Original Article

Outcomes of Renal Transplantation in Elderly Patients: Experience From Two Centers

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Background: Elderly patients are the fastest growing age group in end-stage renal failure. Data from overseas show that transplantation is a safe and reliable mode of treatment for this group of patients. However, local data about the outcome in these patients are lacking. The aim of this study was to determine and compare the outcomes of renal transplantation among elderly recipients and younger recipients.

Methods: Using the Organ Registry and Transplant System in Kwong Wah Hospital and Princess Margaret Hospital, adult patients who had undergone renal transplantation and who had been followed-up by the two medical units were recruited. They were divided into the control group (age < 60) and the elderly group (age \geq 60) according to age at transplantation. The following data were collected for cross-sectional analysis: comorbid illnesses, transplantation details, immunosuppressive therapy, incidence and severity of acute rejections, incidence of infection and malignancy, graft and patient survival, and causes of graft loss and death.

Results: A total of 324 episodes of transplantation were recorded (266 controls and 58 elderly). The incidence of acute rejection was higher in the control group (18% vs. 8.6%, p=0.08). There was a trend towards higher incidence of infection and malignancy in the elderly group, though the difference did not reach statistical significance. The graft survival rate was similar in the two groups, while the 5-year patient survival rate was worse in the elderly group (92.1% vs. 79.3%, p=0.0058).

Conclusion: The transplantation outcomes in elderly recipients are satisfactory, and age *per se* should not be considered a contraindication to transplantation. [*Hong Kong J Nephrol* 2010;12(1):12–9]

Key words: elderly, renal transplantation, treatment outcome

背景:在末期腎衰竭患者群之間,年老病人的數目增長最為快速。對於這些病人,海外的 數據顯示腎臟移植術是安全且可靠的治療方式;然而本地仍然欠缺這方面的研究數據。 本研究的目的,是調查腎臟移植對年老腎衰竭患者的效用,並與較年輕的患者作出比較。 **方法**:本研究透過廣華醫院及瑪嘉烈醫院的器官登錄與移植系統 (ORTS),選出曾經在該兩 院接受腎臟移植及後續追蹤的成年病人,組成對照組 (接受移植時年齡 < 60 歲)及年老組 (≥ 60 歲),並採用以下因素作橫斷面分析:並存疾病、移植狀況、免疫抑制療法、急性排斥 的比率與嚴重性、感染及惡性腫瘤的比率、移植物及病人的存活、及移植物失效與病人死 亡的原因。

結果:研究人員共選出了 324 宗移植個案 (對照組 266 宗;年老組 58 宗)。分析顯示對照組 的急性排斥比率較高 (18% vs. 8.6%、p = 0.08);感染及惡性腫瘤的比率則以年老組稍高於對 照組,但未達統計學差異。兩組的移植物存活率相似,但 5 年病人存活率以年老組明顯較低 (92.1% vs. 79.3%、p = 0.0058)。

結論:腎臟移植術可以為年老病人提供令人滿意的治療效果,因此高齡本身並不應被視為 移植的禁忌。



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INTRODUCTION

The elderly population of Hong Kong is increasing. According to data from the Census and Statistics Department [1], the number of elderly aged ≥ 65 has risen from 629,555 (10.1%) in 1996 to 852,796 (12.4%) in 2006. The accompanying social problems and burden on the health care system is thus of increasing concern.

According to the Hong Kong Renal Registry report [2], more and more elderly are placed on renal replacement therapy. In 2004, 40.1% of patients newly recruited to the dialysis program were older than 60 years of age, which represents a substantial proportion. In terms of survival, transplantation is the preferred modality of renal replacement therapy. In the United States, renal transplantations in patients older than 60 are associated with a 61% decrease in long-term death risk and an increase of 4 years in life expectancy, as compared to hemodialysis [3]. Apart from the survival benefit, transplantations can offer better quality of life and are more cost-effective when compared with hemodialysis or peritoneal dialysis [4]. In the pre-cyclosporine era, the elderly were often rejected from qualifying for transplantation due to the poor graft survival and high mortality rate [5]. Thanks to improvements in immunosuppressant and anesthetic techniques, transplantations are now considered to be safe procedures, and the outcomes have improved dramatically. It has been advocated that age *per se* should no longer be a contraindication to transplantation. Some studies have reported that mortality and graft survival are worse in elderly patients compared to non-elderly patients, while others have contradicted such findings [6,7]. There is a lack of local data on the outcome of renal transplantation in the elderly, so this retrospective study was conducted to compare the outcomes of renal transplantation between elderly and younger recipients.

