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Older does not mean worse – the results of kidney transplantation in seniors

Starszy nie znaczy gorszy – wyniki transplantacji nerek u seniorów

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Summary

Introduction. The prevalence of chronic kidney disease is rising with advancing age. The elderly patients are qualified to the dialysis treatment and are increasingly being considered to the kidney transplantation. They are characterized by specific co-morbidity profile, that compromise graft and patient outcome.

Material and methods. A group of 64 patients aged over 65 years (mean 66.2+/-2.8) were studied during the seven year period after kidney transplantation.

Results. One-year patient survival was assessed as 84.4% and graft survival 76.5%. The death-censored graft survival in the first year after transplantation was 84.4%. The two- years patient and graft survival were 84.4% and 70.3%, respectively. The main causes of death were cardio-vascular diseases and infections.

Conclusions. Our results confirm that renal transplant must be considered in selected patients older than 65 years as patient and graft survivals are similar to those of younger patients. The leading problem is death-censored graft survival.

Key words: elderly, transplantation, immunosuppression, outcome

Streszczenie

Wstęp. Występowanie przewlekłej choroby nerek wzrasta z wiekiem. Starsi pacjenci coraz częściej kwalifikowani są do dializoterapii oraz do zabiegu przeszczepienia nerki. Charakteryzuje ich specyficzny profil współchorobowości, wpływający na przeżycie greftu i pacjenta.

Materiał i metody. Grupę badaną stanowiło 64 pacjentów w wieku powyżej 65. roku życia (średnio 66,2 ± 2,8) poddanych transplantacji nerki, obserwowanych w czasie 7 lat po zabiegu.

Wyniki. Przeżycie pacjenta w pierwszym roku po transplantacji oceniono na 84,4%, a nerki przeszczepionej na 76,5%. Pierwszoroczne przeżycie pacjentów determinowane przez zgony z czynnym greftem stanowiło 84,4%. Dwuletnie przeżycia pacjentów i przeszczepionych nerek wynosiły odpowiednio: 84,4 i 70,3%. Głównymi przyczynami zgonów były incydenty sercowo-naczyniowe i infekcje.

Wnioski. Przedstawione wyniki potwierdzają skuteczność przeszczepiania nerek u wybranych pacjentów powyżej 65. roku życia w porównaniu do młodszych chorych. Głównym problemem w grupie seniorów pozostaje śmierć z czynnym greftem.

Słowa kluczowe: starsi, transplantacja, immunosupresja, rokowanie

INTRODUCTION

Chronic kidney disease become an illness of the elderly. Every year the number of dialyzed patients aged over 65 years increases in Poland and all over the world. It is related to prolonged life expectancy, better medical care and access to replacement therapy. The ageing of the society results in growing morbidity

due to civilization diseases, so we have to look forward the rise of the elderly people population ongoing regular dialysis. From the Medicare data, since 80' in United States patients over 65 years of age accounted for 30% dialyzed ones (1). The Polish renal replacement registry reports 56% patients in this age, who have begun the dialysis in 2007 and 47.5% in the end of this year.

It is worth noting, that patients aged over 75 years constituted 15.43% among dialyzed population in Poland in 2007 (2). A high percentage of dialyzed older people is also caused by their low registration to the transplantation waiting list. This phenomenon is based on the opinion about higher risk than benefits from the renal transplantation in the elderly. In 2006 in United States only 6% of elderly people ongoing regular hemodialysis were enrolled to the waiting list and only 0.8% patients after transplantation were older than 65 years of age (1, 3). The first large study describing a group of elderly people after kidney transplantation was carried out in 1971 and showed very poor outcome (4, 5). However, the introduction of the new immunosuppression strategies with cyclosporine and tacrolimus, the subsequent reduction of steroids, improved the graft and patients survival in this elder recipient group. Currently in qualification to kidney transplantation age itself is not the exclusion criterion, but the general health and so-called “biological age”.

AIM

We evaluate the role of kidney transplantation in the management of end stage renal failure in patients older than 65 years. We analyzed the kidney recipients from our center transplanted between 1999-2012 year.

