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Donetsk, 83003.Corresponding author, ¹e-mail: k.shramenko@gmail.com**Abstract**

Introduction: Development of vasoconstriction of kidney arterioles and reduction of renal blood flow is one of the main mechanism of acute kidney injury (AKI) formation. Methods for evaluation of intrarenal hemodynamics status are rather limited. Evident interest for the clinician is the possibility of rapid and non-invasive assessment of renal hemodynamics using the dopplerography method. The method makes it possible to visualize the kidney vessels and conduct a qualitative and quantitative evaluation of renal blood flow. Peculiarities of disturbed blood flow in the kidneys can determine the individuality of pharmacological correction and intensive care in patients with AKI.

Objectives: The aim of our study was to reveal the peculiarities of renal blood flow disorders, depending on the variant, stage and severity of AKI; to evaluate the opportunities of individual pharmacological correction and intensive care in studied AKI patients.

Methods: A prospective nonrandomized study. Inclusion criteria: patients with prerenal, renal and subrenal AKI in the stage of oligoanuria and restoration of diuresis; exclusion criteria: AKI patients after cardiac surgery and operations on the large vessels. 250 ICU patients with prerenal (130), renal (81) and subrenal (39) AKI were examined by ultrasound dopplerography.

Results and discussion: Comparative data of intrarenal blood flow dopplerographic examination in patients with various variants of AKI are presented. All patients initially, at admission in ICU revealed disorders of renal hemodynamics, the severity of which was different depending on the AKI module. During intensive care, as diuresis was restored, the parameters of renal blood flow improved. The speed and completeness of hemodynamics recovery was determined by both the modulus and severity of AKI. The heterogeneity of the prerenal module of AKI was determined due the data of renal blood flow and the rate of restoration of diuresis. So, we divided prerenal module in 2 groups: 1) real (genuine) prerenal AKI and 2) AKI prerenal for reason. The expediency of such selection is substantiated. It was established that resistive index (RI) in the main trunk of the renal artery is an early criterion of severity of AKI (F), and its dynamics during intensive care makes it possible to diagnose the transformation of AKI in chronic renal failure (CRF). Strong direct correlation RI with the duration of oligoanuria ($r = 0.72$), which is the main retrospective marker of the severity of AKI, was revealed yet upon admission to the ICU. It was found that the peculiarities of renal hemodynamics disturbance are an important criterion for differential diagnosis of the AKI module: renal dopplerometry data significantly ($p < 0.05$) differ in prerenal, renal and subrenal AKI. It was found that the risk of death is statistically significant decreased ($p = 0.001$), OR =

0.009 (95% CI 0.001 – 0.050) when performing individual pharmacological correction (nephroprotection) in the ICU, based on the advanced diagnosis of the AKI module.

Conclusions: The revealed peculiarities of renal blood flow disorders in patients with different AKI modules point to the need for an individual pharmacological correction and intensive care in AKI patients.

Keywords: Acute kidney injury, renal blood flow disorders, dopplerography, pharmacological correction, intensive care.

Introduction

Treatment of AKI is an important social problem. In recent years, the incidence of AKI has increased, accounting for more than 35% of patients in intensive care units (ICU) [1, 2]. This severe complication is increasingly developing as a component of multiorgan failure in patients of the most able-bodied age [3, 4, 5]. Accession of AKI is an independent predictor of adverse outcome in critically ill patients and increases hospital mortality by 3-10 times [6, 7, 8]. With the advent of hemodialysis, the results of treatment of renal failure improved in comparison with the pre-dialysis era. However, at present, despite the high level of dialysis technologies, new classifications (RIFLE, AKIN, KDIGO), the results of treatment AKI patients, especially complicated by multiorgan failure, do not improve [9].

Mortality in this pathology remains high and exceeds 50% [10, 11]. Often the difficulty of conducting adequate intensive care is associated with the lack of timely diagnosis and the late determination of real cause of AKI [12, 13].

The development of vasoconstriction of kidney arterioles and reduction of renal blood flow is one of the main mechanism AKI formation. Spasm of renal arterioles causes the growth of peripheral vascular resistance and reduces the blood supply of the parenchyma. The expressed hypoperfusion leads to damage, first of all, cells of the proximal renal tubules. Tubulosclerosis and necrosis promotes the flow of ultrafiltrate into the interstitium. Interstitial edema, in turn, compresses the blood vessels, worsens blood circulation and aggravates the disorders of the basic processes that provide numerous kidney functions [14].

Methods for assessing the status of intrarenal hemodynamics are rather limited. The active use of traditional radioisotope, radiologic and radiopaque methods for evaluating the kidney in conditions of reduced renal function may be an

additional risk factor for AKI progression and is not always sufficiently informative [14, 15, 16]. Evident interest for the clinician is the possibility of rapid and non-invasive assessment of renal hemodynamics using the dopplerography method. The method allows to visualize the kidney vessels [15, 16]. Performing a complex ultrasound in the regime of pulsed wave dopplerography allows conducting a qualitative and quantitative analysis of arterial and venous blood flow in the kidneys and aorta [17, 18]. Most of the work is limited to the analysis of hemodynamics in patients with non-severe forms of AKI, in cases where persistent oliguria and severe impairment of renal functions have not yet developed [19, 20].

The possibility of dopplerography examination of renal blood flow only in the early stages (1 and 2 according to AKIN, KDIGO classification) is assessed. Some authors prefer resistive index (RI) in comparison with humoral factors, in particular, with an early marker of AKI – cystatin C [18, 21, 22]. A great number of publications are devoted to the possibility of differentiating the prerenal and renal form of AKI with tubular necrosis [19]. The analysis is limited to carrying out correlations between the RI and the possibility of forming the 3rd AKI stage. The main focus is on the resistive index (RI), without assessing the rates of arterial blood flow, on the basis of which RI is calculated [23, 24].

