Contribution of Autologous Omentum Transposition to the Regeneration of Renal Injuries in the Rat Model

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Abstract

Aim

We aimed to evaluate the repair effect of transpositioned autologous omentum on the injured renal tissues in the rat model.

Methods

A total of 30 female Wistar Albino rats were included and they were randomly separated into control and four groups. In all groups, blood samples were taken at preoperatively and at the 7th day postoperatively, additionally they were taken at 18th day postoperatively for creatinine and urea analysis. All rats of control group were sacrificed at 18th day postoperatively and right kidneys were taken for histopathological evaluation. After the created renal injuries were repaired primarily kidney surgery or omentum added kidney surgery.

Results

According to the our results, granulation and inflammation in kidney specimens were moderately and highly positive correlated with granulation, inflammation, fibrosis and foreign body reaction in surrounding tissue (($r:0.478$, $p = 0.008$), ($r:0.591$, $p = 0.001$), ($r:0.394$, $p = 0.031$), ($r:0.635$, $p < 0.001$)). Granulation in kidney specimen was highly possitive correlated with inflammation and foreign body reaction in kidney specimens (($r:0.824$, $p < 0.001$), ($r:0.872$, $p < 0.001$)). We could not show any significant correlation between biochemical values (U, Cr) and histopathological findings.

Conclusion

According to our results, our biochemical results were not correlated with histopathological analysis. But we detected histopathological significant differences between primary kidney repair and omentum added kidney repair groups. And we recommend that kidney injuries should be surgical repaired by stem cell sources as like omentum tissue.

Introduction:

Renal trauma can occur associated with various mechanisms. Etiological factors are generally described as blunt kidney injuries (80–90%) and penetrating kidney injuries (10%). The main sign of renal trauma is hematuria, but it can also happen without it (1). The main purpose of treatment in kidney trauma is to ensure that the kidney functions return to normal as soon as possible (2). Renal injuries are classified according to severity into 5 grades. Especially, grade 4–5 injuries in the renal tissue are candidate for surgical treatment. Major of the kidney injuries cause of blunt traumas are treated with conservative

management. (2, 3). The other preferences of treatment are surgical or endoscopic procedures. The other preferences of treatment are open or endoscopic surgical procedures. Laparoscopic/robot-assisted or open partial/total nephrectomy, nephrorraphy, autotransplantation, embolization can be options for treatment of renal traumas.

It is important to accelerate wound healing in renal traumas requiring surgical treatment in order to decrease morbidity and mortality rates. Wound healing includes three dynamic phases as named as inflammation, proliferation and remodelling (4). Angiogenesis, inflammation, cellular proliferation, collagenization, granulation and epithelialization are important processes in the remodelling of tissue (5). There are many molecules and molecular mechanisms in tissue regeneration such as vascular endothelial growth factor (VEGF), nitric oxide (NO) (6). Synthetic or autologous materials can used for regeneration of injured kidney tissue such as fat tissue, omentum, meshes and fascias.

As we know well, omentum tissue is quite vascular and fatty structure and includes many growth and angiogenic factors inside the progenitor cells (7, 8). Therefore it can migrate to damaged tissue and help to regeneration capacity of the tissue (9, 10). It has been used for many surgical procedures in the treatment of bone fractures, spine injuries and ischemic heart diseases, hepatic injuries. Progenitor stem cells have highly proliferation and differentiation capabilities. But, they can live very short time in the tissue, if they are injected into the target. In many studies, the omentum has been used to wrap the injured tissue and has been shown to be useful. According to the results of the research, the progression to the chronic kidney failure has been shown to more slowly in subtotal nephrectomies that are covered by omentum (11). This is a unique contribution in the context of nephron-sparing.

We aimed to evaluate the repair effect of transpositioned autologous omentum on the injured renal tissues in the rat model. We measured renal injury biomarkers (such as creatinine, urea) and made a histopathological evaluation to determine the degree of injury and repair capacity compared the correlation of the biomarkers with the histopathological findings.

