



## Guideline

# Consensus on the application of negative pressure wound therapy of diabetic foot wounds

Shizhao Ji<sup>1</sup>, Xiaobin Liu<sup>1</sup>, Jie Huang<sup>1</sup>, Junmin Bao<sup>1</sup>, Zhaohong Chen<sup>2</sup>, Chunmao Han<sup>3</sup>, Daifeng Hao<sup>4</sup>, Jingsong Hong<sup>5</sup>, Dahai Hu<sup>6</sup>, Yufeng Jiang<sup>7</sup>, Shang Ju<sup>8</sup>, Hongye Li<sup>9</sup>, Zongyu Li<sup>10</sup>, Guangping Liang<sup>11</sup>, Yan Liu<sup>12</sup>, Gaoxing Luo<sup>11</sup>, Guozhong Lv<sup>13</sup>, Xingwu Ran<sup>14</sup>, Zhongmin Shi<sup>15</sup>, Juyu Tang<sup>16</sup>, Aiping Wang<sup>17</sup>, Guangyi Wang<sup>1</sup>, Jiangning Wang<sup>18</sup>, Xin Wang<sup>19</sup>, Bing Wen<sup>20</sup>, Jun Wu<sup>21</sup>, Hailin Xu<sup>22,23</sup>, Maojin Xu<sup>1</sup>, Xiaofei Ye<sup>1</sup>, Liangxi Yuan<sup>1</sup>, Yi Zhang<sup>24</sup>, Shichu Xiao<sup>1,\*</sup> and Zhaofan Xia<sup>1,\*</sup>

<sup>1</sup>Burn Institute of PLA, Department of Burns, The First Affiliated Hospital of Naval Medical University, No. 168 Changhai Road, Yangpu District, Shanghai, 200433, China, <sup>2</sup>Fujian Burn Institute, Fujian Medical University Union Hospital, No. 29 Xinquan Road, Gulou District, Fuzhou, 350001, China, <sup>3</sup>Department of Burns & Wound Care Center, Second Affiliated Hospital of Zhejiang University, College of Medicine, No. 88 Jiefang Road, Shangcheng District, Hangzhou, 310009, China, <sup>4</sup>No. 3 Department of Burns and Plastic Surgery and Wound Healing Center, The Fourth Medical Center of Chinese PLA General Hospital, No 51 Fucheng Road, Haidian District, Beijing, 100048, China, <sup>5</sup>Foot and Ankle Surgery Department, Guangzhou Zhenggu Orthopedic Hospital, No. 449 Dongfeng Middle Road, Yuexiu District, Guangzhou, 510031, China, <sup>6</sup>Department of Burns and Cutaneous Surgery, The First Affiliated Hospital of Air Force Medical University, No. 127 West Changle Road, Xincheng District, Xi'an, 710032, China, <sup>7</sup>Wound Healing Department, PLA Strategic Support Force Characteristic Medical Center, No. 9 Anxiang North Lane, Chaoyang District, Beijing, 100101, China, <sup>8</sup>Department of Peripheral Vascular, Beijing University of Chinese Medicine, Dongzhimen Hospital, Hai Yun Cang on the 5th, Dongcheng District, Beijing, 100700, China, <sup>9</sup>Department of Orthopedics, Zhejiang University School of Medicine, Sir Run Run Shaw Hospital, No. 3 East Qinchun Road, Shangcheng District, Hangzhou, 310016, China, <sup>10</sup>Department of Burns, The Fifth Hospital of Harbin, No. 27 Jiankang Road, Xiangfang District, 150030, Harbin, China, <sup>11</sup>Institute of Burn Research, State Key Laboratory of Trauma, Burn and Combined Injury, Southwest Hospital, Third Military Medical University, Gaotanyan Street no. 29, Shapingba District, Chongqing, 400038, China, <sup>12</sup>Department of Burn, Shanghai Jiaotong University, School of Medicine Affiliated Ruijin Hospital, No. 197 Ruijin Road (No.2), Huangpu District, Shanghai, 200025, China, <sup>13</sup>Department of Burn Surgery, the Third People's Hospital of Wuxi, No. 585 North Xingyuan Road, Wuxi, 214043, China, <sup>14</sup>Innovation Center for Wound Repair, Diabetic Foot Care Center, Department of Endocrinology and Metabolism, West China Hospital, Sichuan University, No. 37 Guoxue Lane, Chengdu, China, <sup>15</sup>Department of Orthopedics, Shanghai Jiaotong University Affiliated Sixth People's Hospital, No. 600 Yishan Road, Xuhui District, Shanghai, 200233, China, <sup>16</sup>Department of Hand and Microsurgery, Xiangya Hospital of Central South University, No. 87 Xiangya Road, Kaifu District, Changsha, 410008, China, <sup>17</sup>Diabetic Foot Centre, The Air Force Hospital From Eastern Theater of PLA, Nanjing, No.1 Malu Road, Qinhuai District, 210002, China, <sup>18</sup>Department of Orthopedic Surgery, Beijing Shijitan Hospital, Capital Medical University, No. 10 Tieda Road, Haidian District, Beijing, 100038, China, <sup>19</sup>Department of Plastic and Hand Surgery, Ningbo No. 6 Hospital, No. 1059 East Zhongshan Road, YinZhou District, Ningbo, 315040, China, <sup>20</sup>Plastic and Burn Surgery Department, Diabetic Foot Prevention and Treatment Center, Peking University First Hospital, No.8, Xishiku Street, Xicheng District, Beijing, 100034, China and <sup>21</sup>Department of Burn and Plastic Surgery, Second People's Hospital of Shenzhen, Shenzhen University, No. 3002 West Sungang Road, Futian District, Shenzhen, 518037, China,

<sup>22</sup>Department of Orthopedics and Trauma, Peking University People's Hospital, Peking University, No.11 Xizhimen South Street, Beijing, 100044, China, <sup>23</sup>Diabetic Foot Treatment Center, Peking University People's Hospital, Peking University, No.11 Xizhimen South Street, Beijing, 100044, China and <sup>24</sup>Department of Burn and Plastic Surgery, Affiliated Hospital of Nantong University, No. 20 Xisi Road, Nantong, 226001, China

\*Correspondence. Shichu Xiao, Email: huangzhuoxiao4@hotmail.com; Zhaofan Xia, Email: xiazhaofan@163.com

Received 12 January 2021; Revised 17 March 2021; Editorial decision 21 April 2021

## Abstract

Because China is becoming an aging society, the incidence of diabetes and diabetic foot have been increasing. Diabetic foot has become one of the main health-related killers due to its high disability and mortality rates. Negative pressure wound therapy (NPWT) is one of the most effective techniques for the treatment of diabetic foot wounds and great progress, both in terms of research and its clinical application, has been made in the last 20 years of its development. However, due to the complex pathogenesis and management of diabetic foot, irregular application of NPWT often leads to complications, such as infection, bleeding and necrosis, that seriously affect its treatment outcomes. In 2020, under the leadership of Burns, Trauma and Tissue Repair Committee of the Cross-Straits Medicine Exchange Association, the writing group for 'Consensus on the application of negative pressure wound therapy of diabetic foot wounds' was established with the participation of scholars from the specialized areas of burns, endocrinology, vascular surgery, orthopedics and wound repair. Drawing on evidence-based practice suggested by the latest clinical research, this consensus proposes the best clinical practice guidelines for the application and prognostic evaluation of NPWT for diabetic foot. The consensus aims to support the formation of standardized treatment schemes that clinicians can refer to when treating cases of diabetic foot.

**Key words:** Vacuum sealing drainage, Vacuum-assisted closure, Vacuum-assisted therapy, Negative pressure wound therapy, Topical negative pressure therapy, Suction wound closure therapy, Diabetic foot, Diabetic ulcer, Diabetic wound

## Highlights

- Irregular application of NPWT often leads to complications, and seriously affect its treatment outcomes.
- The writing group for the present article was established with the participation of scholars from the specialized areas of burns, endocrinology, vascular surgery, orthopedics and wound repair.
- The consensus aims to support the formation of standardized treatment schemes that clinicians can refer to when treating cases of diabetic foot.

---

## Background

Diabetic foot is a serious complication in patients who have advanced diabetes and refers to foot infections, ulcers and/or deep tissue destruction caused by nerve abnormalities and vascular lesions in the distal lower limb(s) of these patients. According to the International Working Group on the Diabetic Foot [1], an amputation for diabetic foot is performed every 20 seconds and for more than 1 million people every year. In 2017, there were 425 million diabetic patients globally and this is expected to increase to 629 million by 2045. According to an expert opinion published in the *New England Journal of Medicine*, 19–34% of diabetic patients develop diabetic foot ulcers, the mortality rate 5 years post amputation is greater than 70% and the mortality rate 2 years post amputation in those on kidney dialysis is as high as 74% [2]. The mortality risk in patients with diabetic foot is much higher than in those with some malignant tumors. Diabetic foot has become one of the main health-related killers due to

its high disability and mortality rates; therefore, its prevention and treatment has become an urgent clinical issue.

The treatment of diabetic foot requires a cross-disciplinary and systematic approach that comprises blood glucose control, surgical debridement, vascular recanalization, decompression treatment and supportive treatment. Controlling wound infection and promoting tissue repair are vital for preventing amputation or reducing the level of amputation [3, 4]. The concept of negative pressure wound therapy (NPWT) was first established and applied in clinical practice by a German physician, Fleischmann, in 1993 and has, ever since, been recognized for its remarkable effect in improving wound drainage, enhancing perfusion and promoting the growth of granulation tissue. Today, NPWT is widely used for various acute and chronic wounds, such as diabetic foot ulcers. In 2016, NPWT had been recommended with class I evidence by the Wound Healing Society of the United States in its diabetic foot ulcer treatment guidelines. NPWT

improves wound healing by reducing edema, removing bacterial products and approximating wound edges and should be considered as a treatment strategy when others fail [5]. In 2017, the European Wound Management Association had reported that NPWT-assisted treatment for diabetic foot ulcers promotes granulation tissue proliferation and accelerates wound healing [6]. The International Working Group on the Diabetic Foot recommended using NPWT to promote ulcer healing in its 2019 international guidelines on the prevention and management of diabetic foot [1].

As NPWT is an important adjunctive treatment for diabetic foot wounds, it should be standardized in terms of its application conditions, parameter adjustments, evaluations and other important aspects. The consensus committee of Tucson Expert Consensus Conference on V.A.C. Therapy first published 'Guidelines regarding negative wound therapy (NPWT) in the diabetic foot' in 2004 in the United States [7]; this document, which was later updated and revised in 2006, provides suggestions on the clinical application of NPWT for diabetic foot wounds [8]. Although NPWT was developed within 30 years, rapid progress in research and its clinical applications has been made, especially regarding its use in the management of diabetic foot wounds.