Methods

The Organ Registry and Transplant System (ORTS) is a computer database system that records the transplant details of patients followed-up by the respective hospital. Target patients were retrieved by this system from Kwong Wah Hospital and Princess Margaret Hospital. All adult patients (age ≥ 18) who had undergone renal transplantations during the study period (from July 1, 2000 to June 30, 2005) and who were followed-up in the medical unit of the corresponding hospital were included in this cohort study. Patients were divided into two groups according to their age at the time of transplantation. Those who had undergone transplantation at < 60 years of age were classified into the control group, while those aged ≥ 60 were put in the elderly group. Basic demographic data such as age, sex, body weight, serum creatinine level (the most updated one), cause of end-stage

renal failure, duration of dialysis before transplantation, and duration of follow-up were recorded. Those who had not received renal replacement therapy before transplantation were recorded as preemptive transplant. Data for serum creatinine level were skipped for those who had graft loss and were recorded for those who died with functioning grafts. The presence of the following comorbid illnesses was documented: diabetes mellitus (DM), hypertension, ischemic heart disease, and cerebrovascular accident (CVA). Transplantation details, including donor source (cadaveric or living), number of previous transplants, and transplant center, were obtained. The maintenance immunosuppressive regimen, including number, type and dosage of medications, was noted. Data were omitted for those who had primary non-function of the allograft. For those who were on dialysis or who died with functioning grafts, the immunosuppressive regimen just before the event was documented. The dosage of Myfortic (Novartis International AG, Basel, Switzerland) was converted to the equivalent dose of mycophenolate mofetil (MMF) to facilitate calculation. The usage and dosage of calcium channel inhibitor, which inhibits microsomal P450, was recorded.

The following primary outcomes of this study were recorded: incidence of acute rejection, infection requiring hospitalization, cytomegalovirus (CMV) infection, and malignancy. Presence of CMV infection was defined as positive pp65 antigenemia in association with clinical disease. Graft loss was defined as loss of renal function requiring the patient to return to dialysis. The incidence and causes of graft loss and death were documented.

Statistical methods

Continuous data between groups were compared by Student's *t* test or Mann-Whitney test where appropriate. Categorical data were compared by χ^2 test or Fisher's exact test where appropriate. Graft and patient survival rates were analyzed by Kaplan-Meier curve, and log-rank test was used to compare the outcomes between the two groups. All data are presented as mean±standard deviation unless specified. A *p* value <0.05 was considered statistically significant.

RESULTS

From July 1, 2000 to June 30, 2005, using the ORTS database, 120 episodes of renal transplantation were documented in Kwong Wah Hospital and 204 episodes in Princess Margaret Hospital (Table 1). During this period, 266 episodes (82.1%) involved recipients younger than 60 (mean age, 44.0 \pm 9.9 years; range, 19–59 years), while 58 episodes (17.9%) involved recipients aged \geq 60 (mean age, 65.8 \pm 4.6 years; range, 60–79 years).

The baseline demographic data revealed no significant differences in sex, body weight, serum creatinine

