Zentralblatt für
Chirurgie

2018
Volume 143
Pages 609–616

Reprint

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Translation
Publisher and Copyright:

Georg Thieme Verlag KG
Postbox 30 11 20
70451 Stuttgart
ISSN 0044-409X

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Use of Negative Pressure Wound Therapy with Instillation and Dwell Time for Wound Treatment – Results of an Expert Consensus Conference

Einsatz der Vakuuminstillationstherapie für die Wundbehandlung – Ergebnis einer Expertenkonsensuskonferenz

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Key words

wound infection, wound healing, wound debridement, vacuum-associated closure (for) wound dressing, vacuum instillation

Schlüsselwörter

Wundinfektion, Wundheilung, Wunddébridement, V.A.C.®-Therapie, Vakuuminstillation

Bibliography

DOI https://doi.org/10.1055/a-0713-0517
Zentralbl Chir 2018; 143: 609–616 © Georg Thieme Verlag KG Stuttgart · New York | ISSN 0044-409X

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ABSTRACT

Rinsing wounds with wound cleansing solutions has long been a recognised cornerstone in wound management as a means of removing cell debris and surface pathogens in wound exudates. In combination with surgical debridement and topical negative pressure wound therapy (NPWT), this can facilitate the intended progression from the inflammatory to the proliferative phase of wound healing. Procedures of topical negative pressure wound therapy with instillation and a defined exposure/dwell-time of topical solutions under cyclic compression and decompression with foam dressings (NPWTi-d) can remove cellular remnants and debris that may inhibit the healing process. At the same time, it can aid in reducing the bacterial load in contaminated or infected wounds. Since this newer technique is now commercially available and increasingly widespread, recommendations for the proper use and clinical indications were developed by a panel of interdisciplinary experts in the course of a consensus meeting. Although the level of evidence from expert opinions is low, general guidelines for a safe and effective use of NPWTi-d can be worked out that can be of assistance to the clinician. The consensus recommendations derived from this meeting include the objectives of the treatment, the administration modalities of NPWTi-d, the indications for various wounds, including their contraindications, therapy settings, as well as the use of topical instillation solutions, volume and duration (dwell time) based on current scientific data, optimal treatment duration and future developments of the NPWTi-d.

ZUSAMMENFASSUNG

Das Spülen von Wunden mit einer Lösung zur Wundreinigung ist seit Langem ein anerkannter Eckpfeiler in der Wundbehandlung als Mittel zur Entfernung von Zelltrümmern und Oberflächenpathogenen in Wundexsudaten. In Kombination mit dem chirurgischen Débridement und einer lokalen Vakuumtherapie kann sie das Fortschreiten von der entzündlichen zur proliferativen Phase der Wundheilung erleichtern. Verfahren der topischen Vakuumtherapie mit Instillation und einer definierten Einwirk- bzw. Verweilzeit von topischen Lösungen unter zyklischer Kompression und Dekompression mit Schaumverbänden (Negative Pressure Wound Therapy with instillation and dwell time = NPWTi-d) können Rückstände entfernen, die ansonsten hemmend auf den Heilungsprozess wirken. Gleichzeitig helfen sie, die bakterielle Keimbelastung in kontaminierten oder infizierten Wunden zu verringern. Nachdem diese Technik nun kommerziell verfügbar und zunehmend verbreitet ist, wurden im Rahmen eines Konsensusmeetings durch eine interdisziplinäre Expertenkommission Empfehlungen zur Anwendung und zu den klinischen Indikationen erarbeitet. Auch wenn die Evidenzstufe von Expertenmeinungen einen geringeren Level besitzt, können allgemein gültige Richtlinien für einen sicheren und effizienten Einsatz von NPWTi-d ausgesprochen werden, die dem klinisch tätigen Arzt als Handlungsempfehlung dienen können. Die daraus abgeleiteten Konsensusempfehlungen umfassen basierend auf dem Stand der aktuellen wissenschaftlichen Datenlage die Ziele der Behandlung, die Anwendungsmodalitäten die Indikationsstellung bei verschiedenen Wunden einschließlich eventueller Kontraindikationen, Therapieeinstellungen sowie die Verwendung topischer Instillationslösungen, deren Volumen und Verweildauer (dwell time), die optimale Behandlungsdauer und zukünftige Weiterentwicklungen der NPWTi-d.