For these reasons, and for the purpose of establishing evidence-based guidelines, the Tissue Repair of Burns and Trauma Committee and the Cross-Straits Medicine Exchange Association discussed the latest clinical research and drafted this 'Consensus on the application of negative pressure wound therapy for diabetic foot wounds'. By providing guidance on the best clinical practice guidelines for the application and prognostic evaluation of NPWT for diabetic foot, this consensus aims to support the formation of standardized treatment schemes that clinicians can refer to when treating cases of diabetic foot.

## Methods

### Data retrieval

This consensus was compiled by professional scholars from the specialized areas of burns, endocrinology, vascular surgery, orthopedics and wound repair and based on high-quality literature on the application of NPWT for diabetic foot. This article is based on domestic and foreign guidelines, combined with the clinical experience and research results and is written with an emphasis on practicability and feasibility. Each recommendation in this article represents a consensus from the specialists committee. However, due to the lack of sufficient evidence from large-scale randomized controlled trials (RCTs) and a comprehensive understanding from the specialists committee, many of the recommendations in this paper are preliminary and require further evidence before they can be fully recommended.

The key words used in the search for relevant literature were: vacuum sealing drainage, vacuum-assisted closure, vacuum assisted therapy, NPWT, topical negative pressure therapy, suction wound closure therapy, diabetic foot,

diabetic ulcer and diabetic wound. The search was conducted on the PubMed, Embase and Cochrane Library databases. The retrieval time ranged from the time the databases were established to 1 July 2020. References to support manual retrieval were also used for topics limited to human diseases. The types of articles that were reviewed included meta-analyses, systematic reviews, randomized controlled trials, retrospective series reviews, clinical case series and expert panel recommendations.

### Levels of evidence and grades of recommendation

The levels of evidence and grades of recommendation of each article were classified according to a modified version of the evaluation system of Oxford Centre for Evidence-based Medicine levels of evidence (May 2001) (Table 1) [9]. According to the Delphi technique, each evidence guideline underwent independent and repeated evaluations by every member of our panel of experts before a unanimous opinion regarding recommendations was reached.

## Recommendations

### Application of NPWT for diabetic foot wounds

**Overview** The treatment of diabetic foot wounds requires a multi-disciplinary and systematic approach [10, 11]. The therapeutic goal should be to not only prevent the spread of infection and reduce the level of amputation but also prevent the progression of systemic atherosclerotic diseases, delay the occurrence of diabetes-related complications, prevent the occurrence of cardiovascular and cerebrovascular events and reduce mortality [12]. For diabetic foot wounds, the fundamental therapeutic principles are the control of wound infection, improvement of local tissue perfusion and promotion of tissue repair. Due to its excellent effects of enhancing local perfusion, promoting granulation tissue growth and improving wound healing, NPWT has become an important adjuvant treatment in the management of diabetic foot wounds [13–25]. According to many clinical randomized controlled studies, the application of NPWT for diabetic foot wounds may significantly increase the rate of wound healing, shorten healing time and reduce the rate of amputation [26–38]; it is currently recommended by the Wound Healing Society and the European Wound Management Association [39–41].

*(Grade of recommendation: strong; level of evidence: strong.)*

**Prerequisite conditions** NPWT for diabetic foot wounds is recommended under the following conditions:

- (1) Wound infection is well-controlled: after debridement, the necrotic tissue has cleared and infection (especially if hidden in the fascia or interstitial space) has been controlled [42–49].
- (2) The risk of bleeding is well-controlled: bleeding has completely stopped after debridement, there is no active bleeding or exposed vascular damage on the wound, there is no serious risk of coagulation dysfunction or

**Table 1.** Level of evidence and grade of recommendation for the application of NPWT in DFU

<b>Level of evidence</b>	
Strong	Based on well-designed randomized controlled trials, meta-analyses or systematic evaluations
Moderate	Based on well-designed cohort or case-control studies
Weak	Based on well-designed case series and expert advice
<b>Grade of recommendation</b>	
Strong	Indicating a clear treatment effect or highly unanimous recognition by experts
Moderate	Indicating unclear possible risks and effect after treatment
Weak	Indicating expert opinions about a likely treatment choice with low level of evidence at the present stage

This table is modified based on 2001 Oxford Centre for Evidence-Based Medicine 'Levels of Evidence' and 'Grades of Recommendation' [9]  
 NPWT Negative Pressure Wound Therapy, DFU Diabetic Foot Ulcer

potential bleeding and INR range from 1.0 to 2.0 [7, 50, 51].

- (3) The risk of ischemia is well-controlled: there is adequate wound and distal limb perfusion and  $TcpO_2 > 40$  mmHg, ABI range from 0.9 to 1.3 or  $TBI \geq 0.6$  [52–58].

(Grade of recommendation: moderate; level of evidence: moderate.)

#### Parameter settings

**Pressure** For diabetic foot ulcers without vascular lesions, the recommended pressure range is between  $-125$  and  $-80$  mmHg [59, 60]. For vascular stenotic or occlusive lesions, the recommended pressure range is between  $-80$  mmHg and  $-60$  mmHg [61].

**Mode** NPWT may be applied in a continuous, intermittent or variable mode. In clinical practice, the most commonly used mode is continuous, in which a stable level of negative pressure is maintained. Intermittent pressure therapy (IPT) is a relatively newer mode in which the negative pressure device switches on and off at preset time intervals (e.g. 5 minutes on, 2 minutes off). Many studies have shown that the blood flow and granulation tissue growth achieved by the IPT mode are much better than those seen when using the continuous mode. However, due to the tissue deformation that occurs with every cycle of IPT, patients may experience significant pain. Therefore, the variable pressure therapy (VPT) mode was created. The biggest difference between the VPT and IPT modes is that the minimum negative pressure value of the VPT mode is a certain negative pressure value (e.g.  $-10$  mmHg), rather than 0 mmHg. The VPT mode has the same advantages as the IPT mode but causes less pain and is easily accepted by patients. Both preclinical and clinical studies have shown that IPT and VPT modes lead to better granulation tissue growth, wound contraction and wound epithelialization. It is therefore recommended that the continuous mode is applied for the first 48 hours, followed by the IPT (5 minutes on, 2 minutes off) or VPT mode (high:  $-80$  mmHg, low:  $-10$  mmHg).

**Note** The settings should be adjusted according to the patient's condition and the size of the wound [62–65].

- (1) For larger and more complex wounds that are difficult to seal, the negative pressure value may be increased accordingly.
- (2) For patients who have undergone skin grafting or dermal stent grafting, the continuous mode should be applied for 5–7 days.

- (3) For patients who are at risk of bleeding (e.g. coagulation dysfunction or long-term anticoagulant use), the negative pressure value should be reduced accordingly.

- (4) Some patients cannot tolerate even slight amounts of pain; therefore, the NPWT mode should be selected according to the patient's pain tolerance.

(Grade of recommendation: moderate; level of evidence: moderate.)

**Evaluation and management of the effect of NPWT in treating diabetic foot wounds** For surgical debridement of diabetic foot wounds, the 'nibbling' principle, with limited batched debridement, is usually adopted. There are an abundance of soft tissue and fascial spaces in the feet. In clinical practice, a small amount of necrotic tissue may remain within the wound and, even after several rounds of debridement, it is unlikely that hidden foci of infection would have been removed. Therefore, there is a risk that infection may spread after NPWT [66]. In addition, even after revascularization of the ischemic wound, there is a short-term risk of reclosure of blood vessels and wound ischemia. At the same time, for patients who need to take anticoagulants for a long duration, there may be a risk of wound bleeding after NPWT [67]. In order to detect potential risks like infection, bleeding, ischemia, it is recommended that daily evaluation is done to carefully inspect for wound pain, redness and swelling; changes in skin color and temperature around the wound; and color, odor and volume of wound drainage fluid; along with blood tests and imaging to comprehensively evaluate for wound infection, ischemia, bleeding, and the overall condition of the patient [68–71]. If wound infection is not under control, avascular necrosis is aggravated or the wound continues to bleed, the negative pressure dressings should be removed and the wound should be reevaluated. NPWT may be applied again only after infection is controlled, tissue ischemia has improved and the risk of bleeding has reduced [72]. If pain and swelling are aggravated, but without wound infection, tissue ischemia, or other systemic conditions, it is recommended to reduce or suspend the negative pressure, change the mode of negative pressure treatment for observation and remove the negative pressure if necessary [73].

After 1–2 rounds of NPWT application, a comprehensive evaluation of its effects should be conducted. The effectiveness evaluation and recommended treatment measures are as follows [74–77].

- (1) Significantly effective: there is growth of new granulation tissue on the wound surface or a reduction of the wound surface with surrounding epithelialization; it is recommended to continue NPWT.
- (2) Effective: wound infection or tissue ischemia improves, the wound is ruddy and blood perfusion is good; it is recommended to apply NPWT 1–2 times and re-evaluate.
- (3) Ineffective: wound infection or tissue ischemia does not improve, the infection is aggravated or the tissue is more necrotic; it is recommended to stop the NPWT, recanalize the blood vessels and re-evaluate after infection is controlled.

(Grade of recommendation: moderate; level of evidence: moderate.)

**Frequency of replacement** The frequency of NPWT replacement after debridement should be determined based on the condition of the wound [78–81]. In the absence of infection, active bleeding or tissue ischemia, it is recommended that the dressing is replaced after 3–5 days and within 7 days. The frequency of dressing replacement after skin grafting may be extended to 5–7 days.

*Note* Polyvinyl alcohol foam is hydrophilic, so it tends to harden and block the vessels when there is less wound exudation and may even compress the wound site and cause tissue ischemia; thus, close observation and timely NPWT dressing replacement is required. The pore diameters of polyurethane foam are relatively large, providing room for granulation tissue to grow into. Therefore, NPWT should not be applied for a long time to avoid the risk of granulation tissue growing into the porous structure of the foam and causing damage and unnecessary blood loss during foam removal [82].

(Grade of recommendation: weak; level of evidence: weak.)

**Common complications and their management** Before applying NPWT for diabetic foot wounds, the application conditions should be fully understood. Continuous assessment should occur throughout the process and the application should be stopped or the vacuum dressings replaced according to the situation of the wounds [83–85]. Compared with conventional diabetic foot wound treatment methods, NPWT does not significantly increase complications. The possible complications and recommended measures are as follows.

