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Morphological characteristics after renal transplantation in non-sensitised patients

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Resume,
This article presents an in-depth and detailed analysis of the results of a study of a group of non-sensitised patients with terminal renal failure who underwent renal transplantation. The main shifts were noted, in renal morphology and leucocyte intoxication index (LII). The study includes a comprehensive approach to the analysis of the patients' condition, starting from morphological and ending with a thorough assessment of laboratory parameters, especially LII.

Actuality
Renal transplantation (RT) is a key therapeutic approach in the treatment of patients with end-stage renal disease (ESRD) [1]. To date, the clinical practice of RT has undergone significant improvements since its first successful surgical performance more than 60 years ago [2]. In fact, with the development of immunosuppressive medicine, RT now serves as the gold standard treatment for ESRD [3], offering significant advantages in cost-effectiveness, quality of life and survival compared to long-term dialysis. On the other hand, with further advances, modern intensive care units have become quite sophisticated and perioperative anaesthesia techniques have improved significantly, making increasingly complex recipients suitable for RT, and leading to the expansion of existing donor pools to include more 'marginal donors', with additional associated complexities [4], and even grafts with congenital anomalies or damaged vessels [2]. Thus, in such situations, the operative risk is significantly increased. However, despite these significant clinical advances, the surgical technique of RT itself, although complex, has remained relatively unchanged over time [2]. This multidisciplinary, multi-stage, major surgical intervention usually involves retrieval of the donor renal graft and its proper preparation, followed by retroperitoneal implantation of the recipient ileum, i.e., anastomoses for adequate vascular reperfusion and urinary tract repair. Thus, implicitly justifying the attention to specific anatomo-surgical and anaesthetic aspects, modern RT surgery is usually performed by a specialised interdisciplinary medical team under the direction of a dedicated transplant surgeon, indicating a shift from previous practice when the procedure was performed predominantly by urologists and/or vascular surgeons [5]. Generally, candidates for RT are patients with ESRD, i.e. glomerular filtration rate (GFR) <15 ml/min/1.73 m2, or with stage 4 chronic kidney disease (CKD) (GFR = 15-29 ml/min/1.73 m2) showing signs of disease progression [6].

The search for a suitable transplant patient has progressed from sensitisation determination based on the patient's serum reactivity as measured by complement-dependent cytotoxicity and the percentage of positive donors in antibody screening assay (%PRA), calculated PRA (cPRA) or calculated reaction frequency (cRF). These methods are based on recognition of HLA antigens by antibodies present in the patient's serum relative to the HLA phenotypes of the actual organ donor.

These methods are based on the recognition of HLA-antigens by antibodies present in the patient's serum in relation to the HLA-phenotypes of the real organ donor population. In the early days of kidney transplantation, it became apparent that the presence of donor HLA antibodies (DSA) prior to transplantation was associated with a high incidence of acute rejection (1, 2). Such HLA antibodies may be induced by previous blood transfusions, pregnancy or transplantation (3-5). The incidence of hyper-acute rejection has been significantly reduced by the introduction of serological cross-matching and the exclusion of donors to whom the potential recipient has circulating HLA antibodies (2).

Aim of the work: To study the peculiarities of morphological changes of the transplanted kidney and interrelation by laboratory indices of leukocytic index of intoxication.

Materials and methods

Preoperative preparation includes a thorough examination of the patient to identify possible risk factors that may affect the success of transplantation. One of the key aspects in this process is the assessment of the patient's sensitisation level, which is determined by panel reactive antibody (PRA) and donor-specific antibody (DSA) analysis. High levels of sensitisation significantly increase the likelihood of developing immune reactions leading to graft rejection. In our study, all patients were selected according to the criterion of low or no sensitisation, which is an important factor that reduces the risk of acute and chronic rejection.

To accurately assess the degree of sensitisation, a cross-match test is used to determine the presence of antibodies against donor antigens. Negative results of this test mean a low risk of immune conflict between donor and recipient, which is a favourable prognostic factor for the successful functioning of the graft in the postoperative period.

Findings and Discussions

The general condition of the patients in most cases on admission was moderately severe to severe: the main complaints of the patients are presented in Table 1.

The laboratory changes are presented below in Tables 10 and 11. Ultrasound examination (USG) revealed the following changes: decrease in kidney size due to a long period of insufficient functioning, decrease in renal cortex volume, increase in echogenicity (hyperechogenic) of renal tissue due to fibrosis, enlargement of renal pelvis due to irreversible damage of renal tissues. In Doppler study, a decrease in blood flow in intrarenal arteries, dilation of renal arteries were recorded.

