Current possibilities of improving the results of kidney transplantation in patients of the older age group, including those with an aggravated urological history

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Abstract

Introduction. *All over the world and in Russia, the number of patients requiring dialysis therapy and kidney transplantation for chronic renal failure in the end-stage of the renal disease is increasing. In many countries of the world, the number of dialysis patients over 60 years of age accounts for 30 to 45% of all patients with chronic renal failure. Meantime, taking into account the improved methods for early diagnosis of chronic renal failure and the treatment methods for chronic kidney disease, including the renal replacement therapy, we can expect an increase in the number of elderly potential kidney transplant recipients. The likelihood of receiving a renal graft in elderly patients is significantly lower than in young recipients. Elderly patients are known to have a higher risk of death while waiting for a kidney transplant due to higher morbidity and lethality on dialysis. For this reason, the urgency of increasing the availability of kidney transplantation in elderly patients is growing over time. One of the solutions can be the use*

of kidneys from suboptimal donors with a far from ideal graft quality, but which could meet the needs for transplant care of the older age group of patients. The older age of a recipient entails a certain risk of developing a graft dysfunction due to the presence of concomitant diseases, and the potential risk increases even more with kidney transplants from expanded criteria donors. If a reduced functional reserve of kidneys removed from donors with extended criteria is identified, two-kidney transplantation is possible, which provides fairly good long-term results. To reduce the risk of a kidney graft loss, a careful selection of recipients is necessary, taking into account their co-morbidities, including the presence of urological diseases that impair the function of the upper and lower urinary tract. Their timely identification and correction makes it possible to raise the availability of kidney transplantation for elderly patients and improve its results. This review presents the results of the studies conducted in various world transplant centers, covers the mortality rates, kidney graft and recipient survival rates.

The study purpose *was to summarize the actual data and the results of the study on kidney transplantation in elderly patients with urological pathology.*

Keywords: chronic renal failure, kidney transplantation, allograft, urological diseases, old age

CRF, Chronic renal failure

KT, Kidney transplantation

TBI, Traumatic brain injury

Introduction

All over the world, including in Russia, the number of patients with chronic renal failure (CRF) is increasing [1], including those with the end-stage disease requiring dialysis therapy and kidney transplantation (KT). In many countries of the world, the number of dialysis patients over 60 years of age, according to various sources, makes from 30% to 45% of all patients in need of dialysis therapy. According to our data, the proportion of patients over 60 years old on the waiting list for kidney transplantation in N.V. Sklifosovsky Research Institute for Emergency Medicine in different years ranged from 9% to 13% of the total number of potential recipients [2]. Meanwhile, taking into account the improved methods of early diagnosis of CRF and the treatment methods for chronic kidney disease, including renal replacement (dialysis) therapy, we can expect an increase in the number of elderly potential kidney transplant recipients. Over 5 years, the number of patients aged from 50 to 64 years old awaiting for kidney transplantation in the United States had increased by 41%, and the proportion of potential recipients over 65 years old was 16.7% [3].

The likelihood of receiving a renal graft in elderly patients is significantly lower than in young recipients. And, older patients have a higher risk of death while waiting for a kidney graft due to a higher morbidity and lethality on dialysis. In this regard, the relevance of increasing the availability of KT for elderly patients is growing over time [4, 5].

One of the ways to solve this problem is to use kidneys from suboptimal donors with far from perfect graft quality, which were previously considered improper for donation [6]. This category includes donors over 60 years old, as well as younger donors with hypertension, death from stroke, blood creatinine levels above 1.5 mg/dL [7, 8]. Some authors also include donors with type 2 diabetes mellitus who died from traumatic brain injury (TBI) complicated by traumatic or hemorrhagic shock, and donor therapy with high doses of cardiotropic drugs [7]. These donors have been qualified as expanded criteria donors. Donors with cardiac arrest (asystolic donors) can be referred to both an expanded criteria group and optimal donors [8].

A certain parity has been found between the number of recipients over 60 years old in need of kidney transplantation and the probable number of expanded criteria donors who could have been subjected to organ explantation (14% of patients who died from TBI) who could have met the transplant needs for the patients of the older age group [6].

