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ORIGINAL ARTICLE

Physical activity in elderly kidney transplant patients with multiple renal arteries

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ABSTRACT

BACKGROUND: Kidney transplantation (KT) is the gold standard for treatment of patients with end-stage-renal disease. To expand the donor reserve, it is necessary to use marginal/suboptimal kidneys.

METHODS: We retrospectively evaluated the short/long-term outcome of 34 KT elderly patients who received allografts with vascular abnormalities (MRA group), in comparison with 34 KT patients who received a kidney with a single renal artery (SRA group) pair-matched by age, length of time on dialysis, comorbidity and donor age.

RESULTS: All participants completed the International Physical Activity Questionnaire at KT, and then 4, 8, and 12 weeks after transplantation. Our data indicate that kidney with vascular anatomical variants may be successfully transplanted, since the overall rate of surgical complications was 20.6% in the SRA group and 17.6% in the MRA group and that the 5-year survival rate after KT was 100% in both groups.

CONCLUSIONS: The data also underlined that individualized physical activity programs induced similar excellent results in both groups, improving physical capacities, arterial pressure, lipid metabolism, insulin sensitivity, quality of life and physical and mental status.

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KEY WORDS: Kidney transplantation; Elder nutritional physiological phenomena; Vascular malformations; Kidney; Exercise.

Kidney transplantation (KT) is the gold standard for treatment in end-stage-renal-disease patients.[1-11] To increase the number of donors, marginal/suboptimal kidney are used for transplantation ever more frequently and given the donor scarceness the possibility to transplant a kidney with vascular anomalies, *i.e.* sub-optimal kidneys, should always be considered.[12-17]

A kidney is defined suboptimal when it presents arterial anomalies (>2 arteries, with one or more aortic patches, requiring bench reconstruction or double anastomosis), lesion of the parenchyma (focal sclerosis), sutured polar branches

damaged in organ harvesting or excretory tract anomalies. These conditions may determine a reduced nephron mass but not influence on its quality.[18-21]

Today, due to the increasing demand for transplantable kidneys, the criteria for renal transplantation[22-24] was expanded so to include also sub-optimal kidneys.[25-30] During the transplantation, anatomic anomalies are frequently observed, the most common being multiple renal arteries (18-43% of cases)[31, 32] which does not exclude the possibility of using such kidneys for transplantation.

The physical activity is highly recommended for patients who undergo KT by either physician, surgeons in care,[33-36] international guidelines[37] or real-life studies.[38] Due to their sedentary lifestyle,[38-46] KT patients have a higher risk to develop serious cardiovascular events, weight gain and type 2 diabetes than individuals of the general population.[47-54] In addition, post-transplant therapeutic immunosuppression may lead to a severe sarcopenia, which has been found associated with a reduced survival.[43, 45, 51] A physical activity program is highly recommended for these patients since it may improve physical capacities, arterial pressure, lipid metabolism, insulin sensitivity and BMI. Most importantly, it may improve overall morbidity and cardiovascular outcomes.[34, 39, 43, 45, 52-58]

Although the favorable effect of physical activity on quality of life and in prevention of serious side effects in KT patients is widely accepted, the optimal quality, intensity, duration and frequency of physical exercises needs further investigation.[59] Moreover, scanty information is currently available on the effectiveness of physical activity programs in KT patients who had received a kidney with vascular anatomical variants, sub-optimal kidneys used given the donor scarceness.

In this observational study, we analyze the KT short/long-term outcome and the effect of physical activity programs in 34 patients transplanted with a kidney allograft with vascular anomalies in comparison with 34 control KT patients who received a kidney with a single renal artery, paired-matched by age, length of time on dialysis, comorbidity and donor age.

