

Experience of deceased donor kidney transplantation in Brest region

Doświadczenia w zakresie transplantacji nerki od zmarłego dawcy w regionie brzeskim

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Słowa kluczowe: transplantacja nerki, przeżycie pacjentów, niepowodzenie przeszczepu.

Abstract

Introduction: Renal transplantation has progressively increased, and it is the best management of end-stage renal disease.

Aim of the research: To evaluate the outcome of renal transplantation from deceased donors to adults living in a region with a population of about one and a half million.

Material and methods: A retrospective analysis of the outcomes of 126 recipients of allografts in the period 2011–2014 was performed. The mean age of the recipients was 44.5 ± 13.4 years; 71 were male and 55 were female. Kaplan-Meier survival curves were used to assess the graft and recipient survival rates.

Results: The overall mortality rate in our study was 4.7% (6 patients), and the mortality of patients with a functioning kidney graft was 3.9% (5 patients). All of them died due to multiple organ failure caused by septic complications of different aetiologies. The data of in our study show that 1-year and 3-year cumulative patient survival after transplantation was 96% and 93.5%, respectively, and the survival rate of kidney grafts was 93% and 68%, respectively. Mean time spent on the renal transplant waiting list had been 31.6 ± 7.9 years before the start of the Regional Department of Transplantation, and that was 21.4 ± 10.3 (1–141) months in 2014.

Conclusions: Three-years of transplant activity in the Brest region resulted in a significant increase in the availability of deceased donor transplantations since every third of the patients with chronic renal failure had kidney allograft transplantation. The 3-year patient survival after transplantation was over 90% owing to up-to-date immunosuppressive regimens and management of postoperative complications.

Streszczenie

Wprowadzenie: Stopniowo następuje wzrost liczby zabiegów transplantacji nerki, która jest najlepszą metodą leczenia w końcowym stadium choroby nerek.

Cel pracy: Ocena wyników transplantacji nerki od zmarłego dawcy u dorosłych w regionie obejmującym populację 1,5 mln osób.

Materiał i metody: Przeprowadzono retrospektywną analizę wyników 126 biorców i przeszczepów alogenicznych wykonanych w latach 2011–2014. Średnia wieku biorców wynosiła 44,5 ± 13,4 roku; analizie poddano 71 mężczyzn i 55 kobiet. W celu oceny wskaźników przeżycia wśród biorców i przeszczepów wykorzystano krzywe przeżycia Kaplana-Meiera.

Wyniki i wnioski: Ogólny współczynnik umieralności w badaniu wyniósł 4,7% (6 pacjentów), natomiast umieralność wśród pacjentów z funkcjonującym przeszczepem nerki wynosiła 3,9%. Przyczyną zgonu u wszystkich pacjentów była niewydolność wielonarządowa z powodu powikłań septycznych o różnej etiologii. Z danych z przeprowadzonego badania wynika, że kumulatywny wskaźnik przeżycia rocznego i trzyletniego u pacjentów po transplantacji wyniósł odpowiednio 96% i 93,5%, chociaż wskaźnik przeżycia dla przeszczepów nerki wyniósł 93% i 68%. Średni czas oczekiwania na transplantację nerki wyniósł 31,6 ± 7,9 roku przed uruchomieniem rejonowego wydziału transplantacji, a w 2014 r. 21,4 ± 10,3 (1–141) miesiąca.

Wnioski: Trzy lata działalności transplantacyjnej w regionie brzeskim spowodowały znaczny wzrost dostępności transplantacji od zmarłego dawcy, gdyż co trzeci chory na przewlekłą chorobę nerek otrzymał przeszczep alogeniczny nerki. Dzięki najnowszym terapiom immunosupresyjnym i leczeniu powikłań pooperacyjnych trzyletnie przeżycie po transplantacji wyniosło ponad 90%.

Introduction

Renal transplantation from a deceased donor has progressively increased, as well as the positive attitudes of the European population toward organ donation after death [1], and today it is the best management of end-stage renal disease [2], excluding type I diabetics patients with end-stage renal disease [3].