| Table 1. | Demographic | characteristics, | causes of | f end-stage | renal | failure, | and trai | isplant | details | of the | two | group | ps |
|----------|-------------|------------------|-----------|-------------|-------|---------------------------------------|----------|---------|---------|--------|-----|-------|----|
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| | Control $(n=266)$ | Elderly $(n=58)$ | р |
|---|-------------------|------------------|--------|
| Age (yr) | 44.0±9.9 | 65.8±4.6 | _ |
| Male sex | 163 (61.3%) | 31 (53.4%) | 0.27 |
| Body weight (kg) | 63.4 ± 12.3 | 63.7±11.5 | 0.86 |
| Serum Cr (µmol/L) | 116±49.3 | 104.6 ± 44.2 | 0.11 |
| Duration of dialysis before transplant (mo) | 32.3 ± 2.3 | 18.4 ± 8.4 | < 0.05 |
| Length of follow-up after transplant (mo) | 45.1±5.1 | 41.5±1.5 | 0.13 |
| Causes of ESRF | | | |
| Chronic GN | 116 (43.6%) | 9 (15.5%) | < 0.05 |
| DM | 26 (9.8%) | 15 (25.9%) | < 0.05 |
| Polycystic kidney | 13 (4.9%) | 3 (5.2%) | 0.57 |
| HT | 12 (4.5%) | 7 (12.1%) | < 0.05 |
| Unknown | 90 (33.8%) | 23 (39.7%) | 0.40 |
| Others | 9 (3.4%) | 1 (1.7%) | 0.11 |
| Premorbid diseases | | | |
| DM | 72 (27.1%) | 27 (46.6%) | < 0.05 |
| HT | 226 (85.0%) | 53 (91.4%) | 0.20 |
| IHD | 13 (4.9%) | 19 (32.8%) | < 0.05 |
| CVA | 9 (3.4%) | 11 (19.0%) | < 0.05 |
| Transplantation details | | | |
| Cadaveric donor | 254 (95.5%) | 58 (100%) | 0.09 |
| First transplant | 239 (89.8%) | 58 (100%) | < 0.05 |
| Transplantation done in mainland China | 224 (84.2%) | 58 (100%) | < 0.05 |
| Preemptive transplant | 69 (25.9%) | 27 (46.6%) | < 0.05 |

Cr=creatinine; ESRF=end-stage renal failure; GN=glomerulonephritis; DM=diabetes mellitus; HT=hypertension; IHD=ischemic heart disease; CVA=cerebrovascular accident.

| Table 2. Prevalence and | dosage of different | immunosuppressants | among the two | groups |
|-------------------------|---------------------|--------------------|---------------|--------|
| | | | <u> </u> | ~ . |

| | Prevalence | | | Daily dosage (mg) | | | |
|-------------------------|-------------|------------|-------|-------------------|-------------------|------|--|
| | Control | Elderly | р | Control | Elderly | р | |
| Triple therapy | 203 (76.3%) | 47 (81.0%) | 0.44 | | | | |
| Cyclosporin A | 169 (66.8%) | 51 (87.9%) | 0.001 | 136.3 ± 37.4 | 127.0 ± 38.9 | 0.12 | |
| Prednisolone | 239 (94.5%) | 58 (100%) | 0.052 | 6.2 ± 3.41 | 6.1 ± 3.6 | 0.88 | |
| Azathioprine | 53 (20.9%) | 10 (17.2%) | 0.53 | 64.6±17.3 | 65.0 ± 17.5 | 0.95 | |
| MMF/Myfortic | 164 (64.8%) | 37 (63.8%) | 0.88 | 954.3 ± 303.7 | 907.9 ± 269.0 | 0.33 | |
| Tacrolimus | 75 (29.6%) | 6 (10.3%) | 0.003 | 3.1 ± 1.7 | 3.1 ± 2.0 | 0.93 | |
| Diltiazem/Lercanidipine | 114 (44.9%) | 30 (51.7%) | 0.35 | 187.2 ± 114.6 | 205.0 ± 111.2 | 0.45 | |
| Sirolimus | 7 (2.8%) | 0 (0%) | 0.23 | | | | |
| Everolimus | 1 (0.4%) | 1 (1.7%) | 0.34 | | | | |

MMF=mycophenolate mofetil.

level, and length of follow-up between the two age groups. Elderly patients had shorter duration of dialysis before transplantation (32.3 months vs. 18.4 months, p=0.023). Chronic glomerulonephritis was the most common cause of end-stage renal failure in the control group, while DM and hypertension were the most common causes in the elderly group. Other causes of end-stage renal failure, in the control group, were obstructive uropathy (4 cases), interstitial nephritis (2 cases) and nephrocalcinosis (3 cases), and in the elderly group, obstructive uropathy (1 case). For the majority of the control group and all the patients in the elderly group, it was their first transplantation, with most being cadaveric transplantation performed in mainland China.

