

Supplement to the September 2009

WOUNDS

A Multidisciplinary
Approach to

LIMB PRESERVATION

The Role of V.A.C.[®] Therapy

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A Multidisciplinary Approach to Limb Preservation: The Role of V.A.C.[®] Therapy

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Abstract

Many factors and conditions, including trauma, vascular insufficiency, and diabetes mellitus, can lead to an amputation of the lower extremity. A panel of experts convened to discuss their clinical experiences achieving limb preservation through a multidisciplinary, coordinated plan of care comprising peripheral revascularization, serial debridement, infection control, wound management, wound coverage, and correction of biomechanical abnormalities. Negative pressure wound therapy utilizing reticulated open cell foam (NPWT/ROCF) as delivered by Vacuum Assisted Closure[®] (V.A.C.[®] Therapy, KCI Licensing, Inc., San Antonio, TX) is used in conjunction with various surgical techniques and specialized treatment adjuncts to manage acute and chronic wounds. The purpose of this supplement is to present a multidisciplinary approach to limb preservation that employs the use of NPWT/ROCF as an integral part of a treatment algorithm. A cost analysis is also provided as part of the manuscript.

Disclaimer: This peer-reviewed article discusses a multidisciplinary approach to limb preservation and the role of negative pressure wound therapy utilizing reticulated open cell foam (NPWT/ROCF) as delivered by Vacuum Assisted Closure[®] (V.A.C.[®] Therapy, KCI Licensing, Inc., San Antonio, TX) in limb preservation. The information provided is based on an expert panel of podiatric, vascular, orthopedic, general, and plastic and reconstructive surgeons who met April 3-4, 2009, in Charlotte, NC. Additional input was provided from specialists who were unable to attend. This document is intended to help clinicians understand the value of a multidisciplinary approach to limb preservation and role that NPWT/ROCF can play in this process. Recommendations in this article are drawn from both medical evidence and clinical practice experience based on use of the V.A.C.[®] Therapy System. Not all NPWT systems perform in the same manner, and outcomes using other systems may not be the same. Recommendations are not intended as a guarantee of results, outcomes, or performance of the V.A.C.[®] Therapy System. Please note that use of V.A.C.[®] Therapy does not preclude use of other surgical techniques or modalities to manage wounds. Always consult product labeling and instructions for use before initiating V.A.C.[®] Therapy.

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A Multidisciplinary Approach to Limb Preservation: The Role of V.A.C.[®] Therapy

Introduction

Trauma, vascular insufficiency, and diabetes mellitus (DM) are three major conditions that can lead to an amputation of the lower extremity.¹ Amputations to manage wounds date back hundreds of years, making this one of the earliest surgical procedures performed.² An amputation may result from infection, disease (eg, DM, peripheral arterial disease, cancer), or traumatic injury.³ In 2005, approximately 1.6 million people were living with limb loss; this number is expected to more than double by 2050.⁴ Although trauma and cancer can result in amputations, most new amputations occur because of complications associated with DM, such as neuropathic foot ulceration, infection, and peripheral vascular disease (PVD). In 1980, the Centers for Disease Control and Prevention (CDC) estimated that 5.6 million Americans were diabetic. By 1990, the number of diabetics in the United States had increased to 6.6 million. By 2000, that figure had nearly doubled to 12 million.⁵ According to the 2007 CDC National Diabetes Fact Sheet, there are currently 24 million people diagnosed with diabetes,⁶ and the estimated annual direct and indirect costs of diabetes treatment in the United States is approximately \$174 billion.⁶ Studies

by Gordois et al reported that treatment of diabetic foot ulceration and amputations alone in 2001 cost \$10.9 billion, with an average of \$38,077 per procedure.^{7,8} Therefore, preventing ulcerations and/or amputations is critical from both medical and economical standpoints.

The term “limb preservation” refers to the salvage of a limb that would have otherwise required surgical amputation. Limb preservation requires a series of steps including re-establishing adequate perfusion, serial debridements, appropriate wound coverage, aggressive infection management, and correction of underlying biomechanical abnormalities. The cornerstone of limb preservation protocols after required medical and surgical interventions (ie, revascularization procedures) is optimized wound care. Without the latter, the former is usually insufficient to preserve the limb.

