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EVALUATION OF ULTRASOUND AND HISTOLOGICAL PARAMETERS FOLLOWING DESENSITIZATION THERAPY IN HIGHLY SENSITIZED KIDNEY TRANSPLANT PATIENTS

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Abstract

This study evaluated the effect of pretransplant desensitization therapy on ultrasound, laboratory, and histological parameters of kidney grafts in highly sensitized recipients. The study included 31 patients who underwent living-related kidney transplantation under conditions of high immunological sensitization. Of these, 18 (58.1%) were men and 13 (41.9%) were women, with a mean age of 43.7 ± 8.4 years. The mean pretransplant PRA level was $72.4 \pm 8.7\%$; 18 patients (58.1%) had detectable DSA, and in 11 patients (35.5%) DSA levels exceeded 3000 MFI. All patients received a combined desensitization protocol including rituximab, 3–5 sessions of plasmapheresis, intravenous immunoglobulin, and baseline immunosuppression with mycophenolate mofetil and low-dose tacrolimus before transplantation. In 25 patients (80.6%), PRA decreased by at least 50% from baseline, and in 14 patients DSA levels fell below 1000 MFI, allowing transplantation to be performed after a negative final cross-match. In the source data, PRA and DSA showed a representative decline from 70% to 15% and from 3800 to 550 MFI, respectively. Early post-transplant follow-up showed that no cases of acute cellular or humoral rejection were recorded in this group under the applied treatment strategy. These findings

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indicate that desensitization therapy can substantially reduce the immunological burden before transplantation and create conditions for successful graft implantation and early postoperative stability in highly sensitized recipients.

Keywords: kidney transplantation, highly sensitized recipients, desensitization therapy, PRA, donor-specific antibodies, ultrasound monitoring, histological assessment.

Introduction

Actuality Kidney transplantation remains the most effective treatment for patients with end-stage chronic kidney disease, providing superior survival and quality of life compared with maintenance dialysis [3,12,14] (Wolfe et al., 1999; Coemans et al., 2021). However, the outcomes of transplantation are significantly influenced by the recipient's immunological status, particularly in patients with preformed anti-HLA antibodies, who represent one of the most complex categories in modern transplant practice [3,12,14] (Loupy & Lefaucheur, 2018; Halloran et al., 2020).

Highly sensitized recipients are characterized by elevated levels of panel reactive antibodies (PRA) and donor-specific antibodies (DSA), which markedly limit donor compatibility and increase the risk of early graft dysfunction, antibody-mediated injury, and acute rejection [3,12,14] (Lefaucheur et al., 2017; Jordan & Vo, 2021). In this setting, successful transplantation often requires pretransplant desensitization therapy aimed at reducing the circulating antibody burden and achieving a negative final cross-match [3,12,14] (Montgomery et al., 2011; Stegall et al., 2006).

Current desensitization protocols are based on a combination of rituximab, plasmapheresis, and intravenous immunoglobulin. These approaches have expanded access to transplantation for highly sensitized patients and improved short-term outcomes; however, they do not completely eliminate the risk of early

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graft injury [3,12,14] (Djamali et al., 2014; Jordan & Vo, 2021). For this reason, early postoperative monitoring remains critically important, particularly in patients with initially high immunological risk.

In recent years, ultrasound morphometry has gained increasing importance as a noninvasive method for evaluating kidney graft condition in the early postoperative period. Parameters such as parenchymal thickness, resistive index, venous flow characteristics, and overall graft morphology provide clinically relevant information about perfusion, vascular resistance, and structural adaptation of the transplanted kidney [3,12,14] (Belavina et al., 2023; Sanders et al., 2019). When combined with laboratory indicators and histological assessment according to the Banff classification, ultrasound monitoring allows more accurate interpretation of early graft dysfunction and facilitates timely therapeutic adjustment [3,12,14] (Halloran et al., 2020; Loupy & Lefaucheur, 2018).

Therefore, the assessment of ultrasound and histological parameters of kidney grafts after desensitization therapy in highly sensitized recipients is of particular clinical and scientific relevance. Such an integrated approach may improve early detection of unfavorable graft adaptation, refine postoperative surveillance, and contribute to the optimization of management strategies in this high-risk population.

