ORIGINAL RESEARCH PAPER

Nephrology

KEY WORDS:

RENAL TRANSPLANT IN ELDERLY: A VIABLE OPTION?

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Introduction

The number of people requiring renal replacement therapy (RRT) is on a rise, and the elderly population is among the rapidly growing groups, especially in the western world [1–4]. ESRD is increasing in the older patients, with the median age at diagnosis of ESRD in the united Kingdm being 64.9 years [1]. In the USA, the number of waitlisted patients aged over 65 years increased from 7% in 1997 [3] to >15% in 2009 [5]. With increasing numbers of elderly patients with ESRD, it has become increasingly important that we are well aware of the available treatment options and the relative risk to benefit profile of each. Dialysis (Peritoneal dialysis or Hemodialysis) and renal transplant are the principal renal replacement therapy modalities available for the elderly ESRD [3]. Renal transplantation is ideally the modality of choice in ESRD patients. It scores over dialysis with respect to patient survival, cost effectiveness and the quality of life [6–12]. However, option of transplantation is offered infrequently elderly patients. It has been reported that < 5% of patients aged 65 years or more, who are on dialysis will receive a renal transplant (1, 2). It has been shown that, the benefits of renal transplant are similar in elderly as compared to the younger recipients [13–19]. Renal transplantation is still controversial in elderly, and the rates of transplantation in elderly are still modest [7]. This could be because of the various ethical issues involving the allocation of the scarce organs, and the controversies regarding the cost-effectiveness of doing a transplant as well as its efficacy in this cohort, and the hesitancy of the physicians to refer them for transplant [8, 9]. Many physicians consider dialysis as a more stable option with acceptable rates of survival and low short term risks. In contrast, renal transplant though may lead to a longer life expectancy with improvement in quality of life, it is considered to have significant short term risks morbidity and mortality. In a Canadian study, it was found that among patients aged over 65 years, 26.5% were not referred for assessment for renal transplant, despite having no contraindications [10]. In this short review, we will discuss about some common skepticisms holding us back from transplantation in the elderly.

Patient selection and immunosuppression

The challenges for elderly transplant start at the very first step. Patient selection is a very important aspect of transplant in elderly, as many factors have to be taken into consideration. Graft loss in the elderly is related commonly to patient death, and therefore the expected patient survival is crucial so as not to lose graft years, especially from a living donor. The two main causes of morbidity and mortality following transplantation are cardiovascular disease and infection. Cardiovascular disease is predominant in the developed world, while in countries like India, Infection is still the leading cause of death. Therefore, a detailed evaluation of the fitness for transplant and the co-morbidities, including cardiac evaluation using angiography or isotope perfusion scan is mandatory. Also, it is important to rule out occult infections and malignancies and the recipient should be adequately screened.

Apart from patient selection, selection and tailoring of the immunosuppression is important. The pharmacokinetics and effects of many drugs are altered in the elderly due to decreased activity of the metabolising enzymes. Also, rejection occurs less commonly in older patients, a finding that may be attributable to age-related "tolerance". Therefore, lower levels of immunosuppression may be sufficient in elderly patients compared to the younger counterparts. This has to be tailored adequately so as to prevent the drug toxicities and other adverse effects. Initial doses of the calcineurin inhibitors, if given, should be reduced because, at any given dose, higher than normal blood levels result from a decline in cytochrome P450 activity. In addition if corticosteroids are given, it is recommended to do a rapid taper to a low maintenance dose, since corticosteroids have many untoward effects in the elderly.

Donor Selection

Selection of appropriate donors for renal transplant in elderly has been a major hurdle, due to various organ transplant policies, ethical issues etc hampering live transplants. The transplant policies of most organ sharing networks give preference to younger recipients, and the elderly being reserved for expanded criteria donors and discarded kidneys. Hence, Deceased Donor Renal Transplant (DDRT) is the more widely adopted practice, commonly from an expanded criteria donor.

Living donor transplantation helps to alleviate the shortage of deceased donor kidneys in all patients, including the elderly. However, finding a suitable living donor is difficult, which may be even more problematic in case of elderly transplants. The results of live donor transplant are encouraging, with a 5-year survival rate of 76%, as compared to 68% for a non-expanded criteria deceased donor. Deceased donor transplant also do not fare much worse, with a 10 year survival rate of 35% in patients aged >60 years, as compared to 46% in recipients aged 18-30 years. If the availability of donors is sparse, expanded criteria donors can be considered with dual kidney transplant. The kidneys from expanded criteria donors, considered for discarding can be transplanted, maintaining the nephron dose. The results have been promising, with 82% patient survival at 3-years and a graft survival of 70%.