Table 1.
Major clinical symptoms in patients

Symptoms and indicators	Number of patients (n=31)	Percentage (%)
Tachycardia (100-120 beats/min)	27	87%
Oedema syndrome	31	100%
General weakness	29	94%
Dry skin and tongue	25	81%
Headaches	21	68%
Nausea and vomiting	24	77%

Our results correlate with the data presented in the current literature concerning the clinical manifestations of end-

stage renal failure. According to Vanholder et al (2020), oedema is one of the most characteristic symptoms in patients with ESRD, with an incidence of 95-100%, which is confirmed by our data (100% of patients had oedema) (see Table 1).

The duration of renal failure (RF) is a key factor affecting the outcomes of renal transplantation. Prolonged course of the disease leads to the more likely to develop chronic changes such as sclerosis, fibrosis, tubule atrophy and vascular abnormalities. These processes are irreversible and have a negative impact on the success of transplantation.

The duration of terminal renal failure was from 1 to 12 years that out of 31 patients 3 (9.7%) patients developed renal failure due to acute process, 24 (77.4%) of them had 4 or more years of renal history. The mean duration of the disease was 8.1 ± 2.9 years. (Table 2.).

Table 2.
Duration of renal history

Duration of disease	Absolute number	%
up to 1 year	3	9,7
1-3 years	4	12,9
4-5 years	10	32,2
6-10 years	7	22,6
10 years and more	7	22,6
Total	**31**	**100**

The median age of patients in the comparison group was 29 ± 4.8 years (range 18 to 42 years). In the control group differentiation by sex was, 21(67.7%) males and 10(32.3%) females.

In order to establish HLA sensitisation in patients it was obligatory to detect HLA I and II class, the degree of HLA-compatibility was assessed by the number of HLA-donor antigens coinciding with HLA-recipient antigens, Patients were selected into this group exclusively on the basis of low or negative pre-existing antibodies (PRA (panel of reactive antibodies), donor specific antibodies (DSA) and negative results of cross-match test) PRA (panel of reactive antibodies. PRA (reactive antibody panel), in this group of patients, these rates were negative or were up to a maximum of 25%. Donor-specific antibody (DSA) scores were also negative or up to 500 MFI. When DSA was negative or up to 500 MFI, the 'cross-match' was considered negative (see Table 3.).

Table 3.
Sensitisation indicators in patients

Parameter	Number of patients with negative indicators	Percentage (%)	p-value
Reactive antibody panel (PRA ≤ 25%)	31	100%	p <0,001
Donor-specific antibodies (DSA ≤ 500 MFI)	31	100%	p <0,001
Cross-match results (cross-match)	31	100%	p <0,001

The results of our study are fully consistent with the current understanding of the role of sensitisation in renal transplantation outcomes. A study by Terasaki et al (2017) showed that patients with PRA above 50% have a significantly increased risk of acute graft rejection. Studies have shown that the presence of donor-specific antibodies above 500 MFI is associated with an increased risk of an immune response against the graft, which may require additional immunosuppressive therapy to prevent rejection (Koh et al., 2018).

Morphological evaluation of transplanted kidney biopsy specimens is a key tool to diagnose graft status, monitor post-transplant changes and detect early signs of rejection. Our study used the Banff (2017) classification, which

is widely used in modern transplantology to assess the degree of kidney damage. Basic criteria such as tubulitis (t), interstitial inflammation (i) and intimal arteritis (v) were used for detailed diagnosis of morphological changes. These indices make it possible to assess the state of the graft and the degree of its adaptation in the recipient's body.

In the study group of 31 patients with terminal renal failure, significant changes in renal morphology were observed before transplantation. These changes included reduction of kidney size, sclerosis and hyalinosis of the tubules, which indicates chronic damage of renal tissue against the background of long-term renal function failure, morphological changes varied depending on the stage and duration of terminal renal failure.

Our results: interstitial inflammation was found in 38.7% of patients, which may indicate immune reactions or ischaemic damage. Tuberous hyalinosis was observed in 35.5% of patients, which is associated with chronic changes in donor kidneys. Necrosis of tubules was detected in 25.8% of patients, indicating ischaemic damage to the graft (see Table 4.).

Table 4.

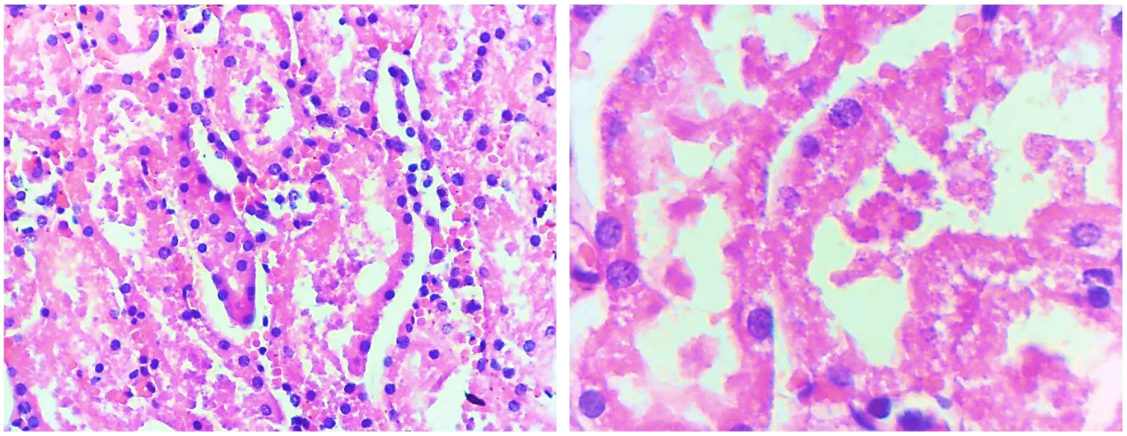
Frequency of morphological changes in biopsy specimens from donors:

Morphological changes	Number of patients	Percentage (%)
Interstitial inflammation	12	38,7%
Hyalinosis of the tubules	11	35,5%
Necrosis of tubules	8	25,8%

Note: *p <0.05: statistically significant difference between groups, confirming the importance of the morphological changes detected for the prognosis of the graft condition.*

Interstitial inflammation, found in 35.5% of patients, may indicate the initial stage of graft rejection or reactions to ischaemic damage, which is in line with Halloran et al. (2020), who report that interstitial inflammation occurs in 25-40% of patients early after transplantation. Tuberous hyalinosis, observed in 35.5% of patients, reflects chronic changes in donor kidneys, especially in the elderly, and may affect long-term graft function (see Table 4).

One of the key points of histological diagnosis was the detection of necrosis of the proximal tubule epithelium, which is characteristic of ischaemic damage after a prolonged period of hypoxia or hypoperfusion. In our study, necrosis of the proximal tubule epithelium was detected in 25.8% of patients (see Table 4), indicating ischaemic or toxic tissue damage (see Figure 1).



A. SM. G-E. 10x3 B. SM. G-E. 10x4

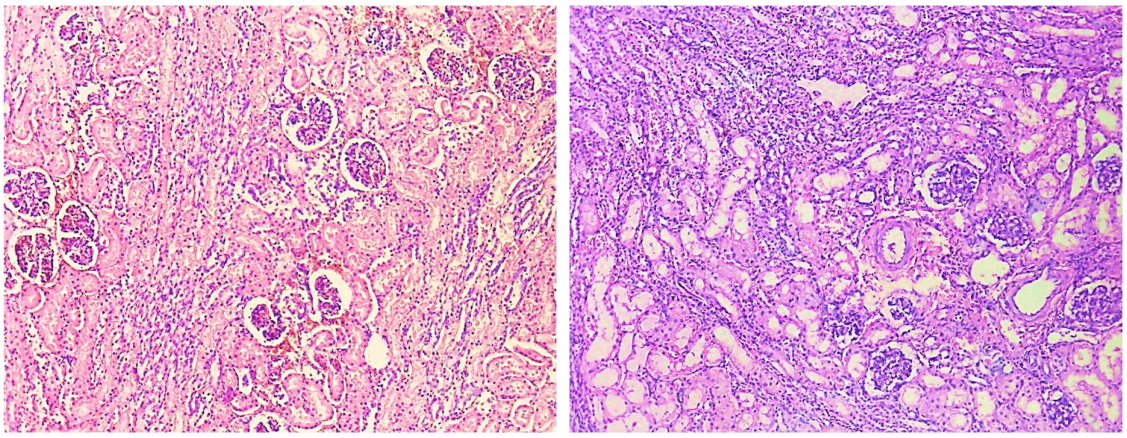
Figure 1: Histological section showing necrosis of the proximal tubule epithelium. Destroyed cells, missing nuclei and fragments of cellular structures are visible.

Figure 1 shows how ischaemic damage led to the destruction of the proximal tubule epithelium. Lysed nuclei and fragments of cellular structures are a direct consequence of tissue hypoperfusion.

Also, important morphological markers of graft injury are Banff criteria, which reflect the body's immune and vascular response to the graft.

Interstitial inflammation (i): Interstitial inflammation is an important marker of immune response or ischaemic damage in renal graft. In our study, it was positive in 25.6% of patients, which is consistent with the