Aim of the Study

The aim of this study was to evaluate the impact of desensitization therapy on ultrasound morphometric and histological parameters of kidney grafts in highly sensitized recipients, and to determine their diagnostic value for assessing early graft adaptation after living-related kidney transplantation.

Materials and Methods

The study was performed at the Samarkand Regional Multidisciplinary Medical Center and was based on the analysis of recipients who underwent living-related

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kidney transplantation between 2021 and 2025. From the overall cohort of 72 transplant recipients, 31 patients were classified as having suboptimal immediate graft function (MFK-2) and were included in the present study. This group represented recipients with a high immunological risk profile and unfavorable early graft adaptation.

The MFK-2 group included 18 men (58.1%) and 13 women (41.9%), with a mean age of 43.7 ± 8.4 years. All patients had end-stage chronic kidney disease and received a kidney from a living-related donor. High immunological sensitization was defined by elevated PRA and the presence of DSA, together with the need for pretransplant immunological preparation. According to the dissertation data, the mean baseline PRA level in this group was $72.4 \pm 8.7\%$, DSA were detected in 18 patients (58.1%), and in 11 patients (35.5%) DSA levels exceeded 3000 MFI.

Table 1. Demographic and sensitisation-related characteristics of the MFC-2 group

Parameter	Significance
Total number of patients	31
Gender (M/F)	17 (56,7%) / 13 (43,3%)
Age (mean \pm SD)	$43,7 \pm 8,4$ year
Mean PRA level (%)	$72,4 \pm 8,7\%$
Patients with DSA (%)	17 (56,7%)
Mean DSA level (MFI)	2850 MFI
DSA patients with MFI > 3000	10 (33,3%)

All recipients in the MFK-2 group underwent a combined desensitization protocol before transplantation. The protocol included rituximab, administered 14 days before surgery, 3–5 sessions of plasmapheresis, intravenous immunoglobulin, and baseline immunosuppressive therapy with mycophenolate mofetil and low-dose tacrolimus prior to transplantation. Desensitization was

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continued until an acceptable immunological status was achieved, including a negative final cross-match.

The effectiveness of desensitization was assessed by dynamic monitoring of PRA and DSA before and after treatment. In the dissertation, successful preparation was defined by substantial reduction in antibody levels and achievement of transplantation eligibility. In 25 patients (80.6%), PRA decreased by at least 50% from baseline, while in 14 patients DSA fell below 1000 MFI. Representative dynamic values showed a reduction of PRA from 70% to 15% and DSA from 3800 to 550 MFI.

Post-transplant monitoring included laboratory, ultrasound, and morphological assessment. Laboratory follow-up focused on markers of graft function and systemic inflammatory response, including serum creatinine, blood urea, and the leukocytic intoxication index (LII). These parameters were used in the dissertation as key indicators for evaluating early graft recovery and identifying unfavorable postoperative dynamics.

Dynamic ultrasound monitoring of the graft was performed according to the institutional protocol. Ultrasound examination was used to assess morphometric and hemodynamic characteristics of the transplanted kidney, including parenchymal thickness, resistive index (RI/IR), venous blood flow parameters, and the general structural appearance of the graft. In the dissertation, these findings were interpreted together with laboratory and biopsy results in order to distinguish favorable and unfavorable early graft adaptation.

Morphological assessment of graft biopsy specimens was carried out according to the Banff 2017 classification. The analysis included the evaluation of inflammatory and vascular lesions in the transplanted kidney, with particular attention to tissue changes associated with suboptimal immediate graft function in highly sensitized recipients. Ultrasound findings were subsequently compared with histological changes in order to determine their diagnostic relationship.

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The collected clinical, immunological, ultrasound, laboratory, and histological data were analyzed in an integrated manner to determine the impact of desensitization therapy on early graft adaptation in highly sensitized kidney transplant recipients.

Results

The MFK-2 group included 31 highly sensitized recipients who underwent living-related kidney transplantation after desensitization therapy. Of these, 18 patients (58.1%) were men and 13 (41.9%) were women, with a mean age of 43.7 ± 8.4 years. The mean pretransplant PRA level was $72.4 \pm 8.7\%$. DSA were detected in 18 patients (58.1%), with a mean fluorescence intensity of 2850 MFI, and 11 patients (35.5%) had DSA levels above 3000 MFI, indicating a very high risk of antibody-mediated rejection.