Pre-emptive transplant has also been attempted in elderly with a better survival benefit. Pre-emptive transplant has also been performed from kidneys discarded of very old donors, with promising results. The death censored 5-year graft survival was 96% as compared to 68% in those receiving transplant after initiation of dialysis. Hence, Elderly patients with end stage renal disease, not on dialysis may benefit from Pre-emptive kidney

transplant from elderly deceased donors whose kidneys were to be discarded.

Patient Survival

Before offering the option of renal transplant to older patients, it is essential to have a detailed evaluation and ensure that the transplant surgery per se and the immunosuppression do not adversely affect their survival.

The initial experience of renal transplant in elderly, especially deceased donors, was dismal. Simmons et al., in 1971 reported patient survival and graft survival at 1 year among patients >45 years age of 40% and 20% respectively. This is significantly worse compared to the younger recipients.2 In the initial reports, patient survival of elderly patients after deceased donor transplant was significantly worse compared to patients on dialysis, with a better survival for patients receiving living donor transplants. As a result, in 1977, it was suggested by Najarian et al. that patients more than 45 years of age should not be offered deceased donor transplants.8 This view changed with the advent of Cyclosporine A based regimens, and in 1987, Fryd et al. found similar outcomes following deceased donor transplant in patients > 50 years of age as compared to those < 50 years of age.17 Since these sentinel studies, the upper age limit for offering renal transplantation is being extended farther. 18-31

In a classic article by Wolfe *et al.* (3), the authors showed that the mortality risk reduction by 68% in patients receiving a renal transplant when compared with the patients who were continuing on the waiting list. Also, they demonstrated a 61% lower mortality among patients aged between 60 and 74 yr and undergoing a renal transplant, compared with the people who remained on the waiting list (3). This mortality reduction translated into a projected 4 years increase in lifespan. The survival advantage was also seen in those aged 70 to 74 years, with an added lifespan of 1 year with renal transplant when compared with the patients on dialysis (3). However, in this study, elderly patients comprised of only 13% of the all renal recipients (3). In an article by Rao *et al,* (8) the authors analysed the survival patterns of elderly renal transplant recipients. Of the 5567 patients aged more >70 yr put on the waiting list between 1990 and 2004, 6% had received living donor transplant while 37% had undergone deceased donor renal transplant. The adjusted relative risk of death for all patients receiving a renal transplant was 0.59 (95% CI 0.53 to 0.65) compared with patients on waiting list (8). The mortality risk varied with time since transplant, with the early post transplant period having the highest risk, higher than dialysis, with a decline decreasing thereafter. The mortality risk equalled that of dialysis at 125 days following renal transplant, and showed a mortality benefit from that time point onwards (8). In view of the high RR for death in the initial period, until 1.8 years after transplant, the transplant patients had a worse survival than the dialysis patients placed on the waiting list (8). The adjusted RR for death was 0.67 (95% CI 0.53-0.86) for patients older than 75 years receiving a renal transplant compared to patients on wait list (8). The survival benefit was significant even for patients with diabetic or hypertension related renal failure, as well as for expanded criteria donor kidneys (8). Another important concern is whether the survival benefit will persist in the elderly patients who were on the waiting list for a prolonged time. This question was analysed by Gill *et al.* (9) in their analysis of 63,783 patients undergoing transplant, from the US Renal Data System database. The authors showed an expected survival of 8.2 years following a renal transplant in patients aged >70 years, compared to 4.5 years survival on the waiting list (9). The authors found that the survival benefit with renal transplant decreased with increasing time for patients on waiting list, but there was some persisting benefit even after 3 years on waiting list, with a 2.5 years increased life span after transplant as compared to dialysis. This studied showed that the survival benefit, although slightly decreased, persisted to show a significant survival benefit in elderly transplant recipients (8). The authors also showed a 42% reduction in mortality in renal transplant recipients even in those with long waiting time (>1350 days) compared to patients on dialysis (*P* <0.0001) (8). Thus, patients with waiting times of even 3 to 4 years have a significant survival benefit in elderly transplant recipients. However, whether transplant after even longer waiting times would lead to a survival benefit in the elderly patients is still not known.