PATIENTS AND METHODS

Between 1999-2012 in our center were performed 796 kidney transplantations. The recipients age ranged from 17 to 76 years. The number of patients older than 65 years was 64, what accounted for 8% of patients after transplantation. This group consisted of 43 men and 21 women. The mean age was 66.2+/-2.8 years. The mean age of the donors for this group was 57.3+/-5.5 years. 63 patients underwent first transplantation. Only one female patient was retransplanted. All patients received kidney from deceased donors. The leading causes of end stage renal disease (ESRD) were diabetes mellitus in 21 subjects, chronic glomerulonephritis in 15 subjects, chronic interstitial nephritis in 5 subjects, autosomal dominant polycystic kidney disease in 6 subjects, hypertension in 7 subjects and other ob unknown causes in 10 subjects. All the examined patients were hemodialysed before transplantation. The mean hemodialysis period was 19.2+/-12.1 months. 9 patients had PRA (panel reactive antibodies) over 20%. The mean CIT (cold ischemia time) was 16.5+/-5.4 hours (tab. 1). The observation period was from 21 days to 7 years (tab. 1).

We evaluated the patient and graft 1 and 2-year survival after renal transplantation in 64 subjects. After this time 23 patients moved for the further care to the other transplant centers so the data from that time were assessed on the smaller group of subjects.

During the whole post transplantation follow up 13 of 64 (20%) recipients have died, including 10 patients (15.6%) in the first year after transplantation. The one- and two-years patient survival was 84.4%

(54 patients). The dominating cause of death with functioning graft in the first year after transplantation were cardio-vascular diseases in seven subjects. The other were infectious complications in two subjects and colon cancer in one subject. The mortality in later years was also related to cardio-vascular events in two patients and gastrointestinal bleeding in one patient (tab. 2).

Table 1. Recipients characteristics.

Parameter	n (%)
Patients age	66.2+/-2.8 years
Cause of renal failure	
DM	21 (32.81%)
GN	15 (23.43%)
HA	7 (10.93%)
Interstitial	5 (7.81%)
ADPKD	6 (9.37%)
Unknown	10 (15.65%)
Hemodialysis	64 (100%)
Panel reactive antibodies over 20% (%)	9 (5.76%)
Cold ischaemia time	16.5+/-6.4 hours
Immunosuppressive protocols	
AZA, CsA, pred	8 (12.50%)
MMF, CsA, pred	23 (35.93%)
MMF, TAC, pred	25 (39.06%)
AZA, TAC, pred	2 (3.12%)
RAPA, TAC, pred	2 (3.12%)
RAPA, MMF, pred	4 (6.25%)
Type of donor	
Deceased donor	64 (100%)

RAPA – rapamycin; MMF – mycophenolate mofetil; CsA – cyclosporine; pred – prednisolone; DM – diabetes mellitus; GN – chronic glomerulonephritis; Interstitial – chronic interstitial nephritis; ADPKD – autosomal dominant polycystic kidney disease; HA – hypertension

Table 2. One-year patient and graft survival with causes of death and graft loss. Two-year patient and graft survival.

Patient and graft survival	n (%)
One-year patient survival	54 (84.4%)
One-year graft survival	49 (76.5%)
One-year death censored graft survival	54 (84.4%)
Causes of death in the first year after transplantation	
Cardio-vascular complications	7 (10.9%)
Infections	2 (3.1%)
Cancer	1 (1.5%)
Causes of graft loss in the first year after transplantation	
Thrombosis of kidney vessels	3 (4.6%)
Acute rejection	1 (1.5%)
Surgical complications	1 (1.5%)
Two-year patient	54 (84.4%)
Two-year graft survival	45 (70.3%)

Among 31 patients who were followed in our center above 2 years post transplant, three returned to haemodialysis due to the graft failure during follow up period up to 7 years.

20 recipients seven years after transplantation had well functioning grafts (eGFR > 60 ml/min). In the same period of observation among the patients below 65 years of age 71 of 732 transplanted patients died, what gives the mortality rate 9.7%. It is two times lower, than in the elder group.

One-year graft survival was 76.5% (46 patients) and death censored 1-year graft survival was 84.4%. Two-year graft survival was 70.3% and no other patients died in the second year.

The lost of the graft in the first year after transplantation concerned 5 subjects and was due to thrombosis of kidney vessels (3 subjects), acute rejection (1 subject) and surgical complications (1 subject).

Analysis of one-year survival within the > 65 age group shows no age – related differences in both patient and graft survival (fig. 1-3).