The persisting shortfall in the availability of organs for transplantation has prompted many countries to re-introduce donation after circulatory death schemes not only for kidney retrieval but also for other organs [4].

Aim of the research

We aim in this study to evaluate the outcome of renal transplantation from deceased donors to adults suffering from end-stage renal disease (ESRD) and living in an Eastern European region with a population of about one and a half million.

Material and methods

We transplanted kidney allografts in 126 recipients from May 2011 to September 2014, and a retrospective analysis of the recipient outcome was performed. All of the patients underwent renal replacement treatment (RRT) before transplantation with haemodialysis (107 patients) or peritoneal dialysis (19), and the mean duration of the RRT was 48.2 ± 16.7 months (range from 3 to 154 months). The rate of early (during hospital stay) and delayed (outpatient follow-up) complications after kidney transplantation, overall mortality rate, and the mortality of patients with a functioning kidney graft were calculated. Renal allograft biopsies were used for evaluation of transplant rejection with Banff classification and morphological confirmation of different tumours in renal allografts. The verification of delayed graft function (DGF) was based on the urine output, serum creatinine changes and dialysis requirements. Those patients ($n = 6$) who died or lost the graft immediately after transplantation were excluded from the statistical processing of the complication-related data.

Statistical analysis

The data analysis was performed using Statistic Version 6 and expressed as mean \pm SD for continuous variables and number (%) for categorical variables.

Kaplan-Meier curves were used to display 1-year and 3-year probability survival rates of the graft and recipient after renal transplantation.

Results

The mean age of the recipients was 44.5 ± 13.4 years (ranging from 18 to 68 years); 71 were male and 55 were female. The patients had end-stage chronic

kidney insufficiency because of glomerulonephritis in 73 (57.9%) cases, polycystic kidney disease – 15 (11.9%), chronic pyelonephritis – 14 (11.1%), hypertension – 6 (4.8%), diabetes mellitus – 8 (6.3%), various congenital kidney and urinary tract anomalies – 3 (2.4%), and other causes in 7 (5.6%) patients.

The mean time spent on the renal transplant waiting list was 21.4 ± 10.3 (1–141) months. However, before the start of the Regional Department of Transplantation, the mean age of patients who needed a kidney transplant had been 37.5 ± 10.3 years and the average time spent on the waiting list – 31.6 ± 7.9 years.

Moreover, the waiting list for cadaveric kidney transplantation has been renewed by 83% since the start of (July 2011) the transplantation department in our region.

The deceased organ-donation rate increased in our region from 11 kidneys per million inhabitants in 2011 to 35 organs per million in 2014.

There were a total of 126 organ donations after brain death (DBD), of which head injury accounted for 72 (57%), brain haemorrhage as a result of severe cerebrovascular disease – 50 (40%), and other causes – 4 cases (3%).

The mean age of DBD donors was 46.8 ± 7.4 years.

After the preservation of donor organs the mean cold ischaemia time (CIT) of the kidney transplant was 120 min when the grafts were retrieved in our transplant centre, 200 min within the intensive care units (ICU) of Brest city hospitals, and 420 min if the organ retrieval was made in other regions within the Brest zone. In the case of delivery of kidney grafts from the National Transplant Centre the CIT was 610 min (maximum 720 min).

Induction immunosuppression with a chimeric monoclonal antibody directed against the α chain of the interleukin-2 receptor (Simulect®) was performed in 116 (92%) patients. The antithymocyte immunoglobulin in combination with plasmapheresis was applied preoperatively in the remaining patients with high risk of the incidence of acute antibody-mediated rejection. The standard immunosuppressive regimens of calcineurin inhibitors (cyclosporine or tacrolimus) with mycophenolate mofetil (MMF) and steroid (methylprednisolone) were carried out in the postoperative period.

The kidney transplantation was unsuccessful in one case due to the hard calcification of iliac vessels that did not allow anastomosis between the graft and recipient arteries.

