

# Negative Pressure Wound Therapy Uses in Orthopedic Open Fracture: A Current Concept Review

Mir Mansour Moazen Jamshidi<sup>1</sup>, Behzad Nezhad Tabrizi<sup>2</sup>, Ehsan Fallah<sup>3</sup>, Mazaher Ebrahimian<sup>4</sup>, Ali Salehi<sup>5</sup>, Alireza Moharrami<sup>1,2,\*</sup>, Seyed Mohammad Javad Mortazavi<sup>6</sup>

<sup>1</sup> Assistant Professor, Department of Orthopedic Surgery, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran

<sup>2</sup> Resident, Joint Reconstruction Research Center, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup> Fellowship, Joint Reconstruction Research Center, Tehran University of Medical Sciences, Tehran, Iran

<sup>4</sup> Resident, Department of Orthopedics, Sina Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

<sup>5</sup> Resident, Department of Radiology, Imam Hossein Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>6</sup> Professor, Joint Reconstruction Research Center, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

\*Corresponding author: Alireza Moharrami; Joint Reconstruction Research Center, Tehran University of Medical Sciences, Tehran, Iran. Tel: 21-61192767, Email: a.moharrami@gmail.com

Received: 02 May 2022; Revised: 16 June 2022; Accepted: 04 July 2022

## Abstract

During an open fracture, the barrier of skin that protects the bones is breached, and the unprotected bones are exposed to the environment, resulting in contamination that leads to hematoma formation. It is often found that open fractures are associated with a high rate of morbidity and infection. In spite of the lack of evidence supporting negative pressure wound therapy (NPWT), open fractures may benefit from it. An increasing number of studies have demonstrated that it can be used to treat open fractures and open complex wounds after failure of arthroplasty or spinal surgery. Based on the recent studies and evidence, we reviewed the role of the NPWT in the open fracture in the present study.

**Keywords:** Negative-Pressure Wound Therapy; Open Fracture; Wounds and Injuries

**Citation:** Moazen Jamshidi MM, Nezhad Tabrizi B, Fallah E, Ebrahimian M, Salehi A, Moharrami A, et al. **Negative Pressure Wound Therapy Uses in Orthopedic Open Fracture: A Current Concept Review.** *J Orthop Spine Trauma* 2022; 8(3): 74-8.

## Background

Among the urban population, fractures from trauma and subsequent trauma are common. The most common type of fracture is considered a closed fracture, which occurs when the skin around the fracture remains intact. These fractures are less likely to be infected. In comparison, if a fracture is 'open', the skin barrier that protects the unprotected bone is breached, which results in contamination from the environment leading to hematoma formation at the fracture site (1).

Open fractures are often associated with a high morbidity rate. The Gustilo-Anderson classification is often used for open fractures, even though there are a number of classification systems. Open fractures, such as those caused by Gustilo-Anderson type III fractures, whose closure is often delayed or impossible, require proper wound management and infection prevention. A type-1 injury is characterized by a laceration less than 1 cm, a type-2 injury has a laceration between 1 cm and 10 cm, and a type-3 wound has a laceration deeper than 10 cm and extensive soft tissue damage (2). Severe open fractures are mangled and crush injuries. Statistics show that severe open fractures have infection rates of 0.021% in type I, 0.101% in type II, and 0.501% in type III (3). However, the duration of antibiotic treatment and the amount of time spent remodeling the wound are indirect factors related to infection (4).

- Knowing how to treat open fractures is crucial because open fractures are associated with an increased risk of infection, complications, and even amputations during treatment (2, 4, 5). As such, the UK Guidelines for Primary Approaches to Open Fractures recommend prescribing antibiotics promptly, surgically removing contaminated

tissue, immobilizing the fracture and fixating it, as well as using conventional dressings on open fractures. Reassessment and possible further wound debridement occur 48-72 hours later (5).

- The mostly used wound care material has been cotton gauze in the past and continues to be today. Using gauze to cover and absorb exudate from simple wounds is a cost-effective way to keep wounds clean and covered. In 1962, Winter found that wounds kept moist healed faster than wounds exposed to the air (6).
- Open fractures may benefit from negative pressure wound therapy (NPWT) despite the lack of evidence for it (2).

The technology was developed almost 20 years ago by Argenta and Morykwas (7) and Morykwas et al. (8) to treat medical conditions. As a result, NPWT has become the method deemed standard in many institutions for treating complex open wounds. A growing body of evidence supports its use in the treatment of open fractures (3, 9) and open complex wounds after failures of arthroplasty (10, 11) or spinal surgery (12). In the present study, we reviewed the role of the NPWT in the open fracture based on recent studies and evidence.

### History of NPWT

Negative pressure has been used since antiquity to treat open wounds. Christine Miller, in her book, examines the historical evolution of negative pressure, which goes back to ancient times when Roman medics employed direct mouth suction to remove poisons or infected fluids from wounded soldiers during battle (13). In the 19<sup>th</sup> century, a British doctor named Dr. Francis Cox developed a wide neck cupping device to use a suction apparatus called the 'glass leech'. In addition to this modification, Dr. Gustav Bier also developed a similar cupping system that included tubing



and a bulb for removing wound exudate (13).