- (1) In cases of wound bleeding or aggravation of wound infection, treatment with NPWT should be stopped immediately, the NPWT device should be removed and the conditions should be reassessed after the infection is controlled by hemostasis or debridement and a dressing change [86].
- (2) In cases of aggravation of ischemia or necrosis, treatment with NPWT should be stopped immediately, the NPWT device should be removed and the conditions should be reassessed after the ischemia improves by increased perfusion [87].

- (3) In cases of eczema around the wound or tension vesicles on the region of normal skin under the applied film (the most common complications), a skin film should be applied to protect the surrounding skin, the vacuum pressure should be reduced and skin stretch when applying the film should be minimized [88].
- (4) In cases of granulation tissue growing into the foam material, NPWT should not be kept for too long and be replaced at intervals of 3–5 days. Foam material should be removed as thoroughly as possible to prevent a secondary infection [89].
- (5) If the wound pain or edema worsens, but wound infection, tissue ischemia and systemic conditions can be excluded, negative pressure might be reduced or paused, the negative mode can be changed and closely observed, or remove it if necessary [90].

(Grade of recommendation: moderate; level of evidence: weak.)

**Economic evaluation** Compared to conventional treatment, NPWT reduces the number of dressing changes, the consumption of medical supplies and the requirement of human resources; this results in lower treatment expenses and medical costs and a higher overall potency ratio. Therefore, NPWT is recommended for the treatment of diabetic foot wounds [91–105].

(Grade of recommendation: moderate; level of evidence: moderate.)

**Application of improved NPWT** In recent years, many improved NPWTs have been used for diabetic foot wounds, including NPWT with instillation [64, 106–114] and local oxygen negative pressure [115]. Preliminary studies have shown that these have certain advantages in preventing and controlling wound infections and promoting wound debridement [107, 116–118]; however, there is limited high-quality research evidence at present and large-scale multicenter clinical verification is still needed.

(Grade of recommendation: weak; level of evidence: weak.)

### Specific applications of NPWT for complicated diabetic foot wounds

**Infected wounds** Diabetic foot wounds are highly susceptible to infection and, if severe, may develop into extensive cellulitis, osteomyelitis or even necrotizing fasciitis, which are life-threatening. For severely infected patients, a comprehensive assessment of the patient's systemic condition is required and amputation should be performed if necessary [119–121]. For limb-salvage patients, multiple debridement operations should be performed. Vascular recanalization and other treatments may be used to improve distal tissue ischemia and ensure sufficient blood perfusion after necrotic tissue removal and infection control [122–125]. NPWT may only be applied on this basis. At the same time, continuous assessment is required during the application and NPWT should be stopped or replaced according to the clinical situation [126–128].

(*Grade of recommendation: moderate; level of evidence: weak.*)

**Wound exposing bone and/or tendon** For wounds exposing bone and/or tendon, it is recommended that a skin flap coverage be used. NPWT may be used to improve the basic condition or cultivate granulation tissue to create a suitable condition for the transfer of a skin flap or skin graft in the following cases.

- (1) The basic conditions of the wound are currently unsuitable for skin flap repair [129–131].
- (2) Skin flap repair cannot be performed due to vascular stenosis or poor blood supply. [132].
- (3) Small wounds exposing bone and/or tendon [96, 133].

(*Grade of recommendation: weak; level of evidence: weak.*)

**Wounds with osteomyelitis** For diabetic foot wounds with osteomyelitis, thorough debridement, removal of sequestrums and systemic antibiotic therapy for 2–4 weeks are required. NPWT should be used until the infection is effectively controlled [134–136]. Continuous assessment and close observation for local infection of the wound are required during the application process and NPWT should be stopped or replaced accordingly [137–139]. For osteomyelitis patients with poorly controlled infection, or in cases for whom the control of infection is yet to be determined, NPWT should be used with caution [140, 141].

(*Grade of recommendation: moderate; level of evidence: weak.*)

**After skin graft or flap transfer** Studies have shown that for both reticular skin grafts and stamp skin grafts, continuous vacuum suction effectively increases the survival rate of the skin and shortens the time required for wound healing [142–145]. It is recommended that NPWT is applied in continuous vacuum suction mode with a pressure between –100 and –80 mmHg for 5–7 days according to wound exudation [146–148].

The conventional use of NPWT devices is not recommended after flap transfer. If NPWT is used, it is necessary to avoid pressing the pedicle of the flap. Continuous vacuum suction should be performed for 48 hours, followed by IPT (suction for 5 minutes, pause for 2 minutes) with a pressure between –80 and –60 mmHg for 3–5 days according to wound exudation [149, 150].

(*Grade of recommendation: moderate; level of evidence: weak.*)

**Wounds grafted with dermal equivalents** Studies have confirmed that the NPWT device effectively promotes vascularization of the dermal equivalent. At the same time, its good drainage effect may prevent fluid accumulation under the dermal equivalent and its decreased need for frequent dressing changes may reduce possible wound exposure and infection, improve the success rate of dermal equivalent grafting and provide good conditions for subsequent skin grafting [151–154]. After dermal equivalent grafting, continuous vacuum suction mode should be applied with a pressure between

–100 and –80 mmHg [155, 156] for 5–7 days according to wound exudation.

(*Grade of recommendation: moderate; level of evidence: weak.*)

**Wounds after extremity or toe amputations (with condition of primary suture)** NPWT is recommended due to its good drainage effect, which reduces the accumulation of exudate in the stump, and for its fixation effect (due to vacuum sealing for stabilizing the stump tissue), which promotes tissue remodeling and wound closure [157–159]. Continuous vacuum suction mode should be applied with a pressure between –80 and –60 mmHg for 5–7 days according to wound exudation.

(*Grade of recommendation: moderate; level of evidence: weak.*)

**Wounds after extremity or toe amputations (without condition of primary suture)** NPWT is recommended for the treatment of stump wounds to promote granulation tissue proliferation and tissue reconstruction after the risks of ischemia and bleeding are reduced, necrotic tissue is cleared and infection is controlled [160, 161]. The IPT (suction for 5 minutes, pause for 2 minutes) or VPT mode should be applied, with pressures between –80 mmHg and –60 mmHg or –80 mmHg and –10 mmHg, respectively, for 3–5 days according to wound exudation.

(*Grade of recommendation: strong; level of evidence: strong.*)

## Conclusion

The treatment of diabetic foot requires a cross-disciplinary and systematic approach, within which NPWT is an important adjunct treatment for diabetic foot wounds. The standardized management and application of NPWT may improve wound exudate drainage, enhance blood perfusion and promote wound healing. In view of the potential risks after its application, we compiled this consensus through a systematic review of the literature, aiming to form standardized treatment schemes for diabetic foot through the use of NPWT. However, it is necessary to point out that the levels of evidence in this consensus are not very high; therefore, more high-quality randomized controlled trials are needed to determine the most appropriate application methods and potential effects of NPWT for diabetic foot wounds.

## Abbreviations

IPT: intermittent pressure therapy; NPWT: negative pressure wound therapy; VPT: variable pressure therapy.

## Funding

Research on in situ skin repair and regeneration based on micro-tissue engineering technology and 3D printing. (The National Key R&D Program of China, Grant Number 2019YFA0110503). The study on natural living micro-angiogenic scaffolds to dynamic regulate immune inflammation

and reconstruct wound repairing. (National Natural Science Foundation of China, Grant Number 81971836). The systemic study of miR-23b\_24-1 cluster in the prevention and treatment of MODS caused by sepsis after burns. (National Natural Science Foundation of China, Grant Number 81930057). The experimental study on regulating the immune inflammatory microenvironment of burn wounds and promoting repair and regeneration based on micro-tissue engineering technology. (National Natural Science Foundation of China, Grant Number 81871559).

### Conflicts of interest

There were no commercial interests between any of the members of the working group during the compilation process. Each member of the working group made a statement regarding his/her conflict of interest.