Materials and methods

The 740 KT from cadaveric donors were performed from January 1999 to December 2018, at the Unit of Kidney Transplants, University Federico II, Naples, Italy. Thirty-four consecutive patients aged >55 years old, that received kidneys with vascular anatomical variants (MRA group) were compared with 34 patients selected from 229 KT patients transplanted in the same period with a kidney with a single renal artery on the basis of a pair-matching by age, period on dialysis, comorbidity and donor age (SRA control group). In this observational retrospective study, we evaluated the incidence of surgical complications, the hypertension, the creatinine clearances, the graft survivals and the impact of physical activity between patients in these two groups. The delayed graft function (DGF) was defined as the need for dialysis in the early days after KT.[60]

Before KT, patients were tested for Cytomegalovirus (CMV) and Epstein-Barr virus (EBV), HBsAg, anti-HCV, total anti-HBc, and anti-hepatitis B surface antibody (HBs) using specific commercial immunoenzymatically assays, as described in previous studies.[61-70]

Physical activity

All patients completed the International Physical Activity Questionnaire (IPAQ) at the time of KT and at 4, 8, and 12 weeks after transplantation.[71] The IPAQ used contained questions on physical activity and demographic parameters (sex, age, educational level, job, etc.). Questions on physical activity related to job, transport and housework were also asked. The IPAQ assessed the daily frequency, duration and intensity of physical activity.[72]

The physical activity program started during the 2nd month after kidney transplantation with 20-minute activity a week, gradually increased up to 2-3 hours during the follow-up. This program consisted of cycling and/or walking activity, vertical row, chest pressure, triceps extension, chest and shoulder extension, biceps curvature, etc. to be performed 3-5 days a week and including 3 series of 3-5 executions for each exercise. This program was adapted to clinical condition, lifestyle and hobbies of each single patient in order to opti-

mize his/her adherence. Before starting the physical activity program, each patient underwent to a clinical checkup, which included the evaluation of clinical conditions, biochemical tests, calculation of body mass index (BMI), electrocardiogram and an evaluation of the nutritional status.

The management of our patients after kidney transplantation lasted 12 months and required a monthly evaluation. Three-check point were established at 1-, 3- and 5-years after KT. During the 1st year follow up and at the 3- and 5-year check points patients declared the type and the level of physical activity they had performed.

Results

Due to the shortage of donors, suboptimal kidneys are also transplanted at our transplant unit. This paper reports the results of a study conducted to compare the clinical aspects and the usefulness of physical activity in a group of 34 patients transplanted with a kidney with multiple renal arteries (MRA group) (Figure 1) with a group of control of 34 patients who received a kidney with a single renal artery (SRA group). All patients in both groups were Caucasian and at their first KT. In the MRA group, the recipients' mean age was 55.8 years old±1.6 (standard deviation ±S D) and the donors' mean age 41±14 (SD); in the SRA group, the recipients' mean age was 55.5±0.9 and the donors' mean age 43±13, a small difference not significant to statistical analysis (Table I). All patients in both groups were re-examined one year after KT, whereas of the 34 patients in the MRA group, 29 were subsequently re-evaluated at the 3-year checking point and 24 at the 5-year checkpoint. Of the 34 patients in the SRA group, 28 were re-examined at the 3-years checkpoint and 23 of these 28 also at the 5-year check point (after 5 years). It should be pointed out that patients absent at the 3-year and 5-year check points did not reach these time-points, but they were still alive, in good clinical condition and with an excellent quality of life.