Using an ordinary polyethylene film over open wounds was described in 1986 by Dr. Nail Bagautdinov in Russia. It was attached to a vacuum pump with petrolatum and secured to the surrounding skin with petrolatum. This construction is similar to modern designs. In Germany, Fleischmann et al. developed a similar system using polyvinyl foam dressings. NPWT systems were developed commercially during the 1990s due to the clinical and scientific research of Dr. Louis Argenta and Dr. Michael Morykwas at Wake Forest University, USA (14).

Originally, the concept was meant to treat patients with chronic diabetic wounds and accelerate their healing by secondary intention.

Dr. Argenta began using this treatment method on a regular basis in 1991. Before NPWT was developed, wound care traditionally included manual dressing changes several times a day. The time and labor burdens placed on healthcare providers and patients were significant. Inflammation, pain, bleeding, and poor healing are associated with this wound treatment method. (7, 15). These issues ultimately led to the creation of the closed system vacuum dressing.

The device included placing an open-cell polyurethane ether foam sponge onto the wound surface, covered by adhesive drapes, and connected to a sub-atmospheric pressure vacuum system through flexible tubing set at 125 mmHg. These studies demonstrated significant improvement in wound healing in both animal models and human patients, including removal of wound exudate, decreased interstitial edema and bacterial load, increased granulation tissue, and improved wound perfusion. Ultimately, these effects resulted in faster wound healing compared with traditional wound care and a shorter hospital stay with cost savings (8). NPWT has had broadening applications over time and continues to evolve.

The use of vacuum-assisted devices as bolster dressings for skin grafts by Dr. Argenta was described in 1998, and further evidence for this technique has been published since then (16-18). It was documented in the literature during the early 2000s that NPWT was used to treat complex soft tissue injuries (associated with tissue loss or exposure of vital structures) in both adult and pediatric populations, including lower extremity injuries with exposed bone and necrotizing infections (10, 19, 20). Further studies have demonstrated the utility of NPWT devices in managing challenging breast wounds and abdominal wall defects, including the use of intra-abdominal NPWT dressings as a bridge to definitive fascial closure following trauma and recovery of abdominal dehiscence after hernia repair (21-25).

Similarly, some practitioners utilized NPWT devices to bridge the gap between debridement and definitive closure of the postoperative sternal wound. Furthermore, NPWT has been found to improve overall survival in patients with mediastinitis following coronary artery bypass grafting (CABG) compared to conventional treatment (26, 27). The use of NPWT has also been reported in orthopedic trauma, perineal and gynecological defects, burn injury, diabetic foot wounds, and head and neck defects. (28, 29).

#### The Physics of NPWT

At sea level, we live in an atmospheric pressure of 760 mmHg. Jet airplane cabins are pressurized to a pressure of about 635 mmHg to ensure passengers' comfort and provide adequate oxygen for their metabolism. In order to

ascend Earth's highest peaks, mountaineers often use supplemental oxygen due to the drop in barometric pressure with altitude. Using the ideal gas equation, we can approximate the behavior of gases in our atmosphere. We can state the following equation:  $P * V = n * R * T$ , where P is the pressure, V is the volume, n is the number of moles of gas, R is the universal gas constant, and T is the temperature. P must always have a positive value since V, n, R, and T are all positive scalars. The pressure in an absolute vacuum is 0 mmHg, like in outer space. A negative pressure is defined as the difference between the pressure applied and the pressure in the atmosphere. However, it is a misnomer commonly used in the literature. The absolute pressure of a chest tube connected to 20 mmHg suction would be 740 mm or the gauge pressure would be 20 mmHg at sea level. During surgical procedures, closed suction drainage systems have been helpful in moving large amounts of liquid out of the body. This system allows air to be evacuated from the pleural space to expand a lung following a pneumothorax. A closed suction can also help treat small bowel obstructions by draining the stomach contents. It is important to control how much suction is used. In the chest, suction levels greater than 40 mmHg can damage the lung. High suction levels can also remove tissues from the body (such as during liposuction).

A subatmospheric pressure environment is composed of three major components: an adhesive-sealed dressing, a vacuum device, and a communication device. Large-pore foam is preferred in most orthopedic trauma cases (30).

#### Mechanisms of Action

There have been several proposed mechanisms of action for NPWT. Through cell signaling effects, the device has four primary mechanisms, as well as potentially numerous secondary mechanisms.

##### Primary Effects

**Macrodeformation:** The open-pore foam pulls the wound edges together depending on the tissue mobility surrounding the wound (31). A NPWT may, for example, bring the scar edges closer together in an obese patient with an open abdominal wound. On the other hand, a large scalp wound will not deform the surrounding tissue.