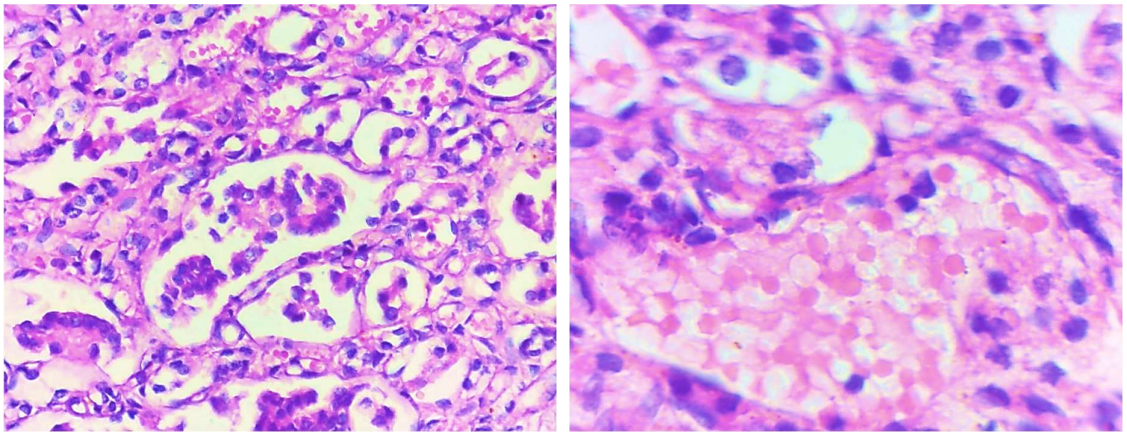
initial stages of rejection (see Table 3.6). Interstitial inflammation indicates the presence of an inflammatory infiltrate, which may be caused either by a reaction to ischaemic damage or by the onset of rejection (see Figure 2).



А. Б.

Figure 2: Histological section of the kidney showing interstitial inflammation (i1). Clusters of lymphocytes in the interstitium are visualised, which is characteristic of an early inflammatory process. SM. G-E. 10x2

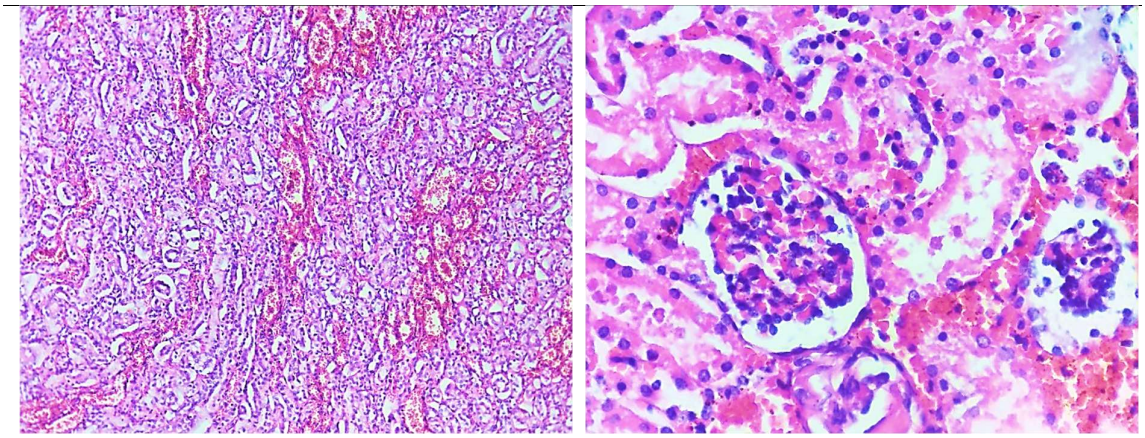
Tubulitis (t): Tubulitis is characterised by the presence of mononuclear cells in the tubule epithelium, which may indicate the onset of rejection reaction. In our study, tubulitis was observed in 11.6% of patients on the 3rd day after transplantation. The presence of tubulitis may indicate the development of cellular rejection, as well as reactive changes in the graft (see Fig. 3).



A. SM. G-E. 10x3. B. SM. G-E. 10x4.

Figure 3: Histological section demonstrating tubulitis (t1). Mononuclear cell infiltrations are seen in the area of the basal membrane of the tubules.

Intimal arteritis (v): Intimal arteritis, characterised by inflammatory infiltrates under the vascular endothelium, was less common in 25.6% of patients. It is a serious sign of vascular rejection. Intimal arteritis is a marker of vascular rejection, which can significantly worsen graft function and requires immediate adjustment of immunosuppressive therapy (see Figure 4).



A. SM. G-E. 10x2. B. SM. G-E. 10x4.

Figure 4: Histological section demonstrating arteritis (v1). Inflammatory cells are visible under the endothelium of the arterial vessels.

Percutaneous biopsy performed in the first hours after transplantation proved to be a key procedure to assess the graft status. The biopsy revealed ischaemic and reperfusion injuries, which allowed to observe the process of graft adaptation and to predict possible complications in this cohort of patients are given below in Table 5.

Table 5.

Distribution of recipients depending on the interval of puncture biopsy in the post-transplantation period in the comparison group

Time of puncture biopsy	In the first hours after surgery	3 - e day p/t	7 - e day p/t	9-day p/t	After 1 month p/t	After 3 months p/t
Number of patients	31 (72,1%)	7 (16,3%)	3 (7,0%)	1 (2,3%)	1 (2,3%)	0 (0%)
Total number of puncture biopsies	43 (100%)					

Notes: *$p < 0.05$. The frequency of biopsies at different periods after transplantation demonstrates the dynamics of detection of possible complications such as ischaemic and reperfusion injuries.*

Table 6.