### References

- Schaper NC, van Netten JJ, Apelqvist J, Bus SA, Hinchliffe RJ, Lipsky BA, et al. Practical Guidelines on the prevention and management of diabetic foot disease (IWGDF 2019 update). *Diabetes Metab Res Rev.* 2020;36(Suppl 1):e3266. doi: [10.1002/dmrr.3266](https://doi.org/10.1002/dmrr.3266).
- Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. *N Engl J Med.* 2017 Jun 15;376(24):2367–75. doi: [10.1056/NEJMra1615439](https://doi.org/10.1056/NEJMra1615439) PMID: 28614678.
- Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. *Ann N Y Acad Sci.* 2018 Jan;1411(1):153–65. DOI: [10.1111/nyas.13569](https://doi.org/10.1111/nyas.13569).
- Bakker K, Apelqvist J, Lipsky BA, Van Netten JJ. International Working Group on the Diabetic Foot. The 2015 IWGDF guidance documents on prevention and management of foot problems in diabetes: development of an evidence-based global consensus. *Diabetes Metab Res Rev.* 2016 Jan;32(Suppl 1):2–6. doi: [10.1002/dmrr.2694](https://doi.org/10.1002/dmrr.2694).
- Lavery LA, Davis KE, Berriman SJ, Braun L, Nichols A, Kim PJ, et al. WHS guidelines update: Diabetic foot ulcer treatment guidelines. *Wound Repair Regen.* 2016 Jan-Feb;24(1):112–26. doi: [10.1111/wrr.12391](https://doi.org/10.1111/wrr.12391).
- Apelqvist J, Willy C, Fagerdahl AM, Fracalvieri M, Malmjö M, Piaggese A, et al. EWMA Document: Negative Pressure Wound Therapy. *J Wound Care.* 2017 Mar 1;26(Sup3):S1–154. doi: [10.12968/jowc.2017.26.Sup3.S1](https://doi.org/10.12968/jowc.2017.26.Sup3.S1).
- Armstrong DG, Attinger CE, Boulton AJ, Frykberg RG, Kirsner RS, Lavery LA, et al. Guidelines regarding negative wound therapy (NPWT) in the diabetic foot. *Ostomy Wound Manage.* 2004 Apr;50(4B Suppl):3S–27 15311482.
- Andros G, Armstrong DG, Attinger CE, Boulton AJ, Frykberg RG, Joseph WS, et al. Consensus statement on negative pressure wound therapy (V.A.C. Therapy) for the management of diabetic foot wounds. *Ostomy Wound Manage.* 2006 Jun;(Suppl):1–32 PMID: 17007488.
- Phillips B, Ball C, Sackett D, Badenoch D, Straus SE, Haynes B, et al. Evidence-based Medicine Levels of Evidence, 2001. Available at: [http://www.cebm.net/levels\\_of\\_evidence.asp](http://www.cebm.net/levels_of_evidence.asp).
- Rys P, Borys S, Hohendorff J, Zapala A, Witek P, Monica M, et al. NPWT in diabetic foot wounds—a systematic review and meta-analysis of observational studies. *Endocrine.* 2020;68(1):44–55. doi: [10.1007/s12020-019-02164-9](https://doi.org/10.1007/s12020-019-02164-9).
- Mohseni S, Aalaa M, Atlasi R, Mohajeri Tehrani MR, Sanjari M, Amini MR. The effectiveness of negative pressure wound therapy as a novel management of diabetic foot ulcers: an overview of systematic reviews. *J Diabetes Metab Disord.* 2019;18(2):625–41 Published 2019 Nov 25. doi: [10.1007/s40200-019-00447-6](https://doi.org/10.1007/s40200-019-00447-6).
- Braun LR, Fisk WA, Lev-Tov H, Kirsner RS, Isseroff RR. Diabetic foot ulcer: an evidence-based treatment update. *Am J Clin Dermatol.* 2014;15(3):267–81. doi: [10.1007/s40257-014-0081-9](https://doi.org/10.1007/s40257-014-0081-9).
- Zhang D, Li Z, Wang Z, Zeng F, Xiao W, Yu A. MicroRNA-126: a promising biomarker for angiogenesis of diabetic wounds treated with negative pressure wound therapy. *Diabetes Metab Syndr Obes.* 2019;12:1685–96 Published 2019 Sep 3. doi: [10.2147/DMSO.S199705](https://doi.org/10.2147/DMSO.S199705).
- Mu S, Hua Q, Jia Y, Chen MW, Tang Y, Deng D, et al. Effect of negative-pressure wound therapy on the circulating number of peripheral endothelial progenitor cells in diabetic patients with mild to moderate degrees of ischaemic foot ulcer. *Vascular.* 2019;27(4):381–9. doi: [10.1177/1708538119836360](https://doi.org/10.1177/1708538119836360).
- Almeida JE, Suárez R, Gibson E. A histological analysis of chronic wounds treated with negative pressure wound therapy to aid healing: a case series. *J Wound Care.* 2018;27(Sup2):S28–34. doi: [10.12968/jowc.2018.27.Sup2.S28](https://doi.org/10.12968/jowc.2018.27.Sup2.S28).
- Ma Z, Li Z, Shou K, Jian C, Li P, Niu Y, et al. Negative pressure wound therapy: Regulating blood flow perfusion and microvessel maturation through microvascular pericytes. *Int J Mol Med.* 2017;40(5):1415–25. doi: [10.3892/ijmm.2017.3131](https://doi.org/10.3892/ijmm.2017.3131).
- Izzo V, Meloni M, Giurato L, Ruotolo V, Uccioli L. The Effectiveness of Negative Pressure Therapy in Diabetic Foot Ulcers with Elevated Protease Activity: A Case Series. *Adv Wound Care (New Rochelle).* 2017;6(1):38–42. doi: [10.1089/wound.2016.0700](https://doi.org/10.1089/wound.2016.0700).
- Wang T, He R, Zhao J, Mei JC, Shao MZ, Pan Y, et al. Negative pressure wound therapy inhibits inflammation and upregulates activating transcription factor-3 and downregulates nuclear factor- $\kappa$ B in diabetic patients with foot ulcerations. *Diabetes Metab Res Rev.* 2017;33(4). doi: [10.1002/dmrr.2871](https://doi.org/10.1002/dmrr.2871).
- Yang SL, Han R, Liu Y, Hu LY, Li XL, Zhu LY. Negative pressure wound therapy is associated with up-regulation of bFGF and ERK1/2 in human diabetic foot wounds. *Wound Repair Regen.* 2014;22(4):548–54. doi: [10.1111/wrr.12195](https://doi.org/10.1111/wrr.12195).
- Wang A, Lv G, Cheng X, Ma X, Wang W, Gui J, et al. Guidelines on multidisciplinary approaches for the prevention and management of diabetic foot disease (2020 edition). *Burns Trauma.* 2020;8:tkaa017. doi: [10.1093/burnst/tkaa017](https://doi.org/10.1093/burnst/tkaa017).
- Lone AM, Zaroo MI, Laway BA, Pala NA, Bashir SA, Rasool A. Vacuum-assisted closure versus conventional dressings in the management of diabetic foot ulcers: a prospective case-control study. *Diabet Foot Ankle.* 2014;5 Published 2014 Apr 8. doi: [10.3402/dfa.v5.23345](https://doi.org/10.3402/dfa.v5.23345).
- Seo SG, Yeo JH, Kim JH, Kim JB, Cho TJ, Lee DY. Negative-pressure wound therapy induces endothelial progenitor cell mobilization in diabetic patients with foot infection or skin defects. *Exp Mol Med.* 2013;45(11):e62 Published 2013 Nov 15. doi: [10.1038/emmm.2013.129](https://doi.org/10.1038/emmm.2013.129).
- Nain PS, Uppal SK, Garg R, Bajaj K, Garg S. Role of negative pressure wound therapy in healing of diabetic

- foot ulcers. *J Surg Tech Case Rep.* 2011;3(1):17–22. doi: [10.4103/2006-8808.78466](https://doi.org/10.4103/2006-8808.78466).
24. Khamaisi M, Balanson S. Dysregulation of wound healing mechanisms in diabetes and the importance of negative pressure wound therapy (NPWT). *Diabetes Metab Res Rev.* 2017 Oct;33(7). doi: [10.1002/dmrr.2929](https://doi.org/10.1002/dmrr.2929).
  25. Jung JA, Yoo KH, Han SK, Lee YN, Jeong SH, Dhong ES, et al. Influence of Negative-Pressure Wound Therapy on Tissue Oxygenation in Diabetic Feet. *Adv Skin Wound Care.* 2016;29(8):364–70. doi: [10.1097/01.ASW.0000483038.18331.a4](https://doi.org/10.1097/01.ASW.0000483038.18331.a4).
  26. James SMD, Sureshkumar S, Elamurugan TP, Debasis N, Vijayakumar C, Palanivel C. Comparison of Vacuum-Assisted Closure Therapy and Conventional Dressing on Wound Healing in Patients with Diabetic Foot Ulcer: A Randomized Controlled Trial. *Niger J Surg.* 2019;25(1):14–20. doi: [10.4103/njs.NJS\\_14\\_18](https://doi.org/10.4103/njs.NJS_14_18).
  27. Liu Z, Dumville JC, Hinchliffe RJ, Cullum N, Game F, Stubbs N, et al. Negative pressure wound therapy for treating foot wounds in people with diabetes mellitus. *Cochrane Database Syst Rev.* 2018;10(10):CD010318 Published 2018 Oct 17. doi: [10.1002/14651858.CD010318.pub3](https://doi.org/10.1002/14651858.CD010318.pub3).
  28. Yang SL, Zhu LY, Han R, Sun LL, Dou JT. Effect of Negative Pressure Wound Therapy on Cellular Fibronectin and Transforming Growth Factor- $\beta$ 1 Expression in Diabetic Foot Wounds. *Foot Ankle Int.* 2017;38(8):893–900. doi: [10.1177/1071100717704940](https://doi.org/10.1177/1071100717704940).
  29. Wang R, Feng Y, Di B. Comparisons of negative pressure wound therapy and ultrasonic debridement for diabetic foot ulcers: a network meta-analysis. *Int J Clin Exp Med.* 2015;8(8):12548–56 Published 2015 Aug 15.
  30. Zhang J, Hu ZC, Chen D, Guo D, Zhu JY, Tang B. Effectiveness and safety of negative-pressure wound therapy for diabetic foot ulcers: a meta-analysis. *Plast Reconstr Surg.* 2014;134(1):141–51. doi: [10.1097/PRS.0000000000000275](https://doi.org/10.1097/PRS.0000000000000275).
  31. Yarwood-Ross L, Dignon AM. NPWT and moist wound dressings in the treatment of the diabetic foot. *Br J Nurs.* 2012 Aug 9-Sep 12;21(15):S26, S28, S30-2. doi: [10.12968/bjon.2012.21.Sup20.S26](https://doi.org/10.12968/bjon.2012.21.Sup20.S26). PMID: 22874828.
  32. Game FL, Hinchliffe RJ, Apelqvist J, Armstrong DG, Bakker K, Hartemann A, et al. A systematic review of interventions to enhance the healing of chronic ulcers of the foot in diabetes. *Diabetes Metab Res Rev.* 2012;28(Suppl 1):119–41. doi: [10.1002/dmrr.2246](https://doi.org/10.1002/dmrr.2246).
  33. Karatepe O, Eken I, Acet E, Unal O, Mert M, Koc B, et al. Vacuum assisted closure improves the quality of life in patients with diabetic foot. *Acta Chir Belg.* 2011 Sep-Oct;111(5):298–302 PMID: 22191131.
  34. Blume PA, Walters J, Payne W, Ayala J, Lantis J. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: a multicenter randomized controlled trial. *Diabetes Care.* 2008;31(4):631–6. doi: [10.2337/dc07-2196](https://doi.org/10.2337/dc07-2196).
  35. Akbari A, Moodi H, Ghiasi F, Sagheb HM, Rashidi H. Effects of vacuum-compression therapy on healing of diabetic foot ulcers: randomized controlled trial. *J Rehabil Res Dev.* 2007;44(5):631–6. doi: [10.1682/jrrd.2007.01.0002](https://doi.org/10.1682/jrrd.2007.01.0002).
  36. Lavery LA, Barnes SA, Keith MS, Seaman JW Jr, Armstrong DG. Prediction of healing for postoperative diabetic foot wounds based on early wound area progression. *Diabetes Care.* 2008;31(1):26–9. doi: [10.2337/dc07-1300](https://doi.org/10.2337/dc07-1300).
  37. Eginton MT, Brown KR, Seabrook GR, Towne JB, Cambria RA. A prospective randomized evaluation of negative-pressure wound dressings for diabetic foot wounds. *Ann Vasc Surg.* 2003;17(6):645–9. doi: [10.1007/s10016-003-0065-3](https://doi.org/10.1007/s10016-003-0065-3).
  38. Chiang N, Rodda OA, Sleigh J, Vasudevan T. Effects of topical negative pressure therapy on tissue oxygenation and wound healing in vascular foot wounds. *J Vasc Surg.* 2017;66(2):564–71. doi: [10.1016/j.jvs.2017.02.050](https://doi.org/10.1016/j.jvs.2017.02.050).
  39. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis.* 2012;54(12):e132–73. doi: [10.1093/cid/cis346](https://doi.org/10.1093/cid/cis346).
  40. Kunze KN, Hamid KS, Lee S, Halvorson JJ, Earhart JS, Bohl DD. Negative-Pressure Wound Therapy in Foot and Ankle Surgery. *Foot Ankle Int.* 2020;41(3):364–72. doi: [10.1177/1071100719892962](https://doi.org/10.1177/1071100719892962).
  41. Isaac AL, Armstrong DG. Negative pressure wound therapy and other new therapies for diabetic foot ulceration: the current state of play. *Med Clin North Am.* 2013 Sep;97(5):899–909. doi: [10.1016/j.mcna.2013.03.015](https://doi.org/10.1016/j.mcna.2013.03.015). Epub 2013 May 4. PMID: 23992900.
  42. Lima RVKS, Coltro PS, Júnior FJA. Negative pressure therapy for the treatment of complex wounds. *Rev Col Bras Cir.* 2017;44(1):81–93. doi: [10.1590/0100-69912017001001](https://doi.org/10.1590/0100-69912017001001).
  43. Deng W, Boey J, Chen B, Byun S, Lew E, Liang Z, et al. Platelet-rich plasma, bilayered acellular matrix grafting and negative pressure wound therapy in diabetic foot infection. *J Wound Care.* 2016;25(7):393–7. doi: [10.12968/jowc.2016.25.7.393](https://doi.org/10.12968/jowc.2016.25.7.393).
  44. Hasan MY, Teo R, Nather A. Negative-pressure wound therapy for management of diabetic foot wounds: a review of the mechanism of action, clinical applications, and recent developments. *Diabet Foot Ankle.* 2015;6:27618 Published 2015 Jul 1. doi: [10.3402/dfa.v6.27618](https://doi.org/10.3402/dfa.v6.27618).
  45. Tansarli GS, Vardakas KZ, Stratoulis C, Peppas G, Kapaskelis A, Falagas ME. Vacuum-assisted closure versus closure without vacuum assistance for preventing surgical site infections and infections of chronic wounds: a meta-analysis of randomized controlled trials. *Surg Infect (Larchmt).* 2014;15(4):363–7. doi: [10.1089/sur.2013.028](https://doi.org/10.1089/sur.2013.028).
  46. Vig S, Dowsett C, Berg L, Caravaggi C, Rome P, Birke-Sorensen H, et al. Evidence-based recommendations for the use of negative pressure wound therapy in chronic wounds: steps towards an international consensus. *J Tissue Viability.* 2011;20(Suppl 1):S1–18. doi: [10.1016/j.jtv.2011.07.002](https://doi.org/10.1016/j.jtv.2011.07.002).
  47. Vikatmaa P, Juutilainen V, Kuukasjärvi P, Malmivaara A. Negative pressure wound therapy: a systematic review on effectiveness and safety. *Eur J Vasc Endovasc Surg.* 2008;36(4):438–48. doi: [10.1016/j.ejvs.2008.06.010](https://doi.org/10.1016/j.ejvs.2008.06.010).
  48. Suess JJ, Kim PJ, Steinberg JS. Negative pressure wound therapy: evidence-based treatment for complex diabetic foot wounds. *Curr Diab Rep.* 2006;6(6):446–50. doi: [10.1007/s11892-006-0077-9](https://doi.org/10.1007/s11892-006-0077-9).
  49. Medical Advisory Secretariat. Negative pressure wound therapy: an evidence-based analysis. *Ont Health Technol Assess Ser.* 2006;6(14):1–38 Epub 2006 Jul 1. PMID: 23074484; PMCID: PMC3379164.
  50. Capobianco CM, Zgonis T. An overview of negative pressure wound therapy for the lower extremity. *Clin Podiatr Med Surg.* 2009;26(4):619–31. doi: [10.1016/j.cpm.2009.08.002](https://doi.org/10.1016/j.cpm.2009.08.002).