In ICU of Donetsk clinical territorial unit (DoCTU) work is performed to improve the pharmacological and non-pharmacologic correction of detected renal blood flow disorders in AKI patients to provide nephroprotection [25, 26].

Objectives. The aim of our study was to reveal the peculiarities of renal blood flow disorders, depending on the variant, stage and severity of AKI; to evaluate the opportunities of

individual pharmacological correction and intensive care in studied AKI patients.

Methods

250 patients were the main group (treated from 2009 to 2014 in DoCTU), 162 male (64.7%), 88 female (35.3%). The age was from 18 to 85 years, an average of 53 ± 8.2 . When enrolling in the ICU, an isolated AKI was only in 5%. All patients after diagnosis clarification were divided into modules: 1) patients with prerenal AKI module (130); 2) patients with renal module AKI (81); 3) patients with subrenal AKI module (39). The module was a relationship of etiology, pathogenetic mechanisms, risk factors, causes of AKI.

Renal replacement therapy was performed in 182 (72.8%) patients, in total 965 sessions, 5.3 sessions per patient on the AK-200, Innova (Hospal), Tina (Baxter), using dialyzers – Alwal GFE, GFS, Polyflux (Gambro), F-5 (Fresenius) and provided intermittent hemodialysis, hemodiafiltration, hemofiltration depending on the mode of operation and the dialysate membrane. The comparison group consisted of 107 patients with a prerenal (60), renal (32) and subrenal (15) variant of AKI treated at the DoCTU before 2009, aged 18 to 77 years, an average of 48 ± 7.9 . 74 male (69.2%) and 33 female (30.8%). Upon admission to the ICU, the isolated AKI was up to 25%. Dialysis treatment was performed in 79 patients (73.8%).

The groups were comparable by sex and age, although the average age group was higher in the main group. In addition, in the comparison group at admission, the percentage of isolated AKI was higher, without polyorganic complications. In the retrospective group, the treatment was performed without taking into account the peculiarities of the renal blood flow and the individual approach.

All patients underwent general clinical, biochemical studies, ultrasound of the kidneys, ECG, chest X-ray; Parts of them, according to the indications – echocardiography, computed tomography (CT) of the abdominal cavity and retroperitoneal space, magnetic resonance imaging (MRI).

In addition to the standard ultrasound, all patients underwent doppler scanning of the vessels of both kidneys (color Doppler mapping and pulsed dopplerography) on the HDI-5000 expert class device (Philips, Holland) in

dynamics. The velocity of blood flow was measured in cm / s. In automatic mode, maximum systolic (Vps), end diastolic (Ved) blood flow velocity was determined in the renal vessels. The resistive index (RI) was calculated. $RI = [(V_{ps} - V_{ed}) / V_{ps}]$.

The systolic-diastolic ratio was determined – V_{ps}/V_{ed} . Each patient was performed 2 complex ultrasound examinations in the stage of oligoanuria and recovery of diuresis.

Statistical processing of data. The analysis of the results was carried out in statistical packages MedStat v.4.1 (Lyakh Yu. E., Guryanov V.G., 2004-2013), MedCalc v. 13.2.2 (MedCalc SoftWare bvba, 1993-2014), Statistica Neural Networks v.4.0 B (StatSoft Inc., 1996-1999). The obtained results are presented in the text in the form of values of the arithmetic mean and its standard error. For the selection of adequate sample comparison procedures, a preliminary verification of the distribution for normality was carried out. The statistical significance of the differences in the mean values in the two samples was estimated using the Student's test (the normal distribution law) or the Wilcoxon test (the distribution law differs from the normal one).

When analyzing the dynamics of change in characteristics during the treatment, the methods of comparing the coupled samples were used. In all cases, the difference was considered reliable when $p < 0.05$. To identify the relationship between the signs used by the method of correlation analysis. The correlation coefficient was used to estimate the degree of linear connection between the two signs. In cases where the distribution was not different from normal, the standard Pearson correlation coefficient (r) was determined. If the distribution deviates from the normal the signs was measured in the rank scale, the Spearman rank correlation coefficient used. At $p < 0.05$, the hypothesis of the existence of a correlation link was accepted. Computer program Excel was used to create diagrams.

To assess the effect on the outcome of AKI in the main group, a number of factors were analyzed that could potentially have an impact on the results of treatment. During the analysis, the results of treatment of 106 patients were reviewed. The task was to identify the factor signs associated with the results of AKI patients

treatment. An estimation of the degree and direction of the influence of these factor signs on the obtained results was carried out.

For the analysis, methods of constructing multifactorial models of classification were used. The quality of the constructed models was estimated by their sensitivity and specificity, a 95% confidence interval (95% CI) was calculated [25]. To determine the factors most associated with the results of treatment, the "genetic algorithm" (GA) method was used. To assess the adequacy of multifactorial mathematical models and predictive efficacy trials, area under the ROC curve (Area Under Curve – AUC) of 95% CI was used. To evaluate the possibility of using the constructed models on new data, a method was used to verify their prognostic characteristics on the confirming variety (a random number generator was used for the selection). To assess the degree of influence of factor characteristics on the resulting characteristics, a method of constructing logistic regression models was used [27]. For the assessment, the odds ratio (OR), as well as their 95% CI, was calculated.

Results and discussion

The development of vasoconstriction of kidney arterioles and reduction of renal blood flow is the main mechanism for the formation of AKI. Normally, the microvascular system of the kidneys is low-resistant. We conducted a comparative analysis of changes in blood circulation in the kidneys with various modules of AKI in the stage of oligoanuria, as well as in the restoration of diuresis.