At the time of the study, the elderly group had a significantly higher prevalence of DM, ischemic heart disease and CVA. Most of the patients in both groups had hypertension. All patients were given dual or triple immunosuppressive therapy. The proportion of patients on dual or triple immunosuppressants was similar between the two groups (Table 2). Data for 13 patients (4.9%) in the control group were missing because their

Control Elderly р Polyclonal antibodies 60 (22.6%) 13 (22.4%) 0.98 Monoclonal antibodies 60 (23.3%) 5 (8.6%) 0.012 Unknown 111 (41.7%) 35 (60.3%) 0.01 No adjuvant therapy 28 (10.5%) 5 (8.6%) 0.66 Combination 5 (1.9%) 0.37 0

Table 3. Comparison of adjuvant induction therapy between the

two groups

| | Control | Elderly |
|------------------------------------|------------|-----------|
| Banff grade I | 18 (31%) | 0 |
| Banff grade II | 6 (10.3%) | 1 (16.7%) |
| Humoral | 2 (3.4%) | 1 (16.7%) |
| Banff grade I+humoral | 2 (3.4%) | 0 |
| Unknown/grading not clearly stated | 11 (19%) | 0 |
| Biopsy not done | 19 (32.8%) | 4 (66.7%) |
| | | |

Table 5. Comparison of rejection grade between the two groups

Table 4. Incidence of acute rejection, infection requiring hospitalization, cytomegalovirus infection and malignancy of the two groups

| | Control | Elderly | р |
|--|-------------|------------|-------|
| Incidence of AR | 48 (18.0%) | 5 (8.6%) | 0.08 |
| Incidence of biopsy-proven AR | 32 (12.0%) | 2 (3.4%) | 0.053 |
| Number of ARs per patient | 0.22 | 0.10 | 0.081 |
| Incidence of infection requiring hospitalization | | | |
| ≥ 1 episode | 158 (59.4%) | 37 (63.8%) | 0.54 |
| ≥2 episodes | 80 (30.1%) | 28 (48.2%) | 0.008 |
| ≥3 episodes | 44 (16.5%) | 13 (22.4%) | 0.29 |
| Incidence of CMV infection | 49 (18.4%) | 14 (24.1%) | 0.32 |
| Malignancy | 8 (3.0%) | 4 (6.9%) | 0.15 |

AR = acute rejection; CMV = cytomegalovirus.

transplantation had been done in mainland China and the details could not be retrieved. The use of tacrolimus was more prevalent in the control group (29.6% vs. 10.3%, p=0.003), while cyclosporin A was more prevalent in the elderly group (66.8% vs. 87.9%, p=0.001). Comparing the two calcineurin inhibitors in all patients, cyclosporin was more frequently used than tacrolimus. The usage of prednisolone, azathioprine, MMF/Myfortic (Novartis International AG), calcium channel blocker, sirolimus and everolimus was similar between the two groups. The dosages of cyclosporin A and MMF were lower in the elderly group, although the differences were not statistically significant (Table 2). The dosages of prednisolone, azathioprine, tacrolimus and diltiazem were similar between the two groups.

Regarding adjuvant induction therapy, monoclonal antibodies were more frequently given to the control group (23.3% vs. 8.6%, p < 0.012), but the corresponding data were missing in many cases (41.7% in control group vs. 60.3% in elderly group). The prevalence of polyclonal antibody usage (22.6% vs. 22.4%, p=0.98) or no adjuvant therapy (10.5% vs. 8.6%, p=0.66) was similar between the two groups. There were five patients in the control group who were given combination induction therapy: three were given polyclonal antibodies plus plasmapheresis. The results are summarized in Table 3.

Forty-eight patients (18.0%) in the control group and five (8.6%) in the elderly group experienced acute

rejections. The incidence of biopsy-proven acute rejection was also lower in the elderly group (12.0% vs. 3.4%, p=0.053). The numbers of acute rejections per patient in the control group and the elderly group were 0.22 and 0.1, respectively. The differences were, however, not statistically significant (Table 4). A large proportion of rejections were diagnosed clinically without renal biopsy (Table 5).

