



# Hypertension in elderly patients with a kidney transplant

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## Abstract

**Introduction:** A large number of patients today with terminal kidney failure are elderly. For a small number of these patients a kidney transplant is a possible method of treatment.

**Aim:** The goal of this work was to investigate the prevalence of hypertension among kidney transplant patients above the age of 65 and to analyze anti-hypertension therapy.

**Methods:** The investigation included 27 patients, 15 male and 12 female, above the age of 65 who received a kidney transplant. The average age of the patients was  $71.2 \pm 5.6$  years. The average time spent on dialysis before the transplant was  $2.7 \pm 2.1$  years. The amount of time that had passed since the transplant was  $6.6 \pm 4.6$  years. The average values of creatinine were  $135 \pm 38.2$   $\mu\text{mol/L}$ .

**Results:** Of the number of patients analyzed, 25 (93%) had hypertension. In the anti-hypertension therapy five (20%) patients were taking one antihypertensive drug, 14 (56%) patients were taking two drugs and six (24%) patients were taking three or more drugs. The most frequently taken medicine was a calcium channel blocker (68%) and together angiotensin receptor blockers (ARB) and ACE-inhibitors (44%;32%). Of the analyzed patients, 13 (52%) achieved the target values for blood pressure.

**Conclusion:** From the data acquired we can conclude that prevalence of hypertension in the elderly group of patients is very high. Also, in half of these patients the target values for blood pressure were achieved. The most frequently used antihypertensives among older patients were calcium channel blocker or ARB and ACE-inhibitors.

## INTRODUCTION

Hypertension appears in a large number of patients after transplants of the kidney and other solid organs. Individual works have evaluated the prevalence of hypertension after a transplant up to 90% patients (1, 2). In addition to the traditional risk factors, it is influenced by factors related to the transplant itself. One of the most important risk factors associated with a transplant is the influence of immunosuppressive therapy, especially cyclosporine, in addition to many other causes, such as the reduced function of the transplanted kidney (4), arterial stenosis of the transplanted kidney (5, 6) and the age of the donor (7).

Arterial hypertension is frequent among elderly people. The aging process itself is related to the increased rigidity of the blood vessels and to reduced vascular elasticity, which increases the frequency of elevated blood pressure, especially systolic (8).

The last several decades have shown an increase in the average lifespan of the population. An increasing share is now made up of elderly people. According to the 1999 census, 17% of the population of Croatia was above the age of 65 (9). A large number of patients with terminal kidney failure who begin dialysis today are elderly. According to data of the Croatia Register for the Replacement of Kidney Functions, the median age of patients who began dialysis treatment in 2009 was 67 years (10). According to data from our center, the average age of patients who began dialysis treatment in recent years was as much as 70 (11).

A great number of older patients who are being treated by one of the types of dialysis have numerous accompanying diseases; most frequently among them is cardiovascular disease (12). A higher age in the general population by itself carried an increased risk of cardiovascular disease. Because of this, a kidney transplant is possible only among a small portion of elderly patients as a method of treating terminal kidney failure. With the advancement and accessibility of diagnostic and therapeutic methods in recent years, there has been a growth in the number of elderly patients waiting for a kidney transplant (12, 13, 14).

The goal of this work was to investigate the frequency of hypertension in patients with a kidney transplant older than 65 and to analyze their anti-hypertension therapy.

## SUBJECTS AND METHODS

### Subjects

Twenty-seven patients older than 65 who received transplants at the Clinical Hospital Center Rijeka were included in the examination, 12 female (44.4%) and 15 male (55.6%). Their average was  $71.2 \pm 5.6$  years (from 65 to 88). The average amount of time on dialysis before a transplant was  $2.7 \pm 2.1$  years. The average amount of time that passed since a transplant was  $6.6 \pm 4.6$  years.