DISCUSSION

Have the survival of patients and transplanted kidneys been better since 1971 year, when the first research was done? The publication of Simmons et al. showed only 60% survival of patients and 20% of grafts in the first year after kidney transplantation in recipi-

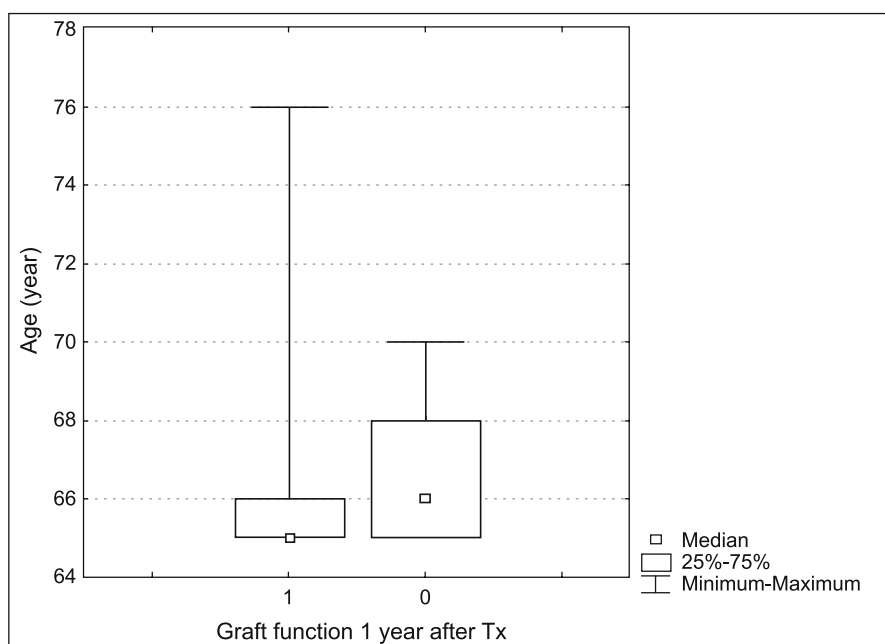


Fig. 1. Relationship between age and graft function in the first year after kidney transplantation. 1 – subjects with functioning graft, 0 – graft lost, Tx – transplantation of the kidney

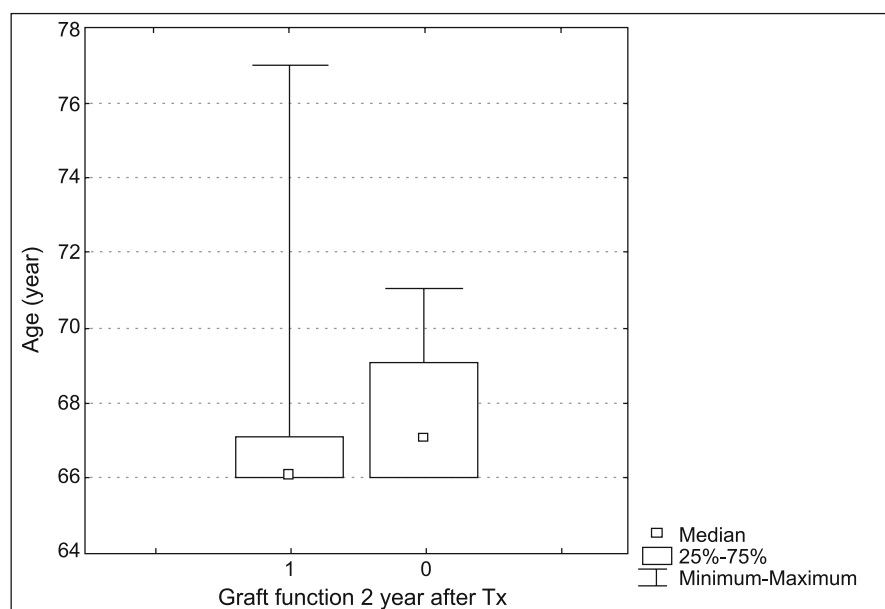


Fig. 2. Relationship between age and graft function in the second year after kidney transplantation. 1 – subjects with functioning graft, 0 – graft lost, Tx – transplantation of the kidney