Regarding the incidence of infections, the elderly group was observed to have more infections requiring hospitalizations (Table 4). One hundred and fifty-eight patients (59.4%) in the control group and 37 patients (63.8%) in the elderly group had at least one such admission, while 80 patients (30.1%) in the control group and 28 patients in the elderly group (48.2%) experienced at least two admissions as a result of infections (p=0.008). There was a trend towards higher incidence of CMV infection in the elderly group (18.4% vs. 24.1%, p=0.32) post transplantation. More patients in the elderly group developed malignancy (3.0% vs. 6.9%, p=0.15). The following eight malignancies in the control group were found: two post-transplant lymphoproliferative disease, one carcinoma of breast, one carcinoma of thyroid, one renal cell carcinoma, one acute myeloid leukemia, one carcinoma of ovary and one metastatic adenocarcinoma of unknown primary origin. Four patients in the elderly group had malignancies post transplantation: one transitional cell carcinoma of the urinary tract, one posttransplant lymphoproliferative disease, one carcinoma of colon and one carcinoma of lung (Table 4).



Figure 1. Kaplan-Meier curve of death-censored graft survival.



Figure 2. Kaplan-Meier curve of patient survival.

Graft survival

Patients who do not require regular renal replacement therapy were defined as having survived graft. For the whole cohort of 324 patients, the overall 1-year and 5-year death-censored graft survival rates were 95.4% and 91.7%, respectively (Figure 1). The death-censored 1-year and 5-year graft survival rates, respectively, were 94.4% and 90.6% in the control group, and 100% and 96% in the elderly group. There were no differences between the two groups (p=0.297 and p=0.178, respectively). The main causes of graft loss in the control group were death with functioning graft (39%), primary nonfunction (9.8%), acute rejection (9.8%), vascular problem (9.8%), and chronic allograft dysfunction (9.8%). The main causes of graft loss in the elderly group were death with functioning graft (83.3%), chronic allograft dysfunction (8.3%), and allograft infection (8.3%).

The overall 1-year and 5-year patient survival rates for the whole cohort were 95.4% and 89.8%, respectively (Figure 2). The 1-year patient survival rates were 95.5%

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Table 6. Comparison of causes of death between the two groups

| | Control | Elderly | р |
|----------------|------------|-----------|------|
| Infection | 10 (47.6%) | 8 (66.7%) | 0.24 |
| Cardiovascular | 3 (14.3%) | 0 | 0.26 |
| Malignancy | 3 (14.3%) | 1 (8.3%) | 0.56 |
| Unknown | 5 (23.8%) | 3 (25%) | 0.60 |

and 94.8% for the control group and elderly group, respectively. However, the 5-year patient survival rate was better in the control than in the elderly group (92.1% vs. 79.3%, p=0.0058).

The main causes of death in the control group were infection (47.6%), unknown (23.8%), cardiovascular (14.3%), and malignancy (14.3%) (Table 6). The main causes of death in the elderly group were infection (66.7%), unknown (25.0%), and malignancy (8.3%). There were no statistically significant differences detected.

DISCUSSION

With this background on the use of immunosuppressive agents in mind, we found that the incidence of acute rejection and biopsy-proven acute rejection was lower in the elderly group than in the control group. The results are similar to those of a retrospective study by Meier-Kriesche et al [8] of 73,707 patients who had undergone primary renal transplantation between 1988 and 1997. The incidence of acute rejection at 6 months decreased from 28% in the youngest age group to 19.7% in the oldest age group. In a retrospective review [9], 1,095 patients were divided into four groups according to their age $(18-49, 50-59, 60-64, \ge 65)$. The incidence of acute rejections showed a decreasing trend across the age groups (34.7%, 25.2%, 27.9%, 23.6%; p=0.09). Friedman et al [10] reported similar findings when 16 patients aged ≥ 60 were compared with 230 patients aged < 60. The overall incidence of acute rejections in the first 90 days was higher in the younger group (33.8% vs. 6.3%, p=0.001).

The observed tendency for older patients to develop less acute rejections could, hypothetically, be related to the immunological change with aging that renders the immune system less active [11]. At the molecular level, aging is associated with a decrease in T cell proliferation in response to T cell receptor- and co-stimulus-mediated stimulation [12]. The level of interleukin-2, an important cytokine in T cell activation, was also found to decrease with age [13]. Thus, as suggested in the current study, the incidence and severity of acute rejections should be lower in the elderly. On these grounds, one may argue that immune senescence may speak for a reduction in immunosuppressive therapy among older transplant recipients. In this study, the incidence of infection requiring hospital admission was higher in the elderly group. The difference becomes more prominent when the frequency is taken into consideration. In other words, elderly patients tend to have more infective complications than younger patients. Similar findings have been reported in the literature. Trouillhet et al [14] compared 40 patients aged ≥ 65 and another 40 aged < 65 who had undergone renal transplantation. The incidence of infection was 80% in the elderly group and 32% in the younger group, with an odds ratio of 5, and a 95% confidence interval of 1.6 to 20. The proposed rationale behind such an observation was the depressed immune system in the elderly.

