Should renal transplantation be offered to older patients?

Claudio Ponticelli

Divisione di Nefrologia e Dialisi, IRCCS Ospedale Maggiore, Milan, Italy

Introduction

At the threshold of the millenium the industrial countries have to face the problem of an increasingly aged population. Between 1900 and 1980 the life expectancy per person at age 65 has risen from 11.9 years to 16.4 years. During the 1980s the number of people aged 75–79 increased by 28.8% and that of persons over the age of 85 years by 52.4% [1]. It should be pointed out that not only has the life expectancy of older persons improved, but also their general health status is substantially better than in the past. The longevity revolution will continue to increase in the future and will represent a major problem for politicians, economists, and sociologists.

If the number of elderly persons in the general population is progressively increasing, the number of elderly uraemic patients requiring renal replacement therapy has increased even more rapidly in recent years, creating a true ‘elderly boom’ in dialysis units. The number of dialysis patients older than 65 years has more than doubled within 10 years in the US [2]. In Europe, more than 50% of new patients admitted to dialysis in 1995 were older than 60 years; in Italy and in France, 35% of dialysis patients were older than 70 years [3].

Although many elderly patients on dialysis are frail [4], a consistent number of older patients are well rehabilitated and do not have comorbid conditions that would be a contraindication to transplantation. Yet many centres are still reluctant to accept patients older than 60–65 years as candidates for renal transplantation. Two main objections for transplanting older patients are generally advanced: (i) patient and graft survival is poor in the elderly; (ii) life-expectancy for elderly patients is better on dialysis than with a transplant.

Patient and graft survival in older recipients

As expected, in renal transplant recipients as well as in general population the more advanced the age the shorter the life expectancy [5]. However, the difference in survival between older transplant patients and the general population of the same age is not striking. A Canadian study compared the patient survival of 284 transplant recipients above age 60 years with that of the sex- and age-matched general population. The survival at 5 years was 75 and 88% respectively [6]. A careful selection of the recipient, paying particular attention to potential evidence of cardiovascular disease, could further reduce the risk.

Even more encouraging are the data about graft survival. An analysis of UNOS showed that the 5-year graft survival was similar in transplant recipients above age 60 years and in those aged 0–60 years. Graft survival declined in older patients after the 5th year because of their high rate of death. However, the so-called functional graft survival, excluding death, was better for patients above age 60 years than for any other age group, mainly because of the lower number of grafts lost by rejection in the elderly group [5]. Two factors may account for the low incidence of rejection in elderly patients: (i) elderly patients are usually more compliant than younger transplant recipients [7]; (ii) in the elderly the inflammatory and immune responses are blunted. Particularly, production of IL-2, expression of IL-2 receptors, cellular and immunological responses, and expression of HLA-DR antigens are attenuated [8].

Probably the most convincing data about the feasibility of renal transplantation in the elderly are those produced recently by the group of Rotterdam. Roodnat et al. [9] subdivided their population of cyclosporin-treated cadaver renal graft recipients into three comparably sized age groups (17–43 years, 44–55 years, and 56–75 years). Patients were transplanted between 1983 and 1997. Three time periods were considered. In each of them the relative risk of graft failure, including death, remained stable. Assuming that the relative risk of graft failure was 1.0 in the period between 1983 and 1990, it decreased subsequently and was 0.49 in the period 1991–1993 and 0.22 between 1994 and 1997.

In each of these periods the older the age of the recipients the higher the risk of graft failure, but the impact of age was considerably attenuated between the first and the third period. Because of the improving results, the risk of graft failure or death was similar for a 20-year-old recipient transplanted between 1983 and 1990 and for a 70-year-old recipient transplanted between 1991 and 1993, while it was halved for a

On the basis of the available data, one may conclude that, thanks to the improving results of transplantation, the impact of the recipient's age on the results of transplantation has been considerably reduced and that today age per se no longer constitutes a contraindication to transplantation.