Material And Methods:

A total of 30 female Wistar Albino rats were included, which were 5 to 6 months old and weighed 250 to 300 grams. They were randomly separated into control and four groups (6 members in per group). In all groups, blood samples were taken at preoperatively and at the 7th day postoperatively, additionally they were taken at 18th day postoperatively for creatinine and urea analysis in control, group 2 and group 4. Sham operation was administered in control group. All rats of control group were sacrificed at 18th day postoperatively and right kidneys were taken for histopathological evaluation. In Group 1 (first kidney repair group), an 8 mm diameter, 4 mm deep parenchymal damage was created with the Stiefel biopsy forceps on the front surface of the right kidneys and primary repaired with atraumatic suture (Ethicon VICRYL Rapid 8 – 0, fastest absorbable, synthetic, braided, composed of a copolymer made from 90% glycolide and 10% L-lactide, absorption time 7–10 days). In Group 1, all rats were sacrificed at 7th day postoperatively and right kidneys were taken for histopathological evaluation. In Group 2 (second kidney

repair group), blood samples were taken at 7th and 18th day postoperatively, same surgical procedure was administered, all rats were sacrificed at 18th day postoperatively and right kidneys were taken for histopathological evaluation. In Group 3 (first kidney omentum repair group), differently from group 1, additional transpositioned autologous omentum was used without primary sutures on the injured renal tissue for repairing. All rats were sacrificed at 7th day postoperatively and right kidneys were taken for histopathological evaluation. In Group 4 (second kidney omentum repair group), different from group 2, additional transpositioned autologous omentum was used without primary sutures on the injured renal tissue for repairing and all rats were sacrificed at 18th day postoperatively and right kidneys were taken for histopathological evaluation. Endpoint of the research was sacrificed time of the rats.

The study was approved by the Turkish Medicines and Medical Devices Agency and the Local Ethical Committee on Animal Experiments (Acibadem Mehmet Ali Aydınlar University, HDK-2018/47). The subjects were kept in standardized laboratory conditions of 20–24 C⁰, 50–60% relative humidity, controlled light (day-night cycle of 12 h: 8/20 h), fed on standardized rodent food, and given filtered and chlorinated water. The animals were anesthetized with an intraperitoneal injection of ketamine (75 mg/kg) and xylazine (5 mg/kg). All rats were protected against the postoperative infections with antibiotic (Cefazolin 15 mg/kg, SC).

The exclusion criteria of this study included whether the rats are male, very young or old. The limitation of this study was that only blood creatinine and urea levels were used for biochemical evaluation of the renal injury and we did not measure the urine concentration due to the technical inadequacy of urine collection in the rats. Moreover, we were able to evaluate histopathological analysis only qualitative. On the other hand, we did not have more rats, so we determined five groups that included six rats per group. This was the minimum level for the statistical methods. There was no data and rat loss during the research.

Tissue sampling and histopathological examination

All samples were fixed in a 10% formaldehyde solution. Kidney tissues were embedded in paraffin and 5 µm tissue sections were obtained for hematoxylin-eosin (H&E) and Masson's Trichrome (MTC) staining protocol for collagen fibers. Addition to macroscopic view, histopathological evaluation was contained granulation, inflammation, fibrosis, foreign body reaction, healing in the injured kidney and around tissue (omentum). All components were scored between from 0 to 5 according to density of the changes in the tissue (normal:0, rare:1, mild:2, modest:3, common:4 and exsecive:5). Macroscopic evaluation was contained only macroscopic view of kidney due to with/without abnormal structure on the surface of kidney. Granulation was evaluated with/without granulation in glomerulus and parenchymal tissue that included eadema, inflammatory cells, angiogenesis, fibroblasts. Inflammation was evaluated with/without acute inflammatory cells, macrophages, lymphocytes. Fibrosis was evaluated with/without fibroblasts and its density. Foreign body reaction was evaluated with/without necrosis, erythrocytes, chronic inflammation findings. Healing in tissue was accepted with/without regeneration and normalization in tissue. The cut sections were examined for completeness and one representative section

of each kidney was selected for tissue processing. The histological damage examined under a light microscope by a pathologist who was blind to the study design (sham vs renal regeneration). All pathological slides were scanned with digital pathology system (3D Histech company, P250 – Flash III Dijital Scanner, 20X) and microscopic photos were taken (3D Histech company, CaseViewer program, .tiff format and 300 dpi). In our research, we preferred sacrifice time at 18th day postoperatively, according to literature (12). J. Miguel, et al reported that posttraumatic necrosis in the tissue disappeared at 18th day. After this period, collagen maturation in the renal capsule and contraction of the connective tissue at the edges of the wound were detected (12).

Biochemical analysis

The creatinine (Cr), urea (U), concentrations in the serum were determined by an enzymatic assay (Roche Diagnostics GmbH, Mannheim, Germany). Serum samples for the measurement were collected and frozen at -80°C until the analysis was carried out. All laboratory investigators were blind to each rat's clinical information.