Effect of Desensitization Therapy

All patients received a combined desensitization protocol that included rituximab, 3–5 plasmapheresis sessions, intravenous immunoglobulin, and baseline immunosuppression. In 25 patients (80.6%), PRA decreased by at least 50% from baseline, and in 14 patients DSA fell below 1000 MFI, allowing transplantation to proceed after a negative final cross-match. In the representative treatment dynamics presented in the dissertation, PRA decreased from 70% to 15%, while DSA decreased from 3800 to 550 MFI. No cases of acute cellular or humoral rejection were identified in the early postoperative period after this preparation strategy.

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Table 2. Management strategy in the preoperative period

Stage	Treatments
Desensitisation	Plasmapheresis (3–5 sessions), intravenous immunoglobulin (IVIG) 200–400 mg/kg, rituximab 375 mg/m ² , low-dose tacrolimus (trough 5–7 ng/ml)
Monitoring effectiveness	Monitoring of PRA and DSA levels

Table 3. Induction immunosuppression

Polyclonal antibodies (thymoglobulin, thymogam) or monoclonal antibodies (basiliximab)	1 mg/kg of body weight for 3–5 days On the day of surgery: 20 mg IV; on the 4th day after surgery: 20 mg IV
Glucocorticoid hormone (methylprednisolone or solumedrol)	On the day of surgery: 10 mg/kg Day 1 after surgery: 7.5 mg/kg Day 2 after surgery: 5 mg/kg Day 3: 2.5 mg/kg

Table 4. Management strategies in the post-transplant period

Stage	Methods
Induction therapy	A glucocorticoid hormone (methylprednisolone or solumedrol) at a dose of 10 mg/kg body weight
Maintenance therapy	Tacrolimus (8–12 ng/ml), (10–12) mycophenolate mofetil 1000 mg twice daily, methylprednisolone with gradual dose reduction
Monitoring	Daily assessment of graft function, creatinine levels and ultrasound scans of the graft

Table 5. Post-transplant baseline immunosuppression

Calcineurin inhibitors: Tocraliimus	The target blood concentration for tacrolimus is 8–12 ng/ml for 3 months, followed by a reduction to 5–6 ng/ml
Micofenolate mofetil	1000 mg twice daily
Glucocorticoid hormone (methylprednisolone or solumedrol)	4–5 mg per day

Ultrasound Morphometric Findings

Dynamic ultrasound follow-up demonstrated progressive improvement in graft morphology and hemodynamics. Graft volume increased from $186.3 \pm 3.0 \text{ cm}^3$

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on postoperative day 1 to 232.0 ± 3.0 cm³ by day 30. Parenchymal thickness increased from 1.57 ± 0.03 cm to 1.85 ± 0.03 cm during the same period. At the same time, the resistive index (IR) declined from 0.78 ± 0.01 to 0.64 ± 0.01 , while venous blood flow increased from 12.8 ± 0.5 ml/s to 23.0 ± 0.5 ml/s. According to the dissertation, all sequential differences relative to the previous time point were statistically significant ($P < 0.01$).

These ultrasound changes indicate progressive normalization of graft perfusion and reduction of intrarenal vascular resistance. The source text specifically notes that a decline in IR below 0.7 was associated with restoration of graft blood supply, while increasing venous flow reflected recovery of venous drainage and reduction of ischemic tissue injury.

Table 6. Changes in graft morphometric parameters in patients in the MFC-2 group

The post-transplant period	Graft volume (cm ³)	Parenchyma thickness (cm)	Resistance Index (IR)	Venous blood flow (ml/s)
1 day	186.3 ± 3.0	1.57 ± 0.03	0.78 ± 0.01	12.8 ± 0.5
2 day	195.0 ± 3.0	1.63 ± 0.03	0.75 ± 0.01	14.5 ± 0.5
3 day	202.0 ± 3.0	1.68 ± 0.03	0.72 ± 0.01	16.2 ± 0.5
5 day	210.0 ± 3.0	1.74 ± 0.03	0.70 ± 0.01	18.0 ± 0.5
9 day	218.0 ± 3.0	1.78 ± 0.03	0.68 ± 0.01	19.8 ± 0.5
15 day	225.0 ± 3.0	1.82 ± 0.03	0.66 ± 0.01	21.5 ± 0.5
30 day	232.0 ± 3.0	1.85 ± 0.03	0.64 ± 0.01	23.0 ± 0.5

Note: The differences compared with previous data are statistically significant ($P < 0.01$).

