Negative-Pressure Wound Therapy: Principles and Usage in Orthopedic Surgery

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1 Introduction

A wound is defined as a disruption of the anatomical structure and function of an organ, such as the skin, resulting from a pathologic process beginning internal or external to the organ [1]. Acute wounds are those that repair themselves or can be repaired in an orderly and timely process, while chronic wounds heal in a delayed fashion (often >1 month) [1]. Skin acts as a protective barrier, and irrespective of the type and etiology of the wound, restoration of this normal barrier is important to prevent loss of body fluids, infection, and injuries to underlying tissues and organs. Dressings have been traditionally used to cover and prevent contamination of wounds [2]. However, with the increasing nature of wound complexities and the various local and systemic factors that affect wound healing, advancements in the types of wound dressings have been made, which can promote wound healing in addition to preventing contamination.

Negative-pressure wound therapy (NPWT) has become an integral part in the management of different types of wounds over the last few decades. It relies on creating a subatmospheric pressure on the surface of wound which is believed to promote wound healing, especially when there are various factors which can affect wound healing [3]. The negative pressure is typically applied until granulation tissue develops or until the local conditions are favorable for an additional surgical procedure, such as skin grafting. Negative-pressure wound therapy can be used for chronic wounds, acute wounds, and even surgical wounds (incisional NPWT) [4, 5]. However, not all types of wounds may benefit from NPWT, and studies have shown mixed results regarding the added clinical benefits of NPWT [6]. A thorough understanding of the mechanisms, indications, and applications of NPWT is crucial to promote the judicious use of NPWT. In this chapter, we focus on the principles of NPWT, and discuss the current evidence in support of its use in various surgical fields, especially orthopedic surgery.

2 History

Approximation of the skin edges and obliteration of dead space have long been recognized as crucial components of wound healing. Use of negative pressure was initially implemented

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Recent Clinical Techniques, Results, and Research in Wounds (2017)
DOI 10.1007/15695_2017_53, © Springer International Publishing AG
Published Online: 07 November 2017

in the 1950s to drain the collection of fluid under the skin associated with certain types of surgeries [7, 8]. These devices were composed of subcutaneously placed drains connected to a vacuum device to drain the excess fluid collection, and were reported to prevent fluid collection formation and promote granulation tissue growth [9]. By the late 1980s, scientists in Europe started to apply negative pressure over the surface of wounds with the use of foam and suction tubing [2, 10]. In the 1990s, a series of basic science and clinical studies performed by Argenta [11] and Morykwas [3], highlighting the positive effects of wound deformation, tissue pressure changes, and cytokine stimulation, led to the widespread implementation of NPWT in the present form in the United States. The first commercially available device that provided NWPT was the vacuum-assisted wound closure device and technology (V.A.C.®) (Kinetic Concepts Inc. (KCI), San Antonio, Texas). While the initial application of NPWT was restricted to large open wounds in debilitated patients, the use of NPWT has expanded to include wounds of varying severities and even as a prophylactic measure over surgical incisions. Although a number of negative-pressure device systems have been described, the most popular and widespread clinically used systems consist of delivery of an open-pore foam dressing, which results in the formation of small, domelike structures at the wound surface called microdeformation [12]. Therefore, some authors have suggested the term microdeformation wound therapy (MDWT) to distinguish the commonly used NPWT system from other systems delivering negative pressure [12]. However, in this chapter we use the term NPWT to refer to the commonly used systems that use foam.

3 Mechanism of Action

Although a number of theories have been described, the effects of NPWT can be broadly explained by two basic theories [13, 14]. The first one is based on the mechanical stain imposed on the tissues at the macroscopic and microscopic level, which leads to approximation of the skin edges and stimulation of growth of granulation tissue. The second is based on the removal of excess fluid, inflammatory markers, and potentially bacteria from the wound and the surrounding tissues. However, this last one is controversial and is discussed further in this chapter. Apart from these two mechanisms, the application of NPWT on wound beds has many indirect effects on wound healing, like modulation of inflammation, angiogenesis, peripheral nerve response, hemostasis, improved lymphatic clearance, and alteration in bioburden [12, 15–17]. However, the clinical relevance of some of these observed effects is unclear [18, 19].

With the application of the negative pressure, the porous foam shrinks in size and exerts strain on the wound bed, which leads to macro- and microdeformation of the wound (Fig. 1) [12]. Macrodeformation refers to the shrinkage of the size of the wound with the application of the NPWT. The foam used in NPWT systems can reduce in size by approximately 80%, and has been shown to result in a substantial decrease in wound sizes [13]. The extent of the contraction depends on the deformability of the tissue being used with larger shrinkage seen with abdominal wounds, compared to less deformable tissues located in the extremities or in a previously irradiated tissue bed [20]. Additionally, the wound contraction is associated with a paradoxical rise in the pressure of the surrounding tissues presumably due to the tension applied on the tissues by the contracting wound [12]. This can decrease the blood supply and can be detrimental in certain types of wounds, especially in ischemic limbs if circumferential NPWT is administered. In addition to the changes at the macroscopic level, the porous surface of the foam results in an undulated wound surface at a microscopic level [21]. This microdeformation results in strain of the tissue's cytoskeleton, which in turn stimulates cell proliferation, migration, and differentiation [22]. These microscopic changes in the surface of the wound