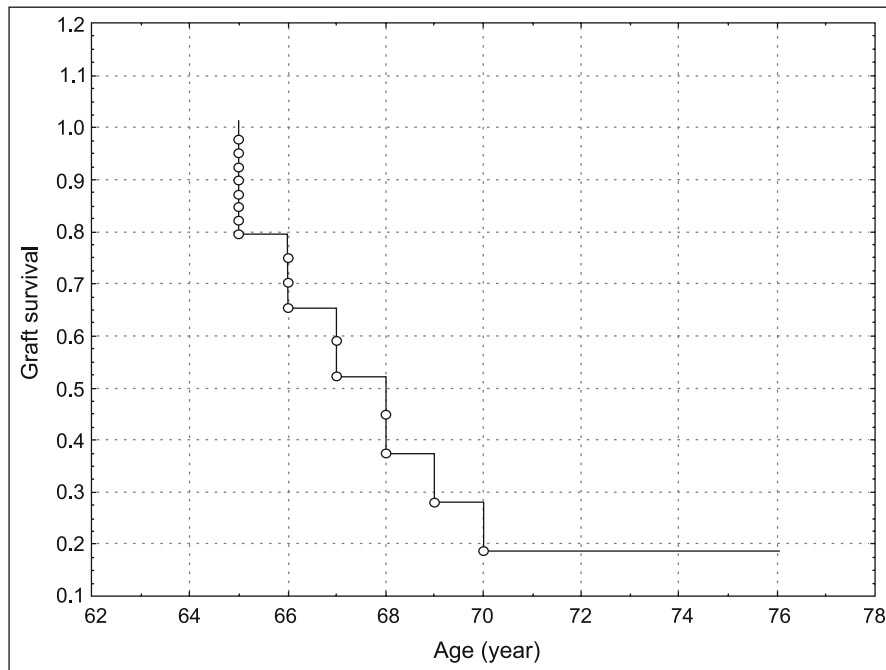


Fig. 3. Relationship between graft survival and recipients age (Kaplan-Meier).

ents aged over 45 years. Today such recipients are qualified as younger ones (4). In the article from the same year Delmonico et al. in the group of patients older than 51 years observed the mortality in the first year after transplantation on the level of 57% and of the grafts 50% (5). It was the time of dual immunosuppressive therapy. The worst survival of patients and transplanted kidneys in this age group was probably related to high dosage of steroids. The effects of kidney transplantation improved during last decades. It is the consequence of more safe and efficient modern immunosuppressive therapy, better post transplant surveillance, antiviral prophylaxis and treatment of viral infections, especially cytomegalovirus and polyoma BK virus. Therapeutic drug monitoring and patient's viral status also play a very important role in a successful kidney transplantation. It is confirmed in the recent research. Fehrman et al. in the group of kidney graft recipients aged over 65, examined 1 and 3-year patients and grafts survival. She found 71% and 63% respectively patients survival, and grafts survival on the level of 57% and 49% respectively (7). Murie et al. observed the group of 63 patients over 65 and showed the 1-year recipient and graft survival rates on the level 87% and 63% respectively (8). These numbers are confirmed in other publications. 4 authors cited in this article examined together 207 patients. An average 1-year patient survival was 76% and graft survival 73% (7, 9-11). None of those researchers found the difference in survival between younger and older recipients. In the ERA-EDTA report from 2009, 2-year survival of the patients aged between 65-75 years ongoing regular hemodialysis was about 67.9% (67.3-68.4%), but over 75 year of age decreased to 53.7% (53.1-54.3%).

The same report showed 84.9% (82.4-85.9%) rate of 1-year survival after kidney transplantation for the group of patients over 65 years (12). The survival of the patient after kidney transplantation is higher than for the same age group of subjects on dialysis treatment. Wolf et al. in their study presented, that the risk of death among elderly patients within 2 years after transplantation is three times higher than on haemodialysis, but over that time the results showed the survival advantage for the transplanted patients (13). The hospitalization frequency and duration are higher in the elderly during the first year after transplantation than in dialyzed patients and younger patients after transplantation. It is caused by many comorbidities in the senior group (14). In our center survival of the patients and grafts does not differ significantly from that shown in the cited articles.

Death with functioning graft

One of the most important problems among the elderly patients after renal transplantation is death with functioning graft. Comparing the young recipients aged from 18 to 29, those aged over 65 years, have 7 times higher risk of death with functioning graft. The main cause of mortality among the seniors after transplantation are cardio-vascular events. In the group from our center the observations were similar (twice lower mortality rate in younger group).