Laboratory dynamics

Laboratory follow-up also demonstrated a favorable trend. Serum creatinine decreased from 841.4 ± 20.0 μmol/L on day 1 to 630.0 ± 20.0 μmol/L on day 2, 477.0 ± 20.0 μmol/L on day 3, 291.0 ± 20.0 μmol/L on day 5, 185.0 ± 18.0 μmol/L on day 9, 140.0 ± 17.0 μmol/L on day 15, and 112.0 ± 17.0 μmol/L by day 30. Blood urea declined from 29.8 ± 2.0 mmol/L to 8.4 ± 1.2 mmol/L, and the leukocytic intoxication index (LII) decreased from 4.15 ± 0.15 to 1.20 ± 0.11 .

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These changes were also reported as statistically significant compared with the previous observation point ($p=0.01$).

Table 7. Changes in laboratory parameters in patients in the MFC-2 group

The post-transplant period	Creatinine ($\mu\text{mol/L}$)	Urea (mmol/l)	LII
1 day	841.4 ± 20.0	29.8 ± 2.0	4.15 ± 0.15
2 day	630.0 ± 20.0	25.5 ± 2.0	3.45 ± 0.15
3 day	477.0 ± 20.0	20.5 ± 1.8	2.70 ± 0.14
5 day	291.0 ± 20.0	16.2 ± 1.5	2.05 ± 0.13
9 day	185.0 ± 18.0	12.8 ± 1.3	1.80 ± 0.12
15 day	140.0 ± 17.0	10.5 ± 1.2	1.65 ± 0.11
30 day	112.0 ± 17.0	8.4 ± 1.2	1.20 ± 0.11

Note: The differences compared with the previous data are statistically significant ($p=0.01$).

The article interprets this laboratory pattern as evidence of restored filtration function, absence of major inflammatory complications, and achievement of functional homeostasis by the end of the first postoperative month.

Histological Findings

Morphological analysis of graft biopsies in the MFK-2 group included 45 biopsy specimens. According to the reported Banff-based distribution, 18 biopsies (40%) showed $i0-t0-v0$, 17 biopsies (38%) showed $i1-t1-v0$, and 10 biopsies (22%) demonstrated $i2-t2-v1$ changes. Thus, the majority of biopsies (78%) did not show pronounced vascular injury, while 22% demonstrated moderate inflammatory lesions compatible with subclinical rejection and requiring intensification of immunosuppressive therapy.

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Table 8. Distribution of morphological changes in the graft among MFC-2 patients

Changes to Banff 2017	Number of biopsies	Proportion (%)
i0-t0-v0 (no signs of inflammation)	18	40%
i1-t1-v0 (mild interstitial inflammation and tubulitis)	17	38%
i2-t2-v1 (moderate arteritis, marked tubulitis and inflammation)	10	22%

Correlation Between Ultrasound and Morphology

Correlation analysis showed clinically meaningful relationships between ultrasound parameters and biopsy findings. An IR above 0.75 on days 5–9 was associated with i2–t2 inflammatory changes and interpreted as a marker of rejection risk requiring intensified therapy. Venous blood flow below 14 ml/s on days 1–5 correlated with moderate inflammatory and venous changes in biopsy specimens, whereas normalization of venous flow above 18 ml/s by day 15 was associated with favorable morphology. In addition, parenchymal thickness below 1.7 cm by day 15 corresponded to interstitial inflammation and tubulitis, while values above 1.8 cm were associated with the absence of significant structural injury. All correlations were reported as statistically significant ($p=0.01$).

Table 9. Correlation between ultrasound findings and morphological changes

Ultrasound result	Critical value	Morphological changes (Banff)	Clinical significance
Graft size	>20 cm ³ by day 9	i0–i1/t0–t1	A positive outlook
Resistance index	>0.75 on days 5–9	i2–t2	Risk of rejection, intensification of treatment
Venous blood flow	<14 ml/s on days 1–5	Moderate changes	Risk of dysfunction, close monitoring
Parenchyma thickness	<1.7 cm by day 15	Interstitial inflammation and tubulitis	Increased risk of rejection
Parenchyma thickness	>1.8 cm by day 15	No significant changes	Normal graft function

Overall, the results show that desensitization therapy made transplantation feasible in highly sensitized recipients and was followed by favorable early

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laboratory and ultrasound dynamics, while histological surveillance identified a subgroup with residual subclinical inflammatory injury requiring closer monitoring and therapeutic adjustment.