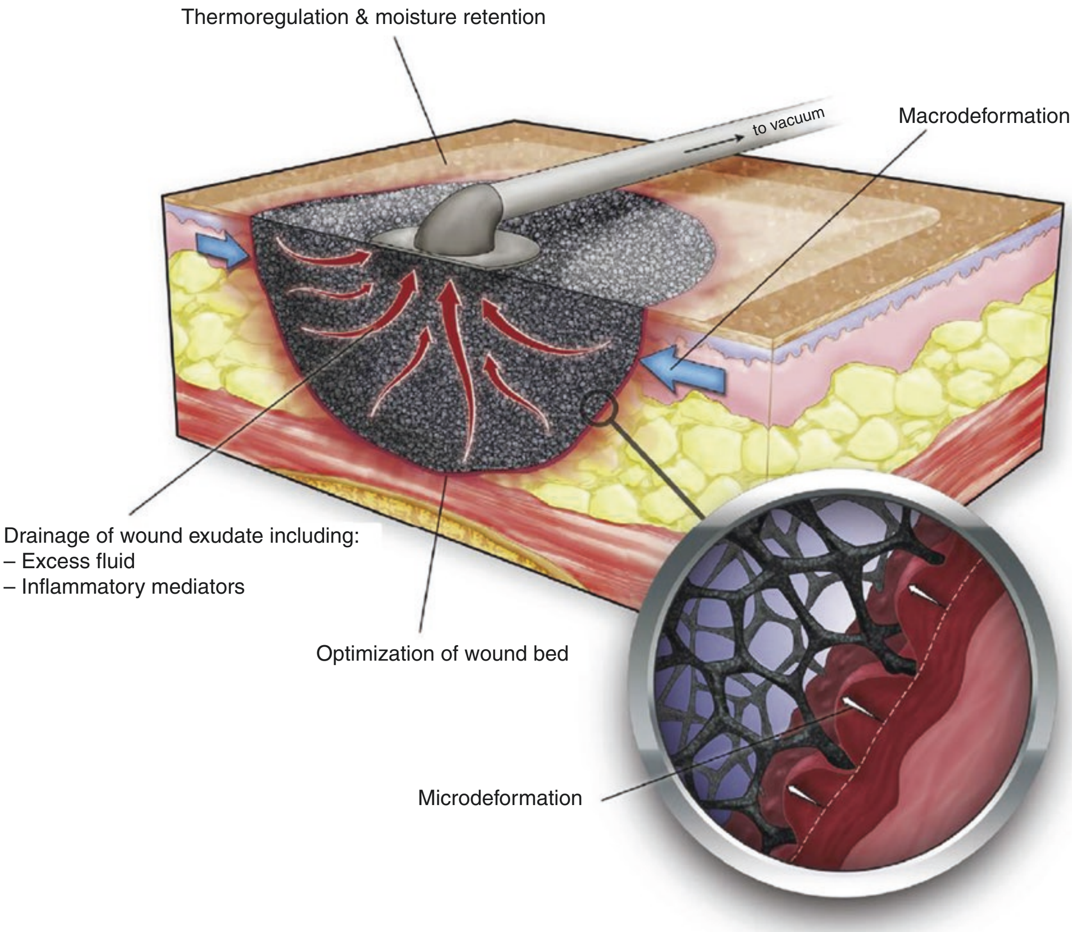

Fig. 1 The proposed mechanisms of action of negative-pressure therapy. Used with permission [12]

result in faster granulation tissue formation and quicker wound healing [13].

The negative pressure applied over the wounds results in the removal of fluids and clears the wound of toxins and exudates. Removal of fluid relieves the compressive effect of extracellular fluid on surrounding tissues and has been shown to improve circulation in the wound bed [23]. Removal of fluid also reduces the amount of fluid that must be cleared by the lymphatics and induces a local increase in lymphatic density [24]. It is also important to understand that the basic science evidence behind incisional NPWT (application over a primarily closed wound) has also been shown to afford similar benefits as application over open wounds, such as decreased tension on the skin, improved blood flow in the dermal location, and decreased seroma/lymphedema formation [17]. The use of NPWT does not appear to reduce the bacterial burden in the wounds. Some studies have even reported that the use of NPWT can increase the bacterial burden although there was enhanced wound healing with NPWT [18, 19].

4 Application of NPWT

NPWT does not replace the basic principles of wound management. Wounds should be thoroughly debrided, and necrotic or infected tissue should be removed prior to the application of NPWT. There are five basic components to the modern-day NPWT system, including wound filler, tubing, drapes, a pump, and a canister. The most commonly used wound filler is open-cell polyurethane foam and is composed of interconnected cells of size ranging between 400 and 600 μm in diameter [15]. The porous nature of the foam allows the pressure to be evenly distributed throughout its entire surface. Once the wound bed is ready, the foam piece is cut into an appropriate size so that the foam stays within the wound edges. After the application of the foam, a semiocclusive adhesive drape is placed over the wound covering the entire foam to ensure an airtight seal. The drape should have at least 3–5 cm of border to ensure maintenance of a tight seal. A small hole is made in the drape and a non-collapsible tube is placed over the hole and connected to a vacuum pump. The fluid drained from the wound is collected in the canister attached to the pump. The pressure applied by the pump can vary depending on the local wound conditions, and the device can be programmed to provide both continuous and intermittent negative pressure. The standard suction pressure is 125 mmHg, as optimal granulation tissue formation has been reported with this pressure [25]. However, other pressures have been reported depending on the size of the wound, location, and predisposition to bleeding. The most common mode of negative-pressure application is the continuous mode, but intermittent suction (for periods of 5 min separated by 2-min intervals) may be associated with greater stimulation of granulation tissue formation [3, 26]. However, intermittent therapy is not routinely used, as sudden and frequent changes in pressure can create varying discomfort for patients. Despite this, it is recommended to advance from continuous suction to intermittent suction in acute wounds, after the initial 48 h, unless there is uncontrolled pain, suction leaks, or an uneven wound surface. The duration of use of NPWT depends on the type of wound and the treatment goals. Chronic wounds often require prolonged treatment with NPWT, sometimes over a period of months, and NPWT might be continued until satisfactory outcomes are obtained. The negative-pressure dressing should be changed once every 48–72 h to prevent fluid saturation of the foam, which can decrease the effectiveness of the treatment. Newer dressings, however, such as the incisional NPWT dressing, can be placed over closed wounds for up to 7 days without changing. For infected wounds, dressings may need to be changed more frequently, though the clinician should be cautious about the use of these dressings over grossly infected wounds.