51. Clare MP, Fitzgibbons TC, McMullen ST, Stice RC, Hayes DF, Henkel L. Experience with the vacuum assisted closure negative pressure technique in the treatment of non-healing diabetic and dysvascular wounds. *Foot Ankle Int.* 2002 Oct;23(10):896–901. doi: [10.1177/107110070202301002](https://doi.org/10.1177/107110070202301002).
52. Meloni M, Izzo V, Vainieri E, Giurato L, Ruotolo V, Uccioli L. Management of negative pressure wound therapy in the treatment of diabetic foot ulcers. *World J Orthop.* 2015;6(4):387–93 Published 2015 May 18. doi: [10.5312/wjo.v6.i4.387](https://doi.org/10.5312/wjo.v6.i4.387).
53. Miller JD, Carter E, Hatch DC, Zhubrak M, Giovinco NA, Armstrong DG. Use of collagenase ointment in conjunction with negative pressure wound therapy in the care of diabetic wounds: a case series of six patients. *Diabet Foot Ankle.* 2015;6:24999 Published 2015 Jan 27. doi: [10.3402/dfa.v6.24999](https://doi.org/10.3402/dfa.v6.24999).
54. A N, Khan WS, J P. The evidence-based principles of negative pressure wound therapy in trauma & orthopedics. *Open Orthop J.* 2014;8:168–77 Published 2014 Jun 27. doi: [10.2174/1874325001408010168](https://doi.org/10.2174/1874325001408010168).
55. Schintler MV. Negative pressure therapy: theory and practice. *Diabetes Metab Res Rev.* 2012;28(Suppl 1):72–7. doi: [10.1002/dmrr.2243](https://doi.org/10.1002/dmrr.2243).
56. Nather A, Chionh SB, Han AY, Chan PP, Nambiar A. Effectiveness of vacuum-assisted closure (VAC) therapy in the healing of chronic diabetic foot ulcers. *Ann Acad Med Singap.* 2010 May;39(5):353–8 PMID: 20535423.
57. Armstrong DG, Lavery LA, Boulton AJ. Negative pressure wound therapy via vacuum-assisted closure following partial foot amputation: what is the role of wound chronicity? *Int Wound J.* 2007;4(1):79–86. doi: [10.1111/j.1742-481X.2006.00270.x](https://doi.org/10.1111/j.1742-481X.2006.00270.x).
58. Mendonca DA, Cosker T, Makwana NK. Vacuum-assisted closure to aid wound healing in foot and ankle surgery. *Foot Ankle Int.* 2005;26(9):761–6. doi: [10.1177/107110070502600915](https://doi.org/10.1177/107110070502600915).
59. Lee KN, Ben-Nakhi M, Park EJ, Hong JP. Cyclic negative pressure wound therapy: an alternative mode to intermittent system. *Int Wound J.* 2015;12(6):686–92. doi: [10.1111/iwj.12201](https://doi.org/10.1111/iwj.12201).
60. Borys S, Hohendorff J, Koblik T, Witek P, Ludwig-Slomczynska AH, Frankfurter C, et al. Negative-pressure wound therapy for management of chronic neuropathic non-infected diabetic foot ulcerations - short-term efficacy and long-term outcomes. *Endocrine.* 2018 Dec;62(3):611–6. doi: [10.1007/s12020-018-1707-0](https://doi.org/10.1007/s12020-018-1707-0) Epub 2018 Aug 11. PMID: 30099674; PMCID: PMC6244911.
61. Lavery LA, Murdoch DP, Kim PJ, Fontaine JL, Thakral G, Davis KE. Negative Pressure Wound Therapy With Low Pressure and Gauze Dressings to Treat Diabetic Foot Wounds. *J Diabetes Sci Technol.* 2014;8(2):346–9. doi: [10.1177/1932296813519012](https://doi.org/10.1177/1932296813519012).
62. Lavery LA, La Fontaine J, Thakral G, Kim PJ, Bhavan K, Davis KE. Randomized clinical trial to compare negative-pressure wound therapy approaches with low and high pressure, silicone-coated dressing, and polyurethane foam dressing. *Plast Reconstr Surg.* 2014;133(3):722–6. doi: [10.1097/01.prs.0000438046.83515.6a](https://doi.org/10.1097/01.prs.0000438046.83515.6a).
63. Venturi ML, Attinger CE, Mesbahi AN, Hess CL, Graw KS. Mechanisms and clinical applications of the vacuum-assisted closure (VAC) Device: a review. *Am J Clin Dermatol.* 2005;6(3):185–94. doi: [10.2165/00128071-200506030-00005](https://doi.org/10.2165/00128071-200506030-00005).
64. Hall KD, Patterson JS. Three Cases Describing Outcomes of Negative-Pressure Wound Therapy With Instillation for Complex Wound Healing. *J Wound Ostomy Continence Nurs.* 2019;46(3):251–5. doi: [10.1097/WON.0000000000000516](https://doi.org/10.1097/WON.0000000000000516).
65. Borys S, Hohendorff J, Frankfurter C, Kiec-Wilk B, Malecki MT. Negative pressure wound therapy use in diabetic foot syndrome-from mechanisms of action to clinical practice. *Eur J Clin Invest.* 2019 Apr;49(4):e13067. doi: [10.1111/eci.13067](https://doi.org/10.1111/eci.13067) Epub 2019 Jan 29 30600541.
66. Kimura T, Watanabe Y, Tokuoka S, Nagashima F, Ebisudani S, Inagawa K. Utility of skin perfusion pressure values with the Society for Vascular Surgery Wound, Ischemia, and foot Infection classification system. *J Vasc Surg.* 2019;70(4):1308–17. doi: [10.1016/j.jvs.2019.01.045](https://doi.org/10.1016/j.jvs.2019.01.045).
67. Sajid MT, MUSTAFA Qu, Shaheen N, Hussain SM, Shukr I, Ahmed M. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers. *J Coll Physicians Surg Pak.* 2015 Nov;25(11):789–93. PMID: 26577962.
68. Salvo P, Calisi N, Melai B, Dini V, Paoletti C, Lomonaco T, et al. Temperature- and pH-sensitive wearable materials for monitoring foot ulcers. *Int J Nanomedicine.* 2017;12:949–54 Published 2017 Jan 31. doi: [10.2147/IJN.S121726](https://doi.org/10.2147/IJN.S121726).
69. Yazdanpanah L, Nasiri M, Adarvishi S. Literature review on the management of diabetic foot ulcer. *World J Diabetes.* 2015;6(1):37–53. doi: [10.4239/wjdv6.i1.37](https://doi.org/10.4239/wjdv6.i1.37).
70. Zheng Y, Wang X, Zhang L, You C, Feng Z, Han C. Successful Treatment of a Patient With Complicated Diabetic Foot Wound: A Case Report. *Int J Low Extrem Wounds.* 2014;13(2):140–6. doi: [10.1177/1534734614529650](https://doi.org/10.1177/1534734614529650).
71. Kim YH, Hwang KT, Kim JT, Kim SW. What is the ideal interval between dressing changes during negative pressure wound therapy for open traumatic fractures?. *J Wound Care.* 2015 Nov;24(11):536, 538–40, 542. doi: [10.12968/jowc.2015.24.11.536](https://doi.org/10.12968/jowc.2015.24.11.536). PMID: 26551646.
72. Abbas M, Uçkay I, Lipsky BA. In diabetic foot infections antibiotics are to treat infection, not to heal wounds. *Expert Opin Pharmacother.* 2015;16(6):821–32. doi: [10.1517/14656566.2015.1021780](https://doi.org/10.1517/14656566.2015.1021780).
73. Schwartz JA, Goss SG, Facchin F, Gendics C, Lantis JC. Single-use negative pressure wound therapy for the treatment of chronic lower leg wounds. *J Wound Care.* 2015;24(Suppl 2):S4–9. doi: [10.12968/jowc.2015.24.Sup2.S4](https://doi.org/10.12968/jowc.2015.24.Sup2.S4).
74. Li X, Liu J, Liu Y, Hu X, Dong M, Wang H, Hu D. Negative pressure wound therapy accelerates rats diabetic wound by promoting agenes. *Int J Clin Exp Med.* 2015 Mar 15;8(3):3506–13. PMID: 26064242.
75. Cigna E, Fino P, Onesti MG, Amorosi V, Scuderi N. Diabetic foot infection treatment and care. *Int Wound J.* 2016;13(2):238–42. doi: [10.1111/iwj.12277](https://doi.org/10.1111/iwj.12277).
76. Georgakarakos E, Charalampidis D, Kakagia D, Georgiadis GS, Lazarides MK, Papanas N. Current achievements with topical negative pressure to improve wound healing in dehiscent ischemic stumps of diabetic patients: a case series. *Int J Low Extrem Wounds.* 2013;12(2):138–45. doi: [10.1177/1534734613483769](https://doi.org/10.1177/1534734613483769).
77. Goudie EB, Gendics C, Lantis JC II. Multimodal therapy as an algorithm to limb salvage in diabetic patients with large heel ulcers. *Int Wound J.* 2012;9(2):132–8. DOI:[10.1111/j.1742-481X.2011.00869.x](https://doi.org/10.1111/j.1742-481X.2011.00869.x).

