



The Effects of Obesity on the Kidneys

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INTRODUCTION. Renal dysfunction is a common manifestation of renal ischemia, along with renovascular hypertension (RVH) and congestive heart failure [1, 3–5]. It is known that a decrease in estimated glomerular filtration rate (GFR) is clearly associated with an unfavorable prognosis both in the general population [2] and in patients with AORLD [1, 3]. Therefore, preserving organ function is one of the priorities in the surgical treatment of ischemic kidney disease (IKD) in patients with atherosclerotic occlusive lesions of the renal arteries (AORLD) [1]. There are few attempts to predict the outcome of RP based on PF based on the initial functional state, organ size, and assessment of intrarenal blood flow [4–12]. In particular, it has been shown that an initially high level of serum creatinine [9] and an increase in the resistive index of more than 0.80 in segmental arteries [8, 11] are associated with worsening PF after RP. In contrast, other studies have shown that these indicators were unreliable predictors of long-term RP functional outcome [7, 14–16]. In this regard, the main goal of the study was to assess the initial Doppler parameters of blood flow and the morphological state of small arteries of ischemic kidneys depending on the long-term functional outcome of their revascularization. **PATIENTS AND METHODS** Duplex scanning (DS) of the arterial blood flow of 85 ischemic kidneys was performed in 64 patients with hemodynamically significant AORLD (stenoses 60–100%), proven angiographically (40 men and 24 women aged 42 to 78 years, on average 60 ± 8 years). Of these, 33 patients had bilateral, and the other 31 had unilateral VA obstruction. Forty-six patients (72%) had varying degrees of renal dysfunction at baseline (estimated GFR < 60 ml/min according to MDRD) [13]. For each patient, the level of serum creatinine and GFR were determined before, after surgery and in the long-term period (from 5 to 72 months, on average 18 ± 13 months after RP). 21 patients underwent bilateral, and the other 43 patients underwent unilateral RP (31 with unilateral and 12 with bilateral AOPCA lesions). Refusal to revascularize the contralateral kidney in patients with bilateral AOPCA was due to the occlusion of their intraparenchymal arteries and at the same time the need to reduce the time of open surgery due to the presence of risks or the initial ineffectiveness of attempts at endovascular recanalization. Renal revascularization ($n = 42$) was performed by bypass and endovascularly, using stents ($n = 43$). The study of the physical parameters of blood flow in the VA and in the intraparenchymal arteries was carried out using a Vivid-6 device (General Electric, USA). Using a convex matrix sensor with a frequency of 7–9 MHz and the computer of the device, the following parameters were automatically determined in the mouth, middle and distal segments of the VA, as well as in the segmental and interlobar arteries of the upper, middle and lower thirds of the kidney: peak systolic blood flow velocity (PSV), of course, diastolic blood flow velocity (BDSV), pulsatility index (PI) (the ratio of the difference between BPSV and BDSV to the average blood flow velocity), resistive index (RI) (the ratio of the difference between BPSV and BDSV to BPSV) and blood flow acceleration time (BAT) [17]. Each blood flow measurement was performed three times and the arithmetic mean was calculated for subsequent analysis. DS was performed by one researcher. Patients who underwent bilateral VA surgery were considered as a single case of RP, since neither the degree of VA stenosis nor Doppler measurements in simultaneously ischemic kidneys were significantly different (data not shown). In this case, for subsequent analysis, the arithmetic mean values of blood flow parameters in both kidneys were used. As a result, all cases of RP were divided into three groups depending on the state of PF in the long-term period: group I – with deterioration of PF (decrease in GFR $> 10\%$ of its initial level) ($n = 18$); group II – with stable PF (GFR within $\pm 10\%$) ($n = 28$); group III ($n = 18$) –



