Negative Pressure Wound Therapy: Mechanism of Action and Clinical Applications

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Abstract

Negative pressure wound therapy (NPWT) promotes healing by evenly applying negative pressure on the surface of the wound. The system consists of a sponge, a semiocclusive barrier, and a fluid collection system. Its effectiveness is explained by four main mechanisms of action, including macrodeformation of the tissues, drainage of extracellular inflammatory fluids, stabilization of the environment of the wound, and microdeformation. Rarely will complications linked to NPWT occur, but special care must be taken to prevent events such as toxic shock syndrome, fistulization, bleeding, and pain. New NPWT modalities have been recently developed to make NPWT suitable for a wider variety of wounds. These include NPWT with instillation therapy (NPWTi-d), different cleansing options, and application of NPWT on primarily closed incisions. Finally, vacuum-assisted wound closure therapy has been demonstrated to be efficient for various clinical settings, such as the management of diabetic foot ulcers, pressure ulcerations, chronic wounds, and skin grafts.

Keywords

- negative pressure wound therapy
- VAC
- wounds
- semiocclusive membrane

History and Design

The concept of using controlled subatmospheric pressure to treat open or infected wounds was initially described by Fleischmann et al in 1993.[1] They created a vacuum-sealed dressing to promote the healing of open fracture wounds in trauma patients. Complementary studies brought the investigators to describe how subatmospheric pressure dressings can be beneficial in the treatment of both acute and chronic infected wounds, as well as fasciotomy wounds of the lower extremity. Based on the same rationale, Argenta et al popularized, in 1997, the vacuum-assisted wound closure (VAC) device as an innovative method of improving secondary intention wound healing. Since then, VAC therapy has significantly evolved over the years and grown to become one of the most powerful tools in the plastic surgeons' armamentarium.[2]

VAC therapy, also known as negative pressure wound therapy (NPWT), refers to a wound dressing system that provides subatmospheric pressure across the entirety of the wound site. The system consists of a polyurethane foam sponge, a semiocclusive adhesive cover, a fluid collection system and a suction pump. The foam has pores ranging in size from 400 to 600 µm and can be trimmed to fit the size and geometry of any wound.[3,4] The open structure of the foam cells ensures the equal distribution of the negative pressure across the entire wound surface.

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Different types of sponges have been designed to meet the needs of a greater variety of wounds. For instance, sponges can be categorized into two distinct subgroups: the GRANUFOAM (3M, KCI) dressing, suitable for both acute and chronic wounds, and the WHITEFOAM (3M, KCI) dressing, which is less adherent, making it ideal for more fragile wounds or underlying tissues. The chosen foam is then sealed to the skin with an adhesive membrane and connected to a suction pump which exerts negative pressures between −50 and −200 mm Hg. The pressure can be applied continuously or intermittently.

Mechanism of Action

VAC therapy is effective via four dominant mechanisms of action[3,4]:

1. Macrodeformation
2. Drainage of fluids
3. Stabilization of the wound environment
4. Microdeformation

Macrodeformation

The subatmospheric pressure applied to the sponge has the effect of reducing its size by approximately 80%.[4] Considering that the sponge is firmly attached to the edges of the wound, this results in a reduction of wound surface area. This three-dimensional shrinkage is dependent on the deformability of the surrounding tissues, which explains why wounds surrounded by loose excess skin will be approximated faster compared with wounds located on high tension surfaces, such as the scalp.[4,5]

Drainage of Fluids

The suction applied by the VAC system helps to remove extracellular fluid which decreases edema. It has been well demonstrated that edema causes swelling that leads to cellular compression and, in turn, diminishes the proliferative cellular response necessary for wound healing. The removal of exudates also releases the pressure caused by the accumulation of fluid around blood vessels, which is beneficial for the perfusion of the wound. Additionally, the flow of fluid created by the suction causes (1) shear forces on the cells and (2) a movement of ions establishing electric fields. Both of these processes promote a cellular proliferation response. Ultimately, the suction of exudates also helps to remove toxic materials, such as TNF-α and matrix metalloproteases (MMP), as was shown by Stechmiller et al.[6]