78. Hafeez K, Haroon-Ur-Rashid KKG, Kumar D, Kumar S. Vacuum Assisted Closure- utilization as home based therapy in the management of complex diabetic extremity wounds. *Pak J Med Sci.* 2015;31(1):95–9. doi: [10.12669/pjms.311.6093](https://doi.org/10.12669/pjms.311.6093).
79. Yao M, Fabbri M, Hayashi H, Park N, Attala K, Gu G, et al. A retrospective cohort study evaluating efficacy in high-risk patients with chronic lower extremity ulcers treated with negative pressure wound therapy. *Int Wound J.* 2014;11(5):483–8. doi: [10.1111/j.1742-481X.2012.01113.x](https://doi.org/10.1111/j.1742-481X.2012.01113.x).
80. Dzieciuchowicz Ł, Kruszyna Ł, Krasiński Z, Espinosa G. Monitoring of systemic inflammatory response in diabetic patients with deep foot infection treated with negative pressure wound therapy. *Foot Ankle Int.* 2012;33(10):832–7. doi: [10.3113/FAI.2012.0832](https://doi.org/10.3113/FAI.2012.0832).
81. McCallon SK, Knight CA, Valiulus JP, Cunningham MW, McCulloch JM, Farinas LP. Vacuum-assisted closure versus saline-moistened gauze in the healing of postoperative diabetic foot wounds. *Ostomy Wound Manage.* 2000 Aug;46(8):28–32. PMID: 11189545.
82. McElroy EF. Use of negative pressure wound therapy with instillation and a reticulated open cell foam dressing with through holes in the acute care setting. *Int Wound J.* 2019;16(3):781–7. doi: [10.1111/iwj.13097](https://doi.org/10.1111/iwj.13097).
83. Schwartz JA, Fuller A, Avdagic E, Gendics C, Lantis JC. Use of NPWT with and without Soft Port technology in infected foot wounds undergoing partial diabetic foot amputation. *J Wound Care.* 2015;24(Suppl 9):S4–12. doi: [10.12968/jowc.2015.24.Sup9.S4](https://doi.org/10.12968/jowc.2015.24.Sup9.S4).
84. Günel Ö, Tuncel U, Turan A, Barut S, Kostakoglu N. The Use of Vacuum-Assisted Closure and GranuFoam Silver® Dressing in the Management of Diabetic Foot Ulcer. *Surg Infect (Larchmt).* 2015;16(5):558–65. doi: [10.1089/sur.2014.093](https://doi.org/10.1089/sur.2014.093).
85. Armstrong DG, Andros G. Use of negative pressure wound therapy to help facilitate limb preservation. *Int Wound J.* 2012;(9 Suppl):1:1–7. doi: [10.1111/j.1742-481X.2012.01015.x](https://doi.org/10.1111/j.1742-481X.2012.01015.x).
86. Desai KK, Hahn E, Pulikkottil B, Lee E. Negative pressure wound therapy: an algorithm. *Clin Plast Surg.* 2012 Jul;39(3):311–24. doi: [10.1016/j.cps.2012.05.002](https://doi.org/10.1016/j.cps.2012.05.002). Epub 2012 Jun 2.
87. Fife CE, Walker D, Thomson B, Otto G. The safety of negative pressure wound therapy using vacuum-assisted closure in diabetic foot ulcers treated in the outpatient setting. *Int Wound J.* 2008;5(Suppl 2):17–22. doi: [10.1111/j.1742-481X.2008.00467.x](https://doi.org/10.1111/j.1742-481X.2008.00467.x).
88. Nather A, Hong NY, Lin WK, Sakham JA. Effectiveness of bridge V.A.C. dressings in the treatment of diabetic foot ulcers. *Diabet Foot Ankle.* 2011;2. doi: [10.3402/dfa.v2i0.5893](https://doi.org/10.3402/dfa.v2i0.5893).
89. Bondokji S, Rangaswamy M, Reuter C, Farajalla Y, Mole T, Cockwill J, et al. Clinical efficacy of a new variant of a foam-based NWPT system. *J Wound Care.* 2011;20(2):62–7. doi: [10.12968/jowc.2011.20.2.72](https://doi.org/10.12968/jowc.2011.20.2.72).
90. Armstrong DG, Lavery LA, Abu-Rumman P, Espensen EH, Vazquez JR, Nixon BP, Boulton AJ. Outcomes of subatmospheric pressure dressing therapy on wounds of the diabetic foot. *Ostomy Wound Manage.* 2002 Apr;48(4):64–8. PMID: 11993062.
91. Delhougne G, Hogan C, Tarka K, Nair S. A Retrospective, Cost-minimization Analysis of Disposable and Traditional Negative Pressure Wound Therapy Medicare Paid Claims. *Ostomy Wound Manage.* 2018 Jan;64(1):26–33 PMID: 29406300.
92. Liu S, He CZ, Cai YT, Xing QP, Guo YZ, Chen ZL, et al. Evaluation of negative-pressure wound therapy for patients with diabetic foot ulcers: systematic review and meta-analysis. *Ther Clin Risk Manag.* 2017;13:533–44. Published 2017 Apr 18. doi: [10.2147/TCRM.S131193](https://doi.org/10.2147/TCRM.S131193).
93. Driver VR, Blume PA. Evaluation of wound care and health-care use costs in patients with diabetic foot ulcers treated with negative pressure wound therapy versus advanced moist wound therapy. *J Am Podiatr Med Assoc.* 2014 Mar;104(2):147–53. doi: [10.7547/0003-0538-104.2.147](https://doi.org/10.7547/0003-0538-104.2.147).
94. Whitehead SJ, Forest-Bendien VL, Richard JL, Halimi S, Van GH, Trueman P. Economic evaluation of Vacuum Assisted Closure® Therapy for the treatment of diabetic foot ulcers in France. *Int Wound J.* 2011;8(1):22–32. doi: [10.1111/j.1742-481X.2010.00739.x](https://doi.org/10.1111/j.1742-481X.2010.00739.x).
95. White R, McIntosh C. A review of the literature on topical therapies for diabetic foot ulcers. Part 2: Advanced treatments. *J Wound Care.* 2009;18(8):335–41. doi: [10.12968/jowc.2009.18.8.43633](https://doi.org/10.12968/jowc.2009.18.8.43633).
96. Wu SC, Armstrong DG. Clinical outcome of diabetic foot ulcers treated with negative pressure wound therapy and the transition from acute care to home care. *Int Wound J.* 2008;5(Suppl 2):10–6. doi: [10.1111/j.1742-481X.2008.00466.x](https://doi.org/10.1111/j.1742-481X.2008.00466.x).
97. Flack S, Apelqvist J, Keith M, Trueman P, Williams D. An economic evaluation of VAC therapy compared with wound dressings in the treatment of diabetic foot ulcers. *J Wound Care.* 2008;17(2):71–8. doi: [10.12968/jowc.2008.17.2.28181](https://doi.org/10.12968/jowc.2008.17.2.28181).
98. Apelqvist J, Armstrong DG, Lavery LA, Boulton AJ. Resource utilization and economic costs of care based on a randomized trial of vacuum-assisted closure therapy in the treatment of diabetic foot wounds. *Am J Surg.* 2008;195(6):782–8. doi: [10.1016/j.amjsurg.2007.06.023](https://doi.org/10.1016/j.amjsurg.2007.06.023).
99. Frykberg RG, Williams DV. Negative-pressure wound therapy and diabetic foot amputations: a retrospective study of payer claims data. *J Am Podiatr Med Assoc.* 2007;97(5):351–9. doi: [10.7547/0970351](https://doi.org/10.7547/0970351).
100. Lavery LA, Boulton AJ, Niezgod JA, Sheehan P. A comparison of diabetic foot ulcer outcomes using negative pressure wound therapy versus historical standard of care. *Int Wound J.* 2007;4(2):103–13. doi: [10.1111/j.1742-481X.2007.00317.x](https://doi.org/10.1111/j.1742-481X.2007.00317.x).
101. Braakenburg A, Obdeijn MC, Feitz R, van Rooij IA, van Griethuysen AJ, Klinkenbijl JH. The clinical efficacy and cost effectiveness of the vacuum-assisted closure technique in the management of acute and chronic wounds: a randomized controlled trial. *Plast Reconstr Surg.* 2006;118(2):390–400. doi: [10.1097/01.prs.0000227675.63744.af](https://doi.org/10.1097/01.prs.0000227675.63744.af).
102. Weng XC, Li C, Zhou SL, Tang Z, Peng BK. Meta Analysis of Effectiveness of Vacuum Sealing Drainage in the Treatment of Diabetic Foot Ulcer. *Journal of Kunming Medical University.* 2017;38(4):80–3.
103. Guan XH, Li BJ, Gao G. Application of continuous negative pressure sealing drainage technique in the treatment of elderly patients with diabetic foot. *Chinese Journal of Injury Repair and Wound Healing.* 2015;10(6):45–6. doi: [10.3877/cma.j.issn.1673-9450.2015.06.012](https://doi.org/10.3877/cma.j.issn.1673-9450.2015.06.012).
104. Xiao L, Li LZ, Wu SB, Yang CZ, Zhang D, Wang LC, et al. Efficacy comparison and health economics evaluation of negative pressure wound therapy and traditional medicine in the treatment of diabetic foot. *Chinese Journal of Injury Repair and Wound Healing.* 2016;5:330–3.
105. Nord D. Kosteneffektivität in der Wundbehandlung [Cost-effectiveness in wound care]. *Zentralbl Chir.* 2006;131(Suppl 1):S185–8. doi: [10.1055/s-2006-921433](https://doi.org/10.1055/s-2006-921433).