During the first seven days early renal graft function of the post-transplant was observed in 92 (73.6%) recipients. Delayed renal graft function was identified in 27 (21.6%) cases, which was confirmed by serum creatinine level $\leq 300 \mu\text{mol/l}$ within the first 7 days. Eight (6.4%) patients underwent RRT after transplantation. One recipient (0.8%) lost his graft for a few

minutes of re-transplantation as a result of hyperacute rejection that occurred despite the preoperative plasmapheresis and antithymocyte immunoglobulin therapy.

In 5 cases the grafts were lost because of intraoperative or early post-transplant complications such as graft vascular thrombosis (3 patients) and uncontrolled graft fungal infections (1 case), and 1 patient died because of sepsis caused by diffuse peritonitis from the perforated colon.

Only 34 of 125 (27%) patients had an uncomplicated early postoperative period. The rate of early and delayed complications after kidney transplantation is shown in Table 1.

Most often, side effects such as hypertension (48 patients) and diabetes mellitus (5 cases) occurred due to calcineurin inhibitors and steroid therapy.

Urinary tract infections affecting renal transplant recipients were observed in 14 (11.7%) out of 120 recipients, and 3 cases of them were complicated by urosepsis.

Type I–IIA acute renal allograft rejection (AR), according to the Banff classification, was diagnosed in 8 patients by kidney transplant biopsies within 3–7 days. A satisfactory result was achieved in all these cases of AR by conservative treatment.

Surgical complications after renal transplantation were observed in 25 (20%) patients, and 5 of them had 2 complications simultaneously.

In the post-hospital period among 120 patients with a functioning allograft, infectious complications

were reported in 13 (10.8%), and 1 of them died due to the generalisation of a fungal infection.

Acute rejection was observed in 9 recipients (7 cases graded I–IIA by Banff and 2 – IIB) due to which chronic graft dysfunction with the need for renal replacement haemodialysis occurred in 3 (2.5%) cases.

In the post-transplant long-term, malignancies such as cancer native kidney with lethal metastases and meningioma appeared in 2 patients.

The overall mortality rate in our study was 4.7% (6 patients), and the mortality of patients with a functioning kidney graft was 3.9% (5). All of them died due to multiple organ failure caused by septic complications of different aetiologies.

The data of in our study show that 1-year and 3-year cumulative patient survival after transplantation was 96% and 93.5%, respectively (Figure 1) although the survival rate of kidney grafts was 93% and 68%, respectively (Figure 2).

Discussion

The 1-year renal allograft survival rates (GSR) at our centre were almost identical (about 90%) to the data presented by Serur *et al.* [5] in recipients treated with prednisone, mycophenolate mofetil, and tacrolimus (1997–2006) or rabbit's antithymocyte globulin, tacrolimus, mycophenolate mofetil, and methyl prednisone (2001–2006).

Recent studies have shown that CIT was the most important risk factor for the occurrence of DGF [6, 7],

Table 1. The rate of early and delayed post-transplantation complications

Complications	Early n = 120	Delayed n = 120
Side effects of immunosuppression drugs	53 (44.2%)	
Urogenital infection/acute pyelonephritis	14 (11.7%)	4 (3.3%)
Sepsis	3 (2.5%)	5 (4.2)
Allograft rejection	8 (6.7%)	9 (7.5%)
Lymphocele	14 (11.7%)	
Leak/stenosis of an uretero- cystic anastomosis	6 (5 %)	
Bleeding and hematomas	4 (3.3%)	
Vascular thrombosis	3 (2.5%)	
Surgical site infections (wound infection)	2 (1.7%)	
Eventration	5 (4.2)	
Mycosis	1 (1.8%)	2 (1.7%)
Cytomegalovirus infection		7 (5.8%)
Post-transplantation malignant tumors		2 (1.7%)

