Kidney Transplantation in the Elderly

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The impact of age on renal graft and recipient survival after kidney transplantation has been the subject of investigation for many years. In general, the dialysis poplulation is steadily getting older. Currently, 50% of new patients entering into the end-stage renal disease (ESRD) program in the United States are older than 61 years of age. As of 1997, the number of patients 65 years of age and older constituted over 35% of the entire ESRD population. However, the percentage of ESRD patients with a functioning renal allograft was only 2% in this age group. As the supply of donor kidneys remains grossly insufficient worldwide, the limited natural life expectancy of elderly patients and perception in some transplant communities that age per se is a high risk factor, has hindered the allocation of kidneys to elderly patients. A growing body of recent data however, reveals that renal transplantation in elderly patients can achieve acceptable outcomes in patient and graft survivals. Renal transplantation not only improves the quality of life of elderly patients, but also has a positive impact on patient survival. These studies also have delineated unique clinical issues relating to transplantation in recipients' geriatric age. Therefore, the management of transplantation in elderly patients requires an understanding of immunology, pathophysiology and pharmacology peculiar to this age group.

The acceptance rate of elderly patients for kidney transplantation is extremely variable from country to country. As of 1980s, the proportion of patients over 55 years of age with functioning allografts was as high as 43% in Norway, 10 to 20% in United Kingdom, Canada and USA, to as low as 1% in the Netherlands. Most kidney transplantations in the elderly are from cadaver donors. The trend in donor organ distribution is that elderly recipients get kidneys from older donors and kidneys with a longer cold ischemic time. These factors may have contributed to inferior graft survival rates observed in some centers. The shortage of cadaver kidney exists worldwide. There is clearly an ethical dilemma in the practice of transplanting either a kidney from a young living donor to elderly recipient or a marginal cadaver kidney into an elderly recipient. However, age per se should not be a basis for exclusion of elderly patients from kidney transplantation. In the future, the ideal solution for this problem is the breaking of biological barriers to successful xenograft transplantation.

The impact of recipients' age, especially old age, on kidney transplant outcomes has been studied. Most of the studies concerning patients who underwent transplantation in 1980s-1990s with cyclosporine based immunosuppression, report one-year patient and graft survival rates ranging 80-90% and 70-80%, respectively. For example, the Minnesota group summarized their experience as follows: For living donor recipients of older patints (60 years or older), patient survival was 90% at 1 and 3

years, and graft survival was 86% at 1 and 3 years. These results were comparable to that of younger patients. For primary cadaver recipients of the same older patients, patient survival was 91% at 1 year and 77% at 3 years, and graft survival was 83% at 1 year and 68% at 3 years. In general, both patient and graft survival rates are better in those recipients who are nondiabetics, those who received kidneys from living donors and those who received a transplant in 1990s rather than 1980s. Although some studies reported graft survival of elderly patients as slightly worse than that of younger patients, the differences between them have steadily decreased in recent years. In addition, if those patients who died with a functioning graft are censored, there is no difference in the graft survival rates between older and younger patients. Relative to a comparable group of dialysis patients, elderly renal transplant patients not only have a better survival, but also their quality of life is greatly improved to a point it is similar to the age matched U.S. poplulation.

The most common causes of death in the elderly patients after kidney transplantation are cardiovascular diseases (19% MI, 13% CVA and 15% other cardiac diseases; all combined 47%), infectious disease (25%) and malignancies (16%). As in chronic dialysis patients, CV diseases and infectious diseases are the most common cause of death in elderly transplant patients. In some series, infection accounted for almost 50% of patient deaths in the older patient as compared with less than 15% in younger patients. The high death rate from infectious complication is, however, very striking in view of the fact that elderly patients have much lower incidence of acute rejection than younger patients and thus require acute rejection therapy less often. The order of leading causes of death thus depends on the degree of preselection, a detailed pretransplant cardiac evaluation, as well as an immunosuppression regimen.

Unfortunately, the most common cause of graft failure is patient death (with a functioning kidney; 60%). Contrary to younger patients, acute (8%) and chronic rejection (20%) are considerably less common cause of graft failure. The findings of the high incidence of death from infectious complications and a relatively low incidence of graft failure from transplant rejection, suggest that these elderly patients have clinically relevant immunological incompetence. This observation suggests that an immnosuppressive therapy protocol for elderly patients should be different than that of younger patients.

Since elderly patients have a degree of immune incompetence resulting in fewer rejection episodes and increased susceptibility to life-threatening infections, the principle of immunosuppression is to use lower doses of drugs. Reduced cyclosporine dose is appropriate and is based on altered pharmacokinetics (reduced hepatic P450 microsomal enzymes in elderly patients). Corticosteroids are very destructive to the elderly, and a more rapid tapering of prednisone to a low maintenance dose is recommended. Some retrospective studies had shown that triple immnosuppressive therapy consisting of prednisone, cyclosporine and mycophenolate mofetil produced the best graft outcome compared to various other combinations of immnosuppressive regimens. However, this point has to be proved in a controlled clinical trial.

In summary, there has been sufficient data to support that kidney transplantation is a reasonable option for elderly ESRD patients. Kidney transplantation can be successful in this population, may extend life expectancy and provide an excellent quality of life. Therefore, elderly patients should not be denied transplantation on the basis of age alone. However,

elderly patients should have a more detailed pretransplant evaluation (adequate cardiac evaluation and preparation in particular), a modified immnosuppressive regimen and detailed preventive measures against infectious complications. They also require other supportive medical care, such as preventive measures against osteoporosis and lipid disorders.

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