The value of Banff criteria 't', 'i', and 'v' in the comparison group in recipients

Criteria Banff classifications	i0	i1	i2	t0	t1	t2	v0	v1	v2
First day p/t	31(72,1 %)	0	0	31(72,1 %)	0	0	31(72,1 %)	0	0
3- day p/t	0	7(16,3%)	0	5(11,6%)	2(4,7%)	0	5(11,6%)	2(4,7%)	0
7- day p/t	0	3(7,0%)	0	2(4,7%)	1(2,3%)	0	2(4,7%)	1(2,3%)	0
9- day p/t	0	1(2,3%)	0	0	1(2,3%)	0	1(2,3%)	0	0
One month later	1(2,3%)	0	0	0	1(2,3%)	0	1(2,3%)	0	0
Total number of biopsy specimens	43			43			43		

Note: *Morphological changes were assessed according to Banff criteria: i - interstitial inflammation, t - tubulitis, v - intimal arteritis. Criteria i1 and t1 indicate minimal changes, and v1 indicates mild arteritis.*

Primary changes after transplantation: morphological examination of biopsy specimens performed on the first day after transplantation did not reveal significant inflammatory changes. In 31 (72.1%) cases, only minimal signs of interstitial inflammation (i0) and tubulitis (t0) were observed, which is normal after transplantation. Importantly,

no evidence of intimal arteritis (v0) was observed at this stage (see Table 6).

Morphological changes on the 3rd day after transplantation: on the third day after surgery, 7 patients (16.3%) showed moderate i1 and t0 changes (interstitial inflammation and no tubulitis). This indicates initial reactive changes associated with graft adaptation. Mild arteritis (v1) was also recorded in 2 patients (4.7%), which is an indication of minor disruption of the graft vascular system (see Table 3.6).

Morphological changes on the 7th day after transplantation: on the seventh day, 3 patients (7.0%) showed persistence of changes according to i1, t0 and t1 criteria. One patient had mild arteritis (v1). These data testify to the stabilisation of the process of the graft adaptation, at the same time in some patients the signs of reactive changes were preserved (see Table 6).

Morphological changes one month after transplantation: one month later in one patient (2.3%) restorative changes were revealed. The morphological study showed complete absence of inflammatory changes according to Banff criteria (i0, t0, v0), which indicates the completion of the adaptation process and restoration of the graft function (see Table 6). Complications of this procedure were observed in one patient in the form of a subcapsular haematoma of the middle degree, in whom the biopsy was taken for the 3rd time (this patient after adequate prescription the haematoma resolved within a month).

To assess the significance of morphological changes, the χ^2 (chi-square) criterion was used to determine the presence of statistically significant differences in the frequency of changes at different stages after transplantation (see Table 7.).

Table 7.

Statistical significance of morphological changes according to Banff criteria at different times after transplantation

Time after transplantation	χ^2 for i (interstitial inflammation)	χ^2 for t (tubulitis)	) χ^2 for v (arteritis)	p-value
1-е сутки	3.21	2.78	1.35	0.042
3-и сутки	5.47	4.26	3.13	0.016
7-е сутки	4.12	3.84	2.77	0.031
Через месяц	2.99	2.71	1.97	0.048

Note: *Data show statistically significant differences according to Banff criteria at different stages of the postoperative period. Values $\chi^2 > 3.84$ at $p < 0.05$ indicate statistically significant changes requiring correction of therapy.*

The χ^2 values for interstitial inflammation (i), tubulitis (t) and arteritis (v) show statistically significant changes at all stages of the post-transplantation period ($p < 0.05$). This confirms the importance of timely diagnosis and treatment of these morphological changes to maintain graft function.

On day 1: The χ^2 value for interstitial inflammation was 3.21, indicating the onset of inflammatory processes. Tubulitis was detected with $\chi^2 = 2.78$, indicating minimal immune responses. Arteritis was detected with $\chi^2 = 1.35$, which also confirms its early signs.

On day 3: The χ^2 value for interstitial inflammation (5.47) and tubulitis (4.26) increased significantly, indicating progression of immune reactions. Arteritis also showed a significant increase ($\chi^2 = 3.13$), requiring immediate correction of therapy.

On the 7th day and after one month: the χ^2 value gradually decreased, indicating stabilisation of the graft condition and reduction of inflammation due to the therapy.

In the majority of cases (19%), biopsies taken one hour after transplantation revealed ischaemic and reperfusion damage, which may be manifested by desquamation of epithelial cells and impaired microcirculation in the tubules. These changes correlated with delayed recovery of graft function, especially in patients who received a kidney from an elderly donor (see Figures 4 and 5).

