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Professional paper

Kidney Transplantation in Elderly Patients

Dean Markić[1], Maksim Valenčić[1], Romano Oguić[1], Sanjin Rački[2] and Željko Fučkar[1]

[1] Department of Urology, Rijeka University Hospital Center, Rijeka, Croatia
[2] Department of Nephrology, Rijeka University Hospital Center, Rijeka, Croatia

A B S T R A C T

The Eurotransplant Senior Program (ESP) allocates kidneys from elderly donors to elderly recipients (≥65 years old). During the last 39 years, 922 kidney transplantations were performed in our transplant center. We retrospectively analysed patients included in the ESP from the our center. Eleven patients ≥65 years old recieved kidney from donors [3] 65 years old. Cold ischemia time was approximately 15 hours. Dual kidney transplantation was performed in one patient. Appropriate immunosuppressive protocol was given to all patients. Surgical complications were relatively common and included dissection of renal artery (1 patient), thrombosis of renal artery (1 patient), ureterovesical obstruction (1), lymphocele (1), bleeding (1), acute abdomen (2) and wound dehiscence (1). One rejection episode was registered. Delayed graft function was observed in the two patients with full recovery of kidney function. Seven patients until now have good functioning graft. Four kidneys were lost. One patient died because of pneumonia. Kidney transplantation in elderly is feasible procedure but with greater number of complications than usually.

Key words: *renal transplantation, elderly renal transplant recipient, Eurotransplant Senior Program, surgical complications*

Introduction

Renal transplantation is now widely considered as treatment of choice for patients with end-stage renal disease (ESRD) because of improved short- and long-term survival and better quality of life over dialysis treatment[1]. The number and age of patients on waiting lists for kidney transplantation has increased almost in all European countries[1]. The average cadaveric donor is older than in the past. In Spain, the percentage of donors over the age of 60 was 27% between 1992 and 1997, and in the USA 44% of donors were over the age of 50 in 1997[2,3]. In the past, older candidates have not been considered as donors because of the increased risk of graft non-function. An increase in the number of elderly patients on waiting lists has heightened interest in the development of special allocation strategies for these patients[4].

Eurotransplant started in 1999 with Eurotransplant Senior Program (ESP) which allocated kidneys from donors ≥65 years old to recipients ≥65 years old. The aims of ESP were: to achieve a more efficient use of kidneys from donors aged over 65 years and to reduce the waiting time for older patients[5]. Kidneys were allocated locally to reduce cold ischemia time. To reduce immunological risk, included patients had to have panel reactive antibodies less than 5% and no previous transplantation. Recipients had to have compatible blood group and negative cross-match. Human leukocyte antigen (HLA) matching was not included. Croatia became member of Eurotransplant in 2007 and implemented ESP. We presented results of kidney transplantations in eldery patients (ESP) in our transplant center.

Patients and Methods

From January 30 1971 to December 31 2010, 922 kidney transplantations were performed in the Department of Urology, University Hospital Rijeka. Cadaveric transplantations were most prevalent (562 patients–60.9%). Patients ≥65 years old who received kidney from donor ≥65 years old, according to the protocol of the ESP, were included in the study. Their medical records were retrospectively reviewed.

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Patients underwent extensive pretransplant evaluation before placement on the waiting list. Those with good clinical status and without significant comorbidities were put on the list, according to the actual pre-transplant evaluation protocol. Special attention was focused on the cardiovascular status of recipient. The transplant procedure was performed with standard technique[6]. The kidney was always transplanted extraperitoneally in iliac fossa. Vascular anastomosis was performed with the iliac vessels and extravesical ureterocystoneostomy (Röhl) was carried out. An ureteral stent was inserted in the graft ureter for approximately 5–8 days and a transurethral Foley catheter placed. The latter was removed one day after the extraction of ureteral stent. Patients were treated according to our regular immunosuppressive protocol consisting of tacrolimus, mycophenolate mofetil, methylprednisolone and initial dose of daclizumab. Standard pre- and post-transplant cytomegalovirus (CMV) screening was performed and preemptive treatment was applied as needed. Patients was daily followed by staff urologist and nephrologist. Ultrasonography of transplanted kidney was performed every day during hospitalization. We recorded age, gender, primary cause of renal insufficiency, operation time, cold ischemia time, surgical complications, delayed graft function defined as need for dialysis seven days after transplantation, length of hospitalization and outcome.

Results

Among the 922 patients who were transplanted in our center eleven were included in the ESP. All of them being transplanted in 2009 and 2010. All donors were allocated locally (in Croatia). Follow-up time was between three to twenty-two months.

Recipient characteristics are listed in Table 1. Mean recipient age was 69.2 years with female predominance (54.5%). More than 80% of patients used hemodialysis before transplantation. Mean cold-ischemia time was 14.55 hours and mean duration of operation was 205 minutes. In one patient dual kidney transplantation was done.