Introduction

Effective wound treatment should consider both the patient in his entirety, with his specific problems, cofactors and comorbidities, and also the special features of the wounds. Wounds that are associated with a risk of delayed healing include, for example, those with extensive tissue loss, critical colonisation and/or infection, high volumes of exudate or exposed critical and/or vital structures. Factors such as how long the wound has been present, how often it was reopened and what attempts have already been made to close the wound play a part in the likelihood of effective and final healing [1–3]. The repertoire of treatments of infected wounds includes, for instance, debridement, antibiotic treatment, local use of antiseptics and the use of drains [4]. In combination with surgical debridement, wound irrigation is an additional wound cleansing method as it removes cell debris, wound exudate and metabolic products [5–9]. Removal of factors that inhibit wound healing is optimal when they do not over-wet the wound and destroy factors that promote healing.

Rising numbers of multimorbid patients and complex medical procedures with the simultaneous spread of multi-resistant bacteria (MRB) increase the number of complicated wounds and wound colonisations and thus the challenge for clinicians and health systems [10–12]. The prevention of such wound infections is becoming ever more important worldwide with the increasing number of surgical procedures in the risk group of multimorbid patients [13, 14]. It is estimated for the US that roughly half of all wound infections would be fundamentally avoidable [15], which has concrete economic as well as medical implications. Because of this increasing number of patients with “problem wounds” with the concomitant increase in microbial resistance and additional poor penetration of systemically administered antibiotics into the wounds, the feasibility of repeated conventional classic wound irrigation and a permanent operative procedure is limited in routine clinical practice, if only because of limited resources. With the introduction of standardised computer-aided cyclic wound irrigation with topical negative pressure (negative pressure therapy with instillation and dwell time [NPWTi-d]), there has been for some time a very efficient new tool that combines continuous and repetitive wound irrigation with the known positive effects of negative pressure wound therapy (NPWT) with surgical debridement. Experience and clinical evidence of efficacy have already been gained with intermittent fluid instillation in combination with NPWT for wound cleansing and treatment of infection. In the German-speaking countries, no clear recommendations on its use have been available to date. As with other newer procedures, however, there are still uncertainties for users as regards suitable indications, possible contraindications, the type of irrigation solutions, treatment duration and future developments of the method. Because of the increasing acceptance and importance of the therapy, however, such a recommendation is regarded as useful and necessary. Based on the available literature and, in addition, on clinical expertise, an expert consensus meeting has formulated recommendations on the indications, contraindications and possible developments of instillation therapy in combination with NPWT.

Negative Pressure Therapy

The modality of additional instillation therapy with a controlled dwell time was developed based on the long-established NPWT [16–24], which is used mainly as a method of temporary soft tissue cover for wound bed preparation to bridge the interval until final wound closure.

The basic principle still consists of the use of electronically controlled systems with a wound filler material (variously configured polyurethane or polyvinyl alcohol foams, foams with antimicrobial silver coating, gauze), a semipermeable, airtight, water vapour-permeable wound dressing with integral drainage tube and an electrically powered suction source designated as therapy unit [25]. Even very large wounds involving the trunk and thorax or an entire extremity can be treated this way [26]. The therapy unit can be set in steps over a pressure range up to 200 mmHg and an exudate volume up to 500 ml can be removed before the collecting

container has to be changed. The electronic control comprises a sensor that detects a drop in pressure or fluctuation in suction by measuring the suction power close to the wound and automatically corrects small losses of suction. This ensures permanent drainage.

Negative Pressure Instillation Therapy

Negative pressure wound therapy with instillation and dwell time (NPWTi-d) is a clinically significant development of NPWT. The first instillation treatments in combination with NPWT were published in the 1990 s [27]. The first specially designed devices have been available commercially since 2003. Since then, they have been further developed and simplified technically to make them more user-friendly.

NPWTi-d (V. A. C. VERAFLO™, KCI Inc., Texas, USA) is characterised by an integral conduit, which makes it possible to deliver fluid into the wound, combined with a multilumen drain, which aspirates the wound fluid and maintains the subatmospheric pressure. To allow the instilled fluid to work, the subatmospheric pressure is set for the intended dwell time. The instilled irrigation solution (NaCl, Ringer solution, antiseptic wound irrigation solutions such as polyhexanide, superoxidised water, povidone iodine (PVP iodine), acetic acid, octenidine etc.) should wet the wound sufficiently and have sufficient time to work [28]. Significant side effects in the form of contact sensitisation, inflammation or necrosis have not been described to date, with the exception of incidents with octenidine [6–9, 29–33].

