 | <0.001 |

eGFR: estimated glomerular filtration rate

The relationship between recipients' graft functions and donor age were presented in Table 2. A statistically significant positive correlation was found between donors' ages and recipients' creatinine levels at 1., 6., 12. And 18. month follow-up ($p < 0.001$). There was significant negative correlation between donor ages and the recipient eGFR levels at 1., 6., 12. And 18. month follow up ($p < 0.001$).

DISCUSSION

Despite the decrease in the functions of transplanted kidneys with the age, transplantation still has an advantageous position when compared to hemodialysis, because the risk of death of hemodialysis patients is approximately 2 fold higher than old-age kidney transplanted recipients.^{10,11} Especially for cadaveric donors, when the age increased over a level, histologic evaluation becomes important for protecting the recipient from age-related side effects.^{11,12} However, this is still

controversial because of the unjustified exclusion of kidneys with insufficiently validated histopathological scoring systems.¹³ In our study, the outcomes of the transplantation in 18 months-long period, got worsened with the increased age of donors. Ultimately, we found that, the creatinine levels increased and eGFR values decreased in older donor's recipients.

Sekito et al. analyzed 45 living kidney transplant patients whose donors were classified as <60 and >60 years old. They found that the older donor kidneys had a lower rate of eGFR and creatinine levels but the decline in 2 years was similar to young ones.⁶ In our study, we analyzed only laboratory findings and found nearly similar results, but we also included the cadaveric donors. It should be noted that this difference may also be due to the inclusion of cadaveric donors. Furthermore, Shahani et al. analyzed donors according to the age of donors and recipients as young to young, young to old, old to young or old to old in their study of kidney transplantation with 500 living donors.³ They found the best creatinine levels and graft survival in the young donor to old recipients group.³ Although we did not perform an age-related matching between donors and recipients in our study, we obtained similar functional results in transplantation with younger donors and older donors. We showed that the younger donor showed better function in the recipient.

Since transplantation is much more advantageous for the patient's life, criteria have been proposed to solve the problem of discarding marginal kidneys in order not to abandon transplantation in cases of high donor age.^{10,11} Both clinical criteria and histological criteria have been investigated but their validity is still debated.¹²⁻¹⁴ A careful preliminary evaluation of donor, and patient selection procedures are crucial for the prognosis of transplanted patient.^{11,12}

Besides the selection criteria, the knowledge about the risk of increased age, makes scientists think about allocating the organs according to adjusted years. Shifting the priority of transplanted young organs to young patients and old organs to old patients is also suggested to improve results and protect both older and younger age groups from age-related factors.¹⁵

The old-for-old program has been used to save marginal donor organs.¹⁶ Single or dual transplantation decision based on donor and recipients characteristics and preimplantation histologic investigations could decrease the graft rejection rate and also contribute to the low donor pool reserve.¹⁶ Despite the Shahani et al reported that transplantation from young donors to older recipients yielded advantageous outcomes,³ some studies have considered transplantation of young kidneys to older recipients as wasted graft years for the whole organ waiting list.¹⁷ Although the results are worse in the old for old transplantation than young for young one, this allocation method may decrease the waiting time of the old recipients and increases the lifetime of that patients compared to hemodialysis.^{10,17}

In conclusion, donor age is an important parameter that influence the results of transplantation. For the allocation procedures, the distribution of the kidneys must be decided after a careful evaluation. Age-matching procedures, preimplantation biopsies, and multiple organ transplantations can be performed to increase the lifespan of the grafts and transplanted patients.

Study Limitations

The limitations of our study include retrospective analysis of the patients, not analyzing patients by dividing

cadaveric or living donors separately, and not being matched the age of donors and recipients each other.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Ethics Committee Permission

Approval was obtained from Ankara City Hospital No. 2 Clinical Research Ethics Committee (IRB number: E2-22-2074 Date: 06.07.2022).

Authors' Contributions

Concept/Design: MEŞ, MEP, MY. Data Collection and/or Processing: MEP, MK, EO. Data analysis and interpretation: MEŞ, MK, EO, MY. Literature Search: MEŞ, MEP, EO, MY. Drafting manuscript: MEP, MY, EO. Critical revision of manuscript: MK, EO, MY, EO.

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