**Microdeformation:** Microdeformation of the wound surface facilitates cell division and proliferation by allowing cells to expand (32).

**Fluid Removal:** The NPWT is capable of removing large amounts of fluid from the extracellular space in many edematous wounds (7, 8, 32-35).

**Environmental Control of the Wound:** NPWT provides an insulated, warm, and moist environment (36).

##### Secondary Effects

**Granulation Tissue Formation:** Users report that NPWT stimulates granulation tissue formation in a robust manner. There are several factors contributing to this response, including microdeformation, which causes hypoxia near the wound surface and, therefore, activates the hypoxia-inducible factor 1 alpha (HIF-1 $\alpha$ )-vascular endothelial growth factor (VEGF) pathway.

**Cell Proliferation:** The involvement of at least three primary mechanisms for proliferation can be made out of microdeformation (32) and fluid removal (35), as well as the maintenance of a warm and moist wound environment (31).

**Modulation of Inflammation:** We are just learning how the NPWT modulates inflammation in response to injury. Mast cells play a critical role in NPWT success in mice lacking mast cells, for example (37, 38).

**Change in Neuropeptides:** NPWT has been previously shown to enhance neurotransmitter production in a mouse model (39).

**Change in Bacterial Levels:** Several studies have shown both an increase and a decrease in bacterial levels following NPWT (31, 40).

#### Indication and Contraindication

NPWT is best suited to treat purely soft tissue traumatic wounds when definitive closure is not possible, such as when significant wound contamination exists, a debridement is necessary, edema is significant, or the patient is critically ill. As a result of this therapy, wounds are prevented from desiccating, microbial contamination is minimized, edema is reduced, and wound drainage is facilitated. NPWT is less labor-intensive for hospital staff since it is changed less frequently than wet-to-dry dressings, thereby causing less discomfort for the patient. With regard to indications for its use, NPWT has been particularly successful in the treatment of fasciotomy incisions, because delayed primary closure allows for edema to subside and compartment pressures to normalize (Table 1) (41, 42).

#### Cost-Effectiveness of NPWT

There is a wide range of cost-effectiveness among commercial NPWT systems and standard dressings. In a recent randomized controlled trial (RCT) of NPWT, average costs of NPWT were found to be significantly higher than those associated with standard dressings (43).

**Table 1.** The indication and contraindication of the negative pressure wound therapy (NPWT)

#### Indication of NPWT

Complex wound (including any of acute, subacute, and chronic wound)  
Traumatic wound  
Dehisced wound  
Burning wound (especially partial thickness types)  
Chronic ulcer (such as diabetic, pressure, or venous insufficiency)  
Flaps and grafts

#### Contraindication of NPWT

It is extremely important to design vacuum (VAC) therapy system to avoid direct contact to exposed blood vessels, anatomic sites, organs, or nerves.  
V.A.C therapy is contraindicated in patient presented with:  
Untreated osteomyelitis  
Fistulas (specially in non-enteric and unexplored types)  
Necrotic tissue provided with eschar  
Malignancy-related wound  
Sensitivity to any component of each brand (e.g., sensitivity to silver in V.A.C GranuFoam Silver® Dressing only)

NPWT: Negative pressure wound therapy

Kim et al. conducted a retrospective analysis comparing the costs of commercial NPWT and gauze-suction dressings to find that lower-cost materials were significantly cheaper than commercial systems (44). However, Shiroky et al. published a meta-analysis of four RCTs demonstrating that closed incision negative pressure therapy (ciNPT) results in a 40 percent reduction in surgical site infections compared with standard dressings, thereby reducing cost indirectly (45). Further, outpatient wound healing time has been found to indirectly reduce the overall cost by using NPWT (16, 46).

#### Complications

NPWT has potential complications and challenges, despite its infrequency. The timing of the NPWT placement in the acute setting must be carefully considered. The management of some wounds (e.g., severe degloving) requires immediate, acute NPWT, while other wounds (i.e., acute wounds) require more thorough surgical interventions. In addition to debridement and identifying neurovascular structures, NPWT can lead to other complications, including bleeding, pain during dressing changes, retained sponges after prolonged placement, and

wound breakdown. NPWT may not prevent wound breakdown, particularly in immunocompromised patients. One report (30) described a 65-year-old, immunocompromised (history of kidney transplantation on lifelong immunosuppressants) patient who, eight weeks after her medial tibial plateau fixation, developed wound drainage and eventually fractured. The patient required irrigation, debridement, hardware removal, and flap coverage. Complications such as these can be avoided with close monitoring and specific strategies. The wound bed or incision must be thoroughly assessed before dressing placement in order to avoid excessive bleeding. The outputs should be monitored closely after dressing insertion since the negative pressure environment may lead to prolonged coagulation and excessive blood loss (47).