To influence wound healing, disinfectants (e.g., polyhexanide, and also Dakin solution in the US) are often used in addition to instillation of neutral fluids (e.g., Ringer solution, local anaesthetics). Anecdotal reports by individual authors regarding wound irrigation with antibiotics (vancomycin, gentamicin, tobramycin, doxycycline, cephalosporins) are not confirmed scientifically and are regarded as problematic because of development of local resistance and contact sensitisation, among other things.

The aim of negative pressure instillation therapy is to influence the course of wound healing by controlling infection and to prevent infection in the case of contaminated wounds. Bacterial growth, factors that inhibit wound healing such as endotoxins and matrix metalloproteinases and any biofilm present should be reduced. Every open wound should be regarded as primarily contaminated. The following categories of bacterial load should be distinguished, depending on the volume of bacteria and the body's reaction:

- Contamination, defined as the presence of non-multiplying or nearly non-multiplying microorganisms;
- Colonisation, defined as the presence of multiplying microorganisms on the wound surface, which do not yet lead to any cellular damage;
- Critical colonisation, defined as the presence of multiplying microorganisms on the wound surface, which inhibit the healing process, without being accompanied by the classic signs of infection as an expression of the body's defence mechanisms;
- Infection, defined as histologically evident invasion of the multiplying microorganisms from the wound surface into the tissue with typical signs of infection as the body's reaction. A distinction must be made between local and systemic infection.

Surgical debridement is regarded as the primary form of avoiding and treating wound infection, that is, the mechanical removal of nonvital tissue as far as possible into healthy tissue. Every debridement leaves behind cellular remnants that can be removed by additional wound cleansing. Wound irrigation is the most common form of wound cleansing. Debridement and wound irrigation are therefore important components of wound treatment, which build on one another. In the narrower sense, they can be understood as macro- and micro-debridement.

Principles of Negative Pressure Instillation Therapy

Negative pressure instillation therapy can be regarded as a supportive measure that supplements debridement. It allows adequate moist wound treatment and at the same time offers the possibility of carrying out intermittent wound cleansing. Cell detritus and pathogenic bacteria can be thereby removed. In the context of infection prevention and treatment, the use of NPWTi-d in an ex vivo model also reduces the biofilm that protects bacteria [37, 38]. Combined regular cleansing, the reduction of the bacterial count by disinfectants and the negative pressure used in NPWTi-d appear to achieve the greatest benefit in critically colonised or infected wounds [28, 29]. Animal studies on porcine full-thickness skin wounds treated with NPWTi-d and instillation of saline solution also show a more marked increase in granulation tissue compared with NPWT without instillation [39].

Clinical Indications for NPWTi-d

In principle, whenever a wound can be covered with a semi-occlusive or occlusive dressing material, use of NPWT or NPWTi-d is also possible. Classic contraindications to a semi-occlusive dressing include, for instance, inadequate debridement with major necrosis, spreading infection, maceration of the wound surroundings or ulcerating neoplasms. In these cases, semi-occlusive dressings such as hydrocolloids, foam dressings with a border or occlusive films would not be used to cover the wound. NPWTi-d is a method that is helpful especially for wounds in which the focus is on the removal of infective material and other wound debris and promotion of granulation (classic NPWT effects).

NPWT with instillation of a topical wound solution enables a sterile wound covering to be combined with active moist wound therapy. This softens and dilutes nonvital tissue and infective material. It can be aspirated with reapplication of the negative pressure and thus be removed from the wound.

In a consensus paper from 2013, acute and chronic infected wounds, contaminated wounds, wounds associated with diabetic foot syndrome, traumatic wounds, decubitus ulcers and wounds with exposed bone or osteomyelitis were presented as an indication for the use of NPWTi-d [9]. In another publication in 2008, wounds with a high volume of exudate and debris and acute traumatic wounds were described as an indication for the use of

NPWTi-d. Support of further wound cleansing of infected wounds by NPWTi-d directly following surgical debridement was also regarded as an indication [40].