**Patient survival with dialysis or transplantation in the elderly**

In the pre-cyclosporin era there were conflicting opinions on whether dialysis should be preferred to renal transplantation in older patients or vice versa. Most studies found no relevant difference in survival between elderly patients on regular dialysis and patients who underwent renal transplantation [8]. The results of kidney allograft have improved after the introduction of cyclosporin and amelioration of supportive therapies. Recently, the US Renal Data System showed that in patients over 65 years renal transplantation reduced the risk of death more than threefold when compared with dialysis. These data could be biased, however, by case selection [8].

More reliable are the results of those studies that compared the survival of older dialysis patients selected for transplantation who did not receive a renal allograft with the survival of patients of the same age who were transplanted and received a cyclosporin-based regimen [6,10,11]. After correction for comorbidity factors, all the studies found a striking difference in patient survival in favour of transplant recipients. In a Canadian study, the 5-year survival for patients older than 60 years was 80% for transplanted patients and 50% for patients who remained on dialysis [6]. In a Spanish study the 1-year survival was better for dialysis patients, but after 5 years the survival was 86% for transplant patients and 77% for dialysis patients [10]. In an Italian study the 5-year survival for patients >55 years was 85% in transplanted patients vs 72% for patients on dialysis [11].

Thus, in patients older than 55–60 years matched by age, diagnosis, and comorbid conditions, renal transplantation may offer a better life expectancy than dialysis, at 5 years. The difference could be even wider if the early post-transplant mortality could be reduced.

**Practical recommendations**

There is now sufficient evidence to conclude that older age per se does not represent a formal contraindication to renal transplantation. Nevertheless the current results could be further improved by decreasing the risk for death in older transplant recipients. Two main measures can be adopted to reduce mortality: (i) accurate selection and preparation of the recipient; (ii) immunosuppression tailored to the characteristics of the older patient.

(i) The risk of death is mainly related to the presence of comorbid conditions. The two main causes of death in elderly patients are represented by cardiovascular diseases and infections. However, colonic perforation [12], gastric haemorrhage, and acute cholecystitis [8] are also frequent causes of mortality. Cardiac risk may be evaluated by thallium scintigraphy and or dobutamine echocardiography, but some investigators advocated routine coronary angiography, particularly in diabetic patients. Coronary revascularization may reduce the post-transplantation cardiovascular events and the silent cardiac infarcts which represent a frequent cause of death in the elderly [13]. An accurate search and correction of infections is also needed. A preemptive treatment with ganciclovir can reduce the risk of cytomegalovirus (CMV) infections, which may expose the patient to opportunistic, life-threatening infections. Antiviral therapy is mandatory for seronegative recipients receiving seropositive CMV transplants. Colonic perforation most often results from diverticulitis. Therefore, barium enema or colonoscopy should be part of the pretransplant evaluation. What to do in the presence of diverticular disease in a transplant candidate is still uncertain. Some centres perform hemicolectomy, particularly in the case of symptomatic diverticulitis; others recommend intestinal disinfection and prevention of constipation. However, it is important to suspect colonic perforation in the presence of abdominal pain and unexplained fever. Gall-bladder ultrasound should be performed before transplantation in order to eliminate choledolithiasis.

(ii) A possible advantage of renal transplantation in older recipients is their blunted inflammatory and immune response and lower incidence of rejection [5,12,14]. This may allow the reduction of the intensity of immunosuppression, so decreasing post-transplant morbidity and mortality. Corticosteroids are mainly responsible for cardiovascular and infectious complications after transplantation. Controlled trials showed that cyclosporin monotherapy may permit a graft survival similar to that obtained with a triple-drug therapy even in younger adults [15]. In view of the weaker immune response, steroid-free immunosuppression may therefore be recommended in the elderly. This may result in reduction of the risk of diabetes, hypertension, hyperlipidaemia, osteoporosis, cataracts, and other disturbing side-effects. Also the doses of calcineurin inhibitors may be reduced to prevent the potential nephrotoxicity of these drugs, which might be of special concern with the increasing use of kidneys from older donors. These changes of immunosuppression may be carried out more safely today with the use anti-CD25 monoclonal antibodies [16] and mycophenolate mofetil [17], that can reduce the risk of rejection.

The careful evaluation of the older candidate coupled with a tailored immunosuppression may further improve the results of renal transplantation and may allow further expansion of indications for kidney allografts in elderly people.
References