Today, a multidisciplinary team approach to preventing amputations has led to the establishment of specialized limb preservation centers across the United States. Limb preservation centers, unlike wound care centers, focus on optimizing limb function in addition to healing the wound. Their teams include experts in many specialties, including podiatric, vascular, orthopedic, and plastic surgeons, infectious disease specialists and endocrinologists. Together, they provide

a multidisciplinary approach ranging from healing wounds to preventing major amputations. This approach provides the best outcomes for patients who are at risk for limb amputation.⁹⁻¹² In 1995, a multidisciplinary limb preservation clinic was established at Madigan Army Medical Center under the leadership of Dr. Charles Andersen, chief of vascular surgery, and Dr. Vickie Driver, chief of limb preservation. Dr. Driver and colleagues reported early results from this initiative in an article describing how the establishment of the Limb Preservation Service, a multidisciplinary, state-of-the-art, diabetic foot care clinic, decreased the number of lower-extremity amputations from 33 in 1999 to 9 in 2003 in patients with diabetes — an 82% drop in amputations.¹¹

One of the biggest advantages of a limb preservation center is that a variety of specialists can assess patients within a brief time period, resulting in a coordinated plan of care along established evidence-based algorithms. The initial screening determines which disciplines need to be involved in each patient’s plan of care. Unfortunately, not all critical components of a multidisciplinary team are available in either general hospitals or wound care facilities. Some individual physicians and surgeons with experience and training across a broad spectrum of disciplines

may appropriately treat conditions in areas that lack dedicated limb preservation centers, but for complex cases, the preservation results will be inferior to the team approach. In the absence of a critical expertise needed to address limb preservation, panelists commented that NPWT/ROCF might be used as a bridge to definitive closure or as a wound-stabilizing device^{13–17} until the necessary specialist was available.

Background

Acute Versus Chronic Wounds

An acute wound is defined as a disruption in the integrity of the skin and underlying tissue that readily progresses through the sequential stages of normal wound healing.¹⁸ Such wounds can be caused by traumatic injury, a disease process, or surgery; they generally follow a wound-healing progression that includes hemostasis, inflammation, cell proliferation, matrix repair and, finally, epithelialization and remodeling of scar tissue.^{19,20}

Acute wound healing can be affected by extrinsic factors, such as infection, medications, and stress, and by intrinsic factors such as age, multiple comorbidities, nutritional status, and vascularization.¹⁸ Although the majority of acute wounds heal without difficulty, amputation is still a risk if the host is compromised, the vasculature is significantly disrupted, infection is uncontrolled, or the wound progresses into a chronic wound with gross functional impairment. Acute wounds created in an extremity with unrecognized vascular insufficiency are especially at risk to heal poorly and develop secondary infection.

In contrast to acute wounds, chronic wounds fail to progress normally through the stages of wound healing²⁰ and may be at greater risk for limb amputation. In addition to some of the extrinsic and intrinsic factors affecting acute wounds, chronic wounds typically occur in patients afflicted with vascular disease, neuropathy, multiple comorbidities, and/or inappropriate wound care.²¹ Chronic wounds often progress to infection of deep structures, including bone, tendon, and joint capsule. These progressive infections require urgent/emergent bone debridement, tendon resection, and additional amputation. Relying on repetitive antibiotics to treat these wounds can make bacteria more resistant and place the limb at greater risk of amputation and limb loss. Chronic wounds, therefore, require debridement/excision, which essentially results in an acute wound that can continue to heal. Post-debridement, the wound can undergo numerous care protocols including NPWT/ROCF, growth factors, offloading, and multiple advanced moist therapies.

Sheehan et al have shown that a wound has an excellent chance of healing when there is a 10% to 15% reduction in area per week (based on a 53% reduction in area over 4 weeks).²² Even with adequate perfusion, no obvious infections, and proper dressing regimens, wound healing may still fail to proceed. When this occurs, a reassessment of the patient, the wound, and the treatment options employed needs to be performed by the treating physician. Several factors should be reevaluated:

vascular system, biomechanics, infection, coagulopathy, malignancy and autoimmune disease. Repeat wound debridement and biopsy are practical initial steps for a stalled wound. Special attention should be placed on chronic wounds, such as diabetic foot ulcers (DFU) or heel pressure ulcers, which can result in an amputation. For example, neuropathic foot ulcerations, complicated by infection, are a common precursor to lower-extremity amputations.^{17,23} Offloading is a critical component in treating diabetic and dysvascular ulcers. Common methods of offloading include bed rest, wheelchair use, crutch-assisted gait, total contact casts, felted foam, therapeutic shoes, and removable cast walkers.²⁴