5 Advancements in NPWT

Since the initial introduction of V.A.C.® in the 1990s, significant advances have been made in the field of NPWT to cope with the expanding indications. One major challenge of the NPWT therapy is the maintenance of a tight seal so the negative pressure can be delivered. Automated alarm systems are currently available which can detect inadequate seal. Additionally these electronic systems can detect excessive fluid output and can be programmed to deliver negative pressure at various intervals. Two major advancements in the field of NPWT have been the availability of incisional NPWT and negative pressure with instillation.

Surgical wounds are closed with either sutures or staples and heal by primary intention. Surgical incisions from trauma-related surgery, total joint arthroplasty, cardiothoracic surgery, vascular surgery repair in the setting of known ischemia, major soft-tissue rearrangement plastic surgery interventions, and neurosurgical procedures are at high risk of wound dehiscence and increased risk of surgical site infections, all being studied in the setting of these recent advancements of NPWT. Traditionally, negative pressure has been used to treat complex open wounds, which usually heal by secondary intention. However, with the increasing popularity of NPWT, the indications for NPWT have extended as a prophylactic measure in the management of closed surgical incisions (incisional NPWT). Currently, there are commercially available NPWT dressings that can be applied over surgical wounds, such as Prevena™ (KCI, San Antonio, Texas) and PICO (Smith and Nephew, St. Petersburg, Florida) [27]. Compared to the traditional NPWT devices, Prevena and PICO are composed of lightweight portable suction devices that allow patients to remain ambulatory with the dressing. The PICO system is different in that it does not have a canister and the fluid is lost by evaporation [28]. In a meta-analysis by Hyldig et al. [29], NPWT significantly reduced the rate of wound infection and seroma when applied to closed surgical wounds compared with the standard postoperative dressings. However, there was heterogeneity between the included studies, meaning that no general recommendations could be made. Also, they reported that a relatively large number of patients were lost to follow-up in the control groups and length of follow-up might have been inadequate to detect surgical site infections [29]. Although, conclusive evidence regarding the benefit of incisional NPWT is lacking, it is believed that they may be beneficial for surgeries in high-risk patients such as those with medical histories characterized by diabetes, obesity, active smoking status, an immunocompromised state, active dialysis, or previously irradiated wounds.

Maintaining a moist wound environment facilitates the wound healing process by prevention of tissue dehydration and cell death, accelerated angiogenesis, and increased breakdown of dead tissue and fibrin. Negative-pressure wound therapy with instillation has recently been introduced in various settings. This technology combines the traditional negative-pressure system with a method to intermittently instill a solution into the wound [30]. In addition to keeping the wound bed moist, it also enables the controlled delivery of topical anesthetic and antiseptic solutions over the wound bed. First, the instillation fluid drips by gravity through a tube to saturate the foam and then the fluid is allowed to bathe the wound for a predetermined period of time (from 1 s to 1 h). Then, the vacuum is applied through a separate (suction) tubing (5 min to 12 h), thereby removing the irrigation fluid and wound exudate and collapsing the sponge. Suction is continuously maintained until the entire cycle is repeated according to the amount of time programmed into the unit. The instillation solutions include normal saline, bacitracin, povidone-iodine, polyhexanide, acetic acid, antifungals, antiseptics, silver nitrate, local anesthetics, and insulin, depending on the type of wound and desired effects [30, 31]. Alcohol-based solutions and solutions that contain alcohol are contraindicated for use with NPWT with instillation as alcohol is not compatible with wound tissue [32, 33]. Hydrogen peroxide solutions are also contraindicated with this system due to the effervescent nature of this solution [30, 32]. The NPWT dressing is a closed system and any effervescence produced by the hydrogen peroxide may lead to air emboli. In addition, hydrogen peroxide is considered highly cytotoxic and deleterious to wound healing [34]. In a study by Gabriel et al. [35], patients with complex infected wounds treated with instillation of silver nitrate and negative pressure had significantly fewer days of treatment and experienced earlier wound healing compared with the control group. In a retrospective study by Timmers et al. [36], patients with osteomyelitis of the pelvis or lower extremities who received instillation NPWT using polyhexanide had a significantly lower rate of infections compared to patients who were treated with gentamicin-impregnated beads only. As contaminated traumatic wounds are at a high risk for infection, NPWT with antimicrobial instillation may potentially be useful in those cases. Strong evidence supporting the prophylactic use of antimicrobial solutions in contaminated wounds, however, is lacking. In a large multicenter randomized clinical trial (RCT) comparing irrigation protocols of open fractures, irrigation with normal saline resulted in lower rates of infection than castile soap solution [37]. In another RCT by Anglen et al. [38], bacitracin solutions did not decrease wound infection rates compared with normal saline irrigation in decreasing wound infection after open fractures, though wound healing problems were higher in bacitracin-treated patients. Most of the scientific evidences supporting antimicrobial use with or without NPWT have been based on observational cohorts without a control group or based on poorly designed trials. However, in view of the >40% infection rate of contaminated traumatic wounds, NPWT with instillation is expected to be beneficial without any clinically relevant adverse effects [31]. Further prospective randomized studies are needed to clarify this issue.

