© Ann Transplant, 2010; 15(2): 21-26

Original Paper

Received: 2009.09.20
Accepted: 2010.03.03
Published: 2010.06.30

Does age of recipient affect outcome of renal transplantation?

Maryam Moghani-Lankarani[1,2], Shervin Assari[1,2], Mirmohsen Sharifi-Bonab[3], Mohammad-Hossein Nourbala[4], Behzad Einollahi[4]

[1] Medicine and Health Promotion Institute, Tehran, Iran
[2] Universal Network for Health Information Dissemination and Exchange (UNHIDE)
[3] Clinical Research Unit, Baqyiatallah University of Medical Sciences, Tehran, Iran
[4] Nephrology and Urology Research Center, Baqyiatallah University of Medical Sciences, Tehran, Iran

Summary

Background: The outcome of renal transplantation in the elderly, with respect to both patient and graft survival, is not as unambiguous as that in the young.

Our aim was to compare the outcomes of kidney transplantation in old and young recipients.

Material/Methods: This historical cohort study, conducted at Baqyiatallah Hospital, Tehran, Iran, enrolled 358 young (<60 years old) and 44 old (≥60 years old) renal recipients. The main outcomes comprised the subjects' estimated glomerular filtration rate (e-GFR), graft survival (death-censored and death-uncensored), and patient survival at 6 months, 1 year, 2 years, 3 years, and 5 years. Additionally, the causes of death were registered in each group.

Results: There was no significant difference as regards 6-month, 1-year, and 5-year e-GFR and death-censored graft survival between the elderly and young recipients ($p>0.05$), but 5-year patient survival and death-uncensored graft survival were significantly worse in the elderly recipients ($p<0.05$). The frequency of death due to cardiac or cerebrovascular disease was not significantly different between the 2 groups ($p>0.05$).

Conclusions: Given the similar death-censored graft-survival rates in our old and young kidney recipients, it would be ill-advised to exclude transplant candidates on the basis of their age.

Key words: **kidney transplantation • outcome • survival • elderly**

Full-text PDF: http://www.annalsoftransplantation.com/fulltxt.php?ICID=880936

Word count: 1758
Tables: 3
Figures: –
References: 38

Author's address: Shervin Assari, Medicine and Health Promotion Institute, Tehran, Iran, e-mail: assarish@yahoo.com

Background

Kidney transplantation in young recipients is believed to augment patient survival, enhance the quality of life, and obviate the need for dialysis [1–3]. The benefits to the elderly, however, have yet to be thoroughly assessed [4–6], and transplantation outcomes have yet to be fully elucidated by prospective studies [7–13].

A substantial number of elderly patients with end-stage renal disease (ESRD) are liable to be excluded from renal transplantation waiting lists on the grounds of lower life expectancy and higher risk of serious infections due to immunosuppressive medications. A majority of these patients, therefore, receive chronic hemodialysis for the remainder of their lives [14–16]. Optimal renal transplantation in the elderly is difficult to achieve because of organ shortage, allocation policies, non-standardized immunosuppressants, and high waiting-list mortality rates.

Scientific incongruities cannot be blamed for this half-hearted interest in renal transplantation for the elderly [17]; on the contrary, recent years have witnessed the advent of countless major scientific advances improving patient and graft survival rates [15,18]. Another significant factor is the recent increase in age at transplantation [19], conceivably due to the general improvement in health care and the concomitant rise in age at onset of ESRD [20].

A comparison of the outcomes of kidney transplantation between old and young recipients is presented.

Material and Methods

This historical cohort study was conducted in the Nephrology Urology Research Center, Tehran, Iran. Other reports have been previously published from this data set [21].

Participants and sampling

This study enrolled 358 young (<60 years old) and 44 old (⩾60 years old) kidney recipients, all having undergone renal transplantation at Baqyiatallah Hospital, Tehran, Iran, between 1995 and 2005. Census sampling was performed, and the participants were selected from all the consecutive first transplants at this hospital during the study period. Patients who had received preemptive transplantation were excluded from this study.