Stabilization of the Wound Environment

The use of VAC therapy assures stability in the environment surrounding the wound. This can in part be explained by the less frequent dressing changes (every 2–3 days[7]) compared with usual gauze dressings that must be removed daily. Furthermore, the VAC sponge is covered by a polyurethane drape that is impermeable to proteins and microorganisms, which helps to prevent bacterial colonization of the wound. The semiocclusive membrane also has limited permeability to gases and water vapor. The latter helps to limit heat transfer secondary to water evaporation, keeping the wound moist and warm. This characteristic of NPWT is beneficial because normothermic wound therapy promotes healing of chronic wounds as was demonstrated by Kloth et al.[8]

Microdeformation

As mentioned above, the suction created by NPWT causes a movement of fluids through the cellular matrix, which produces shear and deformation forces on the cells. Microdeformations are a key element of VAC therapy,[5,9–12] as they promote cellular proliferation, angiogenesis, and granulation tissue formation. Morykwas et al[13] demonstrated that, in pig models, granulation tissue formation was increased by more than 60% when the wound was treated with NPWT compared with gauze dressings, which leads to faster wound closure. Mechanotransduction[14] is the term used to describe how mechanical forces can modify cell function. Huang et al[15] and Huang and Ingber[16] demonstrated that this process mainly occurs in the cytoskeleton. The negative pressure disrupts integrin bridges which release intracellular messengers and alter gene transcription, ultimately leading to cellular proliferation.[9] Additionally, it was shown that standard gauze dressings result in more cell death and less fibroblast proliferation in comparison to VAC therapy.[10] Finally, current literature states that mechanical forces result in inhibition of apoptosis, upregulation of cell signaling molecules, changes in gene expression, and stimulation of proliferation.[17]

Other Mechanisms

Biochemical Changes

NPWT is also thought to be effective because it changes the biochemistry of the wound. As described by Greene et al, wound treated by a VAC system showed a 15 to 76% decrease in MMP-9/NGAL (neutrophil gelatinase-associated lipocalin) and MMP-2.[18] In another study, Shi et al described a decrease in MMP-1 and MMP-13. This is relevant because MMPs are known to disrupt the connective tissue matrix which inhibits wound healing.[19] In a porcine study, it was demonstrated that VAC therapy creates a significant decrease in peripheral blood monocytes, neutrophils, proinflammatory cytokines INF-y and IL-6. Reduced concentrations of IL-8, TGF-β1, and TNF-α were also observed during the inflammatory phase of wound healing.[20]

Alteration of Perfusion

Investigators have stated for many years that NPWT improves perfusion. However, a more recent study accomplished by Kairinos et al demonstrated that perfusion beneath the VAC system decreases proportionally to the increase in suction pressure.[21] These findings explain why VAC therapy must be used carefully in patients whose perfusion is already compromised.

In comparison, Morykwas et al attributed their increase in granulation tissue formation to better perfusion of the wound. They established that when applying −125 mm Hg

pressure to the wound, blood flow was four times superior, which was demonstrated by laser Doppler probes.[13] An enhanced blood flow implies an increase in inflammatory mediators, growth factors, leucocytes, and antibiotics. The latter explains how VAC therapy can stimulate the closure of the wound and reduce bacterial burden. Finally, in Greene et al's study on three debilitated wounds, they demonstrated that wounds had a greater microvessel density after being subjected to negative pressure.[18]

Decrease in Bacterial Load

Morykwas and colleagues were the first investigators to demonstrate that VAC therapy decreases bacterial count inside the wound. In their porcine study, they showed that bacterial count went from 10^8 to 10^3 organisms in 4 to 5 days of NPWT. In the control group, treated with standard gauze dressings, the bacterial count had significantly increased.[13] Finally, according to Kim et al, NPWT with instillation has the potential to dilute and solubilize infectious materials, which explains how VAC therapy decreases the number of gram-positive bacteria found in culture.[22]

Complications

NPWT is considered a safe approach and rarely leads to complications. However, some complications of varying degrees of severity have been reported and most of them were attributable to a poor technique or inadequate patient selection. In other words, most adverse events related to VAC therapy are preventable. The following section describes the most relevant complications associated with VAC therapy as well as key points for their prevention.

Severe Complications

Toxic Shock Syndrome

Toxic Shock syndrome is attributable to the use of VAC therapy and has been described in case reports.[23] The most effective way to prevent this severe complication is to ensure that the wound is clean and healthy before installing the VAC device, and that it is changed at regular intervals.