The older age of a recipient entails a certain risk of developing a graft dysfunction due to the presence of concomitant diseases, which can worsen the immediate and long-term results of transplantation [9]; and the potential risk increases even more with kidney transplant from expanded criteria donors [10-14]. Nevertheless, this approach is recognized by many authors as acceptable, since it still provides a higher survival rate for patients after KT and a better quality of life compared to the elderly patients who have received hemodialysis treatment [15]. Based on the analysis of all KT cases registered in the Scandiatransplant Registry from 1995 to 2011, V.R. Sørensen et al. [16] showed that in case of kidney transplantation from a cadaveric expanded criteria donor, the risk of death in elderly recipients within 15 years of follow-up was reduced by 55% compared to continuing

the treatment of these patients with hemodialysis; and if the Charlson Comorbidity Index was 5 points or higher, the risk of death in these recipients was reduced by 72%. In general, the probability of death decreased by 62% in transplantation from a cadaveric expanded criteria donor, and by 70% in transplantation from a living donor.

Kidney transplantation according to the "old -for-old" system

Taking into account the global trend of population aging and the increasing incidence of CRF in elderly patients, in 1999 the Eurotransplant Senior Program (ESP) was developed for kidney transplantation from elderly donors (over 65 years old) to elderly recipients (over 65 years old) ("old-for-old"), in order to reduce the waiting time for the graft by elderly patients, to reduce the graft cold ischemia time, and raise the availability of transplantation [17], the use of which significantly increased the availability and reduced the waiting time for the graft in elderly patients[15, 18].

In the early years of the "old-for-old" program, the transplantation results were significantly inferior to the efficacy of kidney transplantations from optimal donors to younger recipients. According to P. Saudan et al. [19], a 10-year survival rate after a cadaveric kidney transplantation was 80% in recipients under 60 years of age, and 44% in the recipients aged over 60 years old, and the graft functioning was 59% and 32%, respectively. Similar results were reported by E. Bertoni et al. [20]. When transplanting a kidney to recipients over 55 years old from donors over 50 years old, lower numbers of a 5-year functioning graft cases were noted compared to younger recipients and donors (68.5% and 84.5%, respectively); the same trend was noted for the recipient survival rates (80.6% and 92.6% respectively). According to A. Ghafari et al. [21], the 1-, 3-, 5- and 10-year functioning

graft rates in kidney transplant recipients over 60 years old (60–72 years old) were 92.11%, 87.71%, 72.32%, and 62.12%, respectively, and the recipient survival rates were 92.25%, 87.79%, 73.56%, and 64.32%, respectively.

According to the data from I. Weiss-Salz et al. [22], in kidney transplantation to elderly donors within the framework of the "old-for-old" program, the graft loss in the first year made 46.2% that was significantly higher than 15.5% in the general recipient group, and accompanied by a higher incidence of surgical complications.) When excluding from the analysis the recipients who died with a functioning graft, a 5-year functioning graft rate did not practically differfrom the results obtained during transplantation to young recipients, reaching the values of about 80% [20, 21].

With gaining the experience in the "old-for-old" system and the development of clearer criteria for selecting recipients and assessing the graft quality, the results of such transplants significantly improved and turned out to be comparable with the statistics of kidney transplantations from standard donors [23, 24]. A summarized analysis of the results for more than 10 years showed that a 5-year survival rate of grafts was about 50% at the initiation of using the program, and then had increased to 76.2% by 2009 [25]. O. Gheith et al. [26] who summarized a 15-year experience of KT in 252 recipients over 60 years old, compared to 710 younger recipients, did not reveal significant differences in the recipient survival rates and the timing of graft functioning between these groups. M. Koukoulaki et al. [27] also found that the functioning graft rate within 1, 2, and 3 years in the group of elderly recipients with kidneys from expanded criteria donors made 92%, 82%, and 70%, respectively, and the recipient survival rates in these time frames were 95%, 87%, and 82%, which did not differ significantly from the

results of KT from standard donors; although in follow-up periods over 3 years, the results in the group with expanded criteria donors turned out to be worse.

