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BENEFITS OF VACUUM-ASSISTED CLOSURE THERAPY OVER STANDARD TREATMENTS FOR INFECTED AND CHRONIC NON-HEALING WOUNDS AFTER KIDNEY TRANSPLANTATION

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Objective: to evaluate the effectiveness of vacuum-assisted closure (VAC) therapy in comparison with standard treatments for infected and chronic non-healing wounds after kidney transplantation. **Materials and methods.** From June 2018 to November 2019, 75 kidney transplants from deceased donors were performed at the Transplantation Ward of Botkin City Clinical Hospital. There were 47 men (62.6%) and 28 women (37.4%). Standard surgical technique was used. Immunosuppressive therapy was carried out according to a three-component scheme with anti-CD25 monoclonal antibody induction (basiliximab) intraoperatively and on day 4. All patients received antibiotic therapy with protected third-generation cephalosporins for 7 days after surgery. Postoperative complications were evaluated according to the Clavien–Dindo classification. Standard methods, including daily dressings using modern dressing materials (group I) and VAC therapy (group II) were used for treating infected and chronic non-healing wounds. **Results.** 30-day mortality in the postoperative period was zero. Postoperative complications were recorded in 11 patients (14.6%), of which 7 had postoperative wound complications. Group I included 3 patients (1 with a *Klebsiella pneumonia*-infected wound and 2 with chronic non-healing wounds and no microflora growth). Group 2 had 4 patients (3 with infected wounds (*Esherichia coli* – 1, *Klebsiella pneumonia* – 2) and 1 with chronic non-healing wound). Complete cleansing of wound, absence of bacterial growth according to the microbiological examination, and maturation of granulations according to histological examination were considered as the criteria upon which a wound could be sutured in both groups of patients. The average time between the start of treatment and secondary suturing in group 1 patients was 33.11 ± 5.43 (28–37) and 15.01 ± 3.15 (13–17) days in group 1 and group 2 respectively. **Conclusion.** VAC therapy in patients with wound complications resulting from kidney transplantation, in comparison with standard treatment, can achieve rapid wound cleansing, acute inflammation relief and accelerated maturation of mature granulation tissue, thereby improving treatment outcomes in this category of patients.

Keywords: kidney transplantation, wound infection, VAC therapy.

INTRODUCTION

Healthcare-associated infection is the most common complication in medicine [1]. Postoperative wound infection is the most common type of infectious complications in surgical patients [2]. This complication increases the cost of medical care, and also increases postoperative mortality [3].

In the Russian Federation, 1361 kidney transplant surgeries were performed in 2018, which accounted for 62% of all organ transplants [4]. The incidence of postoperative wound infection following kidney transplantation is 10–15% [5, 6]. Among the risk factors for this complication are 1) recipient-related factors: age, obesity, diabetes, smoking and malnutrition; 2) surgical factors: surgical technique, wound closure method; 3) factors specific to this surgical intervention, such as: immunosuppressive therapy, delayed graft function, need for dialysis after surgery [7].

Therapy of infected wounds after kidney transplantation comes with significant difficulties due to the need for immunosuppressive therapy, which, on one hand, complicates conservative treatment of the infection, and on the other hand, reduces the reparative processes in the wound [8]. All this leads to the fact that it often takes more than 5 weeks to treat such complications [9].

One of the modern methods of treating infected wounds in surgery is application of negative pressure (VAC-therapy), which is associated with a short wound-healing period [10]. The experience of using this technique in patients who have undergone kidney transplantation is extremely limited [11], which requires further studies of the effectiveness of VAC therapy in this category of patients.

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MATERIALS AND METHODS

From June 2018 to November 2019, 75 kidney transplants from a deceased donor were performed at Botkin City Clinical Hospital. There were 47 men (62.6%) and 28 women (37.4%). The average age was 46.01 ± 11.33 (20–70 years old). The average body mass index (BMI) was 26.09 ± 4.47 (17–36). Donor characteristics are presented in Table 1.