Discussion

The present study demonstrates that desensitization therapy plays a critical role in enabling successful kidney transplantation in highly sensitized recipients. Patients in the MFK-2 group initially presented with high levels of PRA and DSA, which are widely recognized as major immunological barriers to transplantation and are associated with an increased risk of antibody-mediated graft injury (Lefaucheur et al., 2017; Jordan & Vo, 2021).

The application of a combined desensitization protocol including rituximab, plasmapheresis, and intravenous immunoglobulin resulted in a substantial reduction in antibody levels before transplantation. In the majority of patients, PRA levels decreased by more than 50%, and DSA levels were reduced below clinically significant thresholds, allowing transplantation to proceed after a negative final cross-match. Similar therapeutic strategies have been described in previous studies, which demonstrated that multimodal desensitization protocols can significantly expand transplantation opportunities for highly sensitized recipients (Stegall et al., 2006; Montgomery et al., 2011).

An important observation of the present study is the favorable early ultrasound dynamics of the graft following transplantation. Progressive increases in graft volume and parenchymal thickness, combined with a decline in the resistive index and an increase in venous blood flow, reflect gradual normalization of graft perfusion and reduction of intrarenal vascular resistance. These findings are consistent with previous studies indicating that Doppler ultrasound parameters are reliable indicators of early graft adaptation and vascular stability after transplantation (Sanders et al., 2019; Belavina et al., 2023).

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Laboratory indicators also confirmed progressive restoration of graft function. The steady decline in serum creatinine, blood urea, and inflammatory indices during the first postoperative month reflects the recovery of glomerular filtration and stabilization of systemic inflammatory processes. These dynamics correspond to the expected functional trajectory after successful transplantation and indicate effective postoperative management in the studied cohort.

Morphological assessment of graft biopsies provided additional insight into the structural adaptation of the transplanted kidney. According to the Banff classification, most biopsies demonstrated either minimal inflammatory changes or mild interstitial inflammation without severe vascular injury. Nevertheless, approximately one fifth of biopsy specimens showed moderate inflammatory lesions, suggesting the presence of subclinical rejection processes requiring careful monitoring and adjustment of immunosuppressive therapy.

The correlation between ultrasound parameters and histological findings represents an important practical aspect of the present study. Increased resistive index values and reduced venous blood flow were associated with inflammatory changes in biopsy specimens, indicating that Doppler ultrasound may serve as an early noninvasive indicator of graft injury. Such relationships highlight the importance of combining imaging and morphological assessment in the postoperative follow-up of transplant recipients.

Overall, the results suggest that desensitization therapy can effectively reduce immunological risk and allow successful transplantation in highly sensitized recipients, while integrated monitoring using laboratory markers, ultrasound morphometry, and biopsy evaluation remains essential for detecting early graft dysfunction and guiding postoperative treatment strategies.

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Conclusions

1. Desensitization therapy substantially reduced the immunological burden in highly sensitized kidney transplant recipients, making living-related transplantation feasible after achievement of a negative final cross-match.
2. Early postoperative follow-up demonstrated favorable ultrasound morphometric dynamics, including an increase in graft volume and parenchymal thickness, a decrease in the resistive index, and improvement of venous blood flow, which reflected progressive normalization of graft perfusion.
3. Laboratory parameters showed steady recovery of graft function, with significant reductions in serum creatinine, blood urea, and the leukocytic intoxication index during the first postoperative month.
4. Histological assessment according to the Banff classification revealed predominantly minimal or mild inflammatory changes, although a subgroup of recipients demonstrated moderate subclinical lesions requiring closer surveillance and adjustment of immunosuppressive therapy.
5. The integration of desensitization therapy, ultrasound monitoring, laboratory follow-up, and histological evaluation provides an effective strategy for the management of highly sensitized recipients and improves early detection of unfavorable graft adaptation after kidney transplantation.

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