Visual assessment of renal blood flow using color Doppler duplex scanning in the oligoanuria stage revealed: 1) signs of its impoverishment in the cortical layer of the kidney parenchyma at the level of the arc and interlobar arteries, weak signals; 2) reduction of the diastolic flow, until its complete absence; 3) an increase in the rate of venous blood flow associated with shunting the

blood into the venous system of the pyramids and overflowing the venous vessels; 4) in 8 patients the presence of reversible blood flow to the diastole; 5) in 11 patients – with thrombosis of the main trunk of the renal artery – complete absence of blood flow.

In the oligoanuria stage, patients of all three modules had abnormalities of renal hemodynamics, which significantly ($p < 0.001$) differed from those in the control group. The blood flow velocity in the main trunk of the renal artery in the oligoanuria stage was significantly lower than the corresponding parameters in the control group.

This involved both V_{ps} and V_{ed} blood flow velocities at the level of the main renal artery and its segments (arc, interlobar and segmental vessels). The ratio S / D was higher than the data in the control group, which can be explained by edema, lymphohistiocytic infiltration of the interstitial tissue of the kidney in AKI. RI in all cases was elevated and significantly ($p < 0.001$) was different from the data in the control group.

In clinical practice, the severity of AKI (F) is determined retrospectively by the duration of the oligoanuria stage. A correlation between RI and the duration of the oligoanuria was performed, a strong ($r = 0.724$) direct correlation was found.

The following data were obtained: if at admission RI in the trunk of the main renal artery was > 0.79 , the duration of the oligoanuria stage was more than 18 days; At an RI in the trunk of the main renal artery from 0.71 to 0.79, the duration of the oligoanuria stage was 8 to 18 days; If $RI < 0.71$, the duration of the oligoanuria was less than 8 days. Thus, already at the admission in ICU it was possible to talk about the severity of AKI (F). In $RI > 0.79$, AKI was assessed as severe, in RI level of 0.70 to 0.79 – moderate, and in $RI < 0.71$ light AKI (F) (Figure 1).

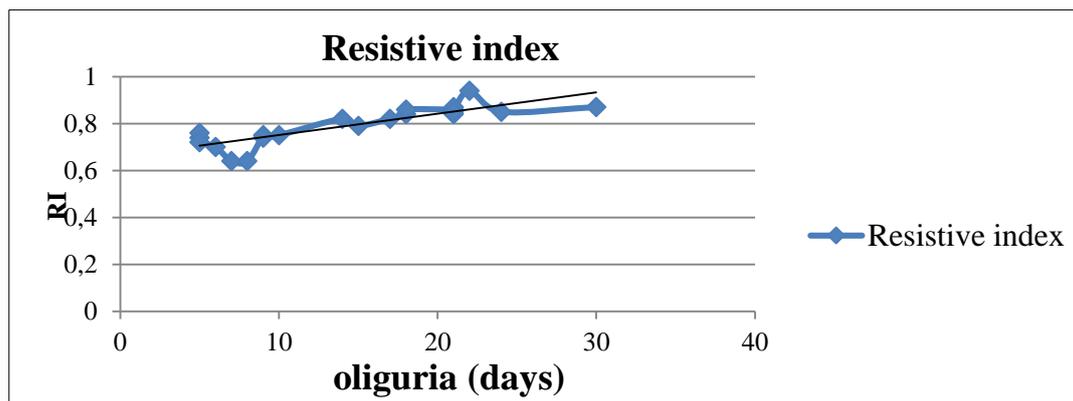


Fig. 1. RI and oliguria (in days) correlation link

Reduction of the rates of renal blood flow and an increase in RI was typical for all patients with AKI in the stage of oligoanuria. However, the studied data significantly ($p < 0.001$) differed in various modules of AKI.

Thus, the most significant decrease in the rate of renal blood flow was observed in renal AKI. In the main trunk of the renal artery Vps was 42.4 ± 0.15 cm / sec; Ved – 6.04 ± 0.03 cm / sec; S / D – 8.96 ± 0.27 ; RI was increased to 0.85 ± 0.01 and was the highest in comparison with RI in other AKI modules. The data of S / D in renal AKI variant were the highest. So, these data reflect, not only the decrease in the total blood flow, but also the edema of the kidney parenchyma, significant shunting of the blood into the venous network with depletion of cortical structures. The most significant edema of the renal parenchyma was revealed in the renal module of AKI.

In prerenal AKI module the following changes were observed according to the data of Doppler ultrasound: Vps was reduced to 59.5 ± 0.2 cm / sec, Ved was 15.2 ± 0.2 cm / sec; the S / D ratio was higher than the data in the control group and was 4.0 ± 0.2 ; RI increased to 0.75 ± 0.02 .

In subrenal AKI, Vps was reduced to 64.01 ± 0.25 cm / sec; Ved – to 20.3 ± 0.3 cm / sec; the S / D ratio was 3.12 ± 0.8 ; RI raised to 0.69 ± 0.02 (Figure 2, 3).

Further analysis of the Dopplerometry data in the oligoanuria stage revealed that groups of patients with prerenal and renal AKI were heterogeneous. And the hemodynamic data differed significantly in them.

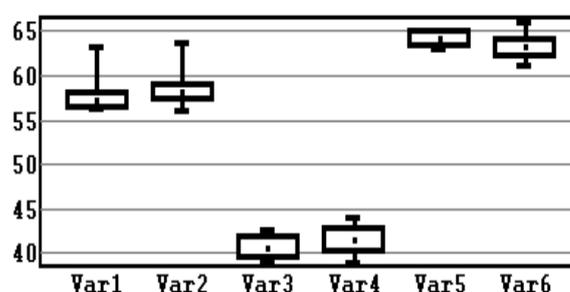


Fig. 2. Comparative characteristics of Vps in the main trunk of the renal artery with prerenal (1, 2), renal (3, 4) and subrenal (5, 6) AKI in oliguria.