Table 1 Major uses of NPWT in orthopedic surgery

Field	Usage
Trauma	• To assist wound closure when there is soft-tissue loss • To assist wound closure in open fracture • Closure of fasciotomy wounds • As incisional dressing over contaminated surgical wounds
Total joint arthroplasty	• To treat dehisced wounds • To treat ongoing drainage • As temporary coverage, till definitive closure can be performed • As prophylactic dressing over high-risk surgical wounds
Orthopedic oncology	• To treat large soft-tissue defects after tumor resection • Contraindicated if wound has known unresected neoplasm • As prophylactic dressing over high-risk surgical wounds (i.e., preoperative radiation)

6 Current Evidence

Although the indications for NPWT have rapidly expanded, there is a paucity of high-level evidence supporting the use of NPWT [39]. While NPWT has proven to be beneficial for certain types of wounds like diabetic wounds, sternal, and abdominal wounds, the benefits are unclear for vascular wounds and surgical wounds [4]. A large number of studies including RCTs and meta-analyses of RCTs have been published in this field and have provided mixed results partly owing to the heterogeneity in terms of wound types, outcome variables, and outcome assessments [40]. Conflict of interest in NPWT-related research is also a matter of concern as most studies were sponsored by the two main device manufacturers [15, 29]. Additionally, a number of RCTs studying the effects of NPWT were not published and the lack of access to unpublished study result data raises doubts about the accuracy of the available evidence [41]. Further, we focus on the current evidence in support of the use of NPWT in orthopedic trauma, total joint arthroplasty (TJA), and orthopedic oncology (Table 1). Additionally, the use of NPWT in other fields is also briefly reviewed.

6.1 Orthopedic Trauma

Since its introduction more than two decades ago, NPWT has had an important impact in orthopedic trauma. The use of NPWT has been adopted in a variety of clinical scenarios in orthopedic trauma, which includes extensive soft-tissue injuries, penetrating trauma, open fractures resulting from high-energy trauma, and fasciotomy incisions. Treatment of traumatic wounds is challenging due to significant wound contamination, need for subsequent debridement, significant edema, or systemic compromising factors from multiple injuries. Negative-pressure wound therapy can be quickly applied and may potentially prevent wound desiccation, minimize microbial contamination, reduce edema, and facilitate wound drainage.

6.1.1 Soft-Tissue Trauma

War wounds pose a challenge to trauma surgeons. These wounds are usually sustained due to energy transfer (gunshots, blasts, and explosives) across multiple tissue planes. These high-energy wounds are heavily contaminated and characterized by extensive loss of soft and/or osseous tissues. Traditionally, these wounds are managed in field hospitals with adequate irrigation and debridement, application of wet-to-dry dressings, and bedside dressing changes. Despite repeated irrigation and debridement of war wounds, wound healing is particularly challenging due to extensive tissue loss, breakdown of traumatized soft tissue, wound necrosis, and infection that requires additional surgical interventions [42]. A systematic approach to war wounds was thus implemented to include eliminating bedside dressing changes and instituting mandatory interval wound examination, re-debridement, and dressing changes in the cleaner environment of an operating room [42]. Negative-pressure wound therapy is advantageous in such settings by keeping the wound covered while simultaneously promoting wound contraction, controlling wound drainage, decreasing wound edema, and augmenting wound granulation and healing [43, 44]. The ease of the application of NPWT is helpful in war injuries as it allows for the temporary coverage of large soft-tissue defects in hospitals located in or near areas of conflict before the patient can be transported to better facilities.

DeFranzo et al. [45] evaluated 75 patients who had open wounds and extensive soft-tissue damage or breakdown, concluding that NPWT decreased tissue edema by diminishing the circumference of the extremity and, thus, decreased the wound surface area allowing for successful wound closure in 71 out of 75 patients. Leininger et al. [46], based in a field hospital, treated 77 patients who sustained a total of 88 high-energy wounds. All wounds were operated on within 24 h of injury, and were covered with NPWT dressings and set to −125 mm Hg continuous pressure for 2–4 days. They reported no acute wound complications, and no reoperations on those who required skin grafts, and all of the patients had clean and closed wounds. In another study by Helgeson et al. [47], 16 patients who had high-energy complex soft tissue with exposed tendon and/or bone that were not amenable to skin graft were initially treated with a bioartificial dermal substitute regeneration template and NPWT. The authors concluded that NPWT had a beneficial effect on the formation of granulation tissue and as a barrier to reduce potential infection.

Stannard et al. [48] randomized 44 patients who suffered injuries from high-energy trauma and developed wound hematomas into two management groups, pressure dressing or NPWT. Dressings were changed daily in the pressure dressing group and every other day in the NPWT group. They found that NPWT was associated with a shorter duration of wound drainage (1.6 vs. 3.1 days, p=0.03) and lower, but not statistically significant, infection rate (8% vs. 16%, p >0.05). Therefore, application of NPWT may offer some advantage in the management of highly complex soft-tissue injuries by promoting wound healing and potentially decreasing incidence of infection.

6.1.2 Open Fracture-Related Wounds

Open fractures are challenging for orthopedic surgeons. High-energy trauma results in not only bone fractures, but also large soft-tissue loss or breakdown. These injuries are at a high risk for infection and osteomyelitis. Open fracture infection rates are reported to range from 16 to 66% depending on the type of fracture, severity of the soft-tissue injury, and patient-related comorbidities [49, 50]. The primary goal of surgical treatment for open fractures is stabilization of the fracture, followed by soft-tissue repair. Careful homeostasis and wound coverage are important for reducing the risk of infection. Traditionally, these wounds undergo a series of irrigations and debridement to ensure that all nonviable tissues are removed to allow for subsequent healing by secondary intention with granulation tissue. Theoretically, NPWT may play an important role in the periods between surgical interventions, where it may be more advantageous than the standard wet-to-dry dressings [51].

In an RCT by Stannard et al. [52], 59 patients who had 63 severe high-energy open fractures were randomized to receive either a standard fine-mesh gauze dressing or a NPWT between irrigation and debridement procedures until definite closure was performed. They found that patients treated with NPWT were less likely to develop an infection compared to the control group (relative risk for infection [RR] = 0.199, 95% confidence interval [CI] 0.05–0.87). Blum et al. [53] retrospectively reviewed 229 open tibia fractures where 72% of patients received NPWT and 28% received a conventional dressing, and found a significantly lower deep infection rate in the NPWT group (8.4% vs. 20.6%, $p = 0.01$). After adjusting for injury severity, NPWT was found to reduce the risk of deep infection by almost 80% (odds ratio [OR] = 0.22; 95% CI, 0.09–0.55; $p = 0.001$).