The similar results on the comparability of the results of kidney transplantation to elderly (up to 6 to 8 years) after KT and young recipients (graft functioning for 1-3 years was 83–90% and 90–93%, respectively; and the recipient survival rates were 88–92% and 94–96%, respectively) were reported by S. Mzoughi et al. [28], M. Moghani-Lankarani et al. [29], and S. Tekin et al. [30]; however, after 5 years, the functioning graft rate in elderly recipients was lower [29].

The significance of the recipient age and of its match to the donor age

With an increased recipient age, the number of concomitant diseases increases, which can limit the possibility of transplantation, raising the question on the maximum recipient age to consider transplantation feasibility.

According to G.L. Adani et al. [31], the 1-, 3-, 5-, and 10-year overall survival rates of elderly recipients after transplantation were 89%, 84%, 72%, and 45%, respectively; however, the results of transplantation in the recipients over 70 years of age were less satisfactory than in the patients aged 65–70 years. Statistical analysis revealed the significance of such risk factors for a recipient death as a more advanced age, delayed graft function, andgraft cold ischemia time.

Meantime, many authors come to the conclusion that the recipient age per se is not a risk factor; and, with the careful selection criteria, taking into account the patient comorbidities, assessing the graft quality, and

considering the peculiarities of the post-transplant period, the results of transplantations will not worsen.

To assess the comorbidities of the potential kidney recipients on dialysis, the Charlson Comorbidity Index (CCI) has a high predictive value, in which 1 point is added to the baseline 2 points for the presence of CRF for every 10 years in the patients over 40 years old and additional points are added if they have concomitant diseases (1 point each for cardiovascular, pulmonary diseases, gastrointestinal tract diseases, systemic diseases, collagenoses, dementia; 2 points each for diabetes mellitus, neurological disorders, malignant diseases without metastases; 3 points each for malignant diseases with metastases, liver cirrhosis; and 6 points for the presence of AIDS). Thus, a potential recipient initially has 4 points by CCI at the age of 60–69, and 5 points at the age over 70 years. The presence of concomitant cardiovascular system diseases usually developing at this age adds another 1-2 points, and the presence of diabetes mellitus adds 2 more points. With the total score increasing above 5, the probability of an unfavorable outcome of transplantation progressively increases. Considering this, when assessing the KT feasibility in elderly patients, it is necessary to weigh the severity of the existing conditions in the recipient against the additional risks associated with the graft quality (including the one from a suboptimal donor) and the need for immunosuppressive therapy. With regard to a graft quality assessment, the relevant data will be provided in the next section. The risks associated with immunosuppression, according to some authors, can be reduced by reducing the aggressiveness of this therapy, given the data on the lower incidence of acute rejection crises in elderly recipients [8, 15, 21, 32].

Taking into account these principles of selecting older recipients for transplantation according to the "old-for-old" principle, in a number of centers, KT is performed for elderly and old recipients from "ultra-old" donors (75 years and older).

According to J. Cabrera et al. [33], with such transplants, the 1- and 5-year recipient survival rates were 82.1% and 60.1%, respectively, which was significantly lower than with KT in younger patients. With the exclusion of deaths cases in patients with a functioning graft, the functioning transplanted kidney rate within 1 and 5 years was 95.6% and 93.1%, respectively. This indicates that the deterioration in transplantation results is associated with a high lethality rate of old recipients, while a graft from an old donor retains functional activity for a long time.

In case of kidney transplantation from old donors to elderly recipients, the results of transplantation were the same as in transplantation from younger donors, which makes this transplantation option acceptable [34].

P. Ruggenenti et al. [35] performed 37 kidney transplantations from donors aged 80 years and older with biopsy control of organ quality before transplantation and did not reveal any significant negative effects of donor age in comparison with the use of younger donors. A. Collini et al. [36] performed 38 transplantations from donors aged 76–90 years (16 cases of a single kidney transplant and 22 cases of dual transplantation). The functioning graft rates at 1, 2 and 3 years were 73.7%, 69.8%, and 64.0%, respectively; the survival rate was 81.2% in all follow-up periods, and a delayed graft function was observed in 57.6% of cases. The authors conclude that, although the results were slightly lower than in the general population of recipients, such transplantation options were acceptable, since they increased the availability of transplantation for elderly recipients.