Contraindications to and Complications of NPWTi-d

There are reasons for not using NPWTi-d. However, they are not usually absolute contraindications. In individual cases, these recommendations may be disregarded. The following circumstances were identified by the expert committee as possible contraindications to NPWTi-d:

- In the case of bleeding wounds, there is a risk that major volumes of blood could be aspirated through the pump and thus could endanger the patient, for example, if the system becomes blocked.
- In patients with an increased bleeding risk or patients who take anticoagulants, there is a risk that the wounds will start to bleed under the negative pressure and mechanical irritation. Close monitoring is indicated in these patients to identify bleeding promptly and institute the necessary measures. The same applies for exposed vessels or bypass grafts. These patients should be treated with NPWTi-d only under close medical supervision.
- Maximal surgical debridement is a precondition for successful use of NPWTi-d. Necrotic wounds are therefore a contraindication. However, NPWTi-d assists autolysis so that smaller areas of necrosis, slough and fibrin deposits are also removed when the wound filler material is changed.
- When there are alterations in the surrounding skin, such as maceration, eczema or atrophy due to advanced age, there is a risk that the systems cannot be attached with a tight seal, that the surrounding skin will deteriorate under the film or that it will tear when the film is removed.
- In the case of neoplasms, there is a theoretical risk that tumour growth will be promoted. To date, however, there are no scientific data in this regard. After tumour resection, negative pressure therapy has become largely established as a bridging treatment until definitive wound closure. A recommendation regarding use on tumours can currently not be given by the expert committee, given the lack of data, similar to NPWT treatment.
- When used over joints, there is a risk that the tight seal of the NPWTi-d system cannot be ensured due to repeated joint movements.
- Situations that require a particular indication definition for NPWTi-d are the management of osteomyelitis, exposed organs and their structures or fistulas.
- Autoimmune wounds such as pyoderma gangrenosum. Here there is a risk that the mechanical irritation will trigger what is known as a pathergy phenomenon in the inflammatory phases and that the wounds will enlarge. If radical surgical debridement of these conditions is performed under therapeutic control of the inflammation, NPWTi-d can be successful in individual cases.

An important aspect for the success of NPWTi-d is patient selection and monitoring by trained staff. NPWTi-d is unsuitable or limitedly suitable for self-treatment by patients.

Treatment Algorithm

Before starting to use NPWTi-d it appears essential to institute therapy of the causes interfering with wound healing. NPWTi-d cannot replace this. However, synchronous or metachronous NPWTi-d can be considered in all patients who do not have any contraindications. It should be used deliberately as part of a clearly defined treatment process for a period of several days to up to 2 weeks to actively influence the wound healing process. A critical assessment of the treatment should take place after 14 days at the latest. 4–8 instillations per 24 hours are necessary as treatment intervals; the instilled fluid should be able to work for 10–20 minutes. This procedure, depending on the type of preparation used, is largely independent of the type of wound and of the instilled fluid. It is based especially on the fact that the cleansing and stimulating effect of NPWTi-d acts a number of times daily and for a sufficiently long time (see algorithm in ▶ **Fig. 1**).

Results of the Expert Consensus Meeting

Which wounds can benefit from NPWTi-d as additional therapy?

With a few exceptions, all wounds can benefit from the use of NPWTi-d. The few exceptions refer to anatomical structures (exposed vessels or nerves) and problems in the surrounding skin (maceration and skin diseases), which present a fundamental problem for the use of negative pressure and/or occlusion. In addition, polyhexanide should not be used directly on cartilage with NPWTi-d, except in high dilution (0.005%).