Enteric Fistula

Rao et al described 6 of 29 patients developed intestinal fistulas secondary to their VAC therapy used for their laparotomy wound.[24] The incidence of enteric fistula is significantly increased when the VAC foam dressing is applied directly over the exposed organ.[25] Therefore, an absorbable biologic or synthetic mesh must be placed between the foam and the organ as an interface to prevent fistulation.[2]

Hemodynamic Instability

Depending on the size and location of the wound, large amounts of fluid can be suctioned during the first days of VAC therapy, occasionally leading to hemodynamic instability. It is important to monitor unstable patients and offer fluid and electrolyte resuscitation when needed.[3]

Minor Complications (Affecting up to 25% of Patients[3])

Bleeding[2]

Major, potentially life-threatening, bleeding can occur if the VAC is placed directly over a major blood vessel or placed on a wound bed that has not undergone adequate surgical hemostasis.[26] When leaving the foam in place for a prolonged time, or when granulation tissue grows rapidly, such as in children, the newly formed granulation tissue can be attached to the foam dressing. When removing the sponge, the capillary buds are disrupted which can lead to bleeding. Most cases of bleeding can be controlled with manual pressure. Electrocoagulation or surgical interventions may be needed if there is significant bleeding. Special care must be taken in anticoagulated patients. An effective method used to prevent bleeding is to increase the frequency of foam dressing changes. The VAC sponge should be changed every 48 hours in adults and every 24 hours in children, particularly in acute settings.

Pain

Variable degrees of pain may occur during VAC therapy. However, it is difficult to determine how much of the pain is attributable to the VAC device and not the wound itself, especially in traumatic settings. Many adjustments can be made to reduce the pain. Pain related to the pressure can be diminished by starting with a −50 mm Hg pressure and increasing it gradually to −125 mm Hg. It is also reported that continuous suction creates less discomfort compared with intermittent suction.[2] Pain caused by the dressing changes can be alleviated by the application of saline or xylocaine before removal of the sponge. Increasing the frequency of sponge changes may also help.[3]

Odor

Odor, although benign, can become a source of discomfort in patients with chronic wounds and can represent one of the first signs of a growing infection. To help with this issue, appropriate cleaning and hydrotherapy can be accomplished when the dressing is being changed. In more severe cases, the VAC device can be removed for 24 to 48 hours to allow the wound to dry.[2] Finally, applying a sheet of silver ion dressing between the wound and the sponge can help reduce the odor.[3]

Infection

Argenta and Morykwas reported the occurrence of infections, which can be prevented by adequate debridement of nonviable tissue prior to VAC installation as well as respecting sterile techniques during sponge changes.[2]

Damage to Adjacent Tissues[3]

To prevent healthy adjacent tissues from being damaged by the VAC device, it is necessary to place the device strategically. Tubes must not be placed on skeletal pressure points to prevent the formation of pressure ulcers. The foam must be trimmed to fit the geometry of the wound and to limit its contact with healthy skin. Skin irritation, maceration, and allergic rashes can also be caused by the sponge or the adhesive cover.

Contraindications

Physicians must avoid NPWT when the following contraindications are present:

Absolute Contraindications

Malignancy[3]

The subatmospheric pressure created by the VAC device is thought to stimulate tumourigenesis by the same mechanisms by which it promotes wound healing (microdeformations promoting cellular proliferation and angiogenesis). Studies have also established a theoretical risk of neoplastic spread secondary to VAC therapy. Neoplasms are also more susceptible to bleeding because of their friable nature. Complete excision of malignant tissue must be performed before considering VAC therapy.[27,28]

Exposed Vital Structures[26]

The application of NPWT directly on vital organs, blood vessels, and vascular grafts can lead to fistulation, erosion, and hemorrhage. Such complications can be prevented by assuring coverage of vital structures with granulation tissue, grafts, or flaps.

Relative Contraindications

Ischemic Tissue[29,30]

Revascularization should be completed before resorting to VAC therapy. The reason behind this is that the subatmospheric pressure applied to the wound transiently reduces the perfusion of the wound, therefore worsening the degree of ischemia.