Virani et al. [54]conducted a RCT to study the effect of NPWT on deep infection and osteomyelitis after open tibia fractures, and they reported a significant reduction in the incidence of infection with use of NPWT compared to controls (4.6% vs. 22%; $p < 0.05$). Wound cultures showed positive growth in 3 patients who received NPWT and 17 in the control group (6.9% vs. 34%; $p < 0.05$), and the probability for infection in the NPWT group for a wound with an open fracture was 5.5 times less compared to controls. However, there was no significant difference in the time required for the wound to be ready for delayed primary closure or coverage. In another RCT by Arti et al. [55], treatment of open fractures with NPWT resulted in a reduction of wound surface volume and lower hospital length of stay. However, the authors did not find a difference in the infection rates. While there are discrepancies in the results of various RCTs evaluating the efficacy of NPWT, overall NPWT appears to have several benefits in the management of open fractures including lowering infection rate, accelerating closure of open wounds, and shortening the hospital length of stay.

6.1.3 Fasciotomy Wounds

Compartment syndrome is considered a surgical emergency, with the treatment goal being to decrease the muscle compartments pressure while maintaining tissue perfusion, which is achieved by open fasciotomy. Primary closure of these wounds would theoretically result in more functional and aesthetic outcomes with decreased morbidity. However, due to muscular edema, protrusion of muscles through the fascia, and significant skin retraction, premature primary closure may increase the compartmental pressure and the forced re-approximation under tension may cause necrosis at the wound edges. Healing by secondary intention had been a commonly used technique, but due to the increased risk of infection, longer hospitalization, increased requirements of frequent dressing changes, delay in rehabilitation, significant scarring, and poor aesthetic outcome, it is no longer considered an appropriate intervention. Serial dressing changes are often needed until definitive primary closure is possible. Primary coverage with NPWT creates a closed environment, which in theory protects the wound from outside infection, reduces local edema, and reduces the need for frequent dressing changes until final closure is achieved.

A large retrospective study by Zannis et al. [56] evaluated 458 patients who had 804 wounds, and demonstrated a significantly earlier time to primary closure (NPWT vs. standard = 5.2 vs. 6.5 days, $p < 0.01$) as well as higher rate of primary closure in fasciotomy wounds treated with NPWT compared to standard wet-to-dry dressings. On the other hand, Kakagia et al. [57] in an RCT comparing NPWT with the shoelace technique (gradual suture approximation technique to facilitate wound closure) found no difference in wound infection rates between the groups. They found that the wound closure time was significantly prolonged in the NPWT group compared to the shoelace method group, and the cost of treatment was also increased in the NPWT group. Although NPWT has become increasingly popular for the closure of fasciotomy wounds, the efficacy of these dressings to decrease infection and shorten time to closure remains uncertain.

6.1.4 Incisional Wounds

The outcomes of NPWT are promising in the management of surgical incisions and prevention of the development of hematomas in closed wounds.

Stannard et al. [48] evaluated NPWT as an adjunct to healing of surgical incisions after fractures that were at high risk for wound complications in terms of wound drainage. They showed that NPWT was associated with a significant reduction in the duration of wound drainage (1.8 vs. 4.8 days; $p = 0.02$). They also showed similar results in a larger randomized controlled trial where they prospectively evaluated the role of NPWT for the prevention of wound dehiscence and infection after high-risk lower extremity trauma in 249 patients who had 263 fractures [58]. In this study, incisional NPWT was applied to the closed surgical incisions in 141 patients, whereas standard postoperative dressings were applied to 122 control patients. The infection rate was significantly lower in the NPWT group compared to the control group (9.7% vs. 18.9%; $p = 0.049$). Similar results were also reported in an RCT by Nordmeyer et al. [59] who compared NPWT to standard dressing after dorsal stabilization of spinal fractures in 20 patients (10 in each group). The NPWT reduced the development of postoperative seromas, nursing time, and material required for wound care. Overall, the use of NPWT appears to be beneficial in the management of surgical incisions in the trauma setting following fixation of high-risk fractures. Negative-pressure wound therapy has been reported to reduce wound drainage, postoperative infection, development of seromas/hematomas, and time and costs related to wound care [60].

6.2 Total Joint Arthroplasty

Total joint arthroplasty (TJA) is a common procedure with approximately one million total knee arthroplasties (TKA) or total hip arthroplasties (THA) being performed annually in the United States [61]. Periprosthetic joint infection (PJI) is a serious complication of TJA with the incidence reported to be from 1 to 2% [62]. The incidence of PJI is even higher after revision surgeries, and can be up to 20% [63]. Approximately 25% of PJIs occur within the first month following the surgery and these early infections are usually associated with wound complications like drainage and wound dehiscence [64]. It has been reported that each day of prolonged wound drainage can increase the risk of wound infection by 42% following THA and by 29% following TKA [65]. Therefore, over the past decade, there has been increased attention placed on NPWT as an effective technique to help prevent wound complications following TJA.

The predominant use of NPWT in arthroplasty is in the form of incisional NPWT dressings. Although a number of observational studies have described the utility of negative-pressure dressings on surgical incisions following TJA, the results of different studies on this topic are inconclusive. In an RCT by Howell et al. [66], no benefits were observed with the use of incisional NPWT in TKA patients at high risk for prolonged wound drainage. However, a higher incidence of blister formation was observed in the NPWT group leading to premature cessation of the trial. But, later RCTs have shown some beneficial effects with the use of incisional NPWTs. In a study by Pachowsy et al. [67], the authors randomized 19 patients undergoing primary THA for osteoarthritis into either a group receiving standard wound dressing or a group receiving NPWT, and showed decreased volume of postoperative seromas on day 10 in the NPWT group (NPWT vs. standard: 1.97 mL vs. 5.08 mL, $p = 0.021$). Although reduction of postoperative seromas can theoretically lead to increased blood flow, better apposition of the wound edges, and decreased risk of drainage, there is currently no evidence to suggest that reduced seroma can decrease rates of clinically relevant complications such as PJI [60, 67]. The use of incisional NPWT has also been reported to decrease wound dressing changes and to eliminate excessive hospital stay following primary TJA [28, 60]. In an RCT of 220 patients undergoing primary TKA/THA, Karlakki et al. [28] found that the use of incisional NPWT decreased the amount of wound drainage and eliminated prolonged length of stay. In another RCT by Manoharan et al. [68] the use of incisional NPWT following primary TKA was associated with improvement in wound leakage and better wound protection, although no benefit was found with respect to hospital cost and wound healing.