Eight patients (29.6%) had interstitial nephritis as the primary kidney disease; 6 patients (22.5%) had polycystic kidney disease; 5 patients (18.5%) had glomerulonephritis; 4 (14.5%) had diabetic nephropathy, and 4 (14.5%) had other diseases (Table 1).

All of the patient received a cadaveric kidney transplant.

The average values of creatinine were  $135.4 \pm 36.4$   $\mu\text{mol/L}$  (from 96  $\mu\text{mol/L}$  to 241  $\mu\text{mol/L}$ ). Fourteen patients had creatinine lower than 120  $\mu\text{mol/L}$ , and thirteen patients had a level higher than 120  $\mu\text{mol/L}$  (ranging from 141  $\mu\text{mol/L}$  to 214  $\mu\text{mol/L}$ ). Average body mass index (BMI) was  $24.1 \pm 2.1$   $\text{kg/m}^2$ .

**TABLE 1**

Demographics, clinical and laboratory parameters of the study group.

Parameter	N (%)
Male	15 (55.6%)
Female	12 (44.4%)
Age (years)	$71.2 \pm 5.6$
Duration HD before transplantation (years)	$2.7 \pm 2.1$
Time passed since transplant (years)	$6.6 \pm 4.6$
BMI ( $\text{kg/m}^2$ )	$24.1 \pm 2.1$
Serum creatinine (mmol/L)	$135.4 \pm 36.4$
creatinine < 120 $\mu\text{mol/L}$	14 (58.2%)
creatinine > 120 $\mu\text{mol/L}$	13 (51.8%)
<b>Causes of end-stage renal failure</b>	
Intrstitial nephritis	8 (29.6%)
Polycystic kidney	6 (22.2%)
Glomerulonephritis	5 (18.5%)
Diabetic nephropathy	4 (14.8%)
Other	4 (14.8%)

Abbreviation: BMI – body mass index, HD – hemodialysis

Eighteen patients were receiving triple immunosuppressive therapy (corticosteroids, cyclosporine or tacrolimus and mycophenolate mofetil or azathioprine). Nine patients had double therapy. Of those, four patients had corticosteroid and cyclosporine as an immunosuppressive therapy. Two patients were taking corticosteroid and mycophenolate mofetil, while another two were taking corticosteroid and azathioprine, and one was taking corticosteroid and sirolimus (Table 2).

**TABLE 2**

Immunosuppressive therapy.

	Patients N (%)
<b>Triple therapy</b>	<b>18 (66.7%)</b>
Cortico+Cyclo/TAC+MMF	12
Cortico+Cyclo/TAC+AZA	6
<b>Dual therapy</b>	<b>9 (33.3%)</b>
Cortico+Cyclo	4
Cortico+MMF or Cortico+AZA	4
Cortico+Sir	1
	<b>27 (100%)</b>

Abbreviations: cortico – corticosteroid, TAC – tacrolimus, MMF – mycophenolate mofetil, Cyclo – cyclosporin, AZA – azathioprine, Sir – sirolimus

**Methods**

We took as the criterion for defining arterial hypertension a systolic blood pressure greater than 140 mmHg and a diastolic pressure greater than 90 mmHg or the routine use of anti-hypertension therapy. Blood pressure was measured with a standard mercury sphygmomanometer during regular out-patient examinations. Immunosuppressive and anti-hypertensive therapy was performed by nephrologists.

**Statistical analysis**

The aims of this study were primarily descriptive. The clinical characteristics of the patients are presented as a mean ± standard deviation.

**RESULTS**

Of the patients examined, 25 (93%) had hypertension. Among all of them hypertension appeared in the first year after a transplant.

Among the patients who had a serum creatinine level higher than 120 µmol/L all had hypertension.

Five patients (20%) took one medicine; 14 (56%) took two medicines; and six patients (24%) took three or more medicines. In monotherapy the most frequently taken medicine was an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blockers (ARB) or calcium channel blockers (seven patients). The most frequent combination in dual therapy was a combination of ACE inhibitors or ARB and calcium channel blockers (seven patients, 50%). The other combination in dual therapy was a combination of ACE inhibitors or ARB blockers with a beta blocker (two patients) and a diuretic (two patients). Six patients (24%) took a combination of three or more anti-hypertension medicines (Table 3).