Fragile Skin[3]

Advanced age, corticosteroid use, collagen disorders, and adhesive allergy can contribute to the weakening of the skin. Thin skin is more susceptible to shearing when lifting the adhesive cover during dressing changes. Therefore, physicians must recognize those patients and adequately protect their skin to prevent skin avulsion and necrosis. In some cases where risks outweigh benefits, clinicians should refrain from using VAC therapy.

Infected or Devitalized Tissue[31]

Adequate debridement of devitalized tissue must be performed before the initiation of a VAC therapy. Ideally, treatment of infection should be undertaken before using NPWT. However, minor wound colonization can be successfully treated with VAC therapy combined with an instillation therapy.[22]

New NPWT Modalities

VAC therapy rapidly proved its effectiveness among physicians, which encouraged the development of multiple new advanced therapies, such as Negative Pressure Wound Therapy with Instillation (NPWTi-d), cleanse choice in VAC systems, and closed incision NPWT.

Negative Pressure Wound Therapy with Instillation[22]

NPWT with instillation consists of the usual VAC system combined with an intermittent delivery of a topical solution into the wound bed. The rationale behind this addition to standard NPWT is to harmonize the power of VAC therapy with the effects of topical solutions frequently used in standard dressings. The solution is delivered to the wound bed according to different pre-established parameters and is then removed through the negative pressure. The type of solution, its dwell time, duration of negative pressure, and the frequency of these cycles are all parameters that can be adjusted depending on the particular needs of every clinical situation. Wound irrigation can be accomplished with different solutions, such as saline, antiseptic solutions, antimicrobial solutions, and debridement solutions.

NPWTi-d has been a subject of interest for many researchers. It was shown that using NPWTi-d with sterile water facilitated the healing of at least 95% of wounds that had previously failed to heal with standard NPWT.[32,33] Lessing et al carried a study on porcine excisional wounds. They demonstrated that, after 7 days of treatment, NPWT combined with instillation of a saline solution resulted in an increase of 43% in granulation tissue formation in comparison to standard continuous NPWT.[34] NPWTi-d not only helps with the granulation of the wound but also with the reduction of its bacterial burden, as was shown by Ludolph et al.[35] In their study, they showed that NPWTi-d with antiseptic solution reduced the mean bacterial number by 46% in pressure ulcers, 22% in chronic wounds, and 56% in chronic ulcers. Additionally, it was also shown in a study conducted by Sibbald et al that polyhexamide antiseptic solution has a beneficial impact on wound healing through biofilm eradication and reduction of infection.[36] Another porcine study demonstrated that NPWTi-d results in a significant decrease in colony-forming units, disrupts *Pseudomonas aeruginosa* biofilms, and damages bacterial cells.[37] Jukema and colleagues demonstrated that NPWTi-d allowed keeping orthopaedic implants in 86.4% of acutely infected wounds and 80% of chronic infections.[38] Finally, Kim et al demonstrated that instillation therapy allows to decrease the number of operative visits, shorten the hospital stay, and reduce the time to the final surgical procedure in comparison to patients who received standard NPWT.[22] For similar reasons, Gabriel et al concluded that NPWTi-d is more cost-effective compared with standard NPWT.[39]

In summary, NPWT combined with instillation therapy is an effective adjuvant therapy for wound healing. However, the optimal parameters for the application and the soak time of the solution have yet to be established. Further studies are also needed to determine which type of solution should be prioritized.

Cleanse Choice[40]

NPWT offers different dressing and cleansing options that should be chosen depending on several factors, such as the geometry of the wound, its location, and its infectious

status. As mentioned above, there are different sponge options, such as the GRANUFOAM and the WHITEFOAM. In addition to these options, there is the VERAFLO cleanse dressing, which is a reticulated open-cell foam polyurethane ester dressing that allows the application of the topical solution on the wound bed. One of its main characteristics is that it is less hydrophobic compared with the GRANUFOAM sponge, which allows even distribution of the solution onto the wound bed. Therefore, it is a great cleansing choice when considering NPWTi-d. Its higher tensile strength ensures that once removed, no foam remains on the wound. This type of dressing is divided into three layers and is designed to remove thicker exudate material (fibrin, slough, viscous exudate, and prokaryotic materials).[41] This represents a great advantage when surgical debridement cannot be accomplished. In a series of case reports, opting for a VERAFLO cleanse combined with instillation therapy resulted in faster closure of the wound in the burn or necrotizing soft tissue infection patient populations.[42] Another study demonstrated that the combination of NPWTi-d with this reticulated open-cell foam dressing helps the formation of granulation tissue and could potentially represent a cost-effective way of reducing surgical debridement.[43]