Although studies have shown that the use of incisional NPWT can decrease wound exudates, decrease in wound infection after primary TJA has not been reported with the use of NPWT. This might be due to the fact that the incidence of PJI is very low compared to the incidence of other wound complications like wound drainage. In an RCT by Gillespie et al. [69], the authors did not find a decrease in surgical site infections with the use of NPWT in patients undergoing primary THA. Furthermore, they suggested that a definitive trial would require approximately 900 patients per group to demonstrate a decrease in SSI after primary arthroplasty. Even though current evidence suggests that wound complications place patients at a higher risk for the development of PJI, there is uncertainty around the benefits of NPWT following elective arthroplasty for decreasing the infection rate [69]. The reasons for the differences in the results of various RCTs are probably related to the heterogeneity of the patient population in terms of the type of arthroplasty (primary or revision) and the indication for arthroplasty (fracture or osteoarthritis) [60, 70]. Although NPWT may not have an added clinical advantage over the standard occlusive dressing in primary elective arthroplasty, it might be helpful in certain high-risk populations like patients who undergo revision arthroplasty. For example, the findings of a comparative study by Cooper et al. [70] suggest that incisional NPWT may decrease wound complications and SSIs in patients who undergo revision hip and knee surgery. The benefits of NPWT may be even more apparent after revision surgery for PJI or in patients with preexisting wound issues. While strong evidence to support the prophylactic use of NPWT in primary or revision arthroplasty is lacking, there are a number of ongoing clinical trials, which might help to better understand the indications for incisional NPWT in TJA.

In addition to the use of incisional NPWT as a prophylactic measure, NPWT can also be used to treat chronically infected, dehisced, or draining wounds in the setting of knee or hip arthroplasty (Fig. 2). In a retrospective study of 109 patients who had persistent drainage after primary THA, Hansen et al. [71] showed that majority of the patients (76%) had cessation of the drainage after being treated with NPWT. Therefore, NPWT can potentially avert morbid surgical procedures which are traditionally performed for persistent drainage. Hansen et al. [71] also demonstrated that patients who failed NPWT therapy and required a subsequent surgical procedure had success rates similar to the published literature, indicating that NPWT might be safely considered as a first-line treatment modality for persistent drainage [72]. Treatment of PJI involves extensive debridement of soft tissues, which can often compromise the soft-tissue coverage required for primary closure, especially for the knee. Therefore, NPWT can be used in such instances to promote granulation tissue formation and to act as a bridge until definite closure can be performed. The benefits and mechanism of action of NPWT dressing in such settings are similar to other open wounds. The availability of instillation therapy offers the additional advantage of providing topical antimicrobial solutions, which may help in the clearance of infections, although the benefits of this remain unclear [73]. Even though NPWT dressing is widely used to treat wound drainage and other wound-related complications after arthroplasty, the majority of studies describing the use of NPWT to treat wound-related complications were performed without a control group. Therefore, the clinical superiority of NPWT over the traditional dressings in terms of faster wound healing and improved infection clearance has not been established. It is reasonable, however, to assume that NPWT can at least decrease the number of wound dressing changes in actively draining wounds, and can remove some tension on the wound edges, and keep them better approximated under lower stress.

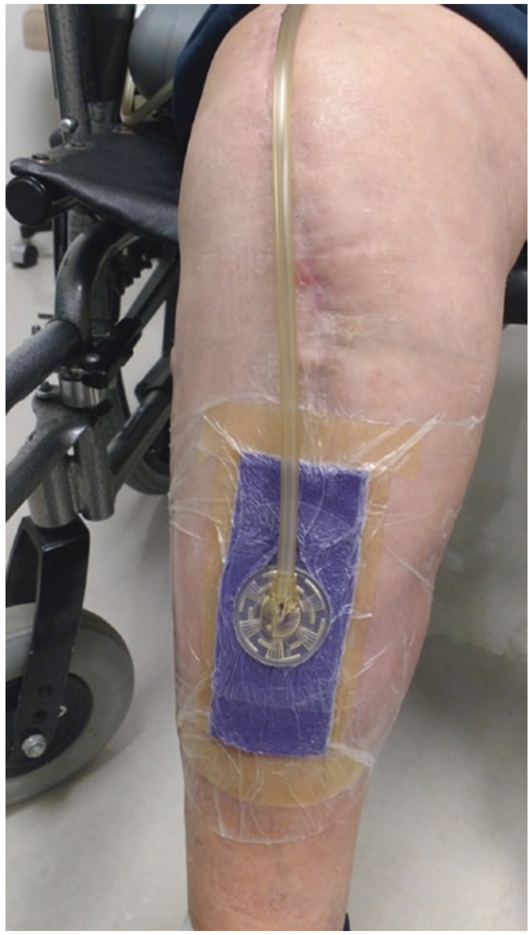

Fig. 2 Negative-pressure dressing applied over a patient who developed postoperative drainage from the distal portion of wound after a complex revision knee arthroplasty. The tubing is connected to a portable suction device allowing the patient to be ambulatory with the dressing