106. Duarte B, Cabete J, Formiga A, Neves J. Dakin's solution: is there a place for it in the 21st century? *Int Wound J*. 2017;14(6):918–20. doi: [10.1111/iwj.12728](https://doi.org/10.1111/iwj.12728).
107. Driver RK. Utilizing the VeraFlo™ Instillation Negative Pressure Wound Therapy System with Advanced Care for a Case Study. *Cureus*. 2016;8(11):e903 Published 2016 Nov 30. doi: [10.7759/cureus.903](https://doi.org/10.7759/cureus.903).
108. Felte R, Gallagher KE, Tinkoff GH, Cipolle MA. Case Review Series of Christiana Care Health System's Experience with Negative Pressure Wound Therapy Instillation. *Cureus*. 2016;8(11):e865 Published 2016 Nov 7. doi: [10.7759/cureus.865](https://doi.org/10.7759/cureus.865).
109. Neas ED, Dunn JA, Silva ED, Chambers AM, Luckasen GJ, Jaskowiak A. Peroxy Pyruvic Acid-Containing Topical Anti-Infective: A Potential Candidate for a Wound Instillation Solution. *Adv Wound Care (New Rochelle)*. 2016;5(10):432–43. doi: [10.1089/wound.2015.0682](https://doi.org/10.1089/wound.2015.0682).
110. Kim PJ, Attinger CE, Steinberg JS, Evans KK. Negative pressure wound therapy with instillation: past, present, and future. *Surg Technol Int*. 2015 May;26:51–6. PMID: 26378290.
111. Dalla Paola L. Diabetic foot wounds: the value of negative pressure wound therapy with instillation. *Int Wound J*. 2013;10(Suppl 1):25–31. doi: [10.1111/iwj.12174](https://doi.org/10.1111/iwj.12174).
112. Armstrong DG, Marston WA, Reyzelman AM, Kirsner RS. Comparative effectiveness of mechanically and electrically powered negative pressure wound therapy devices: a multicenter randomized controlled trial. *Wound Repair Regen*. 2012;20(3):332–41. doi: [10.1111/j.1524-475X.2012.00780.x](https://doi.org/10.1111/j.1524-475X.2012.00780.x).
113. Zelen CM, Stover B, Nielson D, Cunningham M. A prospective study of negative pressure wound therapy with integrated irrigation for the treatment of diabetic foot ulcers. *Eplasty*. 2011 Feb 16;11:e5. PMID: 21369361.
114. Scimeca CL, Bharara M, Fisher TK, Kimbriel H, Mills JL, Armstrong DG. Novel use of insulin in continuous-instillation negative pressure wound therapy as "wound chemotherapy". *J Diabetes Sci Technol*. 2010 Jul 1;4(4):820–4. doi: [10.1177/193229681000400408](https://doi.org/10.1177/193229681000400408).
115. Zhang MG, Li ZQ, Wang JH. Effects of vacuum sealing drainage combined with irrigation of oxygen loaded fluid on chronic wounds in diabetic patients. *Chinese Journal of Burns*. 2014;30(2):116–23. doi: [10.3760/cma.j.issn.1009-2587.2014.02.005](https://doi.org/10.3760/cma.j.issn.1009-2587.2014.02.005).
116. Kim PJ, Attinger CE, Crist BD, Gabriel A, Galiano RD, Gupta S, Lantis IJ, Lavery L, Lipsky BA, Teot L. Negative Pressure Wound Therapy With Instillation: Review of Evidence and Recommendations. *Wounds*. 2015 Dec;27(12):S2–19. PMID: 26966814.
117. Dale AP, Saeed K. Novel negative pressure wound therapy with instillation and the management of diabetic foot infections. *Curr Opin Infect Dis*. 2015;28(2):151–7. doi: [10.1097/QCO.0000000000000146](https://doi.org/10.1097/QCO.0000000000000146).
118. Brinkert D, Ali M, Naud M, Maire N, Trial C, Téot L. Negative pressure wound therapy with saline instillation: 131 patient case series. *Int Wound J*. 2013;10(Suppl 1):56–60. doi: [10.1111/iwj.12176](https://doi.org/10.1111/iwj.12176).
119. Iacopi E, Coppelli A, Goretti C, Piaggese A. Necrotizing Fasciitis and The Diabetic Foot. *Int J Low Extrem Wounds*. 2015;14(4):316–27. doi: [10.1177/1534734615606534](https://doi.org/10.1177/1534734615606534).
120. Sun S, Wang C, Chen D, et al. Combating Superbug Without Antibiotic on a Postamputation Wound in a Patient with Diabetic Foot. *Int J Low Extrem Wounds*. 2016;15(1):74–7. doi: [10.1177/1534734615595736](https://doi.org/10.1177/1534734615595736).
121. Kim BS, Choi WJ, Baek MK, Kim YS, Lee JW. Limb salvage in severe diabetic foot infection. *Foot Ankle Int*. 2011;32(1):31–7. doi: [10.3113/FAI.2011.0031](https://doi.org/10.3113/FAI.2011.0031).
122. Yan Y, Li W, Song Y, Yin P, He Z, Gong Y, et al. Semi-closure wound therapy plus negative pressure wound therapy for an older patient with grade 4 diabetic foot with concomitant vascular occlusion: A case report. *Medicine (Baltimore)*. 2019;98(44):e17786. doi: [10.1097/MD.0000000000017786](https://doi.org/10.1097/MD.0000000000017786).
123. Hajimohammadi K, Makhdoomi K, Zabihi RE, Parizad N. NPWT: a gate of hope for patients with diabetic foot ulcers. *Br J Nurs*. 2019;28(12):S6–9. doi: [10.12968/bjon.2019.28.12.S6](https://doi.org/10.12968/bjon.2019.28.12.S6).
124. Shahi N, Bradley S, Vowden K, Vowden P. Diabetic bullae: a case series and a new model of surgical management. *J Wound Care*. 2014;23(6):326–30. doi: [10.12968/jowc.2014.23.6.326](https://doi.org/10.12968/jowc.2014.23.6.326).
125. Tian M, Jiang YZ, Niu YW, Xiao YR, Lu SL, Wang XQ. A severely infected diabetic foot treated successfully without using systemic antibiotics. *Int J Low Extrem Wounds*. 2012;11(4):296–8. doi: [10.1177/1534734612458286](https://doi.org/10.1177/1534734612458286).
126. Tricco AC, Antony J, Vafaei A, Khan PA, Harrington A, Cogo E, et al. Seeking effective interventions to treat complex wounds: an overview of systematic reviews. *BMC Med*. 2015;13:89 Published 2015 Apr 22. doi: [10.1186/s12916-015-0288-5](https://doi.org/10.1186/s12916-015-0288-5).
127. Kennedy A, Van Zant RS. Diverse applications of negative pressure wound therapy: a multiple case report. *Physiother Theory Pract*. 2006;22(2):83–90. doi: [10.1080/09593980600588781](https://doi.org/10.1080/09593980600588781).
128. Gesslein M, Horch RE. Interdisziplinäres Management von komplexen chronischen Ulzera mittels V.A.C.-Therapie und "Buried Chip Skin Grafts" [Interdisciplinary management of complex chronic ulcers using vacuum assisted closure therapy and "buried chip skin grafts"]. *Zentralbl Chir*. 2006;131(Suppl 1):S170–3. doi: [10.1055/s-2006-921460](https://doi.org/10.1055/s-2006-921460).
129. Abe Y, Hashimoto I, Ishida S, Minoda K, Yoshimoto S. The perifascial areolar tissue and negative pressure wound therapy for one-stage skin grafting on exposed bone and tendon. *J Med Invest*. 2018;65(1.2):96–102. doi: [10.2152/jmi.65.96](https://doi.org/10.2152/jmi.65.96) PMID: 29593203.
130. Hierner R, Degreef H, Vranckx JJ, Garmyn M, Massagé P, van Brussel M. Skin grafting and wound healing—the "dermato-plastic team approach". *Clin Dermatol*. 2005 Jul-Aug;23(4):343–52. doi: [10.1016/j.clindermatol.2004.07.028](https://doi.org/10.1016/j.clindermatol.2004.07.028) PMID: 16023929.
131. Smuđ-Orehovec S, Mance M, Halužan D, Vrbanović-Mijatović V, Mijatović D. Defect Reconstruction of an Infected Diabetic Foot Using Split- and Full-thickness Skin Grafts With Adjuvant Negative Pressure Wound Therapy: A Case Report and Review of the Literature. *Wounds*. 2018 Nov;30(11):E108–15 PMID: 30457564.
132. Ramanujam CL, Zgonis T. Surgical soft tissue closure of severe diabetic foot infections: a combination of biologics, negative pressure wound therapy, and skin grafting. *Clin Podiatr Med Surg*. 2012 Jan;29(1):143–6. doi: [10.1016/j.cpm.2011.10.004](https://doi.org/10.1016/j.cpm.2011.10.004) Epub 2011 Nov 17 22243576.
133. Eneroth M, van Houtum WH. The value of debridement and Vacuum-Assisted Closure (V.A.C.) Therapy in diabetic foot ulcers. *Diabetes Metab Res Rev*. 2008 May-Jun;24(Suppl 1):S76–80. doi: [10.1002/dmrr.852](https://doi.org/10.1002/dmrr.852) PMID: 18393328.
134. Godoy-Santos AL, Rosemberg LA, de Cesar-Netto C, Armstrong DG. The use of bioactive glass S53P4 in the treatment of an infected Charcot foot: a case report. *J Wound Care*. 2019;28(Sup1):S14–7. doi: [10.12968/jowc.2019.28.Sup1.S14](https://doi.org/10.12968/jowc.2019.28.Sup1.S14).