Recent studies have indicated that the results of KT are affected not only by the recipient age or the donor age of, but also by the combination of their age characteristics (I.A. Nesterenko, 2008). The results are worsened with kidney transplants from elderly donors to young recipients [37]. J. Waiser et al. [38] analyzed 1269 cases of KT describing the use of kidneys from young or elderly (over 55 years old) donors to young or elderly recipients. They found that long-term functioning of the graft received from either young or elderly donors, transplanted to elderly recipients, was observed in a greater percentage of cases than in kidney transplantation to younger recipients (at 8 years after transplantation, 66.1% versus 55.2 % for transplants from younger donors and 68.7% versus 22.5% for transplants from older donors). The authors suggested that KT from an elderly donor to younger recipients should be avoided, and the preference should be given to transplanting these kidneys to elderly "old-for-old" recipients.

Meanwhile, a number of authors provide data on more favorable results of kidney transplantation in elderly recipients from younger donors, compared to older donors. M. Nikodimopoulou et al. [18] reported less favorable outcomes of kidney transplantation with the "old-for-old" option (donor and recipient over 65 years old) compared to the "old-for-young" option (recipient under 65 years old): 5-year functioning graft rates were 50% and 72%, respectively, and the recipient survival rates were 58% and 80%, respectively. A.I. Sutherland et al. [38, 39] concluded that kidney transplantations from elderly cadaveric donors yielded fairly good results, although the results were generally better when using younger donors. However, these authors also consider that it is permissible to perform kidney transplants from elderly donors, while giving preference to the "old-for-old" transplant option, which will increase the number of transplantations in

elderly recipients with using elderly cadaveric donors. The same conclusion was made by C. Ponticelli et al. [40].

Criteria for assessing the quality of the graft and the possibility of transplanting kidneys with decreased functional reserves

Organs obtained from expanded criteria donors require a mandatory assessment of their functional status in order to solve the issue of the possibility and option of transplantation, since the decreased functional reserves of these organs can affect the subsequent functioning, development of complications, and mortality of recipients. The decreased functioning of such grafts has was demonstrated by L. Marconi et al. [34], who showed that in KT from donors over 70 years old, higher blood creatinine levels were noted at 1–60 months after transplantation compared to transplantation from younger donors with lower rates of preserved functioning grafts after 1, 3, and 4 years: 90%, 85% and 83% for transplantations from donors under 70 years old and 87%, 79% and 72% in the group with donors over 70 years old. Nevertheless, given the shortage of donor organs, as well as the relatively low availability of transplants for elderly recipients, the current trend is to maximize the use of donor kidneys, even with their suboptimal functional status.

A predictive index of the quality of the renal graft removed from a suboptimal donor has been developed, which includes such parameters as the donor's age, the presence of arterial hypertension, overweight, a long hospital stay until death, and the use of epinephrine in resuscitation measures [11]. According to S. Machado et al. [24], the risk of early graft loss at the donor's age over 60 years increases by 1.9 times compared to KT from younger donors, and in the presence of arterial hypertension in the

donor, it increases by 2.16 times. A similar situation occurs when the blood creatinine concentration in a donor over 60 years of age increases above 1.5 mg/ dL: the risk of early graft loss increases by 2.36 times. If the cause of death of a donor over 60 years old was TBI, then the risk of early graft loss increases by 2.47 times, and with a concomitant increase in blood creatinine concentration, the risk increases to 2.69.

The most complete assessment of the graft quality can be provided by a histological examination ("zero" biopsy) [5].