Closed Incision Negative-Pressure Therapy

NPWT can also be applied to a primary closed surgical wound to improve its healing and reduce its vulnerability to complications. In a retrospective chart review performed from 2008 through to 2011, Condé-Green et al compared the healing of abdominal wall reconstruction wounds treated with incisional NPWT versus conventional dry gauzes. They demonstrated that incisional NPWT results in a significantly lower rate of complications compared with usual gauze dressings (22 vs. 65,9% respectively). Additionally, skin dehiscence occurred in 9% of patients treated with NPWT compared with 39% for patients treated with gauze dressings. Infection, skin and fat necrosis, seroma and hernia recurrence appeared to be lower in the incisional NPWT group, but statistical significance was not established.[44] In another study performed by Stannard et al, incisional VAC therapy reduced the occurrence of infections after high-risk lower extremity trauma. They also demonstrated a significant decrease in wound dehiscence when using NPWT.[45] Similar results were demonstrated in obese women undergoing elective or emergency cesarean section.[46] In summary, incisional NPWT may be an effective way to decrease the incidence of infection and promote wound healing. It was shown to be effective in many various medical settings and specialties.

Evidence

Wound management has continued to evolve since the development of NPWT. An abundance of publications have demonstrated the use of NPWT to promote wound healing in various clinical domains, such as for diabetic foot ulcers, pressure ulcerations, chronic wounds, and skin grafts.[4]

Diabetic Foot Ulcers

In a study conducted by Blume et al, 43.2% of foot ulcers in diabetic patients achieved complete closure when treated with a VAC system, whereas only 28.9% of patients treated with advanced moist wound therapy reached complete re-epithelialization. They also demonstrated that using NPWT resulted in fewer secondary amputations[47] (4.1% compared with 10.2% with standard wound treatment regimen). Finally, the duration of treatment was shorter for the population treated with NPWT.[48] In a similar study, Armstrong et al demonstrated that 56% of diabetic foot wounds achieved full recovery when treated with NPWT compared with 39% for the wounds treated with standard moist wound care. In the same study, granulation tissue formation was significantly faster in the NPWT treated wounds.[49]

Pressure Ulcerations[50]

In Schwien et al's study, they demonstrated the pressure ulcers managed with NPWT had fewer hospitalizations compared with the patients who were treated with standard moist wound healing modalities.[51] Baharestani et al showed that NPWT combined with the VERAFLO cleanse resulted in a shorter length of home care services.[52]

Chronic Wounds

In a quantitative meta-analysis of all randomized trials published before 2011, Suissa et al demonstrated that NPWT resulted in a significantly greater decrease in chronic wound size compared with the standard wound care group. They also concluded that healing time for chronic wounds was shorter with NPWT.[53] In another study aiming to compare NPWT to standard wound care in chronic wounds, they demonstrated that complete healing was obtained after 29 days of VAC therapy compared with 45 days of standard wound care. Furthermore, after 43 days of NPWT, 90% of ulcers were healed compared with 48% of ulcers treated with conventional wound therapy. Additionally, during the preparation stage of the wound treatment (time between surgical debridement and application of the skin graft), VAC therapy results in a significantly shorter preparation time (7 days) in comparison to the control group (17 days). Finally, in this study, VAC therapy was more cost-effective compared with conventional wound care.[54]

Skin Grafts

Scherer et al demonstrated that a vacuum-assisted closure device is a safe and effective way to increase the rate of skin graft survivals. More precisely, their study highlighted the fact that VAC therapy applied on skin grafts resulted in only 3% of repeated skin grafts, whereas 19% of wounds treated with bolster dressings needed a redo of the skin graft.[55] In another study conducted by Moisidis et al, the qualitative appearance of split-thickness skin grafts was significantly better when subjected to NPWT.[56]

Conclusion

In conclusion, NPWT has changed the landscape in the treatment of both acute and chronic wounds. It continues

to play an important role in the plastic surgeon's armamentarium, especially with the new formulations in NPWTi-d and incisional NPWT. This primer aims at describing the understood mechanism of action, contraindications, formulations, and some clinical evidence for use.

Conflict of Interest
None declared.

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