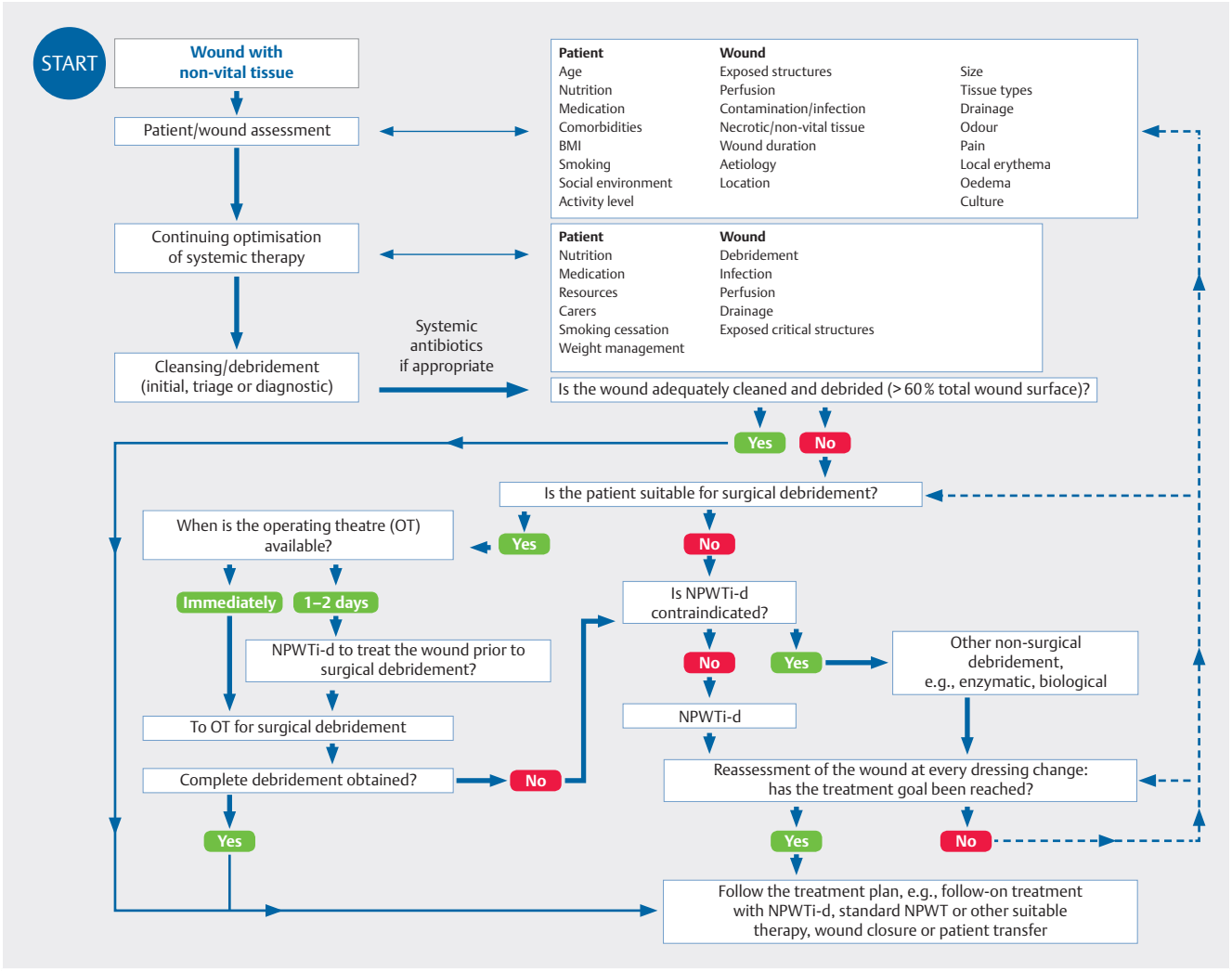
The indication for using NPWTi-d should take the wound situation into account as regards infection. This can be classified into

- Acutely infected wounds
- Chronically infected wounds
- Contaminated wounds and
- Clean wounds.

This infection-related wound situation should suggest the use of NPWTi-d and facilitate the clinician's decision as to whether the treatment should be delivered as NPWT or NPWTi-d. Even with the rather limited study data, the additional value of NPWTi-d compared with NPWT is accepted by all the participants in the expert consensus meeting. The higher the residual bacterial load of the wound after debridement, the more NPWTi-d is indicated. The procedure for the afore-mentioned wound situations is listed in detail below.

Acutely infected wounds

In an acutely infected wound, following surgical debridement, bacteria are found and empirical antibiotic therapy is started, which is then guided by the sensitivity. This measure cannot be replaced by NPWTi-d, especially if there are concomitant systemic symptoms. Synchronous use of NPWTi-d can accelerate wound



▶ **Fig. 1** Algorithm for differential indication for the use of NPWTi-d (negative pressure wound therapy with instillation and solution dwell time) depending on the wound nature and local and systemic factors.

healing, however, and so help to combat the infection and shorten the treatment time (▶ **Fig. 2**).