135. Mikami T, Kaida E, Yabuki Y, Kitamura S, Kokubo K, Maegawa J. Negative Pressure Wound Therapy Followed by Basic Fibroblast Growth Factor Spray as a Recovery Technique in Partial Necrosis of Distally Based Sural Flap for Calcaneal Osteomyelitis: A Case Report. *J Foot Ankle Surg.* 2018;57(4):816–20. doi: [10.1053/j.jfas.2017.11.011](https://doi.org/10.1053/j.jfas.2017.11.011).
136. Drampalos E, Mohammad HR, Kosmidis C, Balal M, Wong J, Pillai A. Single stage treatment of diabetic calcaneal osteomyelitis with an absorbable gentamicin-loaded calcium sulphate/hydroxyapatite biocomposite: The Silo technique. *Foot (Edinb).* 2018;34:40–4. doi: [10.1016/j.foot.2017.11.011](https://doi.org/10.1016/j.foot.2017.11.011).
137. Raphael A, Gonzales J. Use of cryopreserved umbilical cord with negative pressure wound therapy for complex diabetic ulcers with osteomyelitis. *J Wound Care.* 2017;26(Sup10):S38–44. doi: [10.12968/jowc.2017.26.Sup10.S38](https://doi.org/10.12968/jowc.2017.26.Sup10.S38).
138. Dalla Paola L, Carone A, Boscarino G, Scavone G, Vasilache L. Combination of Open Subtotal Calcanectomy and Stabilization With External Fixation as Limb Salvage Procedure in Hindfoot-Infected Diabetic Foot Ulcers. *Int J Low Extrem Wounds.* 2016;15(4):332–7. doi: [10.1177/1534734616667865](https://doi.org/10.1177/1534734616667865).
139. Ramanujam CL, Stapleton JJ, Zgonis T. Negative-pressure wound therapy in the management of diabetic Charcot foot and ankle wounds. *Diabet Foot Ankle.* 2013;4 Published 2013 Sep 23. doi: [10.3402/dfa.v4i0.20878](https://doi.org/10.3402/dfa.v4i0.20878).
140. Lipsky BA, Berendt AR, Deery HG, Embil JM, Joseph WS, Karchmer AW, et al. Diagnosis and treatment of diabetic foot infections. *Plast Reconstr Surg.* 2006;117(7 Suppl):212S–38. doi: [10.1097/01.prs.0000222737.09322.77](https://doi.org/10.1097/01.prs.0000222737.09322.77).
141. Namgoong S, Jung SY, Han SK, Kim AR, Dhong ES. Clinical experience with surgical debridement and simultaneous meshed skin grafts in treating biofilm-associated infection: an exploratory retrospective pilot study. *J Plast Surg Hand Surg.* 2020;54(1):47–54. doi: [10.1080/2000656X.2019.1673170](https://doi.org/10.1080/2000656X.2019.1673170).
142. Gkotsoulis E. Split Thickness Skin Graft of the Foot and Ankle Bolstered With Negative Pressure Wound Therapy in a Diabetic Population: The Results of a Retrospective Review and Review of the Literature. *Foot Ankle Spec.* 2020 Oct;13(5):383–391. doi: [10.1177/1938640019863267](https://doi.org/10.1177/1938640019863267). Epub 2019 Aug 2. PMID: 31370687; PMCID: PMC7493201.
143. Wu CC, Chew KY, Chen CC, Kuo YR. Antimicrobial-impregnated dressing combined with negative-pressure wound therapy increases split-thickness skin graft engraftment: a simple effective technique. *Adv Skin Wound Care.* 2015; 28(1):21–7. doi: [10.1097/01.ASW.0000459038.81701.fb](https://doi.org/10.1097/01.ASW.0000459038.81701.fb).
144. Kisch T, Liodaki ME, Mauss KL, Kalousis K, Wenzel ET, Mailaender P, et al. Reduced Amputation Rate by Circular TNP Application on Split-Skin Grafts After Deep Dermal Foot Scalds in Insulin-Dependent Diabetic Patients. *J Burn Care Res.* 2015;36(5):e253–8. doi: [10.1097/BCR.0000000000000184](https://doi.org/10.1097/BCR.0000000000000184).
145. Chan SY, Wong KL, Lim JX, Tay YL, Nather A. The role of Renasys-GO™ in the treatment of diabetic lower limb ulcers: a case series. *Diabet Foot Ankle* 2014;5:24718 Published 2014 Nov 17. doi: [10.3402/dfa.v5.24718](https://doi.org/10.3402/dfa.v5.24718).
146. Chiummariello S, Del Torto G, Iera M, Arleo S, Alfano C. Negative pressure dressing in split-thickness skin grafts: experience with an alternative method. *Wounds.* 2013 Nov;25(11):324–7 PMID: 25867632.
147. Ross RE, Aflaki P, Gendics C, Lantis Ii JC. Complex lower extremity wounds treated with skin grafts and NPWT: a retrospective review. *J Wound Care.* 2011;20(10):490–5. doi: [10.12968/jowc.2011.20.10.490](https://doi.org/10.12968/jowc.2011.20.10.490).
148. Randall KL, Booth BA, Miller AJ, Russell CB, Laughlin RT. Use of an acellular regenerative tissue matrix in combination with vacuum-assisted closure therapy for treatment of a diabetic foot wound. *J Foot Ankle Surg.* 2008;47(5):430–3. doi: [10.1053/j.jfas.2008.04.012](https://doi.org/10.1053/j.jfas.2008.04.012).
149. Wada A, Ferreira MC, Tuma Júnior P, Arrunátegui G. Experience with local negative pressure (vacuum method) in the treatment of complex wounds. *Sao Paulo Med J.* 2006;124(3):150–3. doi: [10.1590/s1516-31802006000300008](https://doi.org/10.1590/s1516-31802006000300008).
150. Hu KX, Zhang HW, Zhou F. Observation on the therapeutic effects of negative-pressure wound therapy on the treatment of complicated and refractory wounds. *Chinese Journal of Burns.* 2009;25(4):249–52. doi: [10.3760/cma.j.issn.1009-2587.2009.04.004](https://doi.org/10.3760/cma.j.issn.1009-2587.2009.04.004).
151. Cazzell S, Vayser D, Pham H, Walters J, Reyzelman A, Samsell B, et al. A randomized clinical trial of a human acellular dermal matrix demonstrated superior healing rates for chronic diabetic foot ulcers over conventional care and an active acellular dermal matrix comparator. *Wound Repair Regen.* 2017;25(3):483–97. doi: [10.1111/wrr.12551](https://doi.org/10.1111/wrr.12551).
152. Guo X, Mu D, Gao F. Efficacy and safety of acellular dermal matrix in diabetic foot ulcer treatment: A systematic review and meta-analysis. *Int J Surg.* 2017;40:1–7. doi: [10.1016/j.ijssu.2017.02.008](https://doi.org/10.1016/j.ijssu.2017.02.008).
153. Rupert P. Human acellular dermal wound matrix for complex diabetic wounds. *J Wound Care.* 2016;25(4):S17–21. doi: [10.12968/jowc.2016.25.Sup4.S17](https://doi.org/10.12968/jowc.2016.25.Sup4.S17).
154. Cole WE. DermACELL: Human Acellular Dermal Matrix Allograft A Case Report. *J Am Podiatr Med Assoc.* 2016 Mar;106(2):133–7. doi: [10.7547/14-091](https://doi.org/10.7547/14-091). PMID: 27031550.
155. Protzman NM, Brigido SA. Recent advances in acellular regenerative tissue scaffolds. *Clin Podiatr Med Surg.* 2015;32(1):147–59. doi: [10.1016/j.cpm.2014.09.008](https://doi.org/10.1016/j.cpm.2014.09.008).
156. Espensen EH, Nixon BP, Lavery LA, Armstrong DG. Use of subatmospheric (VAC) therapy to improve bioengineered tissue grafting in diabetic foot wounds. *J Am Podiatr Med Assoc.* 2002;92(7):395–7. doi: [10.7547/87507315-92-7-395](https://doi.org/10.7547/87507315-92-7-395).
157. Ahmed ME, Mohammed MS, Mahadi SI. Primary wound closure of diabetic foot ulcers by debridement and stitching. *J Wound Care.* 2016;25(11):650–4. doi: [10.12968/jowc.2016.25.11.650](https://doi.org/10.12968/jowc.2016.25.11.650).
158. Richter K, Knudson B. Vacuum-assisted closure therapy for a complicated, open, above-the-knee amputation wound. *J Am Osteopath Assoc.* 2013 Feb;113(2):174–6. PMID: 23412679.
159. Stansby G, Wealleans V, Wilson L, Morrow D, Gooday C, Dhataria K. Clinical experience of a new NPWT system in diabetic foot ulcers and post-amputation wounds. *J Wound Care.* 2010;19(11):496–502. doi: [10.12968/jowc.2010.19.11.79706](https://doi.org/10.12968/jowc.2010.19.11.79706).
160. Armstrong DG, Lavery LA; Diabetic Foot Study Consortium. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. *Lancet.* 2005;366(9498):1704–10. doi: [10.1016/S0140-6736\(05\)67695-7](https://doi.org/10.1016/S0140-6736(05)67695-7).
161. Ulusal AE, Sahin MS, Ulusal B, Cakmak G, Tuncay C. Negative pressure wound therapy in patients with diabetic foot. *Acta Orthop Traumatol Turc.* 2011;45(4):254–60. doi: [10.3944/AOTT.2011.2283](https://doi.org/10.3944/AOTT.2011.2283).