Statistical analysis

In estimating the sample size of the study, it was calculated that 5 groups of animals comprising 6 per group would be required to detect a 3 units of improvement (with 1.5 units as Standard Deviation) as a significant effect in a wound healing model, assuming a power of 80% and a confidence level of 95%. SPSS 21.0 (SPSS Inc., Chicago, IL) for MacBook Air was used for statistical analysis. The descriptive statistics for categorical variables were given as the number, percentage means $\pm$ standard deviation (SD), and for numerical variables as the median. One-Sample Kolmogorov-Smirnov test was used for normality and normal distribution was obtained for all groups ($p > 0.05$). Histopathologic categorical variables of the groups were compared using the Kruskal Wallis test. After the analyze, binary groups were compared using the Mann-Whitney U test. Nonparametric dependent variables were evaluated using the Wilcoxon test. Spearman's correlation test was used for correlations between groups (Rho: r). Statistical significance was assumed for $p < 0.05$. Details are displayed in the description of the results.

Results:

Results of biochemical analysis (Cr,U) are shown in Table 1 and scores of histopathological evaluation in renal injury and surrounding tissue are shown in Tables 2 and 3. All histopathological changes are shown in Figures (Fig. 1–5).

According to the Cr analysis, Mann-Whitney U test revealed a significant difference between *Sham group Cr sampled on day 18* and *Kidney primary repair second Cr on day 18* ($p = 0.004$), *Kidney repair first Cr on day 7* and *Kidney primary repair second Cr on day 18* ($p = 0.004$), *Kidney repair first Cr on day 7* and *Kidney repair with omentum first Cr on day 7* ($p = 0.041$), *Kidney primary repair second Cr on day 18* and *Kidney repair with omentum first Cr on day 7* ($p = 0.002$).

According to the U analysis, Mann-Whitney U test revealed a significant difference between *Sham group U sampled on day 18* and *Kidney repair first U on day 7* ($p = 0.015$), *Sham group U sampled on day 18* and *Kidney repair with omentum second U on day 18* ($p = 0.026$), *Kidney repair first U on day 7* and *Kidney primary repair second U on day 18* ($p = 0.004$), *Kidney primary repair second U on day 18* and *Kidney repair with omentum first U on day 7* ($p = 0.041$), *Kidney primary repair second U on day 18* and *Kidney repair with omentum second U on day 18* ($p = 0.009$).

Kruskal Wallis test revealed statistically significant differences between groups as *U level in blood* ($p = 0.008$), *Cr level in blood* ($p = 0.005$), *Macroscopy of the kidney specimen* ($p = 0.566$), *Granulation degree in kidney specimen* ($p < 0.001$), *Inflammation degree in kidney specimen* ($p < 0.001$), *Fibrosis degree in kidney specimen* ($p = 0.190$), *Foreign body reaction in kidney specimen* ($p = 0.001$), *Healing process completion in kidney* ($p = 0.004$), *Granulation degree in surrounding* ($p = 0.009$), *Inflammation degree in surrounding tissue* ($p = 0.013$), *Fibrosis degree in surrounding tissue* ($p = 0.010$), *Foreign body reaction in surrounding tissue* ($p < 0.001$).

Mann-Whitney U test was done for evaluate to which groups were statistically different from the other. Analysis of Urea concentration comparison inside groups revealed a significant difference between *Sham group U sampled on day 1* and *Sham group U sampled on day 18* ($p = 0.046$), *Kidney repair first U on day 1* and *Kidney repair first U on day 7* ($p = 0.026$), *Kidney repair with omentum second U on day 1* and *Kidney repair with omentum second U on day 7* ($p = 0.028$), *Kidney repair with omentum second U on day 1* and *Kidney repair with omentum second U on day 18* ($p = 0.027$).

Analysis of Creatinine concentration comparison inside groups revealed a significant difference between *Kidney repair first Cr on day 1* and *Kidney repair first Cr on day 7* ($p = 0.028$), *Kidney primary repair second Cr on day 1* and *Kidney primary repair second Cr on day 7* ($p = 0.042$), *Kidney primary repair second Cr on day 1* and *Kidney primary repair second Cr on day 18* ($p = 0.046$).

Wilcoxon test revealed a significant difference between *Sham group U sampled on day 1* and *Sham group U sampled on day 18* ($z: -1.992$, $p = 0.046$), *Kidney repair first U on day 1* and *Kidney repair first U on day 7* ($z: -2.226$, $p = 0.026$), *Kidney repair with omentum second U on day 1* and *Kidney repair with omentum second U on day 7* ($z: -2.201$, $p = 0.028$), *Kidney repair with omentum second U on day 1* and *Kidney repair with omentum second U on day 18* ($z: -2.214$, $p = 0.027$), *Kidney repair first Cr on day 1* and *Kidney repair first Cr on day 7* ($z: -2.201$, $p = 0.028$), *Kidney primary repair second Cr on day 1* and *Kidney primary repair second Cr on day 7* ($z: -2.032$, $p = 0.042$), *Kidney primary repair second Cr on day 1* and *Kidney primary repair second Cr on day 18* ($z: -1.197$, $p = 0.046$).