Note: Var 1, 3, 5 – right kidney; Var 2, 4, 6 – left kidney. Vps right versus left kidneys $p_{1-2, 3-4, 5-6} \geq 0.05$

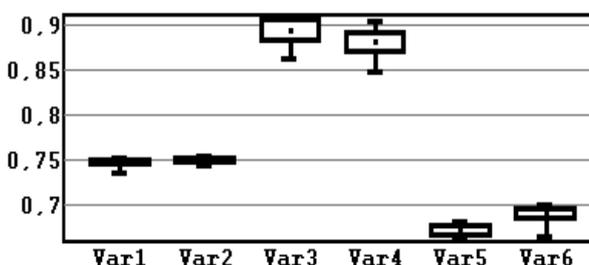


Fig. 3. Comparative characteristic of RI in the main trunk of the renal artery in prerenal (1,2), renal (3,4) and subrenal (5,6) AKI in oliguria.

Note: Var 1,3,5-right kidney; Var 2,4,6-left kidney. Vps right versus left kidneys $p_{1-2, 3-4, 5-6} \geq 0.05$

In some patients (27) with prerenal AKI, Vps and RI significantly ($p < 0.05$) differed from the majority of patients (53) in this group. Disturbances of renal hemodynamics in this subgroup were much less severe. Thus, Vps was 67.4 ± 5.0 cm/ sec, Ved 18.9 ± 1.2 cm / sec, and RI was 0.715 ± 0.01 . While in the majority of patients Vps was less (54.8 ± 6 cm / sec on average), Ved – 13.38 ± 4.2 cm / sec, and RI was $0.75 \pm 0, 05$ (Figure 4, 5).

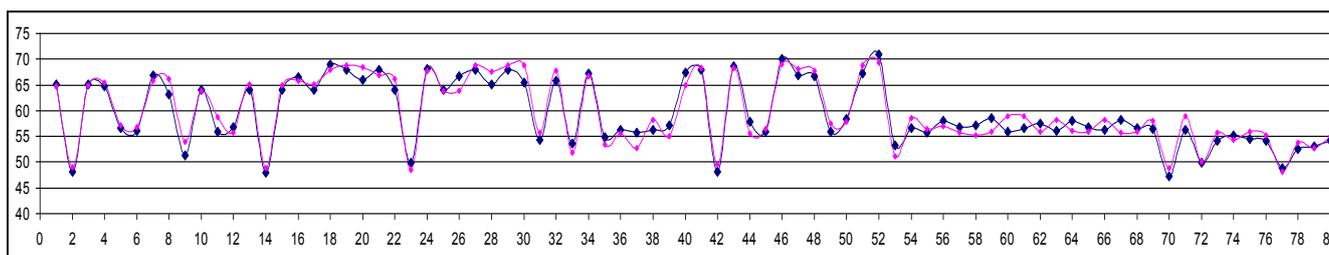


Fig. 4. Variation of Vps in the prerenal AKI group

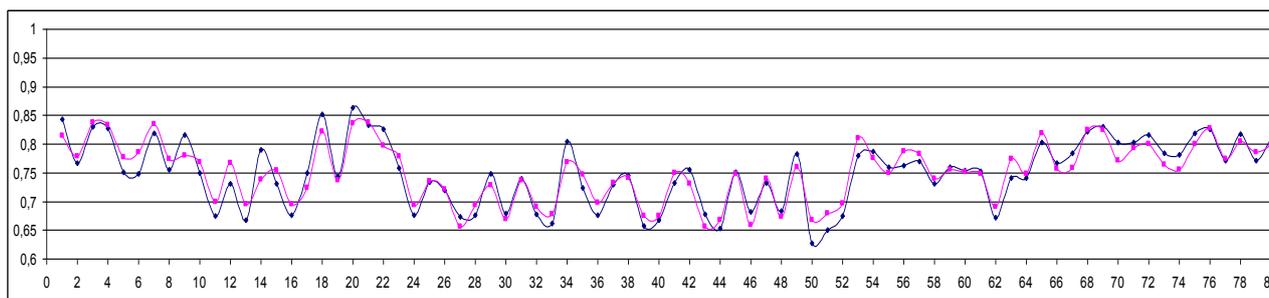


Fig. 5. Variation of RI in the prerenal AKI group

Subsequently it turned out that 27 patients of the prerenal group with less severe renal blood flow disorders responded well to pharmacological correction (nephroprotective measures) and diuresis was restored without hemodialysis treatment or 1-2 sessions were performed. So, we characterized this subgroup as a real prerenal AKI, which is not accompanied by severe tubular damage. In the remaining cases (53), AKI was evaluated as for the causal factor prerenal AKI.

In a group of patients with renal AKI, the significant variation of hemodynamic data was revealed too. Thus, the min value of Vps in the renal AKI group was 31.15 cm / sec, and max – 66.8 cm / sec. Accordingly, the min RI was 0.69, and max was 0.94 (Figure 6, 7).

In 17 patients of this group, very low Vps of 34.4 ± 0.5 cm / s was detected and Ved – 8.7 ± 0.3 cm / sec that was less than in the other patients of this group. The reason of such peculiarities, on our opinion, was the prevalence of nephrosclerosis versus severe oedema of renal parenchyma in these patients. The RI in this subgroup was relatively lower in comparison with the rest of the patients in renal AKI group ($p < 0.05$) and was 0.74 ± 0.02 . Subsequently, in these 17 patients kidney function did not restore definitively. They were isolated as a group of AKI on CRF or – with transformation in CRF. More than 70% of these patients were transferred from the ICU to continue treatment with program hemodialysis or kidney transplantation.