Graft Survival

Transplantation into older individuals with relatively shorter life spans than younger individuals may be associated with the loss of significant allograft years because of death of the older individual before allograft failure. But the positive side is that rejection occurs less commonly in older patients, a finding that may be attributable to age-related "tolerance".

Shannon Doyle et al found 86% one year graft survival in older recipients, which is comparable to younger patients with a 1-year graft survival of 88%. However, they found a significantly reduced 10-year graft survival in the elderly (39% *vs* 53%). Younger recipients had a significantly better overall graft survival ($P < 0.001$). The poorer graft survival in the elderly was explained by the increased number of deaths in the older patients. Graft loss due to death was found to be 61% in the elderly, compared to 45% in younger patients. The authors reported that the death censored graft survival in patients more than 60 years of age was equivalent to the younger recipients.

In their study, the leading causes for graft loss included death, rejection (hyperacute and chronic rejection), and hemolytic uremic syndrome. The major causes of mortality being cardiac disease, sepsis, and recurrent disease. The authors also found a significant difference in the interval between transplant and the last treatment received for any malignancy and mortality with a waiting time of 2.2 ± 0.3 years in non-survivors *vs* 14.0 ± 3.6 years in survivors ($P < 0.0001$).

Poor graft survival has also been associated with other factors like donor age greater than 50, increased time on waiting list, age group 65 to 70 years as compared to those between 60 to 64 years. The presence of delayed graft function, coronary artery disease, or diabetes was not shown to be associated with poor graft outcomes. Use of tobacco was also found to be associated with a poorer graft outcome.

At our centre, the graft survival at 1, 3 and 5 years is 88.9%, 60% and 25% respectively (figure 1) with 21% patients having died with a functioning graft. The major causes for mortality in our centre are sepsis (50%) followed by cardiovascular death (31.3%) (figure 2), with Respiratory infection being the most common cause of sepsis related death (25%). The patient and graft survival at 3 years were better with live donors compared to deceased donors (Table 1).

The immune competence is known to decrease with increasing age and therefore associated with fewer rejections 36-39. *Tesi et al*. found a significantly better death censored graft survival in patients > 60 years of age. The elderly patients had fewer immunological graft losses, 11% *vs* 31% (p = 0.0009) with a relative risk for graft loss of 0.36. Also, they found no graft loss secondary to immunological injury after 36 months. At our centre, three patients > 60 years of age had graft loss secondary to chronic rejection between 28 and 70 months post-transplant. A possible explanation for increased graft loss secondary to rejection in some studies may be due to the tendency to use lower levels of immunosuppressants in elderly patients, and also possibly less aggressive management of episodes of acute rejection. The lower rejection rates in elderly patients translate into a decrease in the rate of re-hospitalization, and more elderly patients are readmission-free.

To assess the effect of co-morbid conditions like diabetes and cardiac disease, Schulak et al. conducted a study and divided the patients aged > 60 years into those without both diabetes and cardiac disease (low-risk) (n = 14), and those who had presence of either diabetes or cardiac disease (n = 12).27 he found that patients at low risk had better patient and graft survival rates (p=0.055). However, Benedetti et al found no such difference.

With improvements in graft survival in the elderly population, there has been more concern about loss of significant allograft

years in the elderly due to death with a functioning graft, which is about 21% at our centre. To overcome this drawback, an approach similar to the Eurotransplant Senior Programme (ESP) policy had been followed. As per this approach, the organs retrieved from donors older than 65 years of age are allocated to patients of similar age. This also leads to better utilisation of expanded criteria donors and also the kidneys considered to be discarded can be transplanted to appropriate recipients. Data from this program revealed that, among 227 patients, one year allograft survival rates were 86 percent which compared favourably with 79 percent survival with the older system.

Quality of Life and Cost effectiveness

Successful renal transplantation improves overall quality of life and relieves the burden and tedium of dialysis among all patients with ESRD. It could be related to amelioration of anaemia, and enhancement of physical, mental and cardiac functions. It has been shown that transplant patients have 18.12% greater quality of life in total aspects of human life (physical, emotional, social, spiritual and financial) compared to patients on hemodialysis.

A 65 year old patient without co-morbidities can gain 1.2 years of life following transplant, and about 1.1 quality-adjusted life years (QALY) at an incremental cost of $67,778 per QALY. The improvement in Life Expectancy (LE) and Quality Adjusted Life Expectancy (QALE) was also observed in those with diabetes and cardiovascular disease, albeit to a smaller extent. Otherwise, patients with no comorbidities continued to have improvement in QALY with transplant even up to the age of 80 yr.