There were not any significant differences between groups according to *macroscopic evaluation*. On the other hand, histopathological analysis of degree of *granulation in renal tissue* revealed a significant difference between *First Kidney Repair day 7* and *Sham day 18* ($p = 0.02$), *Sham day 18* and *Second Kidney Repair day 18* ($p = 0.015$), *First Kidney Repair day 7* and *First Kidney Omentum Repair day 7* ($p = 0.002$), *Second Kidney Repair day 18* and *Second Kidney Omentum Repair day 18* ($p = 0.015$), *First Kidney Repair day 7* and *Second Kidney Repair day 18* ($p = 0.002$).

Histopathological analysis of degree of *inflammation in renal tissue* revealed a significant difference between *Sham day 18* and *First Kidney Repair day 7* ($p = 0.002$), *Sham day 18* and *Second Kidney Repair day 18* ($p = 0.002$), *First Kidney Repair day 7* and *First Kidney Omentum Repair day 7* ($p = 0.002$), *Second Kidney Repair day 18* and *Second Kidney Omentum Repair day 18* ($p = 0.004$). There were not any significant difference between groups according to degree of fibrosis and foreign body reaction in renal tissue. Histopathological analysis of degree of *healing in renal tissue* revealed a significant difference between *First Kidney Repair day 7* and *First Kidney Omentum Repair day 7* ($p = 0.015$).

Histopathological analysis of degree of *granulation in surrounding tissue* revealed a significant difference between *Sham day 18* and *First Kidney Omentum Repair day 7* ($p = 0.041$), *Sham day 18* and *Second Kidney Omentum Repair day 18* ($p = 0.041$), *Second Kidney Repair day 18* and *Second Kidney Omentum Repair day 18* ($p = 0.004$). Histopathological analysis of degree of *inflammation in surrounding tissue* revealed a significant difference between *Second Kidney Repair day 18* and *Second Kidney Omentum Repair day 18* ($p = 0.015$). Histopathological analysis of degree of *fibrosis in surrounding tissue* revealed a significant difference between *Sham day 18* and *First Kidney Repair day 7* ($p = 0.002$), *Sham day 18* and *Second Kidney Repair day 18* ($p = 0.015$), *Sham day 18* and *Second Kidney Omentum Repair day 18* ($p = 0.015$). Histopathological analysis of degree of *foreign body reaction in surrounding tissue* revealed a significant difference between *Sham day 18* and *First Kidney Repair day 7* ($p = 0.002$), *Sham day 18* and *Second Kidney Repair day 18* ($p = 0.002$), *Sham day 18* and *First Kidney Omentum Repair day 7* ($p = 0.002$), *Sham day 18* and *Second Kidney Omentum Repair day 18* ($p = 0.002$), *Second Kidney Repair day 18* and *Second Kidney Omentum Repair day 18* ($p = 0.026$).

Spearman's correlation test was used between all groups. Correlation Coefficient (ρ : r) analysis were not any significant difference between U or Cr levels in the blood and all histopathology groups.

According to correlation analysis of histopathological evaluation between *kidney specimen groups* and *surrounding tissue groups*: *Granulation degree in kidney specimen* was moderately or highly positive correlated with *Granulation degree in surrounding* ($r:0.478$, $p = 0.008$), *Inflammation degree in surrounding tissue* ($r:0.591$, $p = 0.001$), *Fibrosis degree in surrounding tissue* ($r:0.394$, $p = 0.031$), *Foreign body reaction in surrounding tissue* ($r:0.635$, $p < 0.001$). *Inflammation degree in kidney specimen* was moderately or highly positive correlated with *Granulation degree in surrounding* ($r:0.512$, $p = 0.004$), *Inflammation degree in surrounding tissue* ($r:0.507$, $p = 0.004$), *Fibrosis degree in surrounding tissue* ($r:0.434$, $p = 0.017$), *Foreign body reaction in surrounding tissue* ($r:0.660$, $p < 0.001$). *Fibrosis degree in kidney specimen* was moderately positive correlated with *Fibrosis degree in surrounding tissue* ($r:0.429$, $p = 0.018$). *Foreign body reaction in kidney specimen* was highly positive correlated with *Fibrosis degree in surrounding tissue* ($r:0.829$, $p < 0.001$), *Foreign body reaction in surrounding tissue* ($r:0.813$, $p < 0.001$). *Healing process completion in kidney* was moderately or highly negative correlated with *Granulation degree in surrounding* ($r:-0.625$, $p = 0.001$), *Foreign body reaction in surrounding tissue* ($r:-0.425$, $p = 0.039$).