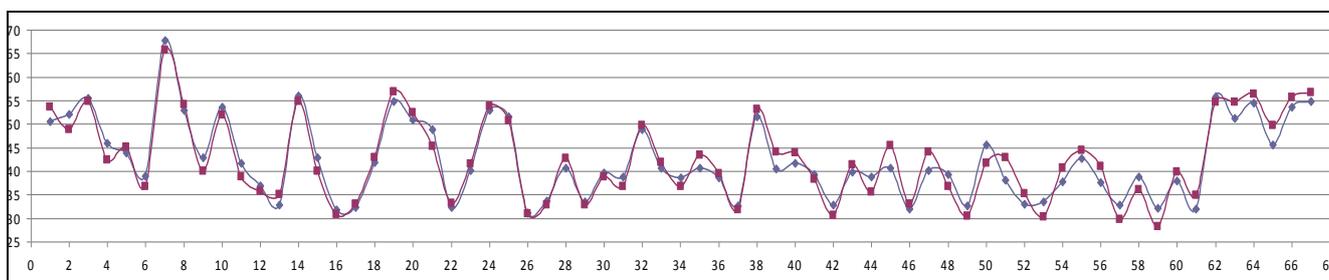


Fig. 6. Variation of Vps in the renal AKI group

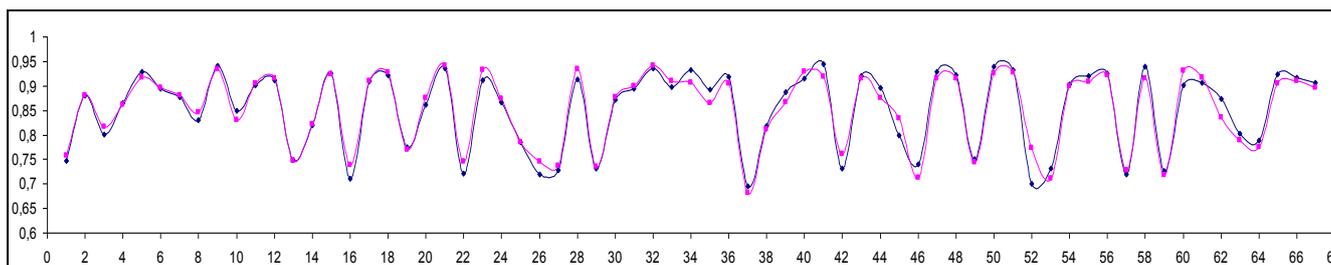


Fig. 7. Variation of RI indices in the renal AKI group

In polyuria phase of AKI, according to the data of complex ultrasound Dopplerography, restoration of arterial blood flow was observed in all groups, beginning with arched and interlobar arteries; normalization of the shape of the Doppler curve; reduction of echogenicity and thickness of the parenchyma, restoration of kidney size and cortico-medullary differentiation. Improvement of the clinical state, restoration of renal functions clearly correlated with improvement of renal hemodynamics and biometric parameters.

The absence of a reliable improvement in the parameters of renal blood flow, according to the data of Dopplerography, even in patients with restoration of diuresis, indicated loss of function and transformation in CRF.

As a model of the study, it is possible to present the diagnosis and treatment of patients with renal artery thrombosis of a single functioning kidney.

1. Diagnostics. The diagnostics based on: clinical manifestations – back pain, oliguria; The presence of risk factors for acute renal blood flow disorders: atherosclerosis, hypertension, permanent atrial fibrillation, history of myocardial infarction or transient cerebral circulatory disorders, malignant neoplasms, old age, wrinkling of one of the kidneys. The absence of expansion of the calyceal system in renal ultrasound examination was the reason for the Dopplerography;

2. Appointment of renal ultrasound in the Doppler mode allow fast, with minimal risk of complications and high accuracy to establish the diagnosis of renal artery thrombosis. Kidney ultrasound in the usual regime was uninformative in this pathology;

3. Carrying out x-ray endovascular intervention, including several steps: catheterization of the renal artery; tromboaspiration and balloon angioplasty of the vessel; selective thrombolysis (actilize 100 mg for 1 hour). Endovascular intervention was advisable, regardless of the oliguria duration, as AKI was

prerenal. High levels of creatinine in this case were not a contraindication for the X-ray-contrast introduction.

In all 11 this group patients, diuresis recovered immediately after intervention and pharmacological correction, despite prolonged anuria (up to 7 days). Conducting hemodialysis was not required.

Figures 8-11 show the renograms of the patient P., 58 years (7 days of anuria), which demonstrate the restoration of blood flow after catheterization of the left renal artery and local thrombolysis.

After removal of the thrombus, intravenous heparin was administered at a dose of 600 to 800 U /h under the control of the coagulogram indices (the target level of APTT was 60-80 s). Heparin therapy was combined with clopidogrel (75 mg / day). Warfarin was prescribed at the stage of diuresis recovery. When target values of INR (2.5-3.5) were reached, heparin was canceled.

Such nephroprotective therapy was organ-preserving, prevented the wrinkling of the kidney and the need for program hemodialysis (in contrast to the comparison group). So, a good quality of life in extremely severe group of patients was provided.

It was principally important to provide the pharmacological correction during endovascular intervention (thrombolytics, anticoagulants), otherwise the effect was short-lived.

To assess the influence of various factors on the outcome in AKI patients, a multifactor analysis was carried out. The results of treatment in AKI patients were evaluated as: survived, died.

