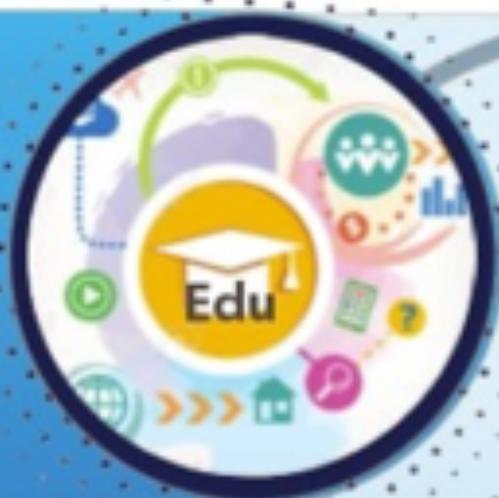




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# Morphological Effects of Vacuum-Assisted Therapy on Experimental Pulmonary Abscesses in a Diabetic Rabbit Model

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## ABSTRACT

**Background.** Pulmonary abscesses in diabetic individuals are often characterized by delayed inflammatory resolution and impaired healing. While vacuum-assisted closure (VAC) therapy is widely used in external wound management, its effects on internal thoracic infections remain insufficiently studied at the tissue level.

**Objective:** To evaluate the histomorphological effects of VAC therapy on pulmonary abscesses in an experimental rabbit model with type 2 diabetes mellitus.

**Materials and Methods:** A controlled animal study was conducted on 36 adult rabbits, divided into three groups: Group 1 (control, no VAC), Group 2 (continuous negative pressure - 80 mmHg), and Group 3 (intermittent pressure -80/0 mmHg, 5/2 cycle). Pulmonary abscesses were induced via transbronchial inoculation with *S. aureus* under general anesthesia. All animals had previously induced type 2 diabetes using streptozotocin. Histological samples were taken on days 3, 7, and 14 to evaluate inflammation, necrosis, granulation, vascularization, and collagen formation.

**Results:** Rabbits in Group 2 showed accelerated granulation tissue formation, reduced necrotic area, and active fibroblast proliferation by day 7. Group 3 showed similar trends but less pronounced. The control group demonstrated persistent inflammation and poor cavity organization. By day 14, continuous VAC led to near-complete epithelialization of the cavity margins and dense neocollagen deposition. Intermittent VAC resulted in slower dynamics, while no-VAC animals retained abscess cavities with inflammatory infiltration.

**Conclusion:** VAC therapy exerts favorable histomorphological effects in pulmonary abscess healing under diabetic conditions. Continuous negative pressure provided superior outcomes compared to intermittent mode. These findings support the biological rationale for applying VAC in thoracic infections, especially in compromised metabolic states.

**Keywords:** Vacuum-assisted closure, pulmonary abscess, experimental model, diabetes mellitus, histology, wound healing, negative pressure therapy.

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## INTRODUCTION

**P**ulmonary abscess remains a serious infectious complication, particularly in individuals with type 2 diabetes mellitus (T2DM), where impaired immune responses, microvascular changes, and delayed wound healing mechanisms contribute to persistent inflammation and poor recovery outcomes [1, 2]. Experimental and clinical studies have shown that diabetes modifies both the progression and resolution of pulmonary infections, resulting in higher risks of cavity persistence, fibrosis, and systemic spread [3].

Vacuum-assisted closure (VAC) therapy, also referred to as negative pressure wound therapy (NPWT), has been extensively studied in external soft tissue infections and chronic wounds, including diabetic foot ulcers, surgical wounds, and mediastinitis [4, 5]. The key mechanisms of VAC include removal of exudate, reduction of edema, enhancement of microcirculation, and stimulation of granulation tissue [6]. However, its application in internal organs, especially in the context of thoracic infections, remains underexplored.

A limited number of studies have addressed the utility of VAC in the thoracic cavity - mostly in the context of empyema or post-resectional spaces - and data on its tissue-level effects are scarce [7]. Furthermore, few experimental studies have evaluated the histological changes induced by negative pressure in pulmonary tissues, particularly under diabetic conditions that may influence healing kinetics.