An often overlooked complication of NPWT is the wound complications secondary to interrupted therapy. Loss of power or error message is often caused by a poor seal or a blockage in the tubing. Negative pressure is lost when this occurs for a long period, resulting in a moist, closed environment that can eventually lead to further skin maceration and breakdown. Collinge and Reddix retrospectively analyzed 123 patients who had interrupted non-progressive wound healing and found a significantly higher rate of wound complications than patients who did not experience interruptions (48). Therefore, all staff must be vigilant about notifying doctors and nurses of any interruptions in therapy, which must be addressed promptly. Some simple principles and strategies can be used to minimize pain during dressing changes. Keeping the duration of two to four days between changes is recommended.

A sponge placed between the soft tissue and the dressing can make it easier to remove it. Additionally, although the senior authors used it anecdotally, the application of a nonocclusive protective dressing between the sponge and the skin (e.g., cellulose acetate silicone dressing, petroleum gauze dressing) might facilitate dressing removal and prevent irritation or maceration of the skin. Christensen et al. investigated the efficacy of topical lidocaine (1%) without epinephrine compared to placebo before dressing removal (49). A lidocaine injection directly into the sponge before removal significantly reduced pain (49). After removing the sponge, the wound bed should be carefully inspected to ensure no foam remains behind. In crush injuries and amputations, NPWT should be used with caution due to the risk of blood loss and skin necrosis, as well as exposing nerves and arteries (50).

#### Conclusion

As of today, NPWT is an excellent option for treating many types of complex wounds such as open fractures, extensive soft tissue loss, and wounds that require secondary treatment. Therefore, this bridging therapy making temporary coverage of wounds has a variety of functions and features that help reduce deep wound infection, soft-tissue edema, failure of the flap and accelerated wound healing, and hospitalization and have significant roles in patient and health service bar. NPWT is now widely used to treat orthopedic trauma and injuries that result in wounds. In order to avoid excessive bleeding, direct exposure to neurovascular bundles, and pain during dressing changes, the use of NPWT should be closely monitored. However, more research is needed to determine the duration of therapy, exact pressure needed for each type of wound, and other areas of surgery to be considered.

## Conflict of Interest

The authors declare no conflict of interest in this study.

## Acknowledgements

None.