According to correlation analysis of histopathological evaluation *among subgroups of surrounding tissue analyses*: *Inflammation degree in surrounding tissue* was moderately or highly positive correlated with

Granulation degree in surrounding ($r:0.490$, $p = 0.006$), *Fibrosis degree in surrounding tissue* ($r:0.397$, $p = 0.030$), *Foreign body reaction in surrounding tissue* ($r:0.431$, $p = 0.017$). *Fibrosis degree in surrounding tissue* was moderately or highly positive correlated with *Inflammation degree in surrounding tissue* ($r:0.397$, $p = 0.030$), *Foreign body reaction in surrounding tissue* ($r:0.708$, $p < 0.001$).

According to correlation analysis of histopathological evaluation *among subgroups of in kidney tissue analyses*: *Granulation degree in kidney specimen* was highly positive correlated with *Inflammation degree in kidney specimen* ($r:0.824$, $p < 0.001$), *Foreign body reaction in kidney specimen* ($r:0.872$, $p < 0.001$) and highly negative correlated with *Healing process completion in kidney* ($r:-0.627$, $p = 0.001$). *Inflammation degree in kidney specimen* was highly positive correlated with *Foreign body reaction in kidney specimen* ($r:0.731$, $p = 0.001$) and highly negative correlated with *Healing process completion in kidney* ($r:-0.608$, $p = 0.002$).

Discussion:

The prevalence of renal trauma is ranged 0.3%-3.25% according to literature. Most of them are caused by blunt trauma, the others are occurred with penetrating factors. The common renal trauma classification is the American Association for the Surgery of Trauma (AAST) classification that is classified grade 1–5 (13). Currently, except the hemodynamically unstable grade 4–5 renal trauma, renal injuries are followed up with conservative approach. If some vital changes occur during this time, it can be treated with surgical interventions.

Partial/total nephrectomy or nephrorrhaphy can be preferred according to the type or degree of injury. Usually transperitoneal surgical approach is more preferable because of this route provides some advantages such as the early control of large veins and arteries. Surgery of the renal trauma contains control of the bleeding by sutures, watertight closure of the collecting system and closure of parenchymal injuries. Even preserving kidney capacity in thirty percent can provide adequate kidney function. The renal capsule should be preserved at all possible cases for successfully repairing (14). Sometimes, if renal capsule is not available, a pedicle flap of omentum, free peritoneal grafts or free fat grafts or polyglycolic acid meshes can be used for coverage of large defect. In the technique, omentum is closed to the injured tissue, with superficially with monofilament absorbable sutures (15–17).

The omentum has long been known to have the capacity to migrate to injured organs and facilitate their healing of injuries such as bones, spinal cords, heart, liver, pancreas. Many studies have shown that a reduction in total nephron capacity may cause kidney failure in the future, thus maximum protection of kidney tissue should be the main purpose. Some suture material and surgical techniques can be harmful to kidney tissue. For this reason, alternative techniques have been developed to better protect the kidney tissue especially in the large tissue lose. One of them is using of the omentum or fatty tissue for repairing of renal injury. As we well known, mesenchymal stem cells (MSCs) can be obtained from adipose tissue, peripheral blood or bone marrow. Another alternative source is omentum for repairing of injured tissue. It is a very vascular structure and suitable for use as its healing capacity contains a large number of growth

and angiogenic factors and progenitor cells for regeneration (18). MSCs were first isolated from adipose tissue in 2001 by Zuk et al (19). As we know, MSCs features are ability of multipotency, self-renewing, proliferation, regeneration, and differentiation (20).

MSCs can able to accelerate tissue repair by direct migration to the injured sites (21, 22). MSCs may be administered by local or systemic for treatment. It is widely agreed that transplanted MSCs can directly reconstruct impaired organs. They have some specific features as endocrine (growth factors, chemokines, cytokines with paracrine and autocrine activities), immunomodulatory (T-cells, Dendritic cells, Natural Killer cells), anti-inflammatory effects (23). These factors suppress the local immune system, inhibit fibrosis and apoptosis, enhance angiogenesis, stimulate proliferation and differentiation. Firstly, Iwai et al. discovered that local injection of adipose derived MSCs was prone to attenuation of fibrosis (24).