Table 1

Characteristics of deceased kidney donors

Average age, years	46.41 ± 10.05 (22–65)
Pressor support Yes No	 71 4
Average BMI	27.12 ± 4.81 (20–43)
Time spent in hospital, hour	64.25 ± 63.52 (13–480)
Average donor creatinine, μmol/L	93.46 ± 27.47 (41–180)

The standard surgical technique was used. The urethral and central venous catheters were removed on day 7 after transplantation. All patients received antibiotic therapy with protected third-generation cephalosporins for 7 days after surgery. The following immunosuppressive therapy scheme was used: anti-CD25 monoclonal antibodies (basiliximab), intraoperatively and on postoperative day 4, tacrolimus with a 8–10 ng/ml target concentration, mycophenolic acid at 1000 mg twice a day and prednisolone at 30 mg per day. The ureteral stent was removed in the operating room under aseptic conditions on days 14 or 21. Postoperative sutures were removed on day 21. Postoperative complications were assessed according to the Clavien–Dindo classification. Delayed renal graft function was defined as the need for dialysis in the first 5 days after surgery. Long-term non-healing postoperative wound was defined as dehiscence of the wound edges after suture removal.

RESULTS

The characteristics of the surgical interventions performed are presented in Table 2.

Table 2

Characteristics of surgical interventions for cadaveric kidney transplantation

Average cold ischemia time, min	594.58 ± 193.95 (133–1180)
Average blood loss, mL	104.32 ± 51.12 (30–300)
Average bed-days in ICU	1.56 ± 0.85 (0–4)
Average total bed-days	16.57 ± 13.23 (8–101)
Graft function: immediate delayed	 53 22
Postoperative complications, abs/(%)	11 (14.6%)
Postoperative mortality	0

There was no 30-day mortality in the early postoperative period. Postoperative complications were registered in 11 patients (14.6%), 7 of whom had complications from postoperative wound: suppuration (4 patients, 5.3%), long-term non-healing wound (3 patients, 4%), lymphocele (3 patients, 4%), and urosepsis (1 patient, 1.3%). According to the Clavien–Dindo classification: class II (3 complications, 4%), IIIA (1 complication, 1.3%), IIIB (6 complications, 8%), and IVa (1 complication, 1.3%). Suppuration of postoperative wound was recorded within 28 to 42 days after the operation. In 3 patients (1 patient with an infected wound (*Klebsiella pneumonia* in microbiological examination (Fig. 1)) and 2 patients with long-term non-healing wounds (no growth in microbiological examination)), standard treatment methods were used, including daily dressings using modern dressing materials to create a humid environment, administration of antibiotic therapy in accordance with the antibiotic chart, reducing immunosuppressive therapy.

After the wound was completely cleansed, there was no bacterial growth, which was confirmed by microbiological examination, and granulation matured, which was confirmed by histological examination of edges of the wound, the wound was then closed (Fig. 2). The patients described above constituted Group I of the study.

The second group included 4 patients (3 patients with infected wounds (1 patient with *Esherichia coli*, 2 patients with *Klebsiella pneumonia*) (Fig. 3) and 1 patient with a long-term non-healing wound).

The treatment strategy for this group of patients was to install a VAC system with 90 mm Hg constant pressure (Fig. 4).

Dressings were performed every week. In the absence of systemic inflammatory response syndrome, antibiotic therapy was not prescribed, and immunosuppressive

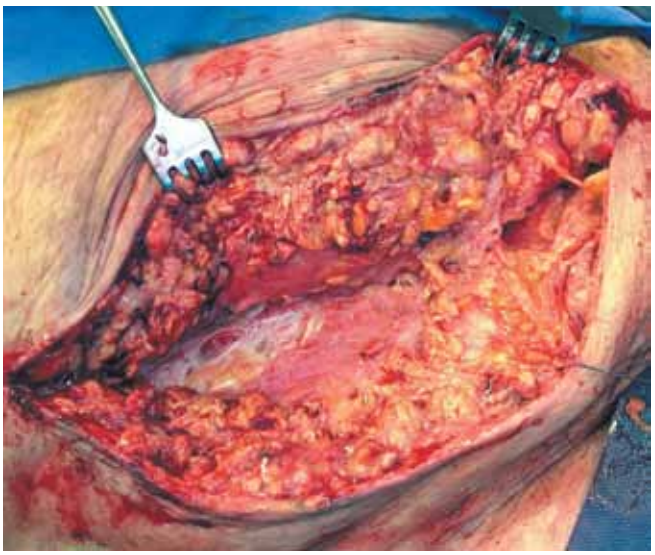

Fig. 1. Infected postoperative wound after kidney transplantation (18 days after transplantation)

therapy was reduced. The wound closure criteria were similar to those of the first group (Fig. 5).