## References

- Suzuki T, Minehara A, Matsuura T, Kawamura T, Soma K. Negative-pressure wound therapy over surgically closed wounds in open fractures. *J Orthop Surg (Hong Kong)*. 2014;22(1):30-4. doi: [10.1177/230949901402200109](https://doi.org/10.1177/230949901402200109). [PubMed: [24781609](https://pubmed.ncbi.nlm.nih.gov/24781609/)].
- Gustilo RB, Anderson JT. JSBS classics. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones. Retrospective and prospective analyses. *J Bone Joint Surg Am*. 2002;84(4):682. doi: [10.2106/00004623-200204000-00029](https://doi.org/10.2106/00004623-200204000-00029). [PubMed: [11940635](https://pubmed.ncbi.nlm.nih.gov/11940635/)].
- Stannard JP, Volgas DA, Stewart R, McGwin G, Alonso JE. Negative pressure wound therapy after severe open fractures: A prospective randomized study. *J Orthop Trauma*. 2009;23(8):552-7. doi: [10.1097/BOT.0b013e3181a2e2b6](https://doi.org/10.1097/BOT.0b013e3181a2e2b6). [PubMed: [19704269](https://pubmed.ncbi.nlm.nih.gov/19704269/)].
- Arti H, Khorami M, Ebrahimi-Nejad V. Comparison of negative pressure wound therapy (NPWT) & conventional wound dressings in the open fracture wounds. *Pak J Med Sci*. 2016;32(1):65-9. doi: [10.12669/pjms.321.8568](https://doi.org/10.12669/pjms.321.8568). [PubMed: [27022347](https://pubmed.ncbi.nlm.nih.gov/27022347/)]. [PubMed Central: [PMC4795891](https://pubmed.ncbi.nlm.nih.gov/PMC4795891/)].
- Grant-Freemantle MC, Ryan EJ, Flynn SO, Moloney DP, Kelly MA, Coveney EI, et al. The effectiveness of negative pressure wound therapy versus conventional dressing in the treatment of open fractures: A systematic review and meta-analysis. *J Orthop Trauma*. 2020;34(5):223-30. doi: [10.1097/BOT.0000000000001750](https://doi.org/10.1097/BOT.0000000000001750). [PubMed: [32079890](https://pubmed.ncbi.nlm.nih.gov/32079890/)].
- Winter GD. Formation of the scab and the rate of epithelization of superficial wounds in the skin of the young domestic pig. *Nature*. 1962;193:293-4. doi: [10.1038/193293a0](https://doi.org/10.1038/193293a0). [PubMed: [14007593](https://pubmed.ncbi.nlm.nih.gov/14007593/)].
- Argenta LC, Morykwas MJ. Vacuum-assisted closure: A new method for wound control and treatment: Clinical experience. *Ann Plast Surg*. 1997;38(6):563-76. [PubMed: [9188971](https://pubmed.ncbi.nlm.nih.gov/9188971/)].
- Morykwas MJ, Argenta LC, Shelton-Brown EI, McGuirt W. Vacuum-assisted closure: A new method for wound control and treatment: animal studies and basic foundation. *Ann Plast Surg*. 1997;38(6):553-62. doi: [10.1097/00000637-199706000-00001](https://doi.org/10.1097/00000637-199706000-00001). [PubMed: [9188970](https://pubmed.ncbi.nlm.nih.gov/9188970/)].
- Blum ML, Esser M, Richardson M, Paul E, Rosenfeldt FL. Negative pressure wound therapy reduces deep infection rate in open tibial fractures. *J Orthop Trauma*. 2012;26(9):499-505. doi: [10.1097/BOT.0b013e31824133e3](https://doi.org/10.1097/BOT.0b013e31824133e3). [PubMed: [22487900](https://pubmed.ncbi.nlm.nih.gov/22487900/)].
- DeFranzo AJ, Argenta LC, Marks MW, Molnar JA, David LR, Webb LX, et al. The use of vacuum-assisted closure therapy for the treatment of lower-extremity wounds with exposed bone. *Plast Reconstr Surg*. 2001;108(5):1184-91. doi: [10.1097/00006534-200110000-00013](https://doi.org/10.1097/00006534-200110000-00013). [PubMed: [11604617](https://pubmed.ncbi.nlm.nih.gov/11604617/)].
- Kilic A, Ozkaya U, Sokucu S, Basilgan S, Kabukcuoglu Y. Use of vacuum-assisted closure in the topical treatment of surgical site infections. *Acta Orthop Traumatol Turc*. 2009;43(4):336-42. [In Turkish]. doi: [10.3944/AOTT.2009.336](https://doi.org/10.3944/AOTT.2009.336). [PubMed: [19809231](https://pubmed.ncbi.nlm.nih.gov/19809231/)].