Measures and measurements

All subjects had the same diagnostic and therapeutic protocols before and after transplantation. In keeping with the screening protocol prior to transplantation, all candidates underwent cardiovascular (physical examination, electrocardiogram, and echocardiography), respiratory (physical examination and plain chest radiography), gastroenterological (physical examination and esophagogastric endoscopy), gynecological (physical examination and pregnancy test), periodontal, and ear-nose-throat (physical examination) evaluations in combination with routine malignancy screening tests (rectal and breast examinations), Prostate-Specific Antigen, and mammography. The kidney recipients were also tested for infectious diseases (human immunodeficiency virus antibody, cytomegalovirus antibody, Epstein-Barr virus antibody, purified protein derivative, Venereal Disease Research Laboratory, Wright, Vidal, urine analysis, urine culture, and stool exam), as well as for blood typing, leukocyte cross-match, and panel test. Those testing negatively were excluded from kidney transplantation. The post-transplant immunosuppressive regimen consisted of Cyclosporine, Prednisolone, and Azathyoprine (before year 2000) or Mycofenolate Mofetil (during and after year 2000).

Out patient charts were retrospectively reviewed for patient and graft status, serum creatinine, and causes of death or graft loss.

Outcomes

Our outcomes were the transplantation outcomes at 6 months, 1 year, 2 years, 3 years, and 5 years. Causes of death were divided into infection, rejection secondary to infection, cerebrovascular or ischemic heart disease, and others [22].

Glomerular filtration rate (GFR) was calculated according to the Jellife formula [23]. Graft survival was the duration of at-risk time from transplantation date to graft-loss date or the study's end, whichever occurred first.

Patient survival was the duration of at-risk time from the date of transplantation to death or the study's end, whichever happened first. Observation for those without events was terminated at the end of the study (January/1/2007).

Table 1. Comparison of demographic and baseline clinical data in the study groups.

	≥60 years	<60 years	P
	n=44	n=358	
ESRD cause			
Hypertension	20 (45.0%)	64 (18.0%)	0.001
Diabetes mellitus	17 (37.5%)	59 (16.4%)	0.001
Urologic	2 (5.0%)	44 (12.4%)	0.168
Glomerulonephritis	0 (0.0%)	28 (7.7%)	0.068
Other causes	0 (0.0%)	3 (0.9%)	0.541
Unknown causes	6 (12.5%)	160 (44.6%)	0.001
Transplant source			
Living related donors	1 (2.3%)	10 (2.9%)	0.666
Living unrelated donors	43 (97.7%)	342 (95.4%)	
Cadaveric donors	0 (0.0%)	6 (1.7%)	

Table 2. Mean (SD) Serum Estimated GFR levels in the study groups (ml/min/1.73 m^2).

Estimated GFR (ml/min/1.73 m^2)	Old recipients	Young recipients	P-value
	≥60 years	<60 years	
6 months	55±20	57±21	0.529
1 year	54±21	56±23	0.539
5 years	51±24	53±25	0.156

Estimated GFR (ml/min/1.73 m^2) = (98 – [0.8 × (age – 20)])/(SCr × [0.90 if female]).

Table 3. Survival of the patient and graft in the study groups.

Graft survival uncensored for patient death	Old recipients	Young Recipients
6 months	93.9	98.3
1 year	93.9	99.6
2 years	89.3	97.1
3 years	81.8	95.9
5 years	72.7	94.2
Graft survival censored for patient death		
6 months	99.2	98.3
1 year	98.9	99.8
2 years	98.2	98.0
3 years	97.3	97.6
5 years	96.0	95.8
Patient		
6 months	97.2	99.9
1 year	93.9	99.9
2 years	87.1	99.2
3 years	83.4	99
5 years	80.0	98.8

Codes of ethics

The study protocol was approved by the Nephrology Urology Research Center.

Statistical analysis

Statistical analysis was performed with SPSS-13 for Windows. The Chi-square and independent samples t-test were employed for comparing the qualitative and quantitative variables between the groups, respectively. The Kaplan-Meier method was utilized to survey patient and graft survival, and the log-rank test was used to compare the survival data between the groups. Graft survival was measured by death-censored and death-uncensored approaches, separately. A P-value less than 0.05 was considered significant.