6.3 Orthopedic Oncology

Bone and soft-tissue sarcomas are relatively uncommon cancers, but over the past decade, the estimated incidence increased from 12,000 to 15,000 new cases per year [74, 75], with the most common soft-tissue sarcomas occurring on the extremities [76]. Historically, the treatment for sarcomas of the extremities was limb amputation; however, there was a shift towards limb salvage procedures with adjuvant chemotherapy and/or radiotherapy [77–79], which has been associated with more patient satisfaction [80], improved physical function [81], and less disability [82]. Limb salvage procedures involve wide surgical margin resection, sometimes necessitating soft-tissue defect, bone defect, or vascular reconstruction in order to minimize recurrence risk and maximize long-term limb function [83–86]. Particularly with soft-tissue sarcoma, wide excision, in combination with neoadjuvant or adjuvant radiotherapy, has been shown to have positive effect in time to local recurrence and overall survival [87]. Despite the benefits of limb salvage procedures, tumor resection and radiotherapy can lead to significant wound complications, which can be a cause of significant morbidity [88]. Surgical resection of bone and soft-tissue sarcomas is often difficult due to involvement of the adjacent fascia and neurovascular structures [77], and depending on the location of the tumor and the surrounding tissues involved, patients may have large open wounds with soft-tissue defects [89]. Despite the benefits conveyed regarding local recurrence, radiotherapy also is strongly associated with various wound-related complications, with a higher rate of wound complications (~30–40%) with neoadjuvant radiation as compared to adjuvant therapy (~20–25%). One study reported on 202 patients who had preoperative radiotherapy and then had surgery for soft-tissue sarcoma of the lower extremity (n = 119), upper extremity (n = 32), trunk (n = 36), and head and neck (n = 15) [90]. The overall wound complication rate was 37%, and a second surgery for the wound complications was required in 16.5%. Similarly, Kunisada et al. [91] evaluated 43 patients who underwent preoperative radiotherapy followed by surgery for soft-tissue sarcomas of the lower leg (n = 28), upper arm (n = 8), and trunk (n = 7). They reported a high complication rate, with preoperative radiotherapy-associated acute skin toxicity that occurred in 84% of cases, and a postoperative wound complication rate of 44%, of which 23% required an additional surgery.

Resection of large bone or soft-tissue tumors can lead to massive soft-tissue defects that cannot be closed at the time of surgery. Bickels et al. [92] reported on 62 patients who underwent resections of either bone or soft-tissue tumors and were left with a large soft-tissue wound defect after surgery, debridement from wound complications, or radiation-associated skin necrosis. Twenty-three of these patients had a NPWT device placed for a mean of 14 days (range 7–19 days), and were followed for a median of 19 months (range 12–27 months). Their outcomes were compared to a similar cohort of 39 patients who were treated prior to the surgeon's use of NPWT. Compared to historical controls, the patients who were treated with the NPWT had a decreased rate of additional surgical wound procedures and a higher rate of primary wound closure, and had shorter hospital length of stay. The soft-tissue defect area decreased by a mean of 25% in those who received NPWT.

In those patients with large soft-tissue defects from resection of bone and soft-tissue tumors, incisional NPWT allows for improved healing and primary wound closure [89]. In addition to the use of negative-pressure dressings, silver has been added to the dressings in order to prevent surgical site infections [93]. Siegel et al. [93] reported on 42 patients who suffered from massive soft-tissue loss resulting in large extremity and/or pelvic wounds and compared a plain NPWT dressing to a NPWT with silver dressing. Tumors were the etiology in 14 of the patients; 11 patients underwent local radiation and 12 patients had immunosuppression either from chemotherapy or from a transplant. The etiology in the remaining patients was infections in 22 and trauma in 6 patients. The patients who had the NPWT with silver dressing had a decreased length of stay compared to the patients with the NPWT alone (7 vs. 19 days, $p < 0.033$). Compared to the patients who only had the NPWT, the NPWT plus silver dressing patients had to undergo fewer surgeries prior to flap coverage (62% vs. 19%, $p = 0.024$) and had required fewer surgical debridements (7.9 vs. 4.1, $p < 0.001$). It seems that the addition of silver to NPWT dressings may have a positive effect for wound healing in such patients. Additional studies are needed to have definitive conclusions.

6.4 Other Major Indications

Perhaps, one of the first indications of NPWT was the treatment of chronic wounds. Chronic wounds pose a great challenge to the medical community, and with the increasing prevalence of bed-ridden patients and those with chronic conditions such as diabetes mellitus and peripheral vascular disease, more patients are being diagnosed with chronic wounds. These wounds are difficult to heal, and may be due to the continuous exposure to the external environment, which can result in colonization with bacteria and fungus. Negative-pressure wound therapy, though, has revolutionized the management of chronic wounds. The primary goals of NPWT in chronic wounds are to achieve wound closure (by surgical or secondary intention), reduce the wound size, improve patient quality of life, manage wound fluid and edema, and prevent wound deterioration. However, the effectiveness of NPWT in achieving these goals depends on the type of wound. Currently there is strong evidence to support the use of NPWT in diabetic foot ulcers. In a multicenter RCT, Armstrong et al. [94] reported that treatment of diabetic foot wounds with NPWT led to a higher proportion of healed wounds, faster healing rates, and potentially fewer re-amputations than standard care. In another multicenter RCT, a greater proportion of foot ulcers achieved complete ulcer closure with NPWT, suggesting that NPWT is more effective than the standard dressings [95]. There is a moderate amount of evidence supporting the use of NPWT in pressure sores and venous stasis ulcers. In an RCT by Vuerstaek et al. [96], the use of NPWT was associated with faster wound healing of venous ulcers and resulted in lower costs. Although a few RCTs have suggested some benefits with the use of NPWT in pressure ulcers, the overall quality of evidence is low and the clinical effectiveness of NPWT is inconclusive [97]. There appears to be no benefit with NPWT in the setting of chronic ischemia ulcers [4]. The benefits of NPWT are usually seen in large edematous wounds, while the wounds arising in the setting of arterial insufficiency are usually in the toes, without much swelling unless there is an associated infection [98]. Additionally, as most of the wounds related to arterial insufficiency are small and surrounded by nonviable tissue, surgical debridement might be preferred over NPWT, which may explain why the literature on the treatment of vascular ulcers is limited [99]. The use of NPWT in an acutely ischemic leg may even have detrimental effects as excessive negative pressure may further compromise blood flow [4].