NPWT/ROCF System and Mechanisms of Action

NPWT/ROCF is form of negative pressure therapy that was developed at Wake Forest University School of Medicine, Winston-Salem, NC, and first marketed in the United States in 1995.²⁵ It is indicated for use in the treatment of chronic, acute, subacute, traumatic, pressure and diabetic ulcers, partial-thickness burns, flaps, and grafts.¹³ The integrated wound care system is composed of a reticulated open-cell polyurethane (V.A.C.[®] GranuFoam[™]) or polyvinyl alcohol foam (V.A.C.[®] WhiteFoam) dressing, a pressure-sensing pad (SensaT.R.A.C.[™]), evacuation tubing, a collection canister, and a software-controlled therapy unit responsible for generating uniform negative pressure.²⁶ The reticulated open-cell foam is also



available as a bridge dressing (V.A.C.[®] GranuFoam™ Bridge Dressing) that enables providers to offload limbs.

NPWT/ROCF's unique mechanisms of action provide a closed, moist wound environment while removing fluids and infectious materials to reduce edema.²⁰ The reticulated open-cell foam, in conjunction with the negative pressure, produces macrostrain and microstrain. Macrostrain draws the wound edges together and microstrain causes deformational changes at the cellular level. These mechanical forces have been shown in a 3D fibrin matrix to result in the production of growth factors (ie, transforming growth factor- β and platelet-derived growth factor) important for wound healing.^{20,27-29} This activity promotes tissue perfusion and healthy granulation tissue formation that help prepare the wound bed for closure by a number of methods, including primary closure, secondary wound closure, split-thickness skin grafts, and flap procedures.^{13,30} Numerous studies, including randomized controlled trials (RCTs), have been published regarding the effective use of NPWT/ROCF for acute wounds and chronic wounds such as DFUs.^{13-15,31-38} Table 1 lists the mechanisms of action for NPWT/ROCF.

Medical Assessments

Patient Assessment

A comprehensive patient assessment is the first step in creating a wound management plan. The initial assessment should obtain a complete history and physical examination that includes patient demographics, current and past

Table 1. NPWT/ROCF Mechanisms of Action

Mechanism of Action
Provides a moist, closed wound healing environment
Promotes granulation tissue formation through cell migration and proliferation
Reduces edema
Removes infectious materials
Draws wound edges together

medical history, medications, nutritional status, social history (eg, smoking, drug abuse, history of depression, mental status) and family history that may shed light on the wound etiology and lack of healing progression.^{16,39,40} The physical examination should provide a good overview of the patient's systemic state of health and the presence of co-morbidities. A careful limb examination is needed to identify bony abnormalities, vascular status, and disturbances in foot biomechanics. These factors become critical when creating care plans, treatment interventions, and overall wound management. To optimize wound healing, comorbidities should be controlled and nutritional status should be optimized.⁴¹

Wound Assessment

There should be a complete wound assessment when the patient initially presents. The assessment should include wound history and characteristics, such as location, date of onset, size (eg, area, volume, depth), base color, amount and

type of exudate, presence of edema, condition of wound edges and surrounding skin, status of granulation tissue, underlying bone involvement, and pain.^{39,42,43} Wound assessments have also been developed that include stages or grades for pressure ulcers and DFUs.⁴⁴ Baseline wound measurements and standardized photographs need to be documented to allow for assessment of wound healing to determine the effectiveness of therapy interventions. Assessment frequency ranges from daily to weekly; however, the major determinant should be the wound characteristics observed at each dressing change.³⁹

The panel agreed that using colors to describe wounds (black, green, yellow, and red) can be helpful in assessing the wound.¹⁹ For example, black eschar may indicate a need for revascularization and/or debridement to look for signs of infection. After removal of the eschar, the wound may appear bright yellow, suggesting healthy fat, or may show a pale yellow intermingled with brown, purple, and blue, suggesting

there is further necrotic tissue. A green wound usually indicates infection or bacterial colonization and would be accompanied by other signs, including purulence, odor, and inflammation, such as erythema, fever, swelling, and pain. In the infected wound, debridement to a clean viable tissue bed and a deep culture to identify the infecting organisms are essential to treatment. A red wound, filled with healthy fine-grained granulation tissue, implies a healing wound, while a purple-red budding granulation implies poor healing.