Assuming a waiting period of 2 year before transplant, renal transplant for 70 year old patients continued to be economically feasible (incremental cost effectiveness [ICE], $79,359 per QALY). But for those more than 75 years of age, and for 70 year old patients with either cardiovascular disease or diabetes, transplant was less economically attractive (ICE $99,553, $126,751 and $161,090 per QALY, respectively). The ICE per QALY increased with age, but remained favourable compared to dialysis even for 80 year old patients (ICE/QALY for transplant $50,000). With increasing time on waiting list, the cost effectiveness ratios increased dramatically (incremental cost/QALY: $15 000, $68 000, and $193,600 for 0, 2, and 4 years on waiting list respectively). The QALE for patients 65 years of age on dialysis equalled that of transplant at 6.7 years. A 65 year old with no co-morbidities on being transplanted has incremental benefits of two life years extra, and savings of more than $100,000.

Humar *et al.* (10) used the SF-36 questionnaire and found that older transplant recipients had a remarkably good quality for life at 1 yr after transplantation. The quality of life scores in the elderly recipients were comparable, and in five of eight domains, they were better than the age matched general population. The three domains where they scored lower were physical functioning, role limitation due to physical health problems, and bodily pain (10). Also, their scores for overall general health perception were similar to younger transplant recipients, and better than the age matched general population (10).

Though transplant is associated with high initial costs, this would be exceeded by the cost of hemodialysis after about 2 years and 10 months. For patients continuing on maintenance hemodialysis, transplantation would lead to a saving of about 3,800 USD per month. And for the elderly patients, it would amount to about 2,400 USD saving per month 16. The cost analysis of patients receiving renal replacement therapy at our centre is as shown in Table 2, with high initial costs of transplant, which reduces over long term and equals that of hemodialysis by about 26 months post transplant. Laupacis *et al.* (1) have shown that the cost of dialysis in patients older than 60 years was $65,270 per year, while transplant cost 63,708$ for the first year and 21,160$ in the second year (1). Thus, transplant becomes even more cost effective with longer follow up compared to dialysis, as the dialysis cost remains constant or increases with longer follow up (1). Jassal *et al.* (11) had performed a decision analysis to examine the cost effectiveness of transplantation in the elderly. They found that the economic results were not favourable in for all subgroups of patients. Patients undergoing a live donor transplant had better economic results regardless of the age at transplant. However, for patients more than 75 years of age, having a wait time of more than 2 years and receiving a deceased donor transplant the transplantation was economically not attractive with the cost per QALY ranging between $99,553 to $231,158 (11). With wait time of more than 4 years, transplant was not economically attractive across all age groups with the cost per QALY ranging from $175,107 to $14,585,442 (11). Their study suggested that live donor transplant would be a better option for the elderly from an economic perspective.

Conclusion

With ageing general population, the ESRD population is also aging. Hence, physicians are expected to have to make increasing number of decisions regarding referral for transplantation and the candidacy in elderly patients. The data suggests that elderly patients on the waiting list experience significant survival benefit with kidney transplantation, even among those who are more than 75 years of age. In addition, older transplant recipients have increased life expectancy and better QALEs and QALYs. From an economic perspective too, transplantation remains a better strategy for the elderly, especially with living donors, or with deceased donors with shorter waiting times. Age alone should not be considered a barrier to kidney transplantation, and until further evidence emerges, treating physicians must consider the option of transplant in all elderly patients with ESRD. The patient must have a detailed evaluation for transplant eligibility and the decision should be made considering the best interests of the patient. The use of rigid age cutoffs for transplant evaluation is not advisable, and should ensure that ageism does not have bias or conflict the decision regarding transplantation.

Conflicts of interest: There were no points of conflicts.