Understanding the morphological effects of VAC on infected lung tissue in the setting of metabolic dysfunction is crucial for validating its use in thoracic surgery. This study aims to evaluate the histopathological impact of VAC therapy - both continuous and intermittent - on pulmonary abscess healing in a rabbit model with streptozotocin-induced type 2 diabetes. Through serial biopsies and standardized scoring of inflammation, granulation, and collagenization, we sought to establish the biological plausibility of VAC in treating internal pulmonary infections.

## MATERIALS AND METHODS

**T**his experimental study was performed on 36 adult male New Zealand white rabbits, each weighing between 2.8 and 3.2 kg. All procedures were approved by the Institutional Animal Care and Use Committee of Tashkent Medical Academy and conducted in accordance with international guidelines on animal welfare.

### Diabetes Induction:

Type 2 diabetes mellitus was chemically induced using a single intraperitoneal injection of streptozotocin at a dose of 65 mg/kg, followed by a high-fat diet. Hyperglycemia (>250 mg/dL fasting glucose) was confirmed after 10 days.

### Pulmonary Abscess Modeling:

On day 11, under general anesthesia with ketamine/xylazine (35/5 mg/kg), transbronchial inoculation of  $1 \times 10^7$  CFU of *Staphylococcus aureus* in 1.5 mL sterile saline was administered via a flexible bronchoscope to the right lower lobe. After 48–72 hours, abscess formation was confirmed using chest X-ray and ultrasonography.

### Group Distribution:

- Rabbits were randomly divided into three groups (n=12 per group):
- Group 1 (Control): drainage without vacuum (passive drain);
- Group 2 (VAC–continuous): continuous negative pressure at –80 mmHg.
- Group 3 (VAC–intermittent): pressure cycling –80/0 mmHg with a 5-min on / 2-min off cycle.

All animals underwent thoracotomy and abscess cavity exposure under sterile conditions. A polyurethane sponge adapted for internal use was placed within the cavity (Groups 2 and 3) and connected to an electronic suction unit. Dressings were replaced on days 3, 7, and 14.

### Histological Evaluation:

Tissue samples were collected on days 3, 7, and 14 post-VAC initiation. Specimens were fixed in 10% formalin, paraffin-embedded, and stained with hematoxylin–eosin (H&E) and Masson's trichrome. Morphological parameters included: degree of inflammation (neutrophilic/mononuclear infiltration); necrosis area (mm<sup>2</sup>); granulation tissue thickness ( $\mu$ m); fibroblast density (cells/hpf); neovascularization (vessels/hpf); collagen deposition (semiquantitative scoring from 0 to 3+).

### Statistical Analysis:

Data were analyzed using SPSS version 26.0. Inter-group comparisons were made using ANOVA with post hoc Tukey correction. A p-value <0.05 was considered statistically significant.

## RESULTS

**B**y day 3, all groups exhibited prominent neutrophilic infiltration and central zones of necrosis within the abscess cavity. However, early differences began to emerge in tissue response. In

the VAC–continuous group (Group 2), peripheral fibroblast infiltration and granulation tissue initiation were already visible, with early capillary budding and decreased necrotic area. In contrast, the control group (Group 1) showed diffuse suppuration, disorganized inflammatory margins, and absence of granulation. The VAC–intermittent group (Group 3) showed intermediate findings: patchy fibroblast zones and limited neovascularization.

By day 7, the differences between groups became more pronounced. In Group 2, granulation tissue became well organized and thicker (mean thickness  $347\pm 39\ \mu\text{m}$ ), with dense fibroblast proliferation and numerous thin-walled capillaries ( $6.8\pm 1.3$  vessels/hpf). Necrosis was largely confined to the center of the cavity, with signs of marginal reepithelialization. Group 3 also demonstrated granulation formation, but to a lesser extent ( $241\pm 34\ \mu\text{m}$ ), with scattered fibroblasts and irregular vascular channels ( $4.2\pm 1.0$  vessels/hpf). The control group continued to exhibit large necrotic areas, dense polymorphonuclear infiltration, and minimal evidence of reparative activity (granulation tissue  $<180\ \mu\text{m}$ ,  $p<0.001$  vs. VAC groups).