18 factors were analyzed, as the factor signs in mathematical models construction: age, sex, AKI module (prerenal -1, renal-2, subrenal-3), duration of the disease before admission to ICU, time of diagnosis, duration of oligoanuria in days before admission to ICU, the presence of multiorgan failure (MOF), the origin of multiorgan disorders (primarily, secondary), the development of AKI in the presence of CRF,

presence of risk factors (no = 0, is = 1), pre-dialysis intensive therapy (early pharmacological correction, nephroprotection) before admission to the ICU (0-none, 1-conducted), pre-dialysis and peridialysis intensive therapy (nephroprotection in ICU) (1- early, 0 late), the need for

hemodialysis (without HD = 0, HD = 1), the number of hemodialysis, the need for artificial ventilation, the level of urea and creatinine on admission to the ICU, the highest level of urea and creatinine.

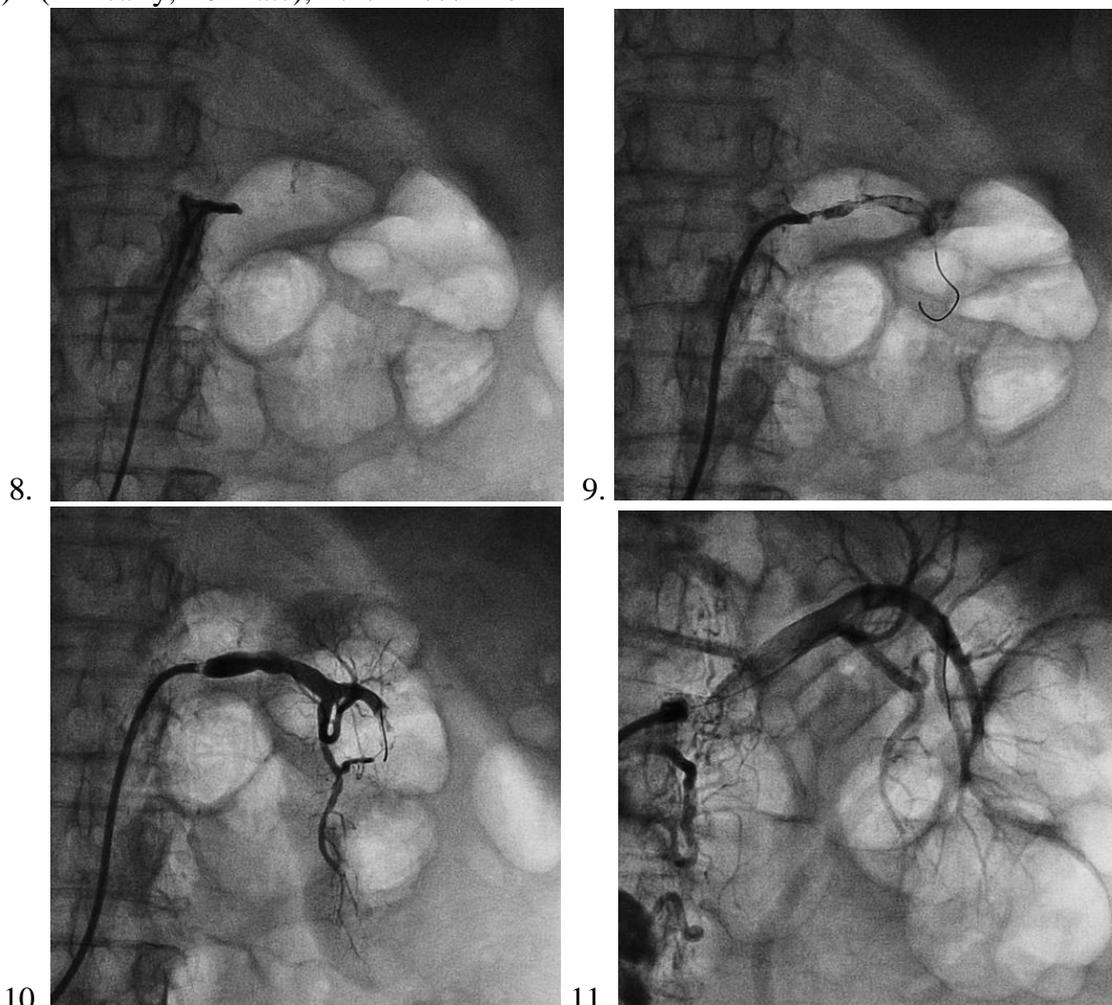


Fig. 8-11. Restoration of blood flow in the main trunk of the renal artery

To identify the factors most associated with the risk of death, a selection of significant sings was performed using the genetic algorithm (GA) method. As a result of the analysis, 2 factors were selected: the presence and origin of multiorgan disorders (primary MOF-1, secondary-2, absence-0) – (X1), nephroprotection in ICU (1 – early, 0 – late) (X2).

On the selected set of factor attributes, a linear neural network model for predicting the risk of death was constructed. The sensitivity of this model on the training set was 82.4% (95% CI 59.4% – 96.9%), specificity – 94.9% (95% CI 87.7% – 99.1%). On the confirming set, the

sensitivity of this model was 83.3% (95% CI 34.3% – 100%), specificity 100% (95% CI 92.3% – 100%).

Sensitivity and specificity on the training and confirming sets are not statistically significant ($p = 0.57$ and $p = 0.63$, respectively, when compared by the criterion χ^2), which indicates the adequacy of the model constructed.

To evaluate the significance of the two isolated factors from the total of 16 factor and assess the adequacy of the constructed models for predicting the risk of death, a method was used to compare the ROC curves of the models (Figure 12).