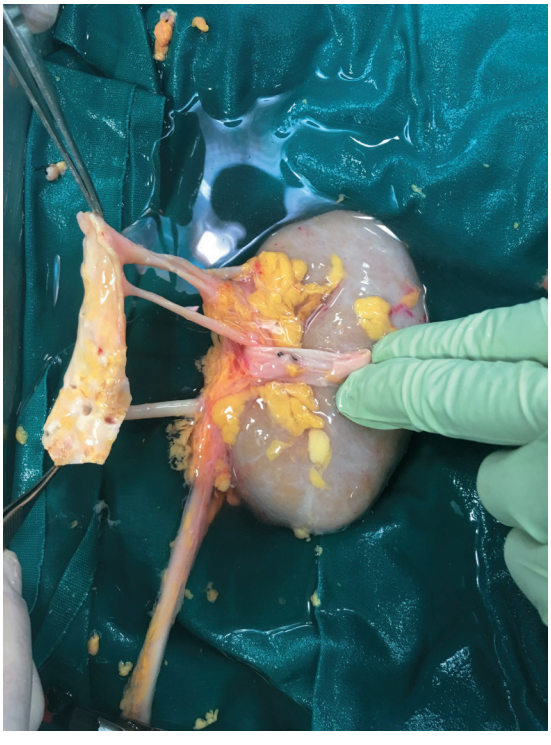

Figure 1.—Multiple renal transplant arteries: renal transplant offering three arteries on one patch.

At the time of KT, the mean BMI was 23.5±3.1 kg/m^2 in the MRA group and 23.7±3.4 in the SRA group. In both groups, there were small not statistically significant variations in BMI values from the initial values those detected at the 3- and 5-year checkpoints (Table I).

Among the deceased donors in the MRA group, 28 died of cerebrovascular accidents and six because of traumatic injuries, whereas in the SRA group the causes of death were cerebrovascular accidents in 30 and traumatic injuries in the remaining four.

At the 1-year checkpoint, the systolic blood pressure was higher in patients in the MRA group, but over time (1 year *versus* 5 years), the arterial hypertension decreased slightly in both groups (Table I). At the 1-year, check point creatinine clearance ranged from 0.6 mg/dL to 2.2 mg/dL in patients in the MRA group and from 0.9 mg/dl to 2.4 mg/dl in the SRA group; these values decreased slightly over time in both groups (Table I).[73-77]

All patients in both groups were alive at the 1-, 3- and 5-year check points with a 100% organ survival rate. The delayed graft function (DGF) occurred in 29.4% of cases in the MRA group and in 20.5% in the SRA group; these KT patients underwent to at least 4 dialytic sessions. The kidney function recovery post-transplanta-

TABLE I.—*Clinical characteristics of patients who underwent kidney transplantation: MRA* versus *SRA groups.*

Characteristic	Group MRA	Group SRA	P value
Number of recipients	34	34	
Recipients' age, years (M±SD)	55.8±1.6	55.5±0.9	0.3
Donors' age, years (M±SD)	41 ±14	43± 13	0.5
BMI (kg/m2), (M±SD)			
At the time of the KT	23.5±3.1	23.7±3.4	0.8
1 years (34 pts MRA group, 34 pts SRA group)	26.5±3.2	26.3±2.0	0.7
3 years (29 pts MRA group, 28 pts SRA group)	24.2±3.8	24.7±3.0	0.5
5 years (24 pts MRA group, 23 pts SRA group)	24.8±0.3	24.9±3.3	0.7
Postoperative Creatinine clearance, mL/min (M± SD)			
1 years (34 pts MRA group, 34 pts SRA group)	2.2±0.6	2.4±0.8	0.2
3 years (29 pts MRA group, 28 pts SRA group)	2.1±0.3	2.2±0.7	0.4
5 years (24 pts MRA group, 23 pts SRA group)	2.0±0.2	1.9±0.4	0.2
Mean Systolic blood Pressure, MmHg (M± SD)			
1 years (34 pts MRA group, 34 pts SRA group)	130±10	125±9	0.03
3 years (29 pts MRA group, 28 pts SRA group)	120±7	120±8	0.3
5 years (24 pts MRA group, 23 pts SRA group)	110±6	110±9	0.3
Delayed graft function, N. (%)	10 (29.4)	7 (20.6)	
Kidney function recovery, days	33	25	
Ischemia time			
1) cold ischemia, hours (range)	7-10	7-10	---
2) banch cold ischemia, minutes (range)	90-120	60	---
3) warm ischemia, minutes (range)	60-75	45-60	---