- Labler L, Keel M, Trentz O, Heinzlmann M. Wound conditioning by vacuum assisted closure (V.A.C.) in postoperative infections after dorsal spine surgery. *Eur Spine J*. 2006;15(9):1388-96. doi: [10.1007/s00586-006-0164-2](https://doi.org/10.1007/s00586-006-0164-2). [PubMed: [16835734](https://pubmed.ncbi.nlm.nih.gov/16835734/)]. [PubMed Central: [PMC2438567](https://pubmed.ncbi.nlm.nih.gov/PMC2438567/)].
- Miller C. The history of negative pressure wound therapy (NPWT): From "Lip Service" to the modern vacuum system. *J Am Coll Clin Wound Spec*. 2012;4(3):61-2. doi: [10.1016/j.jccw.2013.11.002](https://doi.org/10.1016/j.jccw.2013.11.002). [PubMed: [26236637](https://pubmed.ncbi.nlm.nih.gov/26236637/)]. [PubMed Central: [PMC4511545](https://pubmed.ncbi.nlm.nih.gov/PMC4511545/)].
- Fleischmann W, Strecker W, Bombelli M, Kinzl L. Vacuum sealing as treatment of soft tissue damage in open fractures. *Unfallchirurg*. 1993;96(9):488-92. [In German]. [PubMed: [8235687](https://pubmed.ncbi.nlm.nih.gov/8235687/)].
- Langer V, Bhandari PS, Rajagopalan S, Mukherjee MK. Negative pressure wound therapy as an adjunct in healing of chronic wounds. *Int Wound J*. 2015;12(4):436-42. doi: [10.1111/iwj.12132](https://doi.org/10.1111/iwj.12132). [PubMed: [23855645](https://pubmed.ncbi.nlm.nih.gov/23855645/)]. [PubMed Central: [PMC7950602](https://pubmed.ncbi.nlm.nih.gov/PMC7950602/)].
- Driver VR, Eckert KA, Carter MJ, French MA. Cost-effectiveness of negative pressure wound therapy in patients with many comorbidities and severe wounds of various etiology. *Wound Repair Regen*. 2016;24(6):1041-58. doi: [10.1111/wrr.12483](https://doi.org/10.1111/wrr.12483). [PubMed: [27669667](https://pubmed.ncbi.nlm.nih.gov/27669667/)].
- Schneider AM, Morykwas MJ, Argenta LC. A new and reliable method of securing skin grafts to the difficult recipient bed. *Plast Reconstr Surg*. 1998;102(4):1195-8. doi: [10.1097/00006534-199809040-00045](https://doi.org/10.1097/00006534-199809040-00045). [PubMed: [9734445](https://pubmed.ncbi.nlm.nih.gov/9734445/)].
- Scherer LA, Shiver S, Chang M, Meredith JW, Owings JT. The vacuum assisted closure device: A method of securing skin grafts and improving graft survival. *Arch Surg*. 2002;137(8):930-3. doi: [10.1001/archsurg.137.8.930](https://doi.org/10.1001/archsurg.137.8.930). [PubMed: [12146992](https://pubmed.ncbi.nlm.nih.gov/12146992/)].
- Moisidis E, Heath T, Boorer C, Ho K, Deva AK. A prospective, blinded, randomized, controlled clinical trial of topical negative pressure use in skin grafting. *Plast Reconstr Surg*. 2004;114(4):917-22. doi: [10.1097/01.prs.0000133168.57199.e1](https://doi.org/10.1097/01.prs.0000133168.57199.e1). [PubMed: [15468399](https://pubmed.ncbi.nlm.nih.gov/15468399/)].
- DeFranzo AJ, Marks MW, Argenta LC, Genecov DG. Vacuum-assisted closure for the treatment of degloving injuries. *Plast Reconstr Surg*. 1999;104(7):2145-8. doi: [10.1097/00006534-199912000-00031](https://doi.org/10.1097/00006534-199912000-00031). [PubMed: [11149782](https://pubmed.ncbi.nlm.nih.gov/11149782/)].
- de Geus HR, van der Klooster JM. Vacuum-assisted closure in the treatment of large skin defects due to necrotizing fasciitis. *Intensive Care Med*. 2005;31(4):601. doi: [10.1007/s00134-004-2553-5](https://doi.org/10.1007/s00134-004-2553-5). [PubMed: [15666139](https://pubmed.ncbi.nlm.nih.gov/15666139/)].