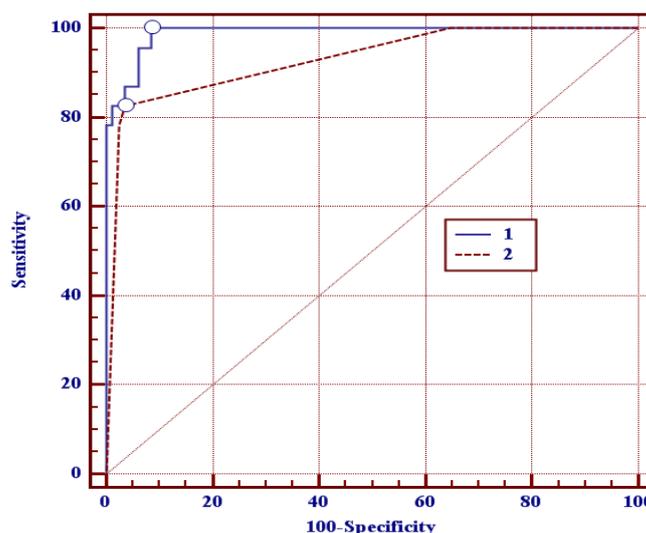


Fig. 12. ROC-curves of models for predicting the risk of death (0 – the optimal values of sensitivity and specificity of models are indicated, the curves are constructed on all 106 cases):

1 – linear neural network model built on all 16 factor attributes, 2 – linear neural network model built on 2 marked factor characteristics

When analyzed, it was established that the area under the ROC curve for the linear neural network model constructed on all 16 factor signs was $AUC_1 = 0.99 \pm 0.01$, for the linear neural network model constructed on the 2 selected factor signs, $AUC_2 = 0.93 \pm 0.03$.

Thus, a decrease in the number of factor signs from 16 to 2 does not lead to a significant change in the predictive qualities of the model, which indicates the high significance of the identified

factors; such as presence and origin of MOF (primary -1, secondary-2, absence-0) (X1), nephroprotection in the ICU (1 – early, 0 – late) (X2) to predict the risk of death. To determine the strength and direction of the influence of the 2 selected factors, a logistic regression model was constructed, the model is adequate ($\chi^2 = 66.0$ with the number of degrees of freedom $k = 3$, $p < 0.001$). The results of analysis of the regression coefficients of the model are presented in table 1.

Table 1

Coefficients of the 3-factor model for predicting the risk of a lethal outcome (logistic regression model)

Factor Sign	The prediction model coefficients value, $b \pm m$	The significance of the coefficient difference from 0, p	odds ratio, OR (95% CI OR)
X1 1. vs 0	17,5±3000	0,995	–
X12vs 0	15,2±3000	0,996	–
X2	–4,8±0,9	<0,001*	0,009 (0,001–0,050)

Note: * – the difference from 0 is statistically significant, $p < 0.05$.

Analysis of logistic regression model coefficients suggests that when early nephroprotection with pharmacological correction is performed in ICU, the risk of death is statistically significant ($p = 0.001$) decreased, OR = 0.009 (95% CI 0.001 – 0.050). The sensitivity of this model was 83.3% (95% CI 34.3% – 100%), specificity 100% (95% CI 92.3% – 100%).

In the study group, out of 250 patients, 38 patients died, the mortality rate was $15.2 \pm 0.5\%$. In the comparison group (107 patients), 28 people died, the mortality was $26.2 \pm 3.7\%$. The absolute risk of death was statistically significant ($p = 0.027$) decreased by 11% (95% CI 2.1-20.8).

Conclusion

Disturbances of hemodynamics in AKI according to Dopplerography of the kidneys are most severe when patients enter ICU (in the stage of oligoanuria). In all groups of AKI, the changes in arterial kidney blood flow are the same and show: a decrease in Vps and Ved, as well as an increase in RI at all levels and a significant increase in systolic-diastolic ratio. At the same time, the renal blood circulation values significantly differ depending on the AKI module, which is convincingly presented when comparing in groups of prerenal, renal and subrenal AKI.

The RI is an indicator that reflects the severity of AKI in the early days (on the first days of oliguria) and reliably correlates with the duration of the oligoanuria stage, the main retrospective marker of the severity of tubulointerstitial kidney damage.

Thus, the implementation of complex ultrasound with Dopplerography of the kidney vessels in AKI patients allowed:

- 1) clarify the cause of AKI;
- 2) to identify patients with real prerenal AKI and AKI prerenal for causal factor.
- 3) in the renal AKI group, reveal patients with AKI on CRF, or transformation AKI into CRF.
- 4) to assess the severity of kidney damage upon admission and appoint an individual intensive care program with pharmacological correction (nephroprotection).

This confirms our hypothesis that evaluation of renal blood flow by the method of Dopplerography and the introduction of individual pharmacological correction in intensive therapy AKI patients in ICU improves the results of treatment of these patients.

Conflicts of interest

The authors have no conflict of interest to declare.