CMV infection was more frequently observed among elderly transplant recipients (18.4% vs. 24.1%, p=0.32) in the present study. This echoed the findings of Moreso et al [15] where the incidence of CMV infection was 29.3% in the elderly compared with 22–29% in the younger adults. In this study, the serology status of CMV for donors and recipients were not included as a result of incomplete data, so it was difficult to conclude whether or not age alone is a risk factor for CMV infection. CMV infection is associated with many adverse outcomes, including increase in acute rejections, decrease in graft and patient survival, and predisposition to infections and malignancy [16]. It is therefore desirable to detect and treat the disease early to improve the outcome of transplant recipients.

The overall incidence of malignancy was 3.7% and was slightly higher in the elderly group (3.0% vs. 6.9%, p=0.15). Similar results were recently reported by Imao et al [17]. In their study, the overall incidence of malignancy was 6.8% (25/366), and age was identified as a risk factor for malignancy (hazard ratio=1.562; 95% confidence interval=1.089–2.240; p=0.0155). One of the possible explanations is age-related decline in immune surveillance, leading to the accumulation of cellular and DNA mutations, and increasing the risk of malignancy development [18]. Another reason would be related to exposure to oncogenic viruses in the elderly [19].

The overall 1-year and 5-year graft survival rates in the present study were 95.4% and 91.7% (death censored), respectively. The results are comparable to local data [2], where the 1-year and 5-year graft survival rates are 92.5% and 84.4% (death censored), respectively. The graft survival rate is better than in a previous larger-scale study [20]. In that review, the author pooled data from the Collaborative Transplant Study [21], United States Renal Data System annual report 1996 [22], United States Network for Organ Sharing and Division of Organ Transplantation 1994 report [23], UK Transplant Services Special Authority newsletter [24] and combined series single center data and determined the overall graft survival rate to be 74% at 1 year and 57% at 5 years. More recent data from the United States Renal Data System [25] showed that the 1-year graft survival rate was 89.5% in 2003 and 65.9% in 1999.

We have demonstrated that graft survival in the elderly is comparable to that in younger patients. Raviňa et al [26] reported that graft survival is not inferior in the elderly when death with a functioning graft was censored in the analysis. Humar et al [27] also revealed no significant difference in the death-censored 5-year graft survival rate in the elderly compared to younger patients.

The main cause of graft loss in the elderly in the current study was death with a functioning graft. This result was consistent with a study in a larger series where 56.5% of graft loss was due to death with a functioning graft among elderly patients [11]. Although the results of graft survival in this study seemed to be superior to those of other countries, we should interpret them with great care because the majority of the transplants were performed in mainland China, where donor information including donor age and human leukocyte antigen typing were not available for analysis. It is suggested that both factors are important determinants of graft survival [28,29].

The overall 1-year and 5-year patient survival rates were 95.4% and 89.8% in this study. This finding was comparable to the local registry data [2] where the 1-year and 5-year patient survival rates for cadaveric kidney transplant recipients were 96.1% and 91.2%, respectively. The results were also similar to figures reported in the United States [25], where the 1-year and 5-year patient survival rates were 94.6% and 79.3%, respectively.

In this study, the 5-year survival rate was lower in the elderly group (79.3% vs. 92.1%, p=0.0058), while the 1-year survival rate was similar. Oniscu et al [9] reported 5-year survival rates of 81–91% in the younger versus 59–66% in the elderly patients (p<0.001), and Giblin et al [30] reported similar findings of 87% versus 60% (p<0.001). This observation can be explained by the more frequent association with comorbid illnesses in the elderly. Although the mortality rate in the elderly was higher than in younger adults, the outcome was still better than those who were on dialysis [31,32].