The immunosuppressant caused toxicity, steroids related weight gain, new onset diabetes mellitus, lipid disorders, hypertension trigger cardio-vascular incidents. The cardio-vascular risk shows linear progression with age, but it is still lower in patients after kidney transplantation than in dialysis population (15). Among 17 patients

over 65 years who undergone kidney transplantation described by Rose et al., 5 of 6 recipients who died with functioning graft had cardio-vascular incidents (11). In Tabsons publication 4 elder patients from 13 died with functioning graft (9). Jordan et al. performed coronarography in all patients aged over 55 years. Only 4 from 67 (5%) needed angioplasty of coronary vessels. Among all patients 3 died due to cardio-coronary event, but 2 of them had no significant changes in coronarography (16). This emphasize the need for pre-transplantation cardiologic diagnostic procedures in the elderly. Howard et al. examined 16 patients over 65 year with the dobutamine stress echocardiography. From this group 8 patients required further invasive diagnostics and coronary angioplasty and one coronary by-pass grafting. Despite this diagnostic procedures after renal transplantation 4 (25%) patients from this group died due to cardio-vascular complications (17). In our center every patient aged over 55 years has routine coronarography and also younger ones with symptoms or suspicion of ischaemic heart disease.

Infections

The mortality connected with infection is the second reason of death among elderly patients after renal transplantation (3). In the first year after transplantation it is related to high doses of immunosuppressive agents, on which elderly people are more sensitive. (18, 19). Elderly patients are more prone to developing drug related adverse effects (20). The studies describe lower age-related clearance of immunosuppressants, for example 34% of cyclosporine. Elders are also more susceptible to pharmacokinetic and pharmacodynamic drug interactions because of frequent in this group of patients polypharmacy. To increased prevalence of infectious complications contribute also disorders of immunological system in the elderly with decreased cell-mediated immunity (20). The older age is the independent risk factor of the urinary tract infections. Chuang et al. described this complication in 55% of patients over 65 years after transplantation comparing with 30% in younger subjects (21). Trouillhet et al. also showed more urinary tract infections among elderly kidney recipients (80%) than in the younger group (32%) (22). Despite this increased post transplant risk, deaths due to infections are more common in haemodialyzed patients in every age group than after kidney transplantation (15).

Acute rejection

Acute rejection is an important reason of graft loss. The actual studies show a tendency of decreasing percentage of acute rejection in seniors recipients. Perhaps, it is connected with age-related higher immunotolerance. In our examined group there was only one graft loss due to acute rejection. More frequent problem in this group is delayed graft function and adverse effects of immunosuppressant (21).

The quality of life

The life expectancy is not the only profit from the treatment of elderly people. The other important aspect is the quality of life. In Westlie research the number of 79 patients aged over 70 years ongoing regular hemodialysis declared high life quality, but the study performed 4 years later showed 54% mortality in that group. 43% from them gave up the dialysis treatment themselves- the reason of such decisions was probably poor life quality (23, 24). Comparison of the group of elderly transplanted patients and hemodialyzed patients in the same age showed higher life quality in people after renal transplantation (25, 26). Other studies presented better subjective improvement of health (physical and psychological) in seniors after transplantation than in healthy population and younger group after kidney transplantation (27). Those findings emphasize the need to consider not only concomitant diseases and direct outcome of renal replacement therapy but also patient expectations when we choose the best option of RRT for individual patient.

Economy

An important factor, which also convince to transplantations of the elderly patients is economy. Wong et al. perform an analytic model based on hemodialyzed and transplanted patients in Australia. It indicated the financial advantage of transplantation over hemodialysis for the health budget. This was obvious not only in the younger population but also in elders. The economy profits not only due to the lower cost of post transplant care compared to hemodialysis but also due to the prolongation of life expectancy and lower hospitalization frequency and costs in this group of patients (13). Analogous observations are valid for Poland and other European countries.

SUMMARY

The attitude to the kidney transplantation in elderly have changed for the last decade. It is caused by better results of this kind of treatment and still increasing population of older patients qualified to hemodialysis and peritoneal dialysis. The studies describes even 41% lower risk of death in patients after renal transplantation comparing to those on the waiting list (28). Seeking the much broader availability of this method older donors and expanded criteria donors are taken under consideration. There are several specific programs for potential older recipients, like: Eurotransplant Senior Program, Old for Old Program and Two Marginal Kidneys for One Recipient Program (29). The success of such treatment implies appropriate proceeding including careful recipient selection, reduction of cold ischemia time, adaptation of immunosuppressive drugs regiments, increase of nephron mass by dual kidney transplantation, using histological criteria in graft selection (30). The kidney transplantation from the living donor becoming also increasingly popular. The results of kidney transplantation in the elderly does not differ significantly from outcome in the younger recipients (31, 32).

The main problem in older patients is death-censored graft survival connected with cardio-vascular diseases

and infections. That gives the basis to conclude, that older really does not mean worse.

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