Figure 1: Patient and graft survival at 3 years – our experience

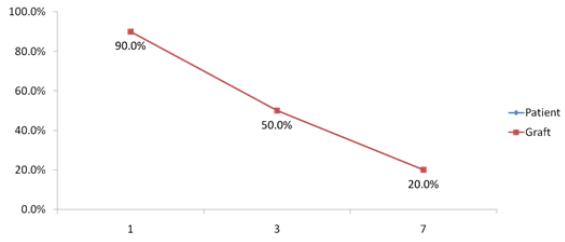

Figure 2: Cause of death in elderly transplant recipients

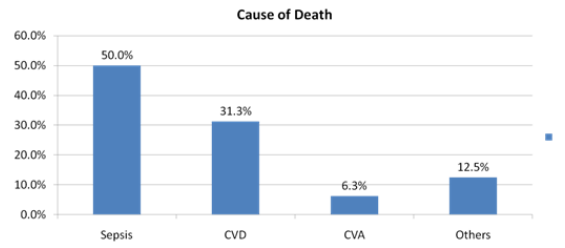

Table 1: Patient and graft survival in live and deceased donors at 3 years post transplant

	Live	DDRT
Patient survival	85.7%	50.0%
Graft survival	71.4%	50.0%

Table 2: Cost analysis of the different renal replacement therapy strategies

Cost	Initiation (in Rs.)	Monthly (in Rs.)
HD	42,500	25,460
PD	33,600	22,550
Early Transplant period	4,50,000	25,600
Late Transplant period	-	9,840