There was a trend in this study towards a higher proportion of patients in the elderly group dying of infection compared with the control group (45.5% vs. 66.7%, p=0.24). This proportion was higher than in previously reported series. Gill et al [33] analyzed the causes of death in 4,741 patients and found that infection accounted for only 17%. In another study involving 1,567 patients, the cause of death due to infection in the elderly group (age>65) was 22%, versus 16% in the younger age group [32]. One can argue that the small sample size and short duration of follow-up in the present study may have affected the results, but over-immunosuppression is another possible explanation. Some studies have reported a changing pattern of causes of death among transplant recipients as a function of the length of follow-up. Jassal et al [34] demonstrated that mortality due to infection decreased from 40.1% to 11.5% from the first year to 5–10 years. At the same time, mortality due to cardiac disease and malignancy rose from 24.3% and 5.0% in the first year to 29.4% and 23.7% at 5–10 years. Since the mean duration of follow-up in the current study was 43 months, the longer-term outcome at 5–10 years may have been different.

The present study has several limitations. First, the samples were collected from two hospitals in Hong Kong, which may not be representative of the whole picture in this locality. In addition, the average duration of follow-up was less than 4 years, and may not be able to determine the long-term outcomes of these patients. More precise data on the immunosuppressants used, such as cumulative dosage of steroid, drug level of calcineurin inhibitors, and combination of immunosuppressants, may enable a more precise correlation with outcome. Most of the patients had undergone transplantation in mainland China, rendering their perioperative data not generally available. Important parameters such as donor age, donor human leukocyte antigen typing, details of induction therapy and postoperative clinical course were thus missing in most of these cases. These parameters are also vital in the precise analysis of patient outcomes. Quality of life is another aspect we would like to investigate, but which was outside the scope of the current study.

This study found that elderly renal transplant recipients were more frequently associated with comorbidities including DM, ischemic heart disease and CVA. The use of cyclosporin A was more prevalent in the elderly than in the control group. The incidence of acute rejection was lower, while the incidence of infection and malignancy was higher in the elderly group. Graft survival in the elderly group was comparable to that in the control group, especially when death with functioning graft was censored. It is thus intriguingly to speculate that there is some sort of senescence of our immune system as aging occurs. As a result, the elderly do not experience graft rejection as often as younger patients, but they do have a higher incidence of complications of over-immunosuppression, namely infections and malignancy. The optimal immunosuppressive therapy for elderly renal transplant recipients may thus be different from that which is universally recommended for all, and needs to be specifically addressed.

References

- Census and Statistical Department. Statistical Table. Population by Age Group, 1996, 2001 and 2006. Available at http://www.censtatd. gov.hk/hong_kong_statistics/statistical_tables/index_t.jsp?charset ID=1&subjectID=1&tableID=137 [Date accessed: March 15, 2007]
- Ho YW, Chau KF, Leung CB, Choy BY, Tsang WK, Wong PN, et al. Hong Kong Registry Report 2004. *Hong Kong J Nephrol* 2005;7:38–46.