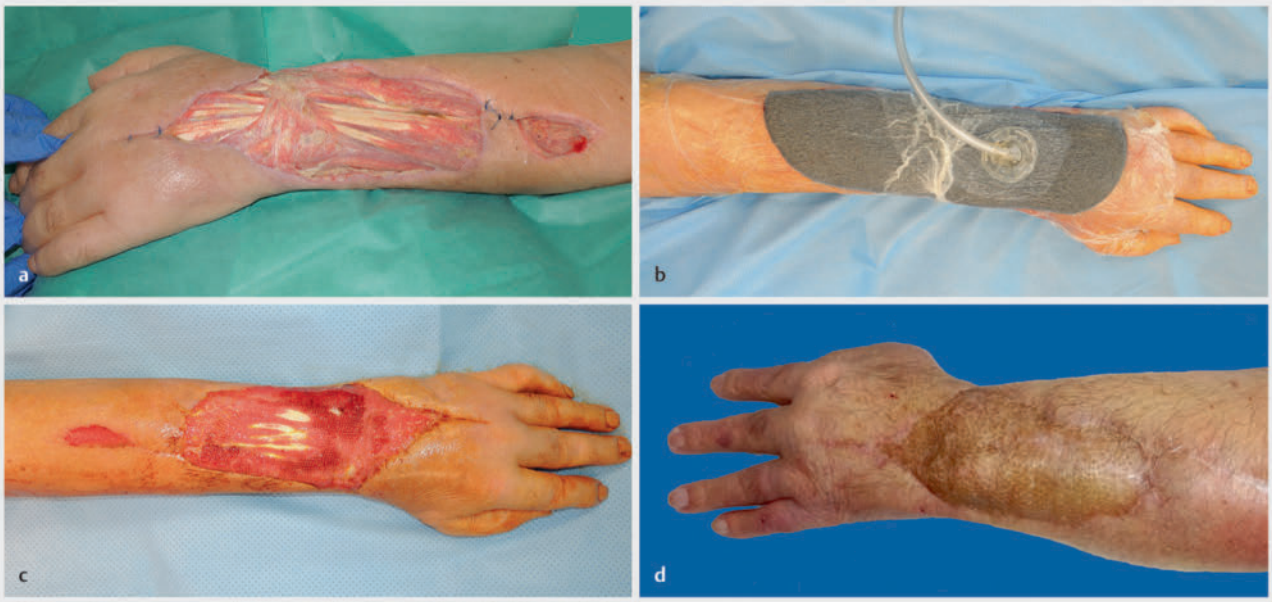
In this situation, polyhexanide in a concentration of 0.1 % or 0.04 % is most often used. Studies of which of these two concentrations is more suitable for NPWTi-d are currently lacking. In the case of wounds with exposed cartilage, however, polyhexanide concentrations no greater than 0.005 % should be used to prevent cartilage damage. The dwell time should be 20 minutes and interval treatments of 4–8 cycles per day are desirable.

Acetic acid can be used in concentrations between 0.25 and 1 %. Here, too, a dwell time of 20 minutes and frequencies of 4–8 cycles per day are useful [45].

Besides these two substances, povidone iodine can also be used. In the literature, a combination of ethanol/propan-2-ol and povidone iodine is recommended (100 ml contain 3.24 g povidone iodine, 38.9 isopropanol and 38.9 g ethanol). Because of its virostatic effect, use should be considered especially in patients with HBV, HBC and HIV infection. The expert committee cannot yet finally comment on the use of this solution.