- Stoeckel WT, David L, Levine EA, Argenta AE, Perrier ND. Vacuum-assisted closure for the treatment of complex breast wounds. *Breast*. 2006;15(5):610-3. doi: [10.1016/j.breast.2005.11.006](https://doi.org/10.1016/j.breast.2005.11.006). [PubMed: [16443363](https://pubmed.ncbi.nlm.nih.gov/16443363/)].
- DeFranzo AJ, Argenta L. Vacuum-assisted closure for the treatment of abdominal wounds. *Clin Plast Surg*. 2006;33(2):213-24. doi: [10.1016/j.cps.2005.12.007](https://doi.org/10.1016/j.cps.2005.12.007). [PubMed: [16638464](https://pubmed.ncbi.nlm.nih.gov/16638464/)].
- Stone PA, Hass SM, Flaherty SK, DeLuca JA, Lucente FC, Kusminsky RE. Vacuum-assisted fascial closure for patients with abdominal trauma. *J Trauma*. 2004;57(5):1082-6. doi: [10.1097/01.ta.0000149248.02598.9e](https://doi.org/10.1097/01.ta.0000149248.02598.9e). [PubMed: [15580036](https://pubmed.ncbi.nlm.nih.gov/15580036/)].
- de Vooght A, Feruzi G, Detry R, Lerut J, Vanwijck R. Vacuum-assisted closure for abdominal wound dehiscence with prosthesis exposure in hernia surgery. *Plast Reconstr Surg*. 2003;112(4):1188-9. doi: [10.1097/01.PRS.0000077233.64957.30](https://doi.org/10.1097/01.PRS.0000077233.64957.30). [PubMed: [12973257](https://pubmed.ncbi.nlm.nih.gov/12973257/)].
- Song DH, Wu LC, Lohman RF, Gottlieb LJ, Franczyk M. Vacuum assisted closure for the treatment of sternal wounds: The bridge between debridement and definitive closure. *Plast Reconstr Surg*. 2003;111(1):92-7. doi: [10.1097/01.PRS.0000037686.14278.6A](https://doi.org/10.1097/01.PRS.0000037686.14278.6A). [PubMed: [12496568](https://pubmed.ncbi.nlm.nih.gov/12496568/)].
- Sjogren J, Gustafsson R, Nilsson J, Malmsjo M, Ingemansson R. Clinical outcome after poststernotomy mediastinitis: vacuum-assisted closure versus conventional treatment. *Ann Thorac Surg*. 2005;79(6):2049-55. doi: [10.1016/j.athoracsur.2004.12.048](https://doi.org/10.1016/j.athoracsur.2004.12.048). [PubMed: [15919308](https://pubmed.ncbi.nlm.nih.gov/15919308/)].
- Sjogren J, Nilsson J, Gustafsson R, Malmsjo M, Ingemansson R. The impact of vacuum-assisted closure on long-term survival after post-sternotomy mediastinitis. *Ann Thorac Surg*. 2005;80(4):1270-5. doi: [10.1016/j.athoracsur.2005.04.010](https://doi.org/10.1016/j.athoracsur.2005.04.010). [PubMed: [16181853](https://pubmed.ncbi.nlm.nih.gov/16181853/)].
- Argenta LC, Morykwas MJ, Marks MW, DeFranzo AJ, Molnar JA, David LR. Vacuum-assisted closure: State of clinic art. *Plast Reconstr Surg*. 2006;117(7 Suppl):1275-42S. doi: [10.1097/01.prs.0000222551.10793.51](https://doi.org/10.1097/01.prs.0000222551.10793.51). [PubMed: [16799380](https://pubmed.ncbi.nlm.nih.gov/16799380/)].
- Gage MJ, Yoon RS, Egol KA, Liporace FA. Uses of negative pressure wound therapy in orthopedic trauma. *Orthop Clin North Am*. 2015;46(2):227-34. doi: [10.1016/j.ocl.2014.11.002](https://doi.org/10.1016/j.ocl.2014.11.002). [PubMed: [25771317](https://pubmed.ncbi.nlm.nih.gov/25771317/)].
- Orgill DP, Manders EK, Sumpio BE, Lee RC, Attinger CE, Gurtner GC, et al. The mechanisms of action of vacuum assisted closure: more to learn. *Surgery*. 2009;146(1):40-51. doi: [10.1016/j.surg.2009.02.002](https://doi.org/10.1016/j.surg.2009.02.002). [PubMed: [19541009](https://pubmed.ncbi.nlm.nih.gov/19541009/)].
- Saxena V, Hwang CW, Huang S, Eichbaum Q, Ingber D, Orgill DP. Vacuum-assisted closure: microdeformations of wounds and cell proliferation. *Plast Reconstr Surg*. 2004;114(5):1086-96. doi: [10.1097/01.prs.0000135330.51408.97](https://doi.org/10.1097/01.prs.0000135330.51408.97). [PubMed: [15457017](https://pubmed.ncbi.nlm.nih.gov/15457017/)].
- Greene AK, Puder M, Roy R, Arsenaault D, Kwei S, Moses MA, et al. Microdeformational wound therapy: effects on