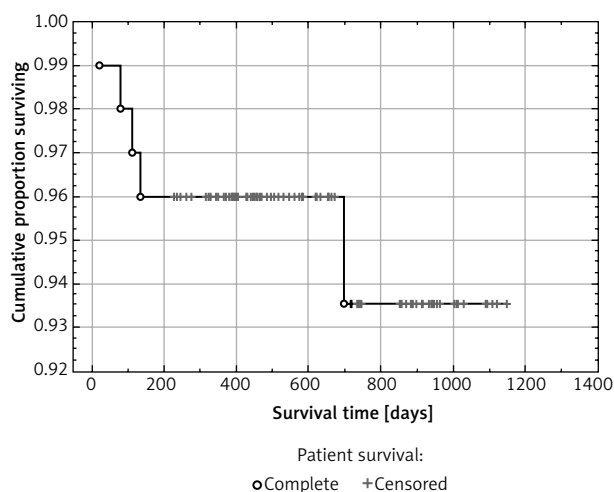


Figure 1. Cumulative proportion surviving of renal transplant recipients

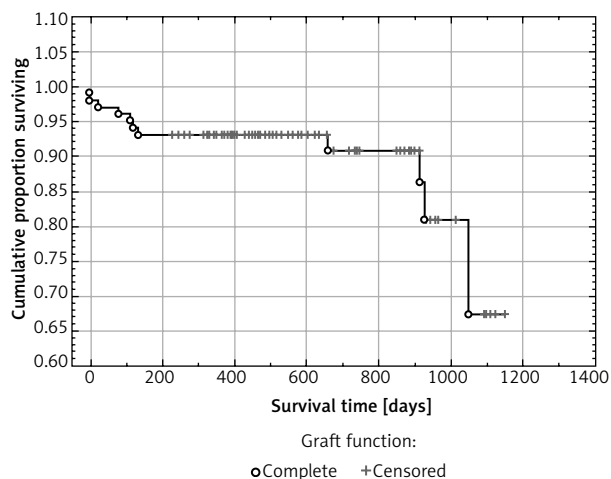


Figure 2. Kaplan-Meier curve of kidney allograft survival

and while the DGF rate has decreased it still remains high (68.7–38.5%, $p < 0.001$) [7].

Among our recipients the DGF rate was relatively low (21.6%), since only 1 out of the 12 grafts had the delayed function, which were retrieved in our centre (8.3%), 3 out of the 23 were received from other hospitals of the city of Brest (13%), and 4 out of the 27 were taken from other regions of Brest zone (14.8%). At the same time, the highest rate of DGF (19, 30%) was observed for 62 allografts received from the National Transplant Centre.

Thus, our data confirm the dramatic impact of CIT on the postoperative recovery of graft function.

The overall mortality was lower (4.7% vs. 6.9%) in our study than in those presented by Nakhjavani *et al.* [8], since only 6 recipients died and 5 of them had a functioning graft, but loss of the transplanted

kidney was observed more often in our patients (4.7% vs. 3.1%).

Despite recent advances in the management of post-operative urological infection, those complications are reported to occur between 2.5% and 30% of all recipients, and our studies have shown significant levels of these complications, but they were lower (11.2%) in comparison to the recently published data of Inez *et al.* (23%) [9] and Lee (21%) [10].

Kidney transplant recipients are at high risk for different infectious complications and for the development of severe life-threatening sepsis of long-term immunosuppressive therapy, which is the main reason for their intensive care unit (ICU) admission [11].

Unfortunately there was no possibility of avoiding development of severe complications such as sepsis, which was diagnosed in 2.4% of patients in hospital and in 4.1% for the first-year follow-up, although this rate was less than, for example, the data of the Taiwan National Health Research Institute in 1999–2007, in which the figures were 6.2% and 10%, respectively [12].

Conclusions

Three years of transplant activity in the Brest region resulted in a significant increase in the availability of deceased donor transplantation: one third of patients with chronic renal failure received kidney allograft transplantation.

Up-to-date immunosuppressive regimens have improved short-term patient survival up to over 90% (1–3 years), but further research should be done to reduce risk factors for patients' death in order to control infections, cardiovascular diseases, and malignancies after renal transplantation.

Conflict of interest

The authors declare no conflict of interest.

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