Normal wound healing process includes endothelial injury, myofibroblast activation, macrophage migration, inflammatory signal stimulation, immune activation, matrix deposition and remodeling. Especially in the first 24–28 hours, many molecular reactions occur in the tissue. Fibroblasts are very crucial members at the inflammation process. Moreover, functional microcirculatory bed has been shown of critical importance in the prevention of epithelial loss and fibrosis (25). Fibrosis is one of the most common and refractory pathological processes. Fibrosis is a redundant accumulation of extracellular matrix (ECM) in tissue by the collagen reaction and end of the recovery a thick fibrotic neocapsule can occur. On the other hand, MSCs can directly release HGF and BMP-7, which are important inhibitors of fibrosis. MSCs have been shown to exert anti-fibrotic effects in animal models by matrix metalloproteinase (26). Autologous MSCs are immune compatible unlike synthetic mash and this is an advantage at the remodeling process.

In our research, time dependently, all histopathological scores were decreased in primary kidney repair group and healing in tissue has improved significantly.

Our results showed *granulation and inflammation in kidney specimen on kidney repair with omentum groups* were lesser than *kidney primary repair groups*. According to our data, histopathological analysis of degree of *inflammation in renal tissue* revealed a significant difference between primary kidney repair and *First Kidney Repair day 7* and *First Kidney Omentum Repair day 7* ($p = 0.002$), *Second Kidney Repair day 18* and *Second Kidney Omentum Repair day 18* ($p = 0.004$). (healing in renal tissue, *First Kidney Repair day 7* vs *First Kidney Omentum Repair day 7* ($p = 0.015$)). On the other hand, histopathological analysis of degree of *granulation in renal tissue* revealed a significant difference between *First Kidney Repair day 7* and *First Kidney Omentum Repair day 7* ($p = 0.002$), *Second Kidney Repair day 18* and *Second Kidney Omentum Repair day 18* ($p = 0.015$)

In many studies, the histological damage of the kidneys has been evaluated on the tissue with the EGTI scoring system (27). The scoring system consists of histological damage in 4 individual components – Endothelial, Glomerular, Tubular, Interstitial (EGTI Scoring system)– and is scored from 0 to 4. This scoring is performed in renal cortex, especially for glomerular unit. Therefore, we preferred to use a new

scoring system for histopathological evaluation, so that it was able to evaluate different components of the regeneration on whole kidney tissue.

Our results showed, there were significant differences among *Urea concentration comparison inside groups* ($p = 0.046$, $p = 0.026$, $p = 0.028$, $p = 0.027$) or *Creatinine concentration comparison inside groups* ($p = 0.028$, $p = 0.042$, $p = 0.046$). Additionally, our results showed there were significant differences among primary kidney repair groups depend on time (on 1st, 7th, 18th day). On the other hand, there were not any significant differences among kidney repair by omentum groups depend on time (on 1st, 7th, 18th day). However, we could not show any significant correlation between biochemical values (U, Cr) and histopathological findings. It can be explained by the fact that we could not produce sufficient nephron damage with our trauma model. In the future, this model should be planned to be repeated with major kidney tissue damage. Contrary to our results, Garcia-Gomez et al reported omentum was effective in treatment of kidney injuries, as was alternative source of adult stem cells. In the context of the use of omentum, progression to CKD (Chronic Kidney Disease) could be reduced in this rat model (11). But in this research kidney injuries were large capacity as like 5/6 subtotal nephrectomy.

According to the our results, granulation and inflammation in kidney specimens were moderately and highly positive correlated with granulation, inflammation, fibrosis and foreign body reaction in surrounding tissue (($r:0.478$, $p = 0.008$), ($r:0.591$, $p = 0.001$), ($r:0.394$, $p = 0.031$), ($r:0.635$, $p < 0.001$)). Healing process completion in kidney was moderately negative correlated with granulation and foreign body reaction in the surrounding tissue (($r:-0.625$, $p = 0.001$), ($r:-0.425$, $p = 0.039$)).

As expected, inflammation in surrounding tissue was moderately and highly positive correlated with granulation, fibrosis and foreign body reaction in surrounding tissue (($r:0.490$, $p = 0.006$), ($r:0.397$, $p = 0.030$), ($r:0.431$, $p = 0.017$)). Moreover, fibrosis in surrounding tissue was moderately and highly positive correlated with inflammation and foreign body reaction (($r:0.397$, $p = 0.030$), ($r:0.708$, $p < 0.001$)).