Preliminary biopsy of the kidneys removed from a suboptimal donor reveals the presence and severity of pathological abnormalities, and makes it possible to exclude severely damaged organs that are unsuitable for transplantation, or to make a conclusion about the possibility of their transplantation in the standard version (in mild disorders) or in the option of simultaneous transplantation of two kidneys (in more significant abnormalities).The percentage of discarded grafts from expanded criteria donors can reach 44% after histological control [41]. To assess the severity of damage in donor kidneys with a "zero" biopsy, a semi-quantitative scoring system has usually been used to identify the proportion of sclerosed glomeruli, the presence of hyalinosis of the intrarenal arteries and their chronic diseases, tubular atrophy, and interstitial fibrosis (from 0 in the absence of a symptom to 3 at maximum severity). With significant, but non-critical pathomorphological alterations (from 5 to 8 points), the feasibility of transplanting a single organ is rejected, as a rule; but it is possible to perform paired transplantation of two kidneys to the recipient to increase the mass of functioning nephrons to a level sufficient to maintain homeostasis of the body, if the recipient's condition allows this [6].

According to a number of authors, satisfactory results can be achieved with biopsy quality control of grafts from non-optimal donors to elderly recipients. Although in the group of kidney recipients from a non-optimal donor, the blood creatinine level at 1-7 years after transplantation was slightly higher than in kidney transplantations from optimal donors; the graft functioning after 7 years did not differ significantly from that after transplantation of kidney (kidneys) from optimal donors (73% versus 83%), the same trend was seen in the recipient survival rate (90.5% versus 95%) [42]. In KT from cadaveric donors over 70 years old with the preliminary biopsy of removed kidneys (both single and dual kidney transplantation) with a mean follow-up of 2.8 ± 1.7 years, the recipient survival and retained graft function were achieved in 80 % and 75 %, respectively [43]. With KT from donors over 65 years old with the pre-transplant biopsy of removed kidneys, the 3-year graft and recipient survival rates were 78.8% and 84.8%, respectively, while with transplantation from younger donors they were 86.9% and 97,5% respectively. When excluding the deaths of the recipients with a functioning graft, the differences disappeared (graft functioning was 89.1% and 88.6%, respectively), which indicated a complete functionality of the transplanted kidneys [44].

It is possible to assess the quality of a donor kidney in the process of its machine perfusion preservation. According to S.F. Bagnenko et al. [6], a 50% or more decrease in the renal vascular resistance index within 4–6 h of hypothermic perfusion indicates a good preservation of the organ and the possibility of its transplantation; whereas with a decrease in resistance by 25–35%, it is advisable to perform dual transplantation; and the persisting high vascular resistance in the kidney is an indication of its marked ischemic damage and casts doubt on the possibility of its transplantation. Using this

algorithm, the authors performed 27 single kidney transplantations and 7 dual transplantations from expanded criteria donors, and compared to the results of 31 KTs from standard criteria donors. Although 21 days after transplantation, the level of blood creatinine in kidney recipients from suboptimal donors was significantly higher than in the group with standard transplantation (158.5 ± 15.6 µmol/L in standard transplantation compared to 340.9 ± 49.3 µmol/L in single and 517.9 ± 0.2 µmol/L in paired transplantation from suboptimal donors); but after 90 days, the differences in this parameter disappeared (blood creatinine 127.2 ± 6.14 µmol/L, 124.6 ± 6.9 µmol/L, and 135.1 ± 0.05 µmol/L, respectively).

The dual kidney transplantation technique is a good alternative for older recipients compared to hemodialysis treatment. The dual kidney transplantation allows providing the recipient with the necessary mass of active nephrons sufficient for nitrogen and water excretory functions. Although with dual transplantation, there is a higher incidence of delayed graft function (59.3% compared to 29% in the group with standard surgery option) and, due to this, a higher blood creatinine level in the first month after transplantation; in a more long-term period (starting from 3 months), the difference in creatinine levels between the compared groups disappeared [45].

According to P. Cravedi et al. [46], despite the fact that the results of such transplantations still do not reach the level obtained with transplantations from younger donors; when performing a biopsy of donor kidneys, it is possible to make a choice between transplanting one or two kidneys and approximate the results of such transplants (even from donors over 70 years old) to the results of standard transplants from younger donors.

A literature review describing the results of dual kidney transplantation by A. Cocco et al. [45] (434 cases), showed that a one-year recipient survival rate was 95% with more than 90% of the functioning grafts. The incidence of delayed graft function ranged from 20% to 30%. R. Snanoudj et al. [47] also showed that dual kidney transplantation from suboptimal donors using adequate methods of clinical and histological assessment of the graft quality provides the same results as single kidney transplantation, despite lower graft quality in the former transplantation option. With double transplantation, the incidence of complications does not increase, with the exception of information from individual authors about a higher incidence of thrombosis.