- Wolfe RA, Ashby UB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, 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;341:1725–30.
- Cameron JI, Whiteside C, Katz J, Devins GM. Differences in quality of life across renal replacement therapies: a meta-analytic comparison. *Am J Kidney Dis* 2000;35:629–37.
- Winkelmayer WC, Weinstein MC, Mittleman MA, Glynn RJ, Pliskin JS. Health economic evaluations: the special case of end-stage renal disease treatment. *Med Decis Making* 2002;22:417–30.
- Ismail N, Hakim RM, Helderman JH. Renal replacement therapies in the elderly: Part II. Renal transplantation. *Am J Kidney Dis* 1994;23:1–15.
- Doyle SE, Matas AJ, Gillingham K, Rosenberg ME. Predicting clinical outcome in the elderly renal transplant recipient. *Kidney Int* 2000;57:2144–50.
- Meier-Kriesche HU, Ojo A, Hanson J, Cibrik D, Lake K, Agodoa LY, et al. Increased immunosuppressive vulnerability in elderly renal transplant recipients. *Transplantation* 2000;69:885–9.
- Oniscu GC, Brown H, Forsythe JL. How old is old for transplantation? Am J Transplant 2004;4:2067–74.
- Friedman AL, Goker O, Kalish MA, Basadonna GP, Kliger AS, Bia MJ, et al. Renal transplant recipients aged over 60 have diminished immune activity and a low risk of rejection. *Int Urol Nephrol* 2004;36:451–6.
- 11. Wick G, Grubeck-Loebenstein B. The aging immune system: primary and secondary alterations of immune reactivity in the elderly. *Exp Gerontol* 1997;32:401–13.
- 12. Hodes JR. Molecular alterations in the aging immune system. *J Exp Med* 1995;182:1–3.
- Globerson A. T lymphocytes and aging. Int Arch Allergy Immunol 1995;107:491–7.
- Trouillhet I, Benito N, Cervera C, Rivas P, Cofán F, Almela M, et al. Influence of age in renal transplant infections: cases and controls study. *Transplantation* 2005;80:989–92.
- Moreso F, Ortega F, Mediluce A. Recipient age as a determinant factor of patient and graft survival. *Nephrol Dial Transplant* 2004; 19 (Suppl 3):16–20.
- Fishman JA, Emery V, Freeman R, Pascual M, Rostaing L, Schlitt HJ, et al. Cytomegalovirus in transplantation—challenging the status quo. *Clin Transplant* 2007;21:149–58.
- Imao T, Ichimaru N, Takahara S, Kokado Y, Okumi M, Imamura R, et al. Risk factors for malignancy in Japanese renal transplant recipients. *Cancer* 2007;109:2109–15.
- Burns EA, Leventhal EA. Aging, immunity, and cancer. *Cancer* Control 2000;7:513–22.
- Muller AM, Ihorst G, Mertelsmann R, Engelhardt M. Epidemiology of non-Hodgkin's lymphoma: trends, geographic distribution, and etiology. *Ann Hematol* 2005;84:1–12.
- Cameron JS. Renal transplantation in the elderly. *Int Urol Nephrol* 2000;32:193–201.
- Opelz G. Factors influencing kidney graft survival in Latin America. Collaborative Transplant Study. *Transplant Proc* 1999;31:2951–4.
- United States Renal Data System. Annual Data Report 1996 and Reference Tables. Available at http://www.usrds.org/adr_1996.htm [Date accessed: March 15, 2007]
- United States Network for Organ Sharing and Division of Organ Transplantation 1994 Report (1988–1993). Bethesda, MD: Bureau of Health Services Development, US Department of Health and Human Services, 1994.
- 24. Belger M. UK Transplant Services Special Authority Newsletter. Bristol: UKTSSA, 1998.

- 25. United States Renal Data System. *Annual Data Report 2006 Reference Tables*. Available at http://www.usrds.org/reference.htm [Date accessed: March 15, 2007]
- Raviňa FO, Martinez MR, Gude F, González-Juanatey JR, Valdés F, Sánchez-Guisande D. Renal transplantation in elderly: does patient age determine results? *Age Aging* 2005;34:583–7.
- Humar A, Denny R, Matas AJ, Najarian JS. Graft and quality of life outcomes in older recipients of a kidney transplant. *Exp Clin Transplant* 2003;1:69–72.
- Pugliese O, Quintieri F, Mattucci DA, Venettoni S, Taioli E, Costa AN. Kidney graft survival in Italy and factors influencing it. *Prog Transplant* 2005;15:385–91.
- 29. Zhou YC, Cecka JM. Effect of HLA matching on renal transplant survival. *Clin Transpl* 1993:499–510.

- Giblin L, Hollander M, Little D, Hickey D, Donohoe J, Walshe JJ, et al. Renal transplantation in the elderly—the Irish experience. *Ir J Med Sci* 2005;174:9–13.
- Johnson DW, Herzig K, Purdie D, Brown AM, Rigby RJ, Nicol DL, et al. A comparison of the effects of dialysis and renal transplantation on the survival of older uremic patients. *Transplantation* 2000; 69:794–9.
- 32. Bonal J, Cleris M, Vela E. Transplantation versus haemodialysis in elderly patients. *Nephrol Dial Transplant* 1997;12:261–4.
- Gill JS, Abichandani R, Kausz AT, Pereira BJ. Mortality after kidney transplant failure: the impact of non-immunologic factors. *Kidney Int* 2002;62:1875–83.
- 34. Jassal JV, Opeltz G, Cole E. Transplantation in the elderly: a review. *Geriatr Nephrol Urol* 1997;7:157–65.