Results

The mean ages (SD) of the young and elderly groups were 34.3±12.8 (18–59) and 69.2±8.1 (60–84) years, respectively. In terms of sex, 229 (64%) patients in the young group and 30 (68%) patients in the elderly group were male (P=0.582). There was no significant difference between the groups in terms of the degree of Human Leucocyte Antigen (HLA) matching (3.9±1.6 vs. 3.4±1.7 HLA-A-B-DR mismatches, p=0.408) and maintenance immunosuppression (62% vs. 68%, received Azathyoprine; transplantation was performed before the year 2000, p=0.364).There was also no difference between the groups as regards the graft source. The frequency of diabetes mellitus (DM) and hypertension (HTN) as the causes of ESRD was higher in the elderly group, whereas the frequency of unknown diseases was higher in the younger group (Table 1).

No significant difference was observed between the study groups with regard to renal function

(estimated GFR) at 6 months, 1 year, and 5 years in the follow-up period (p>0.05) (Table 2).

The 5-year death-uncensored patient- and graft-survival rates in the elderly group were lower than those of the younger group (p<0.05). However, when the graft-survival rates were censored for patient death with a functioning graft, the rates were found to be similar between the study groups (p>0.05) (Table 3).

In-hospital deaths were due to infection (60%) and other causes (40%) in the elderly group, and were due to infection (37%), rejection secondary to infection (26%), rejection (10%), cerebrovascular accident or ischemic heart disease (10%), and other causes (17%) in the young group.

Graft losses leading to re-admission were due to infection (100%) in the elderly group and due to graft rejection (50%), rejection secondary to infection (25%), infection (8%), and cerebrovascular accident (2%) in the young group.

Discussion

Although generally expected to have shorter lives, ESRD patients over 60 years of age can receive the same benefits from renal transplantation as their younger counterparts. This claim is further borne out by the finding of the present study, showing that both elderly and young renal recipients had comparable death-censored graft-survival rates. Achieving acceptable long-term allograft-survival rates in old kidney recipients, therefore, seems to be contingent upon a reduction in the mortality rates of those with functioning grafts.

The lower patient-survival rate of our elderly renal recipients agrees with the previous reports of significantly reduced 5-year patient-survival rates in recipients over the age of 60, compared with patients under the age of 60 [24]. A previous study showed survival rates over a 2-year follow-up in recipients older than 60 were significantly lower than in those younger than 60 years of age, with cardiovascular events the leading cause of death [25]. That should be put in context, as renal transplantation in older patients is believed to reduce cardiovascular mortality [26]. It has also been reported that older patients, if carefully selected, are not at an increased risk of death due to cardiovascular events compared with an age-matched general population [27].

A study from Portugal compared patient and graft survival, hospital stay, the incidence of rejection and rehospitalization, and the cause of graft loss for primary kidney recipients 60 years of age or older with those of a younger group, and reported similar patient- and graft-survival rates. In that study, death-censored graft survival was identical, and there was no difference in the cause of graft loss. Older patients had a longer hospitalization period, but had fewer rejection episodes and fewer rehospitalizations [28]. Comparing renal transplantation long-term outcomes among recipients aged 60 years or older with those in younger patients, another study found no differences in initial graft function, acute rejection rate, and serum creatinine/clearance, but the patient and graft survival rates at 1, 5, and 10 years were lower among the 60+ group, with no differences in graft-survival rates censored for death with a functioning graft [29].

After 5 years, death-uncensored patient- and graft-survival rates in our older patients were lower than those of the younger ones. Nevertheless, when the graft-survival rates were censored for patient death with a functioning graft, the rates were found to be comparable between the study groups. The higher death-uncensored graft-survival rate in the late follow-up, therefore, seems to be in consequence of the higher mortality rate in the elderly group. In some studies, 50% of graft loss has been attributed to patient death in older transplantation recipients as opposed to 15% in younger patients [30,31].