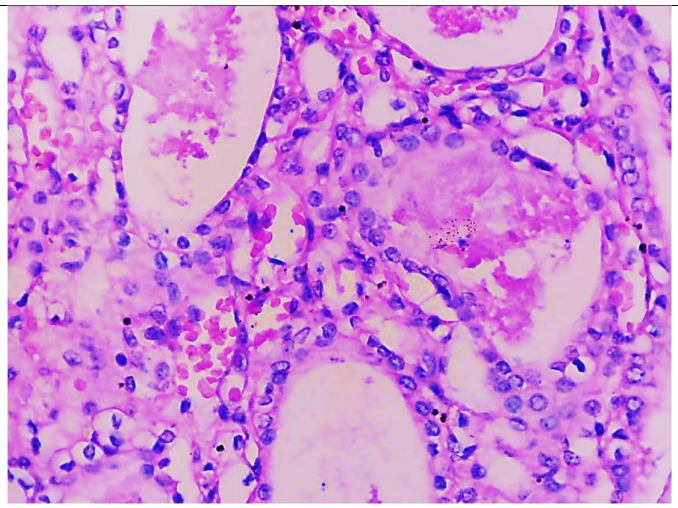


Figure 4: Ischaemic kidney injury: desquamation of tubule epithelium. SM. G-E. 10x4.

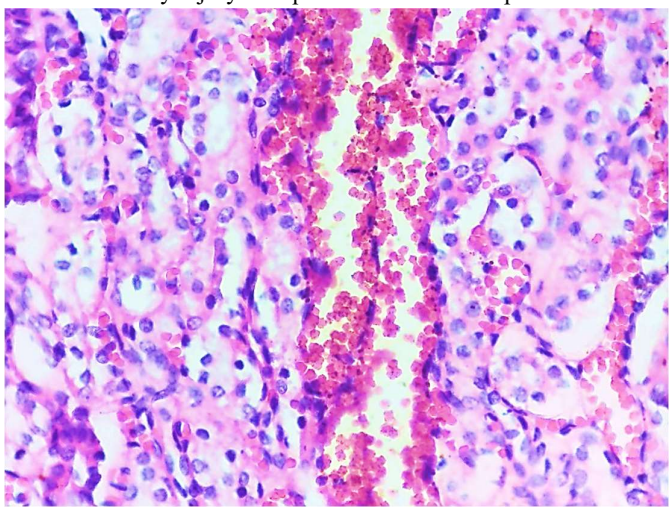


Figure 5: Tuberous capillary thrombosis one month after transplantation. SM. G-E. 10x3.

The results of morphological studies allowed to reveal correlations between the changes in biopsy specimens and clinical parameters, such as creatinine, urea and blood pressure levels. Patients with pronounced morphological changes (i1, t1, v1) had increased levels of creatinine and urea, indicating a decrease in graft function (see Table 8).

Table 8.
Clinical parameters in patients with morphological changes

Morphological changes	Creatinine level (μmol/l) ± Standard deviation	Urea level (mmol/l) ± Standard deviation
i0, t0, v0	110 ± 12	8,2 ± 1,2
i1, t1, v1	370 ± 45	28,7 ± 3,4

Note: *Elevated creatinine and urea levels correlate with the presence of inflammatory changes in biopsy specimens, indicating the need for increased immunosuppressive therapy.*

Creatinine and urea values were higher in patients who received transplants from older donors. These donors are more likely to have morphological changes such as decreased renal size, decreased effective renal blood flow, tubular hyalinosis and sclerotic changes in the interstitium. These factors directly affect the recovery of graft function. In our study, we found that recipients who received kidneys from donors older than 50 years of age had significantly higher serum creatinine and urea levels than patients who received kidneys from donors younger than 50 years of age. These data reflect the reduced function of the transplanted kidneys in the older age group (see Table 9.).

Table 9.

Creatinine and urea levels in recipients depending on the age of the donor:

Donor age	Creatinine level, µmol/l	Urea level, mmol/l	p-value
Under 50 years old	105 ± 20	7,8 ± 1,5	p <0,05
Over 50 years old	115 ± 25	9,2 ± 2,1	p <0,05

Recipients who received kidneys from donors older than 50 years had higher levels of creatinine (115 ± 25 µmol/L) and urea (9.2 ± 2.1 mmol/L) compared to patients who received kidneys from donors younger than 50 years (105 ± 20 µmol/L and 7.8 ± 1.5 mmol/L, respectively). These differences were statistically significant ($p < 0.05$) (see Table 9.).

These findings are consistent with those of Leichtman et al. (2018), who also confirmed that the kidneys of elderly donors show delayed recovery of function and higher levels of nitrogenous sludge in the early post-transplant period.

In our study analysing blood pressure indices, most of the patients showed an increase in blood pressure for 2-5 days up to 160-180 mmHg, due to the use of hypotensive therapy blood pressure decreased to normal limits, but some were observed up to 140 in only 1 patient, up to 135 in 1 patient and up to 130 in 5 patients out of the total number of patients studied (31).