with improved PF (GFR > 10% of baseline). Morphometry of 25 biopsies of ischemic kidneys taken from 20 patients during surgery (including 5 on both sides) was performed, assessing the condition of arteries with an outer diameter of up to 50, from 50 to 100 and more than 100 μm and calculating their vascular index (SI) : (outer perimeter of the artery/inner perimeter of the artery \times 0.5) – 1 [18], as well as by determining the degree of glomerulosclerosis. Microscopic preparations of the kidneys were stained with hematoxylin-eosin, Van Gieson, Masson and Weigert for elastin. A comparative analysis of morphometric data was carried out in two groups of patients: with a 10% decrease in GFR in the long-term period (n = 6) and without it (n = 15). For statistical analysis, Student's t-test, χ^2 test, Mann–Whitney test, and ANOVA were used to assess intergroup differences. Spearman rank correlation was used to identify relationships between indicators. Data are presented as $X \pm \text{SD}$ or median with interquartile range depending on the nature of the distribution of the characteristic. Differences or relationships were considered significant at $p < 0.05$. Calculations were performed using the SPSS 14.0 applied statistical software package (Chicago, Illinois, USA).

RESULTS. Groups of patients with different postoperative dynamics of PF did not have significant differences in gender, age, degree of VA stenosis in ischemic kidneys, severity and duration of RVH, number of antihypertensive drugs, and degree of blood pressure reduction after RP. The initial PF indicators in patients of group III were significantly worse than in groups I and II. Significantly lower RI values were revealed at all levels of the arterial bed, excluding the middle third of the VA, as well as PI in the intraparenchymal arteries of the kidneys in group III. However, there were no differences in any Doppler blood flow parameters between groups I and II of patients. When analyzing the overall trend (ANOVA), significant intergroup differences were detected only for the PI value at the level of the interlobar arteries ($p = 0.019$). Correlation analysis carried out in the combined group showed a close relationship between Doppler parameters of blood flow at all levels of the arterial bed of ischemic kidneys and the relative dynamics of GFR. However, the degree of glomerulosclerosis of ischemic kidneys did not differ between these groups.

DISCUSSION. The traditional goals of treatment for RVH are to control blood pressure [1, 4, 19, 20] and recurrent pulmonary edema [21]. An equally important task is the preservation/restoration of kidney function, which naturally decreases as organ ischemia progresses. Progression of renal dysfunction may be a consequence of increasing degrees of stenosis [22], hypertension, glomerulosclerosis and tubulointerstitial fibrosis [30, 31]. It is logical to expect the maximum effect in terms of renoprotection and preservation/improvement of renal function in patients with relatively intact parenchyma of ischemic kidneys. The traditional clinical indicator used to screen for PF status is serum creatinine, although the benefits of estimating estimated GFR are clear [13]. However, data on the prognostic value of serum creatinine level before RP on long-term results are very contradictory. Thus, it was previously found that when its initial value was more than 0.35 mmol/l, subsequent RP led to a deterioration in renal function, up to the need to start renal replacement therapy [9]. In other studies, creatinine concentrations greater than 0.15 mmol/L before RP were associated with decreased long-term survival [23, 24]. In contrast, other studies have demonstrated that improvement in renal function after VA reconstruction can be achieved even in patients who have already started hemodialysis treatment for RVH [13–15, 25, 26]. Moreover, there is evidence of the absence of a negative effect on the long-term prognosis of a preoperative increase in creatinine [23]. In the patients we examined with improvement in PF as a result of RP, the initial values of creatinine and GFR were significantly higher than in patients with no increase in GFR or its decrease. The data obtained clearly show that the current status of PF in itself is not significant in determining the indications for RP. One could assume that the positive dynamics of GFR is determined mainly by the antihypertensive effect of RP, however, the degree of blood pressure reduction in all three comparison groups was comparable. It is obvious that in some patients with AORLD, a decrease in GFR occurs in response to organ ischemia with relatively intact parenchyma, but is not a consequence of the development of irreversible sclerotic changes in the organ. It is logical to assume that it is in such patients that the renoprotective effect and long-term survival can be maximum possible. The reaction of the unchanged or slightly changed vascular bed of the kidney in response to