MRA: multiple renal artery group; SRA: standard renal artery group; pts: patients; BMI: Body Mass Index; M±SD: Mean±Standard Deviation

tion lasted 25 days in the SRA group *versus* 33 in the MRA group. The cold ischemia time lasted 7-10 hours in both groups, all organs being harvested from the South of Italy. The bench cold ischemia time lasted 55-65 minutes for kidneys in the SRA group and 90-120 minutes for those in the MRA group and the warm ischemia time 45-60 minutes in the SRA group and 60-75 minutes in the MRA group, depending on the surgical preparation of patches and on the need to perform multiple vessel anastomoses.

The surgical complications rate was 20.6% in the SRA group and 17.6% in the MRA group, a difference not statistically significant (Table II). There was no case of vascular complication in the SRA group, while in in the MRA group one patient developed thrombosis of a renal artery, with a partial loss of healthy parenchyma but without graft loss. Urologic complications occurred in 2.9% of cases in the MRA group and in 8.9% in the SRA group (Table II). There were four patients with symptomatic lymphoceles in both groups. (Table II) Patients with complication after surgery were not evaluated for physical activity (7 in the MRA group, and 8 in the SRA group). Once at home, the exercises program

TABLE II.—*Postoperative Complications after Transplantation in the group MRA and in the group SRA*

Complication	Group MRA	Group SRA	P value
Number of recipients	34	34	
Vascular, N. (%)			
Renal Artery thrombosis	1 (2.9%)	0	0.3
Urologic, N. (%)			
Leakage	1 (2.9%)	1 (2.9%)	
Stricture	0	2 (5.9%)	0.3
Lymphocele	4 (11.8%)	4 (11.8%)	1
Total	17.6%	20.6%	0.8

MRA: multiple renal artery group; SRA: standard renal artery group.

favored the hobbies of the patients, including gardening activity for about 10-20 minutes and walking in a row for at least 20 minutes daily and a physical activity of at least 20 minutes, consisting in a fast ride in the open air three times a week and in a moderate physical activity in the remaining two days (30-35 consecutive minutes of cycling at a regular pace).

As compared with the pretransplant period, most patients declared an increase in physical activity after KT, while less activity was reported by 5% of patients in the MRA group and 7% in the SRA group; no change was reported by

5% of patients in the MRA group and 6% in the SRA group.

During the follow-up period, patients in both groups performed a moderate sport activity.

The physical activity program induced similar excellent results in both groups. In fact, there was a clear improvement of quality of life and in physical and mental status in most patients. Most importantly, there were an easier management of comorbidities and a 100% survival rate 5-year after KT.

Discussion

Kidney transplantation is the gold standard in the therapy for the end-stage-renal-disease patients. The transplant of an MRA-kidney has been contraindicated in last decades, due to the increase in urological and vascular complications, sometimes inducing the allograft loss.[77-83] More recently, however, considering the increasing demand for transplantable kidneys and the incidence of multiple renal arteries ranging from 18% to 30% as reported in several large autopsy series,[80, 83-86] the criteria for renal transplantation[22-24] were expanded to MRA-kidneys. These suboptimal kidneys transplanted in 34 patients with an end-stage-renal-disease, provided excellent results and no difference in short/long term renal graft outcomes was observed in comparison with 34 control patients transplanted with an SRA kidney;[80, 84-86] in addition, the presence of an aortic patch did not influence the result of the graft nor the rate of complications.

It is commonly accepted that the lack of physical activity is a major risk factor for mortality in general population and that a weekly exercise program of 3-5 hours increases cardiorespiratory performance, reduces the risk of cardiovascular disease and determines better quality of life in KT setting.[87-91] The beneficial action of physical activity induces changes in the lifestyle directed toward regular physical activity both in hemodialysis and in KT patients.[92-96] A physical activity program based on aerobic exercises including muscle strength with resistance exercises after KT[38] usually induces a cardio-respiratory and muscle strength improvement.[38] In KT patients, muscle function depends on factors such as structure, mass and muscle metabolism, whose dysfunction, typical in post-transplant subjects, is the most important cause of intolerance to exercise.[49, 91] This structural and metabolic hypofunctionality is mostly due to either the use of corticosteroids for immune suppression, or to the reduction of renal function, or to hypomobility.[49, 91] Instead, programmed physical exercise can counteract the muscular depletion induced by these factors.