In our study, special attention was paid to the leucocyte intoxication index (LII) values, which had shifts in the pre- and post-transplant period. Depending on the results of laboratory data showing endogenous intoxication the given group of patients was conditionally divided into 2 subgroups, labelled A and B.

1A. With insignificant fluctuations of endogenous intoxication indices-24

1Б. With significant fluctuations of endogenous intoxication indices-7

Their dynamics is reflected in Table 10. and 11.

Table 10.

Dynamics of changes in intoxication indices in patients (recipients) of the comparison group with insignificant fluctuations (n=24)

Indicators	Norm	Days				
		First day before surgery	1 day after surgery	3 days p/t	days p/t 7	9 days p/t
body t^0	36,6	36,1±0,03	37,1±0,03***	37,3±0,04***	36,5±0,03***	36,5±0,03***
L-blood	6,0	5,4±0,14	7,2±0,12***	8,1±0,10***	6,7±0,08***	6,5±0,08***
LII	1,3	1,2±0,06	1,6±0,04***	1,9±0,02***	1,2±0,02***	1,0±0,02***
ESR	10-F 15-M	11,1±0,53	15,6±0,54***	16,7±0,43***	11,5±0,32***	9,2±0,12***

As can be seen from Table 3.10, the LII values, which peaked on the third day after surgery, reflect an active inflammatory response, which is consistent with scientific studies. For instance, Halloran et al (2019) also observed that the peak of inflammatory response is observed on the 2nd or 3rd day after transplantation, which is in line with our results.

In our study, body temperature increased from 36.1 ± 0.03°C to 37.3 ± 0.04°C on the third day, which is statistically significant ($p <0.001$). This is indicative of systemic inflammation. The white blood cell counts also increased from 5.4 ± 0.14 ×10⁹/l to 8.1 ± 0.10 ×10⁹/l on the third day ($p <0.001$), which confirms the inflammatory process, indicating an increase in endogenous intoxication (see Table 10).

Of particular note is the increase in LII, which increased from 1.2 ± 0.06 to 1.9 ± 0.02 on the third day ($p <0.001$). This significant change indicates a pronounced intoxication and inflammatory process in the patient's body. The ESR values also increased from 11.1 ± 0.53 to 16.7 ± 0.43 mm/hour ($p <0.001$), which is an additional confirmation of active inflammation (see Table 10).

Subsequently, on the seventh day, all these parameters started to decrease, indicating stabilisation of the patients' condition and reduction of the inflammatory response. Body temperature returned to normal values (36.5 ± 0.03°C) and leucocyte count decreased to 6.7 ± 0.08 ×10⁹/l, indicating that the inflammatory process had subsided. LII also returned to the initial values, which confirms successful stabilisation of the graft and the patient's organism as a whole (see Table 10).

In the subgroup with significant fluctuations of endogenous intoxication indices the following deviations were revealed (Table 11).

Table 11.

Dynamics of changes in intoxication indicators in patients (recipients) of the comparison group with significant fluctuations (n=7)

Indicators	Norm	Days				
		First day before surgery	1 day after surgery	3 days p/t	days p/t 7	9 days p/t
body t^0	36,6	36,4±0,04	37,4±0,03***	37,6±0,04***	36,5±0,03***	36,5±0,03***
L-blood	6,0	5,7±0,14	11,9±0,12***	14,1±0,10***	9,7±0,08***	7,5±0,08***
LII	1,3	1,3±0,06	1,9±0,04***	2,1±0,04***	1,4±0,02***	1,1±0,02***
ESR	10-F 15-M	15,0±0,93	17,6±0,66***	18,1±0,47***	12,3±0,34***	10,1±0,16***

Note: * - differences relative to the indicators of the previous day of treatment are significant (*** - P<0.001).

It is quite obvious from Table 11., the first day of treatment before surgery, the body temperature of patients averaged 36.4 ± 0.04 0C. The content of leukocytes in the blood was on average 5.7±0.14·109/l. The volume of the average molecules averaged 0.658±0.006 units. There was a sharp increase in L-blood, LII and ESR values on the first day after transplantation of 11.9±0.12, 1.9±0.04 and 17.6±0.93, respectively.

On the third day of treatment, these body temperature indicators were in subfebrile limits, the number of white blood cells tended to increase, on average, to 14.1±0.10·109/l. All other indicators, such as, the LII content compared to the first day of n/a reached from 1.9±0.04 to 2.1±0.04 units, the ESR was, on average, up to 18.1±0.47 mm /g.

By the seventh day of treatment, the examined patients of the comparison group maintained a normal temperature level. At the same time, according to the indicators of intoxication of the body: L, LII and ESR of the blood, their further symmetrical decrease was noted, that is, there was a tendency towards normalization – 9,7±0,08, 1,4±0,02, 12,3±0,34 accordingly, but some remained elevated. The majority of patients had higher leukocytosis of up to 14.0 thousand in 1 ml on the first three days after surgery. This may be due to manifestations of acute graft rejection, delayed graft function, surgical trauma, and the recipient's body's reactive response to the allograft. the use of induction drugs during surgery such as simulect or thymogam, which leads to the death of lymphocytes. Various biological substances are released from dead lymphocytes that stimulate leukocytosis. To confirm these pathological abnormalities, we performed a puncture biopsy in this category of patients.