Vascular Assessment

Adequate perfusion is critical for wound healing; a well-vascularized wound bed is essential to provide adequate nutrients and oxygen for the granulation tissue formation required for healing.¹⁹ Blood flow is essential for limb preservation and is affected by peripheral arterial disease (PAD), venous insufficiency or thrombosis, edema, coagulopathy, and vasculitis.

A thorough history and physical examination may aid in discovering PVD in the asymptomatic patient. Asymptomatic patients with multiple identified atherosclerotic risk factors should be screened for peripheral arterial and venous disease. Patients with cardiac or pulmonary disease may not be sufficiently ambulatory to trigger complaints of claudication even though significant PVD may be present. Patients with diabetic neuropathy may not experience the pain of claudication. Eight percent of individuals 55 to 74 years of age have asymptomatic

lower-extremity arterial disease when screened.⁴⁵

Additionally, patients with diabetes require routine examinations to assess for vascular insufficiency, ulcer formation, peripheral neuropathy and mechanical foot problems and may benefit from counseling on routine foot care. In patients with diabetes or coronary artery disease (CAD), elective surgery on the leg or foot, such as the harvesting of veins for coronary artery bypass or correction of mechanical foot deformities, should mandate a peripheral vascular assessment even in the absence of specific patient complaints. The traditional approach of “look, listen, and feel” for vascular examination includes inspection of the skin of the extremities, palpation of all peripheral pulses, assessment of extremity temperature, auscultation for bruits, and a thorough neurologic exam.⁴⁶

After the peripheral vascular history and physical examination are complete, the severity of PVD can be assessed on clinical grounds. The affected extremity can be judged to be viable, threatened, or unsalvageable. A viable extremity may have areas of tissue loss, but in general, adequate time is available to conduct further testing. A threatened extremity may require immediate intervention without the luxury of extensive testing. An unsalvageable extremity requires an assessment of amputation level based on clinical judgment with the aid of non-invasive techniques, provided wet gangrene or ascending infection is absent. If time permits an elective work-up, additional

information may be gathered via non-invasive or invasive studies, which serve to confirm the findings of the physical examination through more quantitative means.

When vascular flow is compromised, the patient should be referred for vascular assessment and consideration for a vascular surgery evaluation. The purpose of a non-invasive vascular laboratory work-up is to localize the level of obstructive lesions, assess the adequacy of tissue perfusion, and determine the healing potential of ulcers. These objectives are met by obtaining one or more diagnostic tests, including segmental limb pressures, toe-brachial indices, pulse volume recordings, exercise testing and transcutaneous oxygen (TcPO₂) measurements, and possible invasive testing (eg, arteriograms, CT angiograms) techniques.⁴⁷ A patient may require only selected tests. The need for additional vascular testing depends on the clinical scenario and the recommendations of a consulting vascular surgeon if a lesion is identified. Contrast angiography, for instance, is usually reserved for preoperative vascular surgical planning.

TcPO₂ assesses cutaneous oxygenation and predicts wound healing potential. Values lower than 30 mmHg have been associated with increased risk for amputation.⁴⁸ Bunt et al demonstrated in a study of 147 patients with either acute pedal sepsis or chronic PVD that TcPO₂ values predicted the presence of vascular disease, the need for revascularization, and the success of major/minor amputations



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with or without revascularization.⁴⁹ Once the vascular supply is compromised, revascularization becomes necessary to improve the blood supply either through open procedures (ie, bypass grafting) or endovascular procedures (eg, angioplasty, stenting, and thrombolysis).^{17,48,50,51} Non-interventional management of patients with lower extremity ischemia consists of general wound care measures and use of pharmacologic agents such as anti-coagulants and thrombolytic therapy. As a rule, however, severe ischemia of the lower limb generally requires an interventional approach. The method of revascularization of the affected limb is dependent upon several factors, including the indications for surgery, the patient's risk factors, arteriographic findings, and available graft material. Aggressive revascularization techniques (eg, femoral-popliteal bypass grafts, femoral-tibial bypass grafts) prevent amputations.^{50,51} Thus, revascularization is crucial for preserving limbs because adequate blood supply is a prerequisite for the subsequent wound stabilization techniques required for limb preservation.

Wound Management Principles

Why Wounds Don't Heal

Several factors can prevent a wound from healing. These include the presence of infection, the type of infecting organism, the level of wound colonization, the character of wound exudate, the pH of the wound, the degree of inflammation, the amount of devitalized tissue, the local vascular supply, the vol-

ume of growth factors, the amount of cell senescence, concurrent illnesses, and excessive proteases, such as matrix metalloproteinases (MMPs).⁵² Table 2 lists adverse conditions that may contribute to a non-healing wound;^{40,53} they need to be considered before determining the appropriate treatment options. These factors also need to be reviewed during re-assessment of a stalled, non-healing wound, which may be helpful when deciding to use an advanced therapy such as NPWT/ROCF.