Granulation in kidney specimen was highly positive correlated with inflammation and foreign body reaction in kidney specimens (($r:0.824$, $p < 0.001$), ($r:0.872$, $p < 0.001$)). But it was highly negative correlated with Healing process completion in kidney ($r:-0.627$, $p = 0.001$). Moreover, inflammation in kidney specimen was moderately and highly positive correlated with granulation and foreign body reaction in kidney specimens, contrary to negative correlated with Healing process completion in kidney (($r:0.731$, $p = 0.001$), ($r:-0.608$, $p = 0.002$)).

Finally, we can suggest that renal and perirenal tissues are healed together due to granulation, inflammation, foreign body reaction and fibrosis. Renal insufficiency could be developed according to loss of nephron capacity.

Conclusion:

In most preclinical trials, MSCs exhibit few or no adverse side effects, while the efficacy remains controversial. Although the results are controversial, stem-cell therapy is a new hope for many diseases.

As mentioned above, we aimed to determine repair capacity of omentum tissue on the renal injury at the rat model. According to our results, our biochemical results were not correlated with histopathological analysis. But we detected histopathological significant differences between primary kidney repair and omentum added kidney repair groups. And we recommend that kidney injuries should be surgical repaired by stem cell sources as like omentum tissue. On the other hand, for increase of our knowledge about this topic, there is a need for well-designed and more comprehensive studies on this topic.

Declarations

Ethics approval and consent to participate:

The study was approved by the Turkish Medicines and Medical Devices Agency and the Local Ethical Committee on Animal Experiments

Consent for publication:

N/A

Availability of data and materials:

Data used in this study are included in the manuscript

Competing interests:

The authors declare no conflict of interest to declare

Authors' contributions

TB designed, executed the study, analyzed the results, UI performed pathological contribution, FN supervised the study.

Conflict of interest

The authors declare no conflict of interest.

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Tables

Table 1
Descriptive Statistics of blood creatinine and urea values (First: sacrificed on 7th day, Second: sacrificed on 18th day).

Descriptive Statistics	N	Mean	Std. Deviation	Minimum	Maximum
Sham group urea sampled on day 1	6	43,6667	5,27889	36,00	51,00
Sham group creatinin sampled on day 1	6	0,273	0,041	0,230	0,350
Sham group urea sampled on day 7	6	38,0000	3,74166	32,00	43,00
Sham group creatinin sampled on day 7	6	0,228	0,063	0,170	0,330
Sham group urea sampled on day 18	6	36,1667	2,40139	34,00	40,00
Sham group creatinin sampled on day 18	6	0,273	0,033	0,240	0,330
Kidney repair first urea on day 1	6	39,3333	3,93277	37,00	47,00
Kidney repair first creatinin on day 1	6	0,358	0,043	0,300	0,420
Kidney repair first urea on day 7	6	31,3333	3,07679	28,00	36,00
Kidney repair first creatinin on day 7	6	0,270	0,022	0,240	0,300
Kidney primary repair second urea on day 1	6	43,3333	5,57375	37,00	51,00
Kidney primary repair second creatinin on day 1	6	0,288	0,039	0,240	0,360
Kidney primary repair second urea on day 7	6	37,1667	3,31160	33,00	41,00
Kidney primary repair second creatinin on day 7	6	0,200	0,027	0,170	0,240
Kidney primary repair second urea on day 18	6	39,6667	4,76095	34,00	46,00
Kidney primary repair second creatinin on day 18	6	0,220	0,020	0,200	0,250
Kidney repair with omentum first urea on day 1	6	35,5000	2,88097	32,00	40,00
Kidney repair with omentum first creatinin on day 1	6	0,282	0,037	0,240	0,340
Kidney repair with omentum first urea on day 7	6	33,1667	4,35507	25,00	37,00
Kidney repair with omentum first creatinin on day 7	6	0,357	0,141	0,260	0,640
Kidney repair with omentum second urea on day 1	6	43,1667	5,26941	35,00	51,00

Descriptive Statistics	N	Mean	Std. Deviation	Minimum	Maximum
Kidney repair with omentum second creatinin on day 1	6	0,265	0,037	0,210	0,310
Kidney repair with omentum second urea on day 7	6	33,0000	5,36656	27,00	43,00
Kidney repair with omentum second creatinin on day 7	6	0,227	0,086	0,070	0,330
Kidney repair with omentum second urea on day 18	6	32,8333	2,56255	29,00	37,00
Kidney repair with omentum second creatinin on day 18	6	0,272	0,088	0,160	0,430

Table 2
Score of histopathological evaluation in kidney tissue for control and study groups.