References

1. Waikar SS, Liu KD, Chertow GM. Diagnosis, Epidemiology and Outcomes of Acute Kidney Injury. *Clin. J. Am. Soc. Nephrol.* 2008;3:844-861. doi: 10.2215/CJN.05191107. [PubMed]
2. Case J, et al. Epidemiology of acute kidney injury in the intensive care unit. *Crit. Care Res. Pract.* 2013;2013:479730. doi: 10.1155/2013/479730. [PubMed]
3. Kes P, Jikic N. Acute kidney injury in the intensive care unit. *Bosn. J. Basic. Med. Sci.* 2010.10(Suppl. 1):S.8-12. [PubMed]
4. Singbartl K, Kellum JA. AKI in the ICU: definition, epidemiology, risk stratification, and outcomes. *Kidney Int.* 2012;81(9):819-825. doi: 10.1038/ki.2011.339. [PubMed]
5. Hsu RK, et al. Temporal Changes in Incidence of Dialysis- Requiring AKI. *J. Am. Soc. Nephrol.* 2013;24(1):37-42. doi: 10.1681/ASN.2012080800. [PubMed]
6. Chertow G, et al. Prealbumin, mortality, and cause-specific hospitalization in hemodialysis patients. *Kidney Int.* 2005;68(6):2794-2800. doi: 10.1111/j.1523-1755.2005.00751.x [PubMed]
7. Wang HE, et al. Acute Kidney Injury and Mortality in Hospitalized Patients. *Am. J. Nephrol.* 2012;35:349-355. doi: 10.1159/000337487. [PubMed]
8. Thakar CV, et al. Degree of acute kidney injury before dialysis initiation and hospital mortality in critically ill patients. *Int. J. Nephrol.* 2013;213:1-7. ID 827459. doi: 10.1155/2013/827459. [PubMed]
9. Hoste EA, Schurgers M Epidemiology of acute kidney injury: how big is the problem? *Crit. Care Med.* 2008;36(4):146-151. doi: 10.1097/CCM.0b013e318168c590. [PubMed]
10. Bagshaw SM, George C, Bellomo R. A comparison of the RIFLE and AKIN criteria for acute kidney injury in critically ill patients. *Nephrol. Dial. Transplant.* 2008;23(5):1569-1574. doi: 10.1093/ndt/gfn009. [PubMed]
11. Piccinni P, et al. NEFROINT investigators. Prospective multicenter study on epidemiology of acute kidney injury in the ICU: a critical care nephrology Italian collaborative effort (NEFROINT). *Minerva Anestesiol.* 2011;77:1072-1083. [PubMed]
12. Lameire N, et al. The prevention of acute kidney injury in depth narrative review: Part 2. *NDT Plus.* 2009;1:1-10. doi: 10.1093/ndtplus/sfn199. [PubMed]
13. Tomilina NA, ed.: Gelfand BR, Saltanov AI. Acute Renal Failure. Intensive therapy: national leadership. Vol. 1. Moscow: GEOTAR-Media; 2011:856-879. (In Russian)
14. Gelfand BR, Saltanova AI. Intensive therapy for acute disorders of kidney function. Ch. 7 in book. Intensive therapy: national leadership. Vol. 1. Moscow: GEOTAR-Media; 2011:856-907. (In Russian)
15. Baxter GM, Sidhu PS. Ultrasonic examination of the urinary system/Trans. With English. Moscow: Medpress-inform; 2008. 243 p. (In Russian)
16. Dugan IV, Medvedev VE. Color dopplerography in the diagnosis of kidney disease. Principles and practical recommendations for use. Kiev; 2008. 138 p. (In Russian)
17. Zubarev AV. Doppler ultrasonic methods of research in uronephrology. Method of color duplex

scanning (mapping) in the study of the kidneys and upper urinary tract. Moscow: Medicine; 2004: p. 325-352. (In Russian)

18. Dewitte A. Doppler resistive index to reflect regulation of renal vascular tone during sepsis and acute kidney injury. *Crit Care*. 2012;16(5):R165. doi: 10.1186/cc11517. [PubMed]

19. Gheisari A., Haghihi M. Diagnostic value of Doppler ultrasound in differentiating prerenal azotemia from acute tubular necrosis. *Saudi J. Kidney Dis. Transpl*. 2006;17(2):68-70. [PubMed]

20. Schnell D., Darmon M. Doppler to assess renal perfusion in the critically ill: a reappraisal. *Intensive Care Med*. 2012;38(11):1751-1760. doi: 10.1007/s00134-012-2692-z. [PubMed]

21. Lerolle N, et al. Renal failure in septic shock: predictive value of Doppler – based renal arterial resistive index. *Intensive Care Med*. 2006;32(10):1553-1559. doi: 10.1007/s00134-006-0360-x. [PubMed]

22. Schnell D, et al. Renal resistive index better predicts the occurrence of acute kidney injury than cystatin C. *Shock*. 2012;38(6):592-597. doi: 10.1097/SHK.0b013e318271a39c. [PubMed]

23. Dewitte A, Coquin J, Meyssignac B, Joannès-Boyau O. Doppler resistive index to reflect regulation of renal vascular tone during sepsis and acute kidney injury. *Crit Care*. 2012;16(5):R165. doi: 10.1186/cc11517. [PubMed]

24. Schnell D, Derudder S, Harrois A, Pottecher J, et al. Renal resistive index better predicts the occurrence of acute kidney injury than cystatin C. *Shock*. 2012;38(6):592-597. doi: 10.1097/SHK.0b013e318271a39c. [PubMed]

25. Shramenko KK, Shkarbun L.I. Possibilities of dopplerography in the choice of nephroprotection tactics of acute kidney injury for various etiologies. *Emergency medicine*. 2011;7-8:144-146. [Abstract]

26. Shramenko KK, Shkarbun LI. Comparative Evaluation of Changes in Renal Blood Flow in Different Types of Acute Kidney Injury. *Emergency medicine. [Medicina neotlozhnyh sostoyanij]*. 2014;4:78-82. (In Russian) [eLIBRARY]

27. Lyakh YuE, Gurianov VG. Mathematic modeling for classification problems in biomedicine. *Ukrainian Journal of Telemedicine and Medical Telematics*. 2012;10(2):69-76. [Abstract]

28. Petri A. *Visual statistics in medicine*. Moscow: GEOTAR-MED; 2003. 144 p. [Abstract]

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