In addition, these findings suggest that proinflammatory factors may be reduced and the immune response increased in KT patients after a physical training program, which also provides a better vitality of the graft.[8-10, 19, 31]

The outcome of KT is also influenced by the patient's nutritional status and malnutrition, obesity and other metabolic syndromes must be absolutely avoided because dangerous for the safety of the transplanted organ. Thus, weight control plays a fundamental role. Patients with chronic kidney disease often gain weight after KT because, free from the rigid diet previously practiced, and they can choose an incorrect diet. In addition, the administration of steroids and other immunosuppressants may result in an increase in appetite and retention of sodium and water. It is, therefore, necessary to introduce an adequate diet, supervised by a nutritionist, which can also reduce the symptoms of gastroesophageal pathologies that frequently occur in patients with KT.[97, 98]

Finally, it is of great relevance the favorable effect exerted by physical activity on quality of the life, on mental status (reduction of anxiety and depression) and on working capacity of the KT patients.[51, 97]

Conclusions

Our data, and those found in the literature[1-10, 19] support the more recent opinion that the presence of kidney vascular anomalies is not an absolute limit for KT and that kidneys with multiple renal arteries could be transplanted using the technique that best fits in each surgical situation.[97] Like observed in other studies, 34 of our patients with chronic kidney disease who had received a kidney with multiple renal arteries have shown

a similar graft outcome than the 34 patients in the control group. In fact, in both groups 100% of patients evaluated at the check points of 1-, 3- and 5-years after transplantation were alive with a 100% organ survival rate and DGF occurred only in a quarter of patients; also similar was the length needed to achieve the kidney function recovery post-transplantation.

The success obtained transplanting kidneys with multiple arteries has contributed to the usage of marginal/suboptimal kidneys, good news considering that nearly a quarter of kidneys have multiple renal arteries[1-10, 19] and that the demand for kidney transplantation from nephrologists is increasingly pressing. Another good news is that the incidence of graft-vascular thrombosis and other complications is infrequent (0.3% to 6.1%).[99]

It is a general opinion that education in physical activity improves the quality of life in general population. Therefore, great importance is given to physical activity and sport worldwide and physical education is an official discipline in all schools in most countries. Physical activity plays an important role even in the management of KT patients since it improves the quality of life,[87-90] reduces the risk of cardiovascular unfavorable events and the risk of developing cachexia and sarcopenia. Considering the differences in clinical history and physical clinical condition from a patient to another, a standard physical activity program may not be established, but it is much better to make individual choices for each KT patient and agree them with him. The program of physical activity should also agree with the subject's life habits and hobbies and be as supervised as possible in order to improve the adherence.[87-94, 96, 97] In KT patients, a systematic training program based on aerobic, or endurance exercises leads to positive effects on several physical parameters and allows to optimize the clinical management and to obtain a fast and satisfactory recovery. In fact, physical activity based on aerobic exercises induces an improvement in the performance of cardiorespiratory parameters, while exercises of resistance determine an improvement in muscle strength.[38, 100-102]

The KT patients should adhere to an appropriate diet under the supervision of a dietician to avoid serious complications like malnutrition, obesity, type II diabetes and other metabolic diseases, which may damage the transplanted organ. The dietician should identify a diet suitable for the patient's clinical condition and agree it with him, to obtain good compliance.

Only a few randomized clinical trials have been carried out on the nutritional treatment of KT, but there is a need for international guidelines considering the patients' clinical condition, the different availability of foods in different countries and the alimentary habits related to tradition, culture and religion.

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