References

1. Jager Kj, Van Dijk Pc, Dekker Fw Et Al. The Epidemic Of Aging In Renal Replacement Therapy: An Update On Elderly Patients And Their Outcomes. Clin Nephrol 2003; 60: 352–360.
2. Macrae J, Friedman Al, Friedman Ea Et Al. Live And Deceased Donor Kidney Transplantation In Patients Aged 75 Years And Older In The United States. Int Urol Nephrol 2005; 37: 641–648.
3. Port Fk, Merion Rm, Roys Ec Et Al. Trends In Organ Donation And Transplantation In The United States, 1997–2006. Am J Transplant 2008; 8: 911–921.
4. Danovitch Gm, Cohen Dj, Weir Mr Et Al. Current Status Of Kidney And Pancreas Transplantation In The United States, 1994–2003. Am J Transplant 2005; 5: 904–915.
5. Organ By Age. Organ Procurement And Transplantation. Network Http://Optn.Transplant.Hrsa.Gov/Latestdata/Viewdatareports.Asp
6. Kontodimopoulos N, Niakas D. An Estimate Of Lifelong Costs And Qalys In Renal Replacement Therapy Based On Patients' Life Expectancy. Health Policy 2008; 86: 85–96.
7. Rebollo P, Ortega F, Baltar Jm Et Al. Health-Related Quality Of Life (HRQOL) In End Stage Renal Disease (Esrd) Patients Over 65 Years. Geriatr Nephrol Urol 1998; 8: 85–94.
8. Rebollo P, Ortega F, Baltar Jm Et Al. Health Related Quality Of Life (HRQOL) Of Kidney Transplanted Patients: Variables That Influence It. Clin Transplant 2000; 14: 199–207.
9. Wolfe Ra, Ashby Vb, Milford El Et Al. Comparison Of Mortality In All Patients On Dialysis, Patients On Dialysis Awaiting Transplantation, And Recipients Of A First Cadaveric Transplant. N Engl J Med 1999; 341: 1725–1730.
10. Vincenti F. A Decade Of Progress In Kidney Transplantation. Transplantation 2004; 77: S52–S61.
11. Niakas D, Kontodimopoulos N. Is Renal Transplantation The Most Costeffective And Preferable Therapy For Patients Suffering From End-Stage Renal Disease Or Not? Health Policy 2009; 89: 329–331.
12. Laupacis A, Keown P, Pus N Et Al. A Study Of The Quality Of Life And Cost-Utility Of Renal Transplantation. Kidney Int 1996; 50: 235–242.
13. Albrechtson D, Leivestad T, Sodal G, Bentdal O, Berg Kg, Brekke I, Fauchald P, Flatmark A, Jakobsen A, Lien B, Nordal K, Pfeffer P, Thorsby E, Soreide O: Kidney Transplantation In Patients Older Than 70 Years Of Age. Transplant Proc 27: 86–88, 1995.
14. Schaubel D, Desmeules M, Mao Y, Jeffery J, Fenton Ss: Survival Experience Among Elderly End-Stage Renal Disease Patients. Transplantation 60: 1389–1394, 1995.
15. Heldal K, Leivestad T, Hartmann A Et Al. Kidney Transplantation In The Elderly–The Norwegian Experience. Nephrol Dial Transplant 2008; 23: 1026–1031.
16. Oniscu Gc, Brown H, Forsythe Jl. How Old Is Old For Transplantation? Am J Transplant 2004; 4: 2067–2074.
17. Rao Ps, Merion Rm, Ashby Vb Et Al. Renal Transplantation In Elderly Patients Older Than 70 Years Of Age: Results From The Scientific Registry Of Transplant Recipients. Transplantation 2007; 83: 1069–1074.
18. Oniscu Gc, Brown H, Forsythe Jl. How Great Is The Survival Advantage Of Transplantation Over Dialysis In Elderly Patients? Nephrol Dial Transplant 2004; 19: 945–951.
19. Sener A, Schweitzer Ej, Munivenkatappa R Et Al. Deceased-Donor Renal Transplantation In The Geriatric Population Demonstrates Equal Graft Survival Compared With Younger Recipients. Transplantation 2009; 87: 1549–1554.
20. Johnson Dw, Herzig K, Purdie D Et Al. A Comparison Of The Effects Of Dialysis And Renal Transplantation On The Survival Of Older Uremic Patients. Transplantation 2000; 69: 794–799.
21. Bayat S, Kessler M, Briancon S Et Al. Survival Of Transplanted And Dialysed Patients In A French Region With Focus On Outcomes In The Elderly. Nephrol Dial Transplant 2010; 25: 292–300.
22. Midlöv P. Pharmacokinetics And Pharmacodynamics In The Elderly. Oa Elderly Medicine 2013 Aug 01;1(1):1
23. Jacobson Pa, Schladt D, Oetting Ws, Et Al. Lower Calcineurin Inhibitor Doses In Older Compared To Younger Kidney Transplant Recipients Yield Similar Troughs. American Journal Of Transplantation : Official Journal Of The American Society Of Transplantation And The American Society Of Transplant Surgeons. 2012;12(12):3326-3336. Doi:10.1111/J.1600-6143.2012.04232.X.
24. Cohen, Dj, St. Martin, L, Christensen, Ll, Et Al. Kidney And Pancreas Transplantation In The United States, 1995-2004. Am J Transplant 2006; 6:1153.
25. Tan, Jc, Alfrey, Ej, Dafoe, Dc, Et Al. Dual-Kidney Transplantation With Organs From Expanded Criteria Donors: A Long-Term Follow-Up. Transplantation 2004 Sep 15;78(5):692-6.
26. Enrique Morales, Eduardo Gutiérrez, Ana Hernández, Jorge Rojas-Rivera, Esther Gonzalez,Eduardo Hernández, Natalia Polanco, Manuel Praga, Amado Andrés. Preemptive Kidney Transplantation In Elderly Recipients With Kidneys Discarded Of Very Old Donors: A Good Alternative. Nefrologia. 2015;35:246-55.