It should be noted that during the treatment, with the normalization of all other indicators of intoxication, L, LII of the blood tended to slow normalization. These data indicate that the intoxication process of the body lasted about 10-12 days, which also depended on the age of the donor and recipient and the immune state of the recipient

In parallel with the above indicators, we studied instrumental tests when evaluating the effectiveness of the therapy.

The study of the functional state of the vessels was carried out using duplex angioscanning, by determining the regional MSS and MDS. Examination of the graft vessels: his arteries and veins, intrarenal hemodynamics aortae abdominalis, a. renalis, a. iliaca communis dextra et sinistra on the day of admission showed that MSS, MDS were within normal limits.

Thus, the analysis of the results of the study of the comparison group of patients showed that during kidney transplantation, conducting studies on, determining the HLA of the 1st and 2nd class of donor and recipient, a panel of reactive antibodies (PRA) and donor-specific antibodies (DSA) in the recipient, and a cross-test “cross-

match" between the donor and recipient indicating sensitization of the body to a donor transplant is a mandatory procedure.

In our work, based on the results of the post-transplant period, an increase in the level of laboratory parameters (leukocytes, LII, ESR), and biochemical (creatinine, urea) considered them predictors of functional, organic changes in the kidney and a direct indication of puncture biopsy for a complete morphological assessment of the kidney, the results of which were described above. The leukocyte intoxication index (LEI) has shown itself to be an important marker of the inflammatory process. The peak values of LII on the third day after surgery made it possible to timely adjust immunosuppressive therapy and prevent the progression of inflammatory processes, which emphasizes its importance as a prognostic marker for assessing inflammatory reactions. In a comparative study of the results of the analysis of laboratory and biochemical data with morphological data, changes corresponding to the Banff classification were demonstrated. In this group of patients in the preoperative period, immunoglobulin therapy with human serum immunoglobulin in the amount of 100-200 mg / kg of weight (Octagam 10% 100 ml IV, intrathecum 10% 100 ml, etc.), with serum immunoglobulin was performed for preventive purposes, which helps to reduce various dysfunctional pathologies of the transplant, and prevents all kinds of complications in the postoperative period, which helps to reduce various dysfunctional pathologies of the transplant, and prevents all kinds of complications in the postoperative period.

Conclusions

1. The low level of sensitization of patients is a key factor reducing the risk of transplant rejection. All patients in our study had PRA < 25% and DSA < 500 MFI, which minimized the risk of immunological complications. In 100% of cases, the results of the cross-match were negative ($p < 0.001$), which indicates a high degree of immune compatibility.
2. The age of the donor significantly affects the restoration of kidney function. In patients who received kidneys from donors older than 50 years, creatinine levels were statistically significantly higher (115 ± 25 mmol/l) compared with patients who received kidneys from donors younger than 50 years (105 ± 20 mmol/l), with $p < 0.05$. Urea levels in kidney recipients from older donors were also higher (9.2 ± 2.1 mmol/l versus 7.8 ± 1.5 mmol/L), indicating delayed graft recovery.
3. Morphological changes such as interstitial inflammation (30% of patients, $p < 0.05$), glomerular hyalinosis (25% of patients, $p < 0.05$) and tubular necrosis (18% of patients, $p < 0.05$) detected in transplants indicate ischemic damage and the potential development of graft rejection. These changes require more intensive monitoring and intervention to prevent further deterioration of graft function.
4. Changes in ultrasound examination of the kidneys in non-sensitized patients before and after transplantation have shown the importance of using ultrasound methods and Dopplerography to monitor the condition of the kidneys. A decrease in the size and an increase in the echogenicity of tissues before transplantation indicate chronic changes that require attention. The restoration of normal size and blood flow in 88% of patients after surgery confirms the success of graft revascularization. However, delayed recovery in 12% of patients who received kidneys from elderly donors indicates the need for more thorough postoperative follow-up. Regular ultrasound monitoring is key to maintaining long-term graft function and timely therapy adjustments.
5. The leukocyte intoxication index (LEI), which peaked on the third day after transplantation, was 1.9 ± 0.02 ($p < 0.001$) compared with the initial values of 1.2 ± 0.06. This statistically significant increase reflects an active inflammatory process. Along with this, the leukocyte level increased from $5.4 \pm 0.14 \times 10^9$/l to $8.1 \pm 0.10 \times 10^9$/l ($p < 0.001$), which also indicates systemic inflammation. These data make it possible to adjust therapy in a timely manner to minimize the risk of acute rejection.

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