**TABLE 3**

Antihypertensive therapy.

	Number of patients (%)
<b>Monotherapy</b>	<b>5 (20%)</b>
ACE-inhibitors or ARB	2
Calcium channels blockers	2
β-blockers	1
<b>Dual therapy</b>	<b>14 (56%)</b>
ARB or ACE inhibitors + calcium channels blockers	7
ARB or ACEinhibitors + β-blockers	2
ARB or ACEinhibitors + diuretics	2
Calcium channels blockers + β-blockers	2
other	1
<b>Triple therapy or more</b>	<b>6 (24%)</b>

Abbreviations: ACE – angiotensin converting enzyme, ARB – angiotensin receptor blockers

**TABLE 4**

Correlation between antihypertensive and immunosuppressive therapy in the kidney transplanted patients.

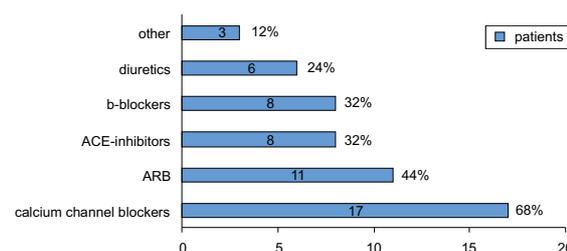
Immunosuppressive therapy (Patients N)	Antihypertensive therapy (Patients N)
<b>Triple immunosuppressive therapy (N =18)</b>	
Cortico+Cyclo/TAC+MMF (N=12)	Monotherapy 2
	Dual therapy 6
	Triple therapy or more 4
Cortico+Cyclo/TAC+AZA (N=6)	Without hypertension 0
	Monotherapy 1
	Dual therapy 4
	Triple therapy or more 1
Cortico+Sir (N=1)	Without hypertension 0
	Monotherapy 1
	Dual therapy 2
	Triple therapy or more 1
Cortico+MMF or Cortico+AZA (N=4)	Without hypertension 0
	Monotherapy 1
	Dual therapy 2
	Triple therapy or more 0
Cortico+Sir (N=1)	Without hypertension 1
	Without hypertension 1

Abbreviations: Cortico – corticosteroid; TAC – tacrolimus, MMF – mycophenolat mofetil, Cyclo – cyclosporin, AZA – azathioprim, Sir – sirolimus

Correlation between immunosuppressive therapy and number of antihypertensive drugs see Table 4.

If all anti-hypertension medicines are analyzed, then the most frequently taken medicine was a calcium antagonist in 17 (68%) patients, an ARB in 11 (44%) patients, an ACE inhibitor in eight (32%) patients, as well as a beta blocker, while six (24%) patients were taking a diuretic (Figure 1). Also, all elderly patients with hypertension had a hypolipemic as well as acetylsalicylic acid.

Of the patients analyzed, 13 (52%) achieved the target blood pressure of 140/90 mmHg, while nine (36%) achieved a blood pressure of 130/80 mmHg.



**Figure 1.** The most frequently used drugs

## DISCUSSION AND CONCLUSIONS

The purpose of this investigation was to establish the frequency of hypertension in elderly kidney transplant patients. Of those patients analyzed, almost all (93%) had hypertension. According to numerous studies, the frequency of hypertension among kidney transplant patients is very great (1, 2, 4). Elderly person also have a high frequency of hypertension compared to the general population (more than 50%) (8). Since our study analyzed elderly kidney transplant patients, this high percentage of patients with hypertension was to be expected.