	N	Mean	Std. Deviation	Minimum	Maximum
Descriptive Statistics					
Urea level in blood	30	34,6333	4,47586	25,00	46,00
Creatinin level in blood	30	,2783	,08408	,16	,64
Macroscopy of the kidney specimen	30	4,7333	,52083	3,00	5,00
Granulation degree in kidney specimen	30	,9000	1,37339	,00	4,00
Inflammation degree in kidney specimen	30	1,5000	1,40810	,00	4,00
Fibrosis degree in kidney specimen	30	1,1667	,46113	,00	2,00
Foreign body reaction in kidney specimen	18	,9444	,80237	,00	2,00
Healing process completion in kidney	24	4,5000	,72232	3,00	5,00
Granulation degree in surrounding	30	1,9667	,76489	1,00	3,00
Inflammation degree in surrounding tissue	30	2,7333	,73968	2,00	4,00
Fibrosis degree in surrounding tissue	30	1,7333	,58329	1,00	3,00
Foreign body reaction in surrounding tissue	30	3,0333	1,62912	,00	5,00

Table 3

Scoring evaluation of histopathological findings in surrounding tissue for control and study groups.

Kidney (Right)	Macroscopy		Granulation	Inflammation	Connective Tissue	Foreign Body Rx	Healing
Control	1	5	0	0	1	0	NA
	2	5	0	0	1	0	NA
	3	5	0	1	1	0	NA
	4	5	0	0	0	0	NA
	5	5	0	1	1	0	NA
	6	5	0	0	1	0	NA
Group-I	1	4	3	3	1	2	4
	2	5	4	3	1	2	3
	3	5	3	3	1	1	4
	4	4	4	3	1	2	4
	5	5	3	4	1	2	5
	6	5	3	3	1	1	4
Group-II	1	5	1	2	1	1	5
	2	4	1	3	2	1	4
	3	3	0	2	1	1	3
	4	5	2	2	1	2	4
	5	5	1	4	2	1	3
	6	5	2	4	1	1	5
Group-III	1	5	0	0	2	NA	5
	2	5	0	1	1	NA	5
	3	4	0	0	1	NA	5
	4	5	0	1	2	NA	5
	5	4	0	0	1	NA	5
	6	5	0	1	1	NA	5
Group-IV	1	5	0	1	1	NA	5
	2	4	0	0	1	NA	5

Kidney (Right)	Macroscopy		Granulation	Inflammation	Connective Tissue	Foreign Body Rx	Healing
	3	5	0	0	2	NA	5
	4	5	0	0	1	NA	5
	5	5	0	1	1	NA	5
	6	5	0	2	2	NA	5

Surrounding Tissue		Granulation	Inflammation	Connective Tissue	Foreign Body Rx
Control	1	2	2	1	0
	2	2	2	1	0
	3	2	3	1	0
	4	1	2	1	0
	5	2	2	1	0
	6	3	4	1	0
Group-I	1	2	3	2	4
	2	3	3	2	4
	3	3	4	2	4
	4	2	3	2	4
	5	3	3	2	4
	6	2	4	2	4
Group-II	1	2	3	2	4
	2	3	3	2	4
	3	3	2	1	4
	4	2	3	2	5
	5	3	3	2	4
	6	2	4	2	5
Group-III	1	1	3	2	3
	2	2	4	3	4
	3	2	2	2	4
	4	3	3	3	4
	5	1	3	1	3
	6	1	2	1	3
Group-IV	1	1	2	2	3
	2	1	2	1	3
	3	2	2	2	3
	4	1	2	2	4

Surrounding Tissue	Granulation	Inflammation	Connective Tissue	Foreign Body Rx
5	1	2	2	4
6	1	2	2	3

Figures

Figure 1

Macroscopic view of kidney and omentum. Left Bottom, Cross section of the whole kidney slice (4μ), Hematoxylin & Eosin staining (57.6X). Right Bottom, Cross section of the whole kidney slice (4μ), Masson Trichrom staining. (28.8X)

Figure 2

Kidney, parenchyma, trauma line– microscopically, Hematoxylin & Eosin staining (377.6X)

Figure 3

Kidney, parenchyma, trauma line– microscopically, Masson Trichrom staining. (256X)

Figure 4

Kidney, parenchyma–microscopicKidney, parenchyma–microscopically, Hematoxylin & Eosin staining. (1120X)ally, Hematoxylin & Eosin staining. (1120X)

Figure 5

Kidney, parenchyma, surrounding area – microscopically, Masson Trichrom staining. (438.4X)