An important objective criterion for determining the time of wound closure is the histological examination of the edges of the wound with the determination of granulation tissue maturation. During the primary and subsequent surgical interventions, sampling was performed from the superficial and deep edges of the wound with dynamic monitoring of the reparative process (Fig. 6).

During primary surgical interventions for infected postoperative wounds, the edges of the wound presented as gangrenous-like acute inflammation with a scab on the wound surface. Inflammatory infiltration was present in the lower layers with the presence of numerous segmented granulocytes. The vascular walls were pareticly dilated with necrosis of the muscular layer (Fig. 7).

On day 5–7 after VAC therapy, formation of young granulation tissue on the wound surface with lymphoid infiltration along the interfatty connective tissue layers was noted. Inflammatory infiltrates were represented

Fig. 2. Outcome of infected wound treatment. Secondary sutures (31 days of treatment)

Fig. 3. Infected postoperative wound after kidney transplantation (14 days after surgery)

Fig. 4. Application of VAC system on an infected postoperative wound

Fig. 5. Complete cleansing of the postoperative wound after VAC therapy (13 days after treatment)

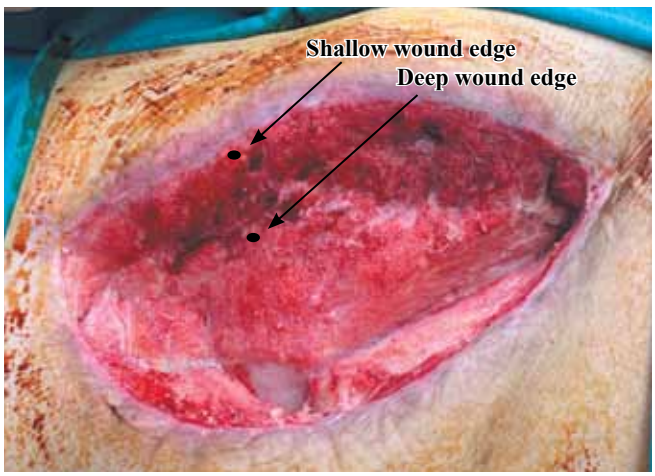

Fig. 6. External view of the wound. Locations from where material was taken for histological examination are marked

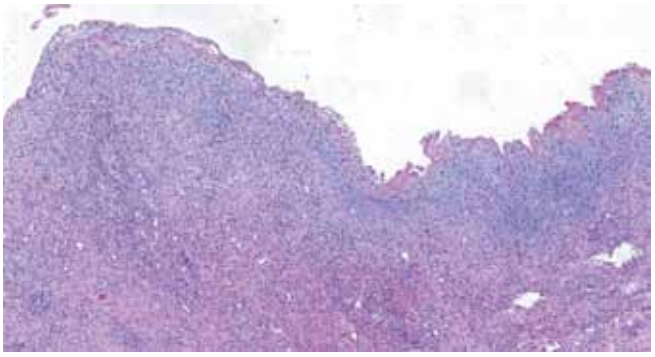

Fig. 7. Muscle fibers are not visible, the scab is represented by an inflammatory shaft in the form of a homonized structureless mass. No granulation tissue was formed. H&E stain