The impact of aggravated urological history

Today, despite many years of experience with KT, the prognosis of KT long-term results in elderly patients is significantly impacted by the aggravated urological history, the condition of the upper and lower urinary tract, as well as previously performed operations on the urinary system organs (B.R. Cabello, 2011) [42].

According to P. Jaeger et al. [48], pathological abnormalities are detected in the urinary tract in 25% of patients with end-stage chronic renal disease. These patients may need to have been operated on to correct urological pathology both before and after KT [49]. According to M. Giessing et al. [50], knowledge about the urological state of both the donor and the recipient is the key in assessing the risk of developing urological complications after KT, which is especially important in elderly recipients.

Earlier, patients with the dysfunction of the lower urinary tract were considered ineligible candidates for KT, however, due to the improved

methods of diagnosis and treatment of these diseases, such patients began to be included in candidates for transplantation [51–53]. The task of urologists before KT is to optimize the condition of the urinary tract that should be sterile, continent and functionally adequate [54]. Meanwhile, potential recipients may have some unrecognized urological diseases with minimal symptoms, which can have activated after KT and should be particularly considered that in patients with anuria, in whom it is especially difficult to assess the functional state of the upper and lower urinary tract [55]. The incidence of urological complications in patients with aggravated urological history has increased from 2.5% to 14% and, according to a number of authors, this increase is accompanied by a higher incidence of graft loss, and recipient mortality rates [56].

According to K.S. Bae et al. [57], 21 of 281 kidney transplant recipients underwent surgery on the urinary system organs either before or after transplantation. In 17 patients, 19 surgical operations were performed at 2–8 months before KT, in most cases being bilateral nephrectomy for polycystic kidney disease or for severe vesicoureteral reflux with persisting urinary infection, and less often being dilating enterocystoplasty for neurogenic or wrinkled bladder. In 3 cases, bladder reconstruction was performed during KT. In one case, an internal urethrotomy was performed for urethral stricture at one month before transplantation. Four patients underwent urological surgery (nephroureterectomy, nephrectomy, orchiopexy, and transurethral resection of the prostate) at 2–122 months after kidney transplantation. Good results of transplantation were obtained in 21 patients. Two patients died from rejection, constrictive pericarditis, and sepsis.

Nephrectomy is the most frequently performed operation in patients before KT. Indications for bilateral nephrectomy in potential KT candidates with polycystic kidney disease include recurrent infection, cyst hemorrhage, and significant enlargement of the kidney, impairing the lung function [58]. However, B. Stiasny et al. [59] showed that the recipient survival rate and the graft functioning duration did not differ in the groups of patients with removed and preserved polycystic kidneys. The main cause of death in these patients was infectious complications resulting in sepsis.

According to M.D. Tyson et al. [60], who compared the results of bilateral nephrectomy in patients with polycystic kidney disease as a preliminary stage (2297 patients) or simultaneously with KT (271 patients), and revealed a more frequent development of hemorrhagic complications, the need for blood transfusion and urological complications with simultaneous nephrectomy and transplantation, however, hospital mortality in these patients was even lower.

An important point is the timing of nephrectomy before transplantation, which should be minimal, so as not to delay the transplantation, and sufficient for complete wound healing and completely coping with urinary infection, if any. Y. Reinberg et al. [61] recommended performing nephrectomy of the native kidneys at 6 weeks to 3 months before transplantation, except for the cases of the need for urethral surgery to prevent the development of dry urethral syndrome. K.S. Bae [57] performed nephrectomy 2–8 months (mean, 2.9 months) before kidney transplantation with no complications developed.