Chronically infected wounds

The same approach applies for chronically infected as for acutely infected wounds. The priority of any treatment is the question of why the wound is chronically infected. This is often due to inadequate surgical debridement, proximity of non-sterile body orifices or intrinsic, unaddressed factors. Chronic infected wounds on the extremities or over the sternum with concomitant osteomyelitis must be investigated by deep biopsies to discover the bacteria causing the infection, which is the basis for targeted antibiotic therapy. Chronic wounds in the region of non-sterile body orifices cannot be rendered free from bacteria by antibiotic therapy. In both situations, the additional cleansing and bacteria-reducing action of NPWTi-d is an important basis. Even though the use of NPWTi-d cannot be underpinned by randomised studies for this



▶ **Fig. 2** **a** At the time of first diagnosis, the 77-year-old multimorbid patient needed intensive care because of sepsis with cholecystitis and prior severe cardiac disease with cardiac output of 15%. He developed necrotising fasciitis on the forearm, which was first excised radically. Skin and soft tissue defect and exposed extensor tendons on the forearm. **b** Until his overall condition stabilised in intensive care, the wound bed was prepared with negative pressure wound therapy with instillation and disinfectant solution. **c** Increasing wound cleansing with negative pressure wound therapy with instillation and induction of granulation therapy. **d** Now 79-year-old patient 2 years after split skin graft with stable healing.

indication, the members of the expert consensus meeting support the use of NPWTi-d in chronically infected wounds.

Contaminated wounds

There is no primary infection in a contaminated wound. Nevertheless, contamination should be assumed based on the mechanism by which the wound developed, and there is an infection risk in the course of therapy due to biofilm development. The combination of surgical debridement and irrigation therapy of these wounds is the established standard and can be usefully assisted or extended by NPWTi-d. International guidelines recommend irrigation with physiological saline or Ringer solution without other additives [41, 42]. Against these recommendations, antiseptic irrigation solutions are also used today in many areas [43]. Even if the indication for NPWTi-d in contaminated wounds is still the subject of discussion, the members of the expert consensus meeting agree that NPWTi-d is a very good temporary wound treatment in addition to all other standard treatments to prevent infection, depending on the extent of the injury and exposure to infective material.

Clean wounds

In a clean wound, by definition there is no infection and also no colonisation. Wound debridement is therefore not indicated. The use of NPWTi-d can therefore only have the objective of keeping the wound in this state and promoting granulation. However, some patients have increased infection risks. To what extent elderly patients, patients with diabetes mellitus and other immunosuppressive states (cachexia, immunosuppressant therapy, need for dialysis etc.), for instance, can benefit from NPWTi-d is currently unclear due to a lack of corresponding evidence. However, if these patients have major wounds that cannot be managed primarily by surgery, they have a high risk for secondary contamination or infection. The use of local antiseptics to prevent infection is then regarded as rational. The members of the expert consensus meeting agree that NPWTi-d can be of benefit in the short term and prophylactically in patients with diabetes mellitus and other immunosuppressive states when wound closure by secondary suture or skin grafts is not yet possible for other reasons. Independent of this, negative pressure methods over closed clean surgical wounds will attain increasing importance in future [44].

The consensus experts can currently recommend NPWTi-d only under inpatient conditions. The experts explain this with the fact that neither topical negative pressure wound therapy nor negative pressure instillation therapy has been included to date by the G-BA (Joint Federal Committee) in the statutory health insurance list of benefits for outpatient care. Moreover, the method has features that imply that intervention in the system can be necessary at any time to ensure uncomplicated negative pressure instillation therapy. This is provided better by the closer monitoring during inpatient hospitalisation.

Conclusion

NPWTi-d is a newly established method for wound cleansing and prevention and for treatment of wound-associated infections in combination with the effects of NPWT; it is still not regarded as sufficiently important, given the knowledge of the positive effect in contaminated wounds that already exists. In the era of increasingly multimorbid patients, ever more complex surgical procedures and ever wider spread of multi-resistant bacteria, NPWTi-d may become highly important in future for local therapy. A central important aspect is the potential to avoid wound infections and thereby shorten wound healing and reduce the use of antibiotics. Even if the scientific data are still very limited at present regarding the statements made above, the members of the expert consensus meeting are convinced of the strengths of targeted use of NPWTi-d. NPWTi-d should be available in every area where patients with acute or chronic wounds are treated and therapists should be trained in its use. Only in this way can the advantages of NPWTi-d compared with NPWT and other wound treatment methods benefit patients and the health system.

Conflict of Interest

The expert consensus was sponsored by the KCI-Acelity company; the members of the expert group worked for KCI-Acelity in the past as consultants or scientific experts.

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Please note: The treating physician can choose between 500 ml and 1000 ml canisters for V.A.C. VERAFLO™ Therapy, depending on duration of therapy, level of instilled solution and exudate.

PRA-PM-EU-00126 (02/19)