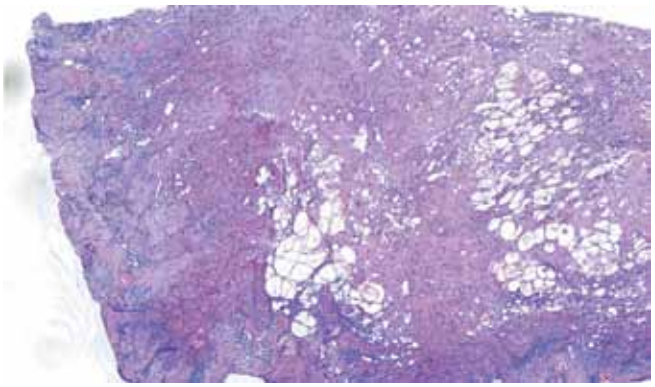

Fig. 8. Young granulation fields can be seen around adipose tissue "islets"

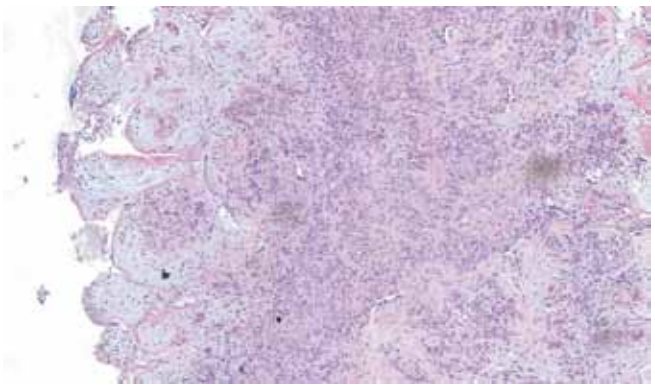

Fig. 9. Mature granulation tissue. No inflammation. Formation of rough papillary structures on the wound surface

predominantly by mononuclear cells. Myofibroblasts, sinusoidal capillaries surrounded by delicate intercellular substance with metachromasia were seen in the "young" granulation tissue (Fig. 8).

In the later stages, mature granulation tissue with thicker vessels and collagen fibrosis was formed. There was maturation zoning in the form of rough papillae on the wound surface. Inflammatory infiltration was scanty, single mature lymphocytes were visible (Fig. 9).

The average times between the beginning of treatment and the application of secondary sutures in group 1 and group 2 were 33.11 ± 5.43 (28–37) and 15.01 ± 3.15 (13–17) days, respectively.

DISCUSSION

In the experience of Botkin City Clinical Hospital, wound complications are the most frequent type of complications after kidney transplantation, and accounts for 9.3%. Development of this type of complication increases the patient's hospital stay by an average of 31.67 ± 5.43 days, thereby increasing treatment costs. The need for prolonged antibacterial therapy due to an open wound surface also carries a potential threat of complications, the most frequent of which is pseudomembranous colitis. All this necessitates the introduction of modern wound treatment methods into clinical transplantology.

The use of the VAC system in patients with wound complications after kidney transplantation, compared to standard daily dressings, made it possible to achieve wound cleansing at significantly early periods (15.01 ± 3.15 vs 33.11 ± 5.43, $p < 0.05$) and maturation of granulation wound, which was confirmed by histological examination. Other important advantages of VAC therapy are early de-escalation of antibiotic therapy, as well as patient convenience compared to daily dressings.

Direct adjacency of vascular anastomosis or neocystoureteroanastomosis to the wound bed, and active diffuse tissue bleeding are contraindications to the use of the technique.

Based on the data obtained, we have developed our own protocol for the use of VAC therapy in patients with wound complications after kidney transplantation: during the first intervention, a wound culture is performed, the wound is debritched with removal of non-viable tissues, the VAC system is installed with 100 mm Hg constant pressure. In the absence of intoxication syndrome, the dressing is changed every 7 days. With repeated dressings, the edges of the wound are taken for microbiological and histological examination. The criteria for application of secondary sutures are: absence of bacterial growth in the wound, absence of systemic inflammatory reaction syndrome, presence of mature granulation tissue in the superficial and deep edges of the wound.

CONCLUSION

VAC therapy in patients with wound complications after kidney transplantation, in comparison to standard treatment methods, allows to achieve rapid wound cleansing, relief of acute inflammation and acceleration of maturation of mature granulation tissue, thereby improving treatment outcomes in this patient cohort.

The authors declare no conflict of interest.

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