Similar to other studies, our findings illustrate that e-GFR at 5 years in old patients with functioning grafts are indicative of a good renal function [29,32]. Cantarovich et al. found that 5-year graft-survival rates did not differ between their young and old patients [33]. Kappes et al. reported that 5-year graft survival was even superior in the older recipients compared with the younger ones, [34] which may be attributable to less acute rejection in elderly patients as a result of the diminishing impact of age on their immune system [35]. Doyle et al. discriminated between low-risk and high-risk recipients among the elderly and found graft survival in low-risk recipients to be equal to that of younger patients [36].

In the current study, a higher percentage of death due to infection was seen in the older recipients. In one study, recipients older than 50 years showed a higher proportion of admission due to infection [37]. In another study, both age at transplantation and age at admission were the independent predictors of post-renal transplantation

in-hospital death, in addition to admission for surgical complications, admission for cerebrovascular accident-ischemic heart disease, and diabetes begetting ESRD [38].

Limitations

First and foremost among the limitations of the present study is the small sample size, which means that non-significant P-values may reflect type I error. A marked predominance of living unrelated transplants among the samples can be cited as another weak point, as can the exclusion of 2 variables, waiting time on dialysis and age of donor, from the analysis. Despite these limitations, given the increasing number of elderly patients requiring renal transplantation [19,32] and the increasing age of those receiving an organ [9,13], the results of this study are hoped to further encourage renal transplantation in the elderly in Iran.

Conclusions

In light of the findings of the current study, we suggest that elderly patients not be excluded from kidney-transplantation waiting lists soley on the grounds of age.

Acknowledgment

This paper is the result of a secondary analysis conducted by Universal Network for Health Information Dissemination and Exchange (UNHIDE) on an existing health data. The secondary analysis and manuscript preparation have been done by this international network.

References:

1. Liem YS, Weimar W: Early living-donor kidney transplantation: a review of the associated survival benefit. Transplantation, 2009; 87(3): 317–18
2. Rees L: Long-term outcome after renal transplantation in childhood. Pediatr Nephrol, 2009; 24(3): 475–84
3. Marcén R: Immunosuppressive drugs in kidney transplantation: impact on patient survival, and incidence of cardiovascular disease, malignancy and infection. Drugs, 2009; 69(16): 2227–43
4. Waiser J, Budde K, Böhler T, Neumayer HH: The influence of age on outcome after renal transplantation. Geriatr Nephrol Urol, 1997; 7(3): 137–46
5. Foley DP, Patton PR, Meier-Kriesche HU et al: Long-term outcomes of kidney transplantation in recipients 60 years of age and older at the University of Florida. Clin Transpl, 2005: 101–9
6. Kwon OJ, Lee HG, Kwak JY: The impact of donor and recipient age on the outcome of kidney transplantation. Transplant Proc, 2004; 36(7): 2043–45
7. Singh N, Nori U, Pesavento T: Kidney transplantation in the elderly. Curr Opin Organ Transplant. 2009; 14(4): 380–85
8. Ladrière M: [What is the best immunosuppression for the elderly kidney transplantation patient?] Nephrol Ther, 2008; 4(Suppl.3): S179–83
9. Saxena R, Yu X, Giraldo M et al: Renal transplantation in the elderly. Int Urol Nephrol, 2009; 41(1): 195–210
10. Arns W, Citterio F, Campistol JM: 'Old-for-old' – new strategies for renal transplantation. Nephrol Dial Transplant, 2007; 22(2): 336–41
11. Pascual J, Marcén R, Liaño F, Ortuño J: Cadaveric kidney transplantation for the elderly. Nephron, 2002; 91(3): 361–78
12. Loreno M, Boccagni P, Rigotti P et al: Combined liver-kidney transplantation in a 15-year-old boy with alpha1-antitrypsin deficiency. J Hepatol, 2002; 36(4): 565–68
13. Cameron JS: Renal transplantation in the elderly. Int Urol Nephrol, 2000; 32(2): 193–201
14. Ismail N, Hakim RM, Oreopoulos DG, Patrikarea A: Renal replacement therapies in the elderly: part I. Hemodialysis and chronic peritoneal dialysis. Am J Kidney Dis, 1993; 22: 759–82
15. Ismail N, Hakim RM, Helderman JH: Renal replacement therapies in the elderly: Part II. Renal transplantation. Am J Kidney Dis, 1994; 23(1): 1–15
16. Fauchald P, Albrechtsen D, Leivestad T et al: Renal replacement therapy in elderly patients. Transplant Int, 1988; 1: 131–34
17. Mallick L, el Marasi A: Dialysis in the elderly: to treat or not to treat? Nefrol Dial Transplant, 1999; 14: 37–39
18. Fabrizii V, Winkelmayer WC, Klauser R et al: Patient and graft survival in older kidney transplant recipients: Does age matter? J Am Soc Nephrol, 2004; 15(4): 1052–60
19. Cecka JM: The UNOS Scientific Renal Transplant Registry. Clin Transpl, 1999;: 1–21
20. Villar E, Rabilloud M, Berthoux F et al: A multicentre study of registration on renal transplantation waiting list of the elderly and patients with type 2 diabetes. Nephrol Dial Transplant, 2004; 19(1): 207–14
21. Lankarani MM, Assari S, Nourbala MH: Improvement of renal transplantation outcome through matching donors and recipients. Ann Transplant. 2009; 14(4): 20–25
22. Moghani Lankarani M, Noorbala MH, Assari S: Causes of re-hospitalization in different post kidney transplantation periods. Ann Transplant, 2009; 14(4): 14–19