By day 14, nearly complete organization of the abscess cavity was observed in Group 2. The cavity was replaced by dense collagenous stroma, lined with epithelial cells, and rich in neocapillaries and fibroblasts. Collagen deposition was scored at 3+ (mature bands with Masson staining) in 10 of 12 animals. In Group 3, cavity resolution was partial, with persistent fibrin and incomplete epithelialization. Collagen score reached 2+ in most animals. In the control group, 8 out of 12 rabbits retained residual abscess structures with disorganized inflammation, incomplete resorption of purulent material, and minimal collagen synthesis (score 1+ or 0,  $p<0.01$ ).

Throughout the study, Group 2 consistently outperformed the other groups in every histological marker: earlier reduction in necrosis, accelerated granulation formation, increased fibroblast density, and superior vascularization (all  $p<0.01$ ). Group 3 showed a moderate response, suggesting that intermittent pressure had partial efficacy. The control group failed to show significant reparative progression.

These findings clearly demonstrate the biological advantage of continuous vacuum-assisted therapy in promoting structured wound healing and resolving intrapulmonary infection under diabetic conditions.

## DISCUSSION

The findings of this experimental study provide compelling evidence that vacuum-assisted closure (VAC) therapy significantly improves the histological dynamics of pulmonary abscess healing under diabetic conditions. The accelerated resolution of inflammation, earlier granulation tissue development, and enhanced collagen deposition observed in the continuous VAC group confirm the favorable impact of negative pressure on infected lung tissue.

Our results are in line with the established benefits of VAC therapy in surface wounds, where negative pressure has been shown to stimulate angiogenesis, reduce local interstitial edema, and enhance fibroblast proliferation [1]. These effects are particularly important in diabetic tissues, where microcirculatory impairment and delayed cellular responses hinder spontaneous recovery [2]. The improved neovascularization and granulation quality observed in this study suggest that VAC therapy may mitigate diabetes-induced impairments in wound healing at the pulmonary level.

Notably, the continuous VAC regimen ( $-80\ \text{mmHg}$ ) outperformed the intermittent protocol, indicating that sustained mechanical tension and uninterrupted fluid evacuation are critical to optimizing tissue remodeling. This observation is consistent with the work of Morykwas et al., who demonstrated a direct correlation between negative pressure magnitude and granulation tissue thickness in animal models [3]. While intermittent VAC may reduce the risk of pressure-induced ischemia, our data suggest that it may also limit the biological stimulus required for robust healing in metabolically compromised environments.

The control group outcomes - characterized by persistent necrosis, minimal neocapillary formation, and disorganized fibroplasia - highlight the inadequacy of passive drainage alone in managing intrathoracic abscesses in diabetic hosts. The absence of structured granulation tissue and weak collagenization further underscore the necessity for active wound modulation in such cases [4].

Few studies have investigated VAC therapy in the context of internal thoracic infections. However, recent clinical observations by Saadi et al. and Filaire et al. suggest that adapted VAC systems can be safely used for pleural empyema and post-resectional cavities with promising results [5]. Our study expands this perspective by providing morphologically documented evidence that VAC is not only safe but also biologically active in the pulmonary parenchyma itself.

The main limitations of our study include the single animal model (rabbit), relatively short observation period (14 days), and lack of long-term functional assessments. However, the strong statistical differences in key histological endpoints support the robustness of our conclusions. Future studies may include molecular markers (e.g., VEGF, TGF- $\beta$ ), longer follow-up, and comparisons across various VAC pressure protocols.

In conclusion, this study provides morphological confirmation that VAC therapy accelerates abscess healing in diabetic pulmonary tissue, with continuous negative pressure proving superior to intermittent mode. These findings validate the extension of VAC therapy into thoracic applications and support its further exploration in clinical practice.

### CONCLUSION

This experimental study demonstrates that vacuum-assisted closure (VAC) therapy significantly enhances the healing of pulmonary abscesses under diabetic conditions. Continuous negative pressure at  $-80$  mmHg provided superior histological outcomes compared to both intermittent VAC and passive drainage. The therapy led to reduced necrosis, earlier granulation tissue formation, enhanced neovascularization, and more complete collagen deposition.