TABLE 1
RECIPIENT CHARACTERISTICS (N=11)

Characteristic	Value
Age (years)	69.2 (65–77)
Gender (male – %)	5 (45.5%)
Renal replacement therapy (%)	9 (81.8%)
Hemodialysis	2 (18.2%)
Peritoneal dialysis	
Primary cause of renal insufficiency:	9 (81.8%)
Chronic glomerulonephritis	2 (18.2%)
Diabetic nephropathy	14.55 (9.30–27.50)
Cold-ischemia time (hours)	
Duration of operation (minutes)	205 (170–300)

Values are presented as medians (range) unless otherwise noted.

TABLE 2
RESULTS OF TRANSPLANTATION DURING FOLLOW-UP

Outcome	Value
Patient survival (%)	10 (90.9%)
Graft survival (%)	8 (66.6%)
Delayed graft function (%)	2 (16,6%)
Acute rejection (%)	1 (8.3%)
Days of hospitalization (n)	48.1 (17–120)
Major infections (%)	2 (16.6%)
Surgical complications:	1 (8.3%)
Dissection of renal artery	1 (8.3%)
Thrombosis of renal artery	1 (8.3%)
Lymphocele	1 (8.3%)
Stenosis of ureterovesical anastomosis	1 (8.3%)
Bleeding	2 (16.6%)
Acute abdomen (apendicitis,bowel perforation)	1 (8.3%)
Wound dehiscence	
Transplantectomy	3 (25%)

Results of follow-up were presented in the Table 2. One patient died one month after transplantation as consequence of bacterial pneumonia with well functioning graft. Transplantectomy was performed in the three patients. The causes for transplantectomy were: dissection of renal artery, thrombosis of renal artery and refractory acute rejection. Two major infections included CMV disease treated with ganciklovir and bacterial pneumonia (lethal outcome). Lymphocele was succesfully treated with percutaneous drainage and instillation of povidone-iodide during three weeks. In the 70 year old female two weeks after transplantation hydronephrosis become evident on ultrasonography with deterioration of renal function and oliguria. Retrograde stenting of the ureter failed because of extensive oedema of ureterovesical anastomosis. Than percutaneous nephrostomy was placed and antegrade pyeloureterography showed stenosis of anastomosis. With nephrostomy, values of urea and creatinine was normalized. Three weeks after, nephrostomy was removed and graft had good function without hydronephrosis seen on the ultrasound. Probably, obstruction was caused by transient oedema of ureterovesical anastomosis. One patient had severe bleeding immediately after transplantation and ligation of bleeding polar vessel was succesfully performed. In the two patients acute abdomen was developed because of appendicitis (appendectomy) and sigmoid colon diverticular perforation (anus praeter construction). Wound dehiscence was treated using wound vacuum device. Acute rejection (mixed humoral and cellular) was detected in one patient. Rejection was resistant to plasmapheresis and immunoglobulins so graftectomy was done.

In one patient during the first postoperative day ultrasonography showed graft without vascularization

and urgent computerized tompography (CT) angiography was performed. CT angiography showed dissection of graft renal artery but also severe arteriosclerosis (Leriche syndrome) and transplantectomy was performed. Graft was sent on the pathohystological analysis which found renal cell carcinoma (clear cell – pT1a) and carcinoma in situ pyeli. In 72 years old female, after initial diuresis, anuria was observed and CT showed thrombosis of renal artery but also ovary tumor on the right side. Transplantectomy was performed and postoperative course was complicated with prolonged febrility, formation of the lymphocele in the iliac fossa and arrest of arteriovenous fistula. Construction of new arteriovenous fistula was made. Percutaneous drainage of lymphocele with instillation of povidone-iodide during two months was sucessfully performed. Fifty eight days after transplantation patient was discharged and renal function was again replaced with haemodialysis. Gynecological procedure removed benign ovarian tumor.

Discussion and Conclusion

Elderly patients benefit from kidney transplantation. Wolfe showed that renal transplantation doubles the life expectancy of patients with ESRD compared with patients on the dialysis[7]. Among 60–74 years old patients, survival improved after the first year with projected increased life span of 5 years and 61% decrease in the long term risk of death. In the last decade kidney transplantation in elderly (≥65 years old) become more frequent. In Europe ESP is the most famous programe for this subgroup of patients. Our results, as a part of ESP, showed that kidney transplantation is effective treatment for these patients.

Cold ischemia time (CIT) in our patients is relatively short (approximately 15 hours) what is similar to the time reported by other authors[4,8]. This was possible because kidneys were allocated locally and kidney transplantations are handled as urgent operations which are performed at any time and other operations are postponed in favour of transplantation. Short cold ischemia time (in standard Eurotransplant program in our center is about 18 hours) is one factor which can contribute to better outcome because ischemic damage of renal parenchyma is lesser. For every hour of CIT, the risk of graft loss is increased by 3%[9].

Delayed graft function (DGF) in ESP was between 8.3–64%[4,9,10]. In our study two patients (16,6%) had delayed graft function. There is a strong connection between cold ischemia time and delayed graft function. Study group of Giessing had a CIT of 8.3 hours and DGF in 12% of recipients while Smits with CIT of 12 hours reported DGF in 33% of recipients[4,10]. DGF was identified as a strong independent risk factor for patient surival, graft survival and rejection[11].