Of course, in this group nonpharmacological measures for the regulation of blood pressure, such as the limitations on salt intake, maintaining an adequate body weight and physical activity, etc., were not enough. They required antihypertension therapy that often included more than one antihypertension drug. Only 20 % of the patients took one drug in antihypertension therapy; 56% of the patients were using two drug, and 24% of the patients were using three or more drug in antihypertension therapy. Patients with triple immunosuppressive therapy, which included kalcineurinske inhibitors often require the treatment of hypertension with three or more drugs.

The optimal antihypertension therapy is difficult to prescribe for transplant patients. It depends most frequently on the values of the blood pressure, immunosuppression therapy, the functioning of the kidney transplant, and on any accompanying diseases (1). The usefulness of antihypertension therapy in reducing blood pressure and lowering cardiovascular mortality and morbidity has also been shown among elderly patients with elevated blood pressure in the general population (8).

The most frequently prescribed antihypertension medicines among our patients were calcium channel blockers (68%). Vasoconstriction is one of the basic mechanisms in the appearance of hypertension in transplant patients and the positive effect of calcium channel blockers (15). on it is important in regulating blood pressure in this group of patients. ACE inhibitors and ARB blockers were the next most frequently used medicines in anti-hypertension therapy. Since this group of medicines works on the renin-angiotensin system, it is today indispensable in regulating blood pressure and is frequently used by a large number of patients as the medicine of choice in hypertension therapy. This group of medicines has also been shown in several studies to be successful in reducing blood pressure and cardiovascular mortality and morbidity among elderly people and in transplant patients (16). On the other hand, the possibility of causing hyperkalemia, anemia (17), and even a reduction of glomerular filtration (18) to a certain extent limits their use among elderly patients with a kidney transplant. We must be cautious in introducing them into an antihypertension therapy. Such patients required at the outset more frequent check-ups not only of blood pressure but also for laboratory findings. According to the clinical guidelines do not exist the first choice antihypertensive drug in this group of patients. The choice of antihyper-

tensive drug may be determined by the presence of post-transplant complications and comorbid disease (19, 20).

Arterial hypertension is a primary and independent factor in cardiovascular risk. According to data from the World Health Organization, it is the leading risk factor for death in the world. Cardiovascular diseases are most frequently the cause of death among dialysis patients, more than 50% (21). Kidney transplant also have a very high percentage of death from cardiovascular diseases. According to the United States Renal Data System, 37% of patients with a kidney transplant die from cardiovascular disease (21). Of course, the percentage of deaths from cardiovascular disease is higher in elderly transplant patients. According to data from an earlier study of our elderly transplant patients, cardiovascular disease was the cause of death in 43.2% of the patients. Detection of hypertension after a transplant and its adequate treatment will help in reducing cardiovascular disease and mortality in this group of patients (22).

Of the number of patients analyzed, half of them achieved the targeted blood pressure of 140/90 mmHg. If the target blood pressure of 130/80 mmHg is taken as a criterion, which in this group patients is a desired and recommended value, 36% of the patients achieved the target blood pressure. We cannot conclude from this work if the reason for this is the reduced compliance of the patient as a consequence of taking a large number of medicines and completely neglecting the recommended therapy or if it involves a group of patients for whom it is more difficult to achieve the target blood pressure. In European countries achievement of the target blood pressure is between 17 and 35% (24). According to a study carried out in 2001, in Croatia the target blood pressure was achieved in 19% of patients (25). Compared to this data from the general population, we can be satisfied with the target blood pressure achieved in the group of older kidney transplant patients of almost 50%, or 36%. From personal experience in working with this group of patients, frequent and regular check-ups, very frequent monitoring of the patient over many years by the same specialist, and their confidence in the method of treatment have contributed to this achievement.

Finally, we can conclude that the appearance of hypertension in an group of elderly kidney transplant patients is almost unavoidable and that its treatment is vital and can be partially successful. In selecting an antihypertension therapy, we must not forget the two basic goals in treating hypertension in this group of patients: the reduction of cardiovascular risk and safeguarding the functioning of the kidney transplant.

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