These results offer biological validation for the clinical use of VAC therapy in the thoracic cavity, particularly in high-risk metabolic states such as type 2 diabetes mellitus. VAC therapy, especially in continuous mode, should be considered a promising adjunct in the treatment of deep pulmonary infections where standard drainage is insufficient.

#### **Ethical Approval:**

All experimental procedures were reviewed and approved by the Institutional Animal Care and Use Com-

mittee (IACUC) of Tashkent Medical Academy. All efforts were made to minimize animal suffering.

#### **Conflict of Interest:**

The author declares no conflict of interest.

#### **Funding:**

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#### **Author Contributions:**

Khamdamov Sh.A. – Conceptualization, experimental design, animal surgery, histological analysis, data interpretation, manuscript writing.

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**DIABETIK QUYON MODELLASHTIRILGAN  
O‘PKA ABSTSESSIDA VAKUUM-TERAPIYANING  
MORFOLOGIK SAMARALARI**

**Khamdamov Sh.A.**

**Toshkent tibbiyot akademiyasi**

**ANNOTATSIYA**

Vakuum-assistensiyalangan terapiya (VAC) yuzaki yaralarda samaradorligi isbotlangan bo‘lsa-da, uning ichki organ infeksiyalariga, xususan o‘pka abstsesslariga morfologik ta’siri yetarlicha o‘rganilmagan. Ushbu eksperimental tadqiqotda 36 nafar streptozotsin orqali diabet modellashtirilgan quyonlarda sun’iy o‘pka abstsessi hosil qilindi. Guruhlar quyidagicha bo‘lindi: nazorat (drenajsiz), doimiy vakuum (–80 mmHg) va interval vakuum (5/2 rejim). 3, 7 va 14-kunlarda olingan biopsiyalar histologik jihatdan baholandi. Doimiy VAC-terapiya yallig‘lanishni tez bartaraf etgan, granulatsiya to‘qimasining erta shakllanishi va kollagen hosil bo‘lishini ta’minlagan. Interval vakuum o‘rtacha natija bergan. Nazorat guruhida esa abstsess to‘liq saqlanib qolgan. Ushbu natijalar o‘pka infeksiyalarini VAC yordamida davolashda biologik asos mavjudligini ko‘rsatadi.

**Kalit so‘zlar:** Vakuum terapiya, o‘pka abstsessi, eksperimental model, qandli diabet, histologiya, yallig‘lanish.

**МОРФОЛОГИЧЕСКОЕ ВЛИЯНИЕ ВАКУУМ-  
ТЕРАПИИ НА ЭКСПЕРИМЕНТАЛЬНЫЕ  
АБСЦЕССЫ ЛЕГКИХ В МОДЕЛИ САХАРНОГО  
ДИАБЕТА У КРОЛИКОВ**

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**АННОТАЦИЯ**

Несмотря на широкое использование вакуум-ассоциированной терапии (VAC) при поверхностных инфекциях, ее тканевое воздействие при внутригрудных процессах остается малоизученным. Целью данного исследования было морфологическое изучение динамики заживления абсцессов легких под влиянием VAC-терапии в условиях индуцированного сахарного диабета у кроликов. В исследовании участвовали 36 животных, разделенных на три группы: контрольная (без VAC), VAC с непрерывным отрицательным давлением (–80 мм рт. ст.) и VAC с интервальным режимом (5/2). Гистологическое исследование биопсийных образцов, полученных на 3, 7 и 14 сутки, показало, что непрерывная VAC значительно ускоряет грануляцию, уменьшает зону некроза, усиливает ангиогенез и способствует раннему формированию зрелого коллагена. Интервальная VAC имела умеренный эффект, а в контрольной группе сохранялись признаки активного воспаления. Эти данные подтверждают целесообразность применения VAC-терапии при лёгочных инфекциях у пациентов с нарушением метаболизма.

**Ключевые слова:** Вакуум-терапия, абсцесс легкого, сахарный диабет, эксперимент, морфология, заживление.