Malformations of the urinary system often lead to the development of the end-stage chronic renal disease requiring KT. The preliminary correction of the defect and the control of the chronic urinary infection accompanying

this abnormality may improve the results of KT in these patients [62]. The authors compared the results of transplantation in 47 patients mainly from a living related donor with developmental anomalies of the urinary system (Group 1) with 446 patients without this pathology (Group 2). Vesicoureteral reflux was the most common developmental abnormality (78.7%). The development of acute tubular necrosis of the graft in the postoperative period was revealed, being less frequent in patients of Group 1 (8.5% versus 22.1% in Group 2), while the incidence of rejection crises in both groups was nearly similar (27.6 % and 23.1%, respectively). The graft function rates for 1, 5, and 10 years in patients of Group 1 made 97.8%, 93.2%, and 79.9%, respectively, which did not differ significantly from these results in Group 2 (95.9%, 87.6%, and 78.9%, respectively). The recipient survival rates during these periods were also nearly similar in the groups (100%, 88.5% and 82.6% in Group 1, and 96%, 87.6% and 79.6%, in Group 2, respectively). These results allowed the authors to conclude that the presence of urinary tract malformations with their timely correction does not worsen KT results in these patients.

To obtain good long-term results of transplantation, it is important that adequate evacuation of urine from the bladder is ensured. Patients with long-existing CRF and anuria, as well as the central nervous system involvement, may develop detrusor hypofunction or bladder puckering (shrunken or neurogenic bladder). In the period up to 2000, according to A. Crowe et al. [63], the presence of an abnormally functioning bladder was the factor that negatively influenced the results of KT, even if the preliminary urinary diversion operations had been performed, using an intestinal conduit. These patients had a higher incidence of graft loss within 5 years after

transplantation (43% versus 14% in the total group of KT recipients), with chronic urinary infection being its main cause.

Impaired evacuation functions of the bladder and its wall reduced elasticity have quite often been revealed in candidates for KT during urodynamic investigation. Although this investigation is not necessary for all recipients, but in patients with anuria or with the symptoms of impaired urination, it will allow a timely identification of existing disorders and their timely treatment, and can also influence the decision on the appropriateness of transplantation [64]. When performing cystography, it is possible to reveal a decreased bladder capacity and the presence of abnormalities in this organ development that may increase the risk of urological complications after KT [65]. Moreover, their preoperative correction improves the surgery prognosis [49, 56].

In patients with a shrunken or neurogenic bladder, extravesical urine diversion or dilated enterocystoplasty can be performed before transplantation [66, 67]. According to L. Teng et al. [68], in patients with a shrunken or neurogenic bladder, it is possible to perform surgical dilatation of the bladder, using a small intestine segment, simultaneously with a kidney transplantation, since this does not lead to an increased complication rate and provides good long-term results of transplantation (with a follow-up period of 50–120 months, the level of blood creatinine was 1.1–1.8 mg/dL).

At the same time, in some authors' opinion, an impaired bladder function accompanied by a decrease in its capacity, an increased intravesical pressure and decreased compliance, do not significantly negatively affect the results of KT for the follow-up period of up to 10 years [69]. Graft functioning in the groups of kidney recipients with bladder dysfunction and a normally functioning organ for 1, 3 and 5 years was 90%, 88%, and 82%

in the group with bladder dysfunction, and 97%, 91%, and 87% in the group without organ dysfunction, respectively. Meanwhile, in a more long-term period (10–20 years), in the group of patients with bladder dysfunction, the results were significantly worse: 63% of functioning renal grafts versus 83% in the group with a normally functioning bladder.

Sometimes urological operations have to be performed after KT due to the development of late complications or new diseases. According to M.F. Trapeznikova et al. [70], such diseases as chronic pyelonephritis, vesicoureteral reflux, chronic prostatitis, chronic cystitis can be treated conservatively on an outpatient basis, while the detection of kidney stones, benign prostatic hyperplasia with severe obstructive symptoms requires a surgical treatment in a hospital setting. In this case, it is preferable to use minimally invasive methods of surgical interventions.

Elderly patients often have problems with urination due to the progression of benign prostatic hyperplasia, which requires a surgical treatment. If necessary, transurethral resection of the prostate can be performed either before or after KT. Moreover, Y. Reinbergetal. [71] note that performing transurethral resection of the prostate immediately after transplantation is possible only with sterile urine, adequate antibacterial and steroid therapy, with flushing of the urethra at low pressure, and with careful hemostasis.