In addition to major orthopedic indications for NPWT, other areas of application that have been studied include open abdominal wounds, sternal wounds, and skin graft host environments [4, 100–102]. While not the scope of this book chapter, these large defects and scenarios can mimic many of the situations in orthopedic surgery and add important insight into the applications for NPWT in the treatment of major appendicular and axial wound concerns.

7 Adverse Events

There have been few complications associated with NPWT, and they can often be avoided or minimized with proper application. The most common complications of NPWT are skin related, which can range from a simple rash to a large blister. Blister formation is an important adverse effect with the use of incisional NPWT due to the direct application of negative pressure over the normal skin. In an RCT by Howell et al. [66] the study was prematurely interrupted when a total of 60 patients were enrolled and a significant difference in blister formation about the knee was detected between the NPWT group and the control group. In order to address the issue of blistering, a non-adherent dressing has been recommended for use over unprotected skin to avoid direct contact with the foam [15, 66]. The study by Howell et al. [66] was one of the initial studies that used an incisional NPWT dressing and blistering was not found to be an issue in the subsequent studies, where the normal skin was protected [103]. Allergy to the components of the NPWT dressing (e.g., adhesive or silver) can also cause skin rashes. The skin of patients who have been treated with immunosuppressive drugs may be fragile and more prone to desiccation from the use of negative pressure [104, 105].

If the sponge is left deep in a wound for prolonged periods (more than 48 h), it can be difficult to extract because of the overgrowth of exuberant granulations. Extraction of the sponge may be associated with minor bleeding due to the highly vascular granulation tissue. To prevent the ingrowth of granulation tissue, dressings are recommended to be changed every 48–72 h. Since this is not an issue with incisional dressings, NPWT can be kept over wounds for longer periods (7 days or longer). Although NPWT is used in tumor surgeries to help with wound closure and prevent wound complications, the effects of negative pressure on neoplasms are unknown. As NPWT is known to stimulate the cytoskeleton and promote granulation tissue, it is thought to maybe have stimulatory effects on the neoplasm as well. Therefore, NPWT is contraindicated for use over neoplastic wounds. However, NPWT may be used for wound closure after resection of deep or superficial tumors. Patients on anticoagulants and those with a history of a bleeding disorder may develop hematomas from the application of negative pressure, especially when wounds are large, and these patients need to be monitored. Lower levels of negative pressure can be used in such cases. When NPWT is used in deep and tunneling wounds, care should be taken to remove the entire piece of foam from the wounds when dressing changes are performed.

8 Cost-Effectiveness

Although the vast majority of the literature supports the efficacy and safety of NPWT, it is important to know whether NPWT is cost effective compared to conventional dressings. A number of studies have suggested NPWT to be a cost-effective method and most insurance companies cover the commercially available NPWT devices. In a study of more than 1000 patients with advanced-stage pressure ulcers, Philbeck et al. [106] demonstrated that wounds treated with NPWT healed faster (97 vs. 247 days) and at a lower cost ($14,546 vs. $23,465) compared to the traditional dressings, suggesting that NPWT is cost effective. However, the cost-effectiveness of NPWT is not fully established for all of the current uses of NPWT. When NPWT is used as a prophylactic agent on surgical incisions, the cost of NPWT ranges from $15/day to $495/week depending on whether the device is a self-made or a commercially tailored for incisions [107]. Since one of the major reasons for the use of incisional NPWT is to prevent surgical site infections, use of prophylactic NPWT might be cost effective due to high costs associated with infections such as PJI [108]. Since NPWT is changed less frequently than wet-to-dry dressings, NPWT can be less labor intensive for hospital staff and may result in overall reduction of cost [109]. The quality of the current evidence supporting the use of NPWT to prevent infection is low and cost-effective analyses are limited [107]. Nevertheless, NPWT is expected to be cost effective at least in patients with well-established risk factors for infections.

The majority of the negative-pressure dressings applied in North America are commercially available preparations [110]. However, these devices can be expensive and may not be readily available throughout the world. Nguyen et al. [110] demonstrated that standard gauze sealed with an occlusive dressing and connected to wall suction was able to achieve similar outcomes to the commercially available devices, but at a lower cost. Further studies are needed to establish such cost-effectiveness.

Conclusions

Negative-pressure wound therapy continues to gain popularity in various specialties including orthopedic surgery, since the indications for its use have grown dramatically since it was first introduced. While efforts have been made to provide an evidence-based guide for its use, this has been limited by a lack of good-quality evidence. The majority of support for the use of NPWT comes from retrospective studies that either fail to compare it to other wound management techniques or are underpowered with both heterogeneous and small patient populations. The majority of the published literature concludes that NPWT is an effective technique but requires more prospective research to support its use. Currently, NWPT is considered superior to traditional dressings for the management of chronic wounds and pressure ulcers. Additionally, in orthopedic surgery, trauma patients experience the most benefit with the use of NPWT especially when there are large soft-tissue defects precluding primary closure. The NPWT is also used as prophylactic dressing after hip and knee arthroplasty in high-risk patients although this is based on observational data. One of the key problems with research in the field of wound healing is founded in the fact that wounds are very difficult to standardize—varying in size, shape, position, and chronicity. Objective assessments of wound healing are not easy to define and labeling wounds based on arbitrary scales is not evidence based. Furthermore, adequate wound healing relies on multiple local and systemic factors and consequently wounds vary from one another. Although the efficacy of NPWT in wound healing is well established, well-designed randomized controlled trials tailored to a specific patient population characterized by a specific wound environment dilemma are needed to give definitive answers regarding the clinical superiority of NPWT over the conventional less expensive dressings.

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