23. Jellife RW: Creatinine clearance: bedside estimate. Ann Intern Med, 1973; 79: 604–5
24. Ponticelli C: Should renal transplantation be offered to older patients? Nephrol Dial Transplant, 2000; 15: 315–17
25. Mourad G, Cristol JP, Vela C et al: Cadaveric renal transplantation in patients 60 years of age and older: Experience with 58 patients in a single centre. Nephrol Dial Transplant, 1995; 10: 105–7
26. Meier-Kriesche HU, Ojo AO, Hanson JA, Kaplan B: Exponentially increased risk of infectious death in older renal transplant recipients. Kidney Int, 2001; 59: 1539–43
27. Cantarovich D, Baatard R, Baranger T et al: Cadaveric renal transplantation after 60 years of age: A single center experience. Transpl Int, 1994; 7: 33–38
28. Pedroso S, Martins L, Fonseca I et al: Renal transplantation in patients over 60 years of age: a single-center experience. Transplant Proc, 2006; 38(6): 1885–89
29. Nunes P, Mota A, Parada B et al: Do elderly patients deserve a kidney graft? Transplant Proc, 2005; 37(6): 2737–42
30. Martins PNA, Pratschke J, Pascher A et al: Age and immune response in organ transplantation. Transplantation, 2005;; 79(2): 127–32
31. DeLuca L, Cardella CJ: How can the care of elderly dialysis. patients be improved? Semin Dial, 1992; 5: 28–29
32. Saudan P, Berney T, Leski M et al: Renal transplantation in the elderly: a long-term, single-centre experience. Nephrol Dial Transplant, 2001; 16: 824–28
33. Austrian Dialysis and Transplant Registry: ÖDTR Jahresbericht 2001 (Annual Report of the Austrian Dialysis and Transplant Registry), p 43; Wels, Austria. Available at: *http://www.nephro.at/oedr2001/JB_11SEP2002.pdf.* Accessed May 5, 2003
34. Kappes U, Schanz G, Gerhardt U et al: Influence of age on the prognosis of renal transplant recipients. Am J Nephrol, 2001; 21: 259–63
35. Wenisch C, Patruta S, Daxbock F et al: Effect of age on human neutrophil function. J Leukoc Biol, 2000; 67: 40–45
36. Doyle SE, Matas AJ, Gillingham K, Rosenberg ME: Predicting clinical outcome in the elderly renal transplant recipient. Kidney Int, 2000; 57: 2144–50
37. Nemati E, Saadat A-R, Hashemi M et al: Causes of Rehospitalization After Renal Transplantation; Does Age of Recipient Matter? Transplant Proc, 2007; 39: 970–73
38. Nemati E, Pourfarziani V, Jafari AM et al: Prediction of Inpatient Survival and Graft Loss in Rehospitalized Kidney Recipients. Transplant Proc, 2007; 39: 974–77