ischemia is to reduce peripheral vascular resistance [27], which is aimed at maintaining organ perfusion. This situation can be largely reflected by changes in blood flow when using the Doppler sonography method, which allows it to be assessed at almost all levels of the intraparenchymal arterial bed of the kidneys [1, 10–12, 28, 29]. It is known that the peripheral resistance of the arterial bed of the organ under study is reflected by indicators of diastolic blood flow, diastolic-systolic ratio, PI and RI [6, 11, 17]. A number of data are presented to assess the significance of these indicators for long-term prognosis after RP in patients with atherosclerosis of the VA. Lower RI and PI at the level of segmental arteries of ischemic kidneys were observed in patients with a clear correction of RVH and/or an increase in GFR after RP compared with patients in whom there was no treatment effect [6, 8, 11]. End-diastolic blood flow velocity > 90 cm/s in the VA in combination with $RI < 0.65$ in the segmental arteries after acute captopril administration and a longitudinal kidney size of more than 9.3 cm were associated with a good effect of RP both in terms of PF and correction BP [10, 12, 28]. In patients with no antihypertensive and renoprotective effect after RP, the initial RI in segmental arteries exceeded 0.8 [11]. In addition, such an increase in RI was associated with a decrease in GFR and an increase in mortality in the postoperative period in a combined group of patients undergoing endovascular or open RP [29]. Our data to a greater extent emphasize the importance of increasing CDSC and decreasing PI/RI, apparently reflecting a decrease in peripheral renal vascular resistance in response to ischemia. Thus, in a correlation analysis of the overall group, we showed that the relative dynamics of GFR in the long-term period after renal revascularization is directly related to CDSC and vice versa - with RI/PI at all studied levels of the arterial bed of the kidneys with atherosclerotic stenosis of the VA. In the group of patients with a clear renoprotective effect of RP, preoperative PI and RI indices were significantly lower than in patients with no obvious improvement in GFR or its decrease. Patients with no change in GFR in the pre- and postoperative periods (i.e., stabilization of GFR) could be classified as having achieved a partial renoprotective effect of revascularization. However, we did not find the expected differences in the studied Doppler indicators of blood flow in ischemic kidneys between the groups of patients with stable GFR and its decrease, obviously due to the small number of observations. In our opinion, this is the main limitation of the study, which does not allow us to determine Doppler ultrasound criteria for the prognosis of RP for this group of patients. Assuming that a decrease in RI and PI in the intraparenchymal arterial bed of these kidneys indicates their relatively intact ability to respond to current ischemia of the organ by reducing resistance, we conducted their morphometric study. Significant differences were clearly shown between the groups of patients with no and clear/partial renoprotective effect after RP in the condition of small arteries with a diameter of more than $100 \mu\text{m}$. In patients with a decrease in GFR, the degree of remodeling of vessels of this caliber, assessed by the vascular index, media thickness and internal diameter, was significantly greater. In addition, the internal diameter of the arteries had a close direct relationship with CDSC and an inverse relationship with RI at the level of segmental arteries, confirming the assumption that Dopplerographic indicators can be useful in assessing the condition of small arteries of the organ with atherosclerotic occlusive lesions of the VA. We did not find significant differences in the degree of glomerulosclerosis between patients with and without deterioration of PF after RP; however, it should be noted that the degree of global changes in the glomeruli in the examined group was relatively small. At the same time, there is no doubt that the functional effect after revascularization of ischemic kidneys can be significantly influenced by pronounced sclerotic changes in their parenchyma, manifested by glomerulosclerosis, interstitial fibrosis and a decrease in the size of the organ when visualized [30, 31].

CONCLUSION. Thus, assessment of the state of the arterial bed of ischemic kidneys in patients with atherosclerotic occlusive lesions of the VA showed a relationship between the morphofunctional state of the arteries of the intraparenchymal bed and the functional result of their revascularization. Our data allow us to conclude that the renoprotective effect of this operation, determined by the relative dynamics of GFR in the pre- and postoperative period, is largely independent of the reduction in blood pressure and is determined by the state of the intrarenal arterial bed. An increase in GFR after restoration of blood flow in the kidneys with stenotic arteries, despite the severity of their initial



dysfunction, can be expected in the presence of Dopplerographic signs of reduced intrarenal peripheral vascular resistance in the form of preserved CDSC and low PI and RI values.

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