There was one rejection episode among our patients. There are contrary reports about immunological response in the elderly. Some authors reported lower number of immunologic graft losses in old recipients while others, in contrast, observed an increased number of rejections (30% in standard kidney transplantation population and 42% in ESP group)[10,12]. Another group from Croatia, which implemented ESP but with HLA matching, had very low rejection rate (4.5%)[13]. In the largest study on ESP patients Frei reported acute rejection in 29% compared to 24% in standard transplant population[9]. They found that HLA mismatches, in particular clas II, is significant independent factor which increases the risk of acute rejection by >20% for mismatch[9]. To improve results Eurotransplant in 2009 was introduced »Eurotransplant Senior DR-compatible program« which is based to full HLA-DR compatibility while maintaining the ESP principle of local organ allocation and reduced CIT.

Our recipients had significant comorbidities as syndrome Leriche, ovary tumor which was not recognised before transplantation. All of them underwent extensive evaluation before they were included on the waiting list. It is obvious that preoperative evaluation of older recipients must be made more rigorously. On the other side we noticed serious problems with cadaveric kidneys: kidney cancer, carcinoma in situ pyeli, severe arteriosclerosis of renal artery, on explantation transected ureter. Clearly, the evaluation of older donors must be improved.

Surgical complications were frequent in our recipients (Table 2). Bentas reported surgical complications in 47% of ESP cases and in the 28% in control group[14]. Fascial dehiscence and vascular complications were the most frequent complications[14]. The fact that 50% of the donor vessels in ESP group showed significant arteriosclerosis (half of that severe arteriosclerosis), about 30% of recipients had significant arteriosclerosis, prolonged vessel anastomosis time and increased intraoperative complications reflect the increasing surgical difficulties in managing old donors and recipients[10]. Special attention must be focused on the iliac vessels with their annual control. Some transplant surgeons suggest a lower midline incision in case when iliac vessels had inconclusive finding on the imaging technique, leaving the possibility to performed transplantation in side with less arteriosclerosis and in that way is abandoned second incision[10].

More than 50% of graft losses in old recipients are due to death with a functioning graft, mostly from cardiovascular causes[13,15,16]. The three year patient survival for ESP group was 55% against 81% in standard transplant kidney population[10]. At five years graft survival was 47% for ESP group and 64% for standard group[9]. In our ESP group two grafts were lost because of surgical complications (dissection and thrombosis of renal artery), one because of immunological complications (refractory acute rejection) and one patient died with well functioning graft. All patients, except one, are alive.

The hospitalization time was prolonged mainly due to numerous complications. Similarly was observed in the other studies[13,14]. Surgical complications had a major impact on rehabilitation, hospitalization time, hospital readmissions and re-operation, as well as on the transplant cost[14]. That also significantly influence on patients and doctors acceptance of the procedure. Potential recipients

must be informed of possible surgical complications prior to making their decision of being transplanted[17–19].

The main limit of our study is small number of patients and short follow-up. With time the number of patients will be increase and follow-up extended which will show us a more representative results.

We have concluded that age alone should not be a barrier to kidney transplantation or donation. The preoperative assessment of recipient and donor ia crucial for successful kidney transplantation in elderly. Surgical complications are frequent in this group of patients but patient survival and quality of life remains higher than during dialysis.

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D. Markić

Department of Urology, Rijeka University Hospital Center, Tome Strižića 3, 51 000 Rijeka, Croatia
e-mail: dean.markic@ri.htnet.hr

TRANSPLANTACIJA BUBREGA U LJUDI STARIJE ŽIVOTNE DOBI

SAŽETAK

Eurotransplant Senior Program (ESP) je temeljen na korištenju bubrega darivatelja starije životne dobi za primatelje starije životne dobi (≥65 godina). Tijekom 39 godina u našem transplantacijskom centru učinili smo 922 transplantacije bubrega. Retrospektivno smo analizirali bolesnike u našem centru koji su transplantirani u sklopu ESP. U jedanaestoro pacijenata ≥65 godina presađen je kadaverični bubreg davatelja starog ≥65 godina. Vrijeme hladne ishemije je prosječno bilo 15 sati. Dvostruka transplantacija bubrega je učinjena u jednog bolesnika. Odgovarajuća imunosupresivna terapija je primijenjena kod svih bolesnika. Kirurške komplikacije su bile relativno česte i uključivale su disekciju renalne arterije (1 pacijent), trombozu renalne arterije (1 pacijent), ureterovezikalnu opstrukciju (1), limfocelu (1), krvarenje (1), akutni abdomen (2) i dehiscijenciju rane (1). Reakcija odbacivanja je zamijećena u jednog pacijenta. Odgođena funkcija presatka je zabilježena u dva bolesnika čija se bubrežna funkcija kasnije potpuno oporavila. Sedam pacijenata ima za sada dobro funkcionirajući graft. Četiri grafta su izgubljena. Jedan pacijent je umro zbog upale pluća Transplantacija bubrega u ljudi starije životne dobi je efikasna metoda, ali s većim brojem komplikacija.