A timely identification of urological problems in potential donors is equally important. The improvement of diagnostic methods has led to an increased rates of detecting urological diseases (stones, cysts or tumors of the kidneys, microhematuria) in potential donors in recent years, which even more urgently raises the question of the possibility of using these patients as donors. According to S. Tonyali et al. [72], kidney diseases were identified

in 51 of 251 (20.3%) potential living related donors. After removal of these kidneys, if cysts were detected (32 cases), all cortical cysts were decorticated; in 3 kidneys, where a tumor was detected, its resection was performed, followed by an urgent histological examination and a decision on the possibility of transplantation after establishing a low grade of malignancy and a negative surgical margin. Kidney stones in donors (8 cases) were removed by ex vivo urethroscopy (2 cases) or pyelotomy (1 case). In other donors, microliths were found to be asymptomatic and potentially harmless. In the future, their negative effect was not noted within the follow-up periods of up to 28 months after transplantation of such kidneys. There were no negative consequences after kidney transplantation from donors with microhematuria (2 cases). These data confirm the high incidence of previously unrecognized urological diseases in potential kidney donors and the need for their thorough urological examination.

To solve the issue of possible KT from donors with microhematuria, it is recommended to perform a graft biopsy [73]. Of 14 transplants from donors with microhematuria, membranous nephropathy was detected in 7 cases, IgA nephropathy in 2 cases, focal glomerulosclerosis in one case, and nonspecific changes in 4 cases. Nine grafts were found to be suitable for transplantation. Their function remained relatively stable for a mean follow-up of 57 months. Two cases of graft loss were not related to the identified pathology: acute irreversible rejection in one, and the death of a recipient with a functioning graft in the other.

Discussion and conclusion

The analysis of the literature has shown that the problem of increasing the availability of renal grafts for elderly and senile patients with chronic

renal failure is still relevant. The use of sub-optimal expanded criteria donors for donation opportunities helps to solve this problem. While the number of foreign publications on this issue has been progressively increasing in recent years, there are significantly fewer such published reports in homeland literature. The results of such transplantations analyzed both in foreign and homeland transplant centers over the recent 10–15 years have shown that the introduction of special programs to increase the availability of kidney transplantation for elderly patients has led to a significant improvement in the results of such transplants. This is largely due to the careful selection of recipients with an assessment of their comorbidity grade using a special scale, as well as the control of graft quality based on the analysis of the present risk factors for kidney dysfunction associated with the donor's condition, and, if necessary, to perform a histological examination of a removed kidney biopsy sample ("zero" biopsy). If a reduced functional reserve of the kidneys removed from expanded criteria donors has been revealed, two-kidney transplantation is possible in order to increase the mass of functionally active nephrons, which provides fairly good long-term results. Although the results of kidney transplantation in elderly patients from a non-optimal donor are inferior to the efficacy of transplantation from standard donors, they provide a higher survival rate and quality of life for recipients as compared to continuing the dialysis treatment.

The issues of the urological diseases leading to the development of chronic renal failure or being concomitant to the underlying disease in relation to the kidney transplantation risk in elderly recipients have been much less published, and such publications are practically absent in the homeland press. Moreover, such diseases are detected in approximately ¼ of patients with chronic renal failure. Published studies mainly discuss the

situations associated with the need to perform nephrectomy, which most authors recommend performing in the pre-transplant period. Significantly fewer publications have been devoted to assessing the impact of dysfunction of the upper and lower urinary tract, which diagnosis presents significant difficulties in patients with end-stage chronic renal disease. The presence of the bladder dysfunction caused by neurogenic disorders, prolonged non-functioning in anuric patients, infravesical obstruction in benign prostatic hyperplasia or urethral strictures, as well as in the presence of vesicoureteral reflux, worsen the long-term results of transplantation in such patients. With a timely correction of these conditions in the pre-transplant period, although the incidence of complications after transplantation in these patients is higher than in groups of elderly recipients without an aggravated urological history, the long-term results of transplantation practically do not differ.

Thus, the presence of an aggravated urological history in elderly patients can be considered an additional risk factor, but taking this factor into account, and a timely diagnosis and correction of disorders can reduce this risk to a minimum.

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