27. Simmons Rl, Kjellstrand Cm, Buselmeier Tj, Najarian Js. Renal Transplantation In High-Risk Patients. Arch Surg 1971; 103:290-298.
28. Najarian Js, Kjellstrand Cm, Simmons Rl. High-Risk Patients In Renal Transplantation. Transplant Proc 1977; 9:107- 111.
29. Fryd Ds, So Sks, Kruse L, Et Al. Improving Results Of Renal Transplantation With Multidrug Therapy In Patients Over 50 Years Of Age. Clin Transplantation 1987; 1:75-80.
30. Shah B, First Mr, Munda R, Et Al. Current Experience With Renal Transplantation In Older Patients. Am J Kidney Dis 1988; 12:516-523.
31. Lauffer G, Murie Ja, Gray D, Et Al. Renal Transplantation In Patients Over 55 Years Old. Br J Surg 1988; 75:984-987.
32. Howard Rj, Pfaffvww, Scornik Jc, Et Al. Kidney Transplantation In Older Patients. Clin Transplantation 1990; 4:181-186.
33. Andreu J, De La Torre M, Oppenheimer F, Et Al. Renal Transplantation In Elderly Recipients. Transplant Proc 1992; 24:120-121.
34. Velez Rl, Brinker Kr, Vergne-Marini Pj, Et Al. Renal Transplantation With Cyclosporine In The Elderly Population. Transplant Proc 1991; 23:1749-1752.
35. Fauchald P, Alberchtsen D, Leivestad T, Et Al. Renal Replacement Therapy In Patients Over 60 Years Of Age. Transplant Proc 1988; 20:432-433.
36. Pirsch Jd, Stratta Rj, Armbrust Mj, Et Al. Cadaveric Renal Transplantation With Cyclosporine In Patients More Than 60 Years Of Age. Transplantation 1989; 47:259-261.
37. Roza Am, Gallagher-Lepak S, Johnson Cp, Adams Mb. Renal Transplantation In Patients More Than 65 Years Old. Transplantation 1989; 48:689-725.
38. Fehrman I, Brattsrom C, Duraj F, Groth Cg. Kidney Transplantation In Patients Between 65 And 75 Years Of Age. Transplant Proc 1989; 21:2018-2019.
39. Schulak Ja, Mayes Jt, Johnston Kh, Hricik De. Kidney Transplantation In Patients Aged Sixty And Older. Surgery 1990; 108:726-733.
40. Morris Ge, Jamieson Nv, Small J, Et Al. Cadaveric Renal Transplantation In Elderly Recipients: Is It Worthwhile? Nephrol Dial Transplant 1991; 6:887-892.
41. Vivas Ca, Hickey Dp, Jordan Ml, Et Al. Renal Transplantation In Patients 65 Years Old Or Older. J Urol 1992; 147:990-993.
42. 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.
43. Tesi Rj, Elkhammas Ea, Davies Ea, Et Al. Renal Transplantation In Older People. Lancet 1994; 1:462-464.
44. Gill Js, Tonelli M, Johnson N, Kiberd B, Landsberg D, Pereira Bj: The Impact Of Waiting Time And Comorbid Conditions On The Survival Benefit Of Kidney Transplantation. Kidney Int 68: 2345–2351, 2005.
45. Shannon E. Doyle, Arthur J. Matas, Kristen Gillingham, And Mark E. Rosenberg. Predicting Clinical Outcome In The Elderly Renal Transplant Recipient. Kidney International, Vol. 57 (2000), Pp. 2144–2150.
46. Fox Ra. Immunology Of Aging. In Brockelhurst Jc, Ed. Textbook Of Geriatric Medicine And Gerontology. New York: Churchill Livingstone, 1985, Pp 82-104.
47. Murasako Dm, Weiner P, Nelson B, Et Al. Decline In Mitogen Induced Proliferation Of Lymphocytes With Increasing Age. Clin Exp Immunol 1987; 70:440-445.
48. Powers Dc, Nagel Je, Hoh J, Adler Wh. Immune Function In The Elderly. Postgrad Med 1987; 81:355-359.
49. Hirokawa K. Understanding The Mechanism Of The Age-Related Decline In Immune Function. Nutr Rev 1992; 50:361-366.
50. Enrico Benedetti, Arthur J. Matas, Nadey Hakim Et Al. Renal Transplantation For Patients 60 Years Of Age Or Older. A Single-Institution Experience. Annals Of Surgery Vol. 220, No. 4,445-460.
51. Rudge, C. Long-Term Patient And Graft Survival In The Eurotransplant Senior Program: A Single-Center Experience. Transplantation 2005; 80:571.
52. Fabrizii, V, Kovarik, J, Bodingbauer, M, Et Al. Long-Term Patient And Graft Survival In The Eurotransplant Senior Program: A Single-Center Experience. Transplantation 2005; 80:582.
53. Saša Perović, Slobodan Janković. Renal Transplantation Vs Hemodialysis: Cost-Effectiveness Analysis. Vojnosanit Pregl 2009; 66(8): 639–644.
54. Sarbjit V. Jassal, Murray D. Krahn, Gary Naglie Et Al. Kidney Transplantation In The Elderly: A Decision Analysis. J Am Soc Nephrol 2003; 14: 187–196.
55. Wong G, Howard K, Chapman Jr, Chadban S, Cross N, Et Al. (2012) Comparative Survival And Economic Benefits Of Deceased Donor Kidney Transplantation And Dialysis In People With Varying Ages And Co-Morbidities. Plos One 7(1): E29591. Doi:10.1371/Journal.Pone.0029591.
56. Humar A, Denny R, Matas Aj, Najarian Js: Graft And Quality Of Life Outcomes In Older Recipients Of A Kidney Transplant. Exp Clin Transplant 1: 69–72, 2003.
57. Kaló Z, Járay J, Nagy J. Economic Evaluation Of Kidney Transplantation Versus Hemodialysis In Patients With Endstage Renal Disease In Hungary. Prog Transplant 2001; 11(3): 188–93.