- angiogenesis and matrix metalloproteinases in chronic wounds of 3 debilitated patients. *Ann Plast Surg.* 2006;56(4):418-22. doi: [10.1097/01.sap.0000202831.43294.02](https://doi.org/10.1097/01.sap.0000202831.43294.02). [PubMed: [16557076](https://pubmed.ncbi.nlm.nih.gov/16557076/)].
34. Gabriel A, Gialich S, Kirk J, Edwards S, Beck B, Soroceanu A, et al. The Haiti earthquake: The provision of wound care for mass casualties utilizing negative-pressure wound therapy. *Adv Skin Wound Care.* 2011;24(10):456-62. doi: [10.1097/01.ASW.0000406473.36176.79](https://doi.org/10.1097/01.ASW.0000406473.36176.79). [PubMed: [21926673](https://pubmed.ncbi.nlm.nih.gov/21926673/)].
  35. Morykwas MJ, Simpson J, Pungler K, Argenta A, Kremers L, Argenta J. Vacuum-assisted closure: State of basic research and physiologic foundation. *Plast Reconstr Surg.* 2006;117(7 Suppl):121S-6S. doi: [10.1097/01.prs.0000225450.12593.12](https://doi.org/10.1097/01.prs.0000225450.12593.12). [PubMed: [16799379](https://pubmed.ncbi.nlm.nih.gov/16799379/)].
  36. Scherer SS, Pietramaggiore G, Mathews JC, Prsa MJ, Huang S, Orgill DP. The mechanism of action of the vacuum-assisted closure device. *Plast Reconstr Surg.* 2008;122(3):786-97. doi: [10.1097/PRS.0b013e31818237ac](https://doi.org/10.1097/PRS.0b013e31818237ac). [PubMed: [18766042](https://pubmed.ncbi.nlm.nih.gov/18766042/)].
  37. Erba P, Ogawa R, Ackermann M, Adini A, Miele LF, Dastouri P, et al. Angiogenesis in wounds treated by microdeformational wound therapy. *Ann Surg.* 2011;253(2):402-9. doi: [10.1097/SLA.0b013e31820563a8](https://doi.org/10.1097/SLA.0b013e31820563a8). [PubMed: [21217515](https://pubmed.ncbi.nlm.nih.gov/21217515/)]. [PubMed Central: [PMC3403722](https://pubmed.ncbi.nlm.nih.gov/PMC3403722/)].
  38. Younan GJ, Heit YI, Dastouri P, Kekhnia H, Xing W, Gurish MF, et al. Mast cells are required in the proliferation and remodeling phases of microdeformational wound therapy. *Plast Reconstr Surg.* 2011;128(6):649e-58e. doi: [10.1097/PRS.0b013e318230c55d](https://doi.org/10.1097/PRS.0b013e318230c55d). [PubMed: [22094766](https://pubmed.ncbi.nlm.nih.gov/22094766/)].
  39. Younan G, Ogawa R, Ramirez M, Helm D, Dastouri P, Orgill DP. Analysis of nerve and neuropeptide patterns in vacuum-assisted closure-treated diabetic murine wounds. *Plast Reconstr Surg.* 2010;126(1):87-96. doi: [10.1097/PRS.0b013e3181da86d0](https://doi.org/10.1097/PRS.0b013e3181da86d0). [PubMed: [20595860](https://pubmed.ncbi.nlm.nih.gov/20595860/)].
  40. Moues CM, Vos MC, van den Bemd GJ, Stijnen T, Hovius SE. Bacterial load in relation to vacuum-assisted closure wound therapy: A prospective randomized trial. *Wound Repair Regen.* 2004;12(1):11-7. doi: [10.1111/j.1067-1927.2004.12105.x](https://doi.org/10.1111/j.1067-1927.2004.12105.x). [PubMed: [14974959](https://pubmed.ncbi.nlm.nih.gov/14974959/)].
  41. Yang CC, Chang DS, Webb LX. Vacuum-assisted closure for fasciotomy wounds following compartment syndrome of the leg. *J Surg Orthop Adv.* 2006;15(1):19-23. [PubMed: [16603108](https://pubmed.ncbi.nlm.nih.gov/16603108/)].
  42. Zannis J, Angobaldo J, Marks M, DeFranzo A, David L, Molnar J, et al. Comparison of fasciotomy wound closures using traditional dressing changes and the vacuum-assisted closure device. *Ann Plast Surg.* 2009;62(4):407-9. doi: [10.1097/SAP.0b013e3181881b29](https://doi.org/10.1097/SAP.0b013e3181881b29). [PubMed: [19325346](https://pubmed.ncbi.nlm.nih.gov/19325346/)].
  43. Petrou S, Parker B, Masters J, Achten J, Bruce J, Lamb SE, et al. Cost-effectiveness of negative-pressure wound therapy in adults with severe open fractures of the lower limb: evidence from the WOLLF randomized controlled trial. *Bone Joint J.* 2019;101-B(11):1392-401. doi: [10.1302/0301-620X.101B11.BJ-2018-1228.R2](https://doi.org/10.1302/0301-620X.101B11.BJ-2018-1228.R2). [PubMed: [31674241](https://pubmed.ncbi.nlm.nih.gov/31674241/)].
  44. Kim JJ, Franczyk M, Gottlieb LJ, Song DH. Cost-effective alternative for negative-pressure wound therapy. *Plast Reconstr Surg Glob Open.* 2017;5(2):e1211. doi: [10.1097/GOX.0000000000001211](https://doi.org/10.1097/GOX.0000000000001211). [PubMed: [28280658](https://pubmed.ncbi.nlm.nih.gov/28280658/)]. [PubMed Central: [PMC5340473](https://pubmed.ncbi.nlm.nih.gov/PMC5340473/)].
  45. Shiroky J, Lillie E, Muaddi H, Sevigny M, Choi WJ, Karanicolas PJ. The impact of negative pressure wound therapy for closed surgical incisions on surgical site infection: A systematic review and meta-analysis. *Surgery.* 2020;167(6):1001-9. doi: [10.1016/j.surg.2020.01.018](https://doi.org/10.1016/j.surg.2020.01.018). [PubMed: [32143842](https://pubmed.ncbi.nlm.nih.gov/32143842/)].
  46. Dowsett C, Davis L, Henderson V, Searle R. The economic benefits of negative pressure wound therapy in community-based wound care in the NHS. *Int Wound J.* 2012;9(5):544-52. doi: [10.1111/j.1742-481X.2011.00913.x](https://doi.org/10.1111/j.1742-481X.2011.00913.x). [PubMed: [22321132](https://pubmed.ncbi.nlm.nih.gov/22321132/)]. [PubMed Central: [PMC7950552](https://pubmed.ncbi.nlm.nih.gov/PMC7950552/)].
  47. Li Z, Yu A. Complications of negative pressure wound therapy: A mini review. *Wound Repair Regen.* 2014;22(4):457-61. doi: [10.1111/wrr.12190](https://doi.org/10.1111/wrr.12190). [PubMed: [24852446](https://pubmed.ncbi.nlm.nih.gov/24852446/)].
  48. Collinge C, Reddix R. The incidence of wound complications related to negative pressure wound therapy power outage and interruption of treatment in orthopaedic trauma patients. *J Orthop Trauma.* 2011;25(2):96-100. doi: [10.1097/BOT.0b013e3181de0134](https://doi.org/10.1097/BOT.0b013e3181de0134). [PubMed: [21245712](https://pubmed.ncbi.nlm.nih.gov/21245712/)].
  49. Christensen TJ, Thorum T, Kubiak EN. Lidocaine analgesia for removal of wound vacuum-assisted closure dressings: A randomized double-blinded placebo-controlled trial. *J Orthop Trauma.* 2013;27(2):107-12. doi: [10.1097/BOT.0b013e318251219c](https://doi.org/10.1097/BOT.0b013e318251219c). [PubMed: [23343829](https://pubmed.ncbi.nlm.nih.gov/23343829/)].
  50. Khajeh R, Moharrami A, Farzan M, Molaei H, Moazen Jamshidi MM, Zarei M. Forearm amputations and crush injuries, different scenarios and treatments: Educational corner. *J Orthop Spine Trauma.* 2022;7(3):105-13. doi: [10.18502/jost.v7i3.8109](https://doi.org/10.18502/jost.v7i3.8109).