Principle of TIME

The fundamental principles of TIME (Tissue, Infection/Inflammation, Moisture balance, and Edge of wound) were developed based on the management of chronic wounds (ie, non-healing wounds).^{19,44,54} Table 3 describes the TIME principles. Briefly, the wound bed needs to be examined for necrotic tissue or slough/fibrinous material that can impair healing. The level of infection and type of infecting organism need to be determined in order to decide whether bacteria are slowing or preventing healing. Prolonged inflammation can also prevent the wound from progressing through the normal healing stages. Obtaining an optimal moisture balance within the wound bed facilitates healing. Excessive fluid macerates the wound whereas excessive desiccation slows the epidermal regeneration necessary for wound healing. Finally, non-advancing epidermal margins affect wound closure even when the other three principles of TIME have been addressed.^{19,44,54}

Table 2. Factors That Prevent Wounds from Healing*

Poor circulation
Edema
Infection
Diabetes mellitus
Immobilization
Anemia
Use of steroids
Age
Smoking
Obesity
Coagulopathy
Vasculitis

*Adapted from Riou et al.⁴⁰

Wound Bed Preparation

Wound bed preparation is "the management of the wound to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures."^{19,42,54} Applying the TIME principle to maximize wound healing includes an assessment of the overall health status of the patient to determine the underlying basis of the non-healing wound.^{44,55} In some instances, this is merely addressing the nutritional status of the host; in others, it may require the intensive monitoring and adjustment of the patient's metabolic state through the use of insulin, dialysis, and hormone therapy. The main compo-

Table 3. TIME Principle*

Clinical Observations	Pathology	Clinical Actions	Effect of Clinical Action
Tissue (non-viable or deficient)	Defective matrix and cell debris impair healing	Debridement	Restoration of wound base and functional extracellular matrix
Infection or inflammation	High bacteria counts or prolonged inflammation	Remove infected foci	Low bacterial counts or controlled inflammation
Moisture imbalance	Desiccation slows epithelial cell migration Excessive fluid causes maceration	Apply moisture balancing dressing Remove fluid	Restored epithelial cell migration, desiccation avoided, and maceration avoided
Edge of wound not advancing or undermined	Non-migrating keratinocytes Non-responsive wound cells	Reassess cause or consider corrective therapies	Keratinocyte migration restored

*Adapted from Chin et al.⁵²

nents of wound bed preparation include

- serial debridement,
- microbiologic management,
- moisture control, and
- addressing the wound margin/epidermal edge.^{19,42,56}

One example using the TIME principle was demonstrated by Foley, who presented a case report in which the principles of TIME were implemented to treat a difficult-to-heal (approximately 8 years) chronic heel ulcer. The final outcome was complete healing.⁵⁷ In addition, several studies, including RCTs, have demonstrated the successful use of NPWT/ROCF for wound bed preparation by promoting granulation tissue formation and decreasing wound size.^{13,14,35,37,58}

Debridement

The panel agreed that debridement is a key step in wound healing with the main goal of achieving a viable wound bed.⁵⁹ Debridement is the removal of damaged, necrotic and infected tissue from an acute or chronic wound until surrounding healthy tissue is revealed.^{47,60–62} The material frequently debrided includes eschar, slough, non-viable tissue, and any foreign material (eg, retained hardware, clothing from burns).⁶² The wound should be debrided until normal tissue colors (yellow, red, and white) and texture are attained. Debridement allows the provider to assess the wound accurately by revealing size and depth of wound, signs of infection, and possible undermining or tunneling. Necrotic tissue provides an optimal growth environment for bacteria that promote inflam-

mation as well as infection.⁴⁴ Removing non-viable tissue decreases infection by eliminating bacteria and biofilm, and reducing proinflammatory mediators that can impede wound healing.⁵⁹ The various methods of debridement include autolytic, sharp/surgical, enzymatic, mechanical, and biosurgical debridement.^{45,59,60,62,63} Table 4 describes each method and includes advantages and disadvantages for each.

Debridement for acute and chronic wounds differs in that a single debridement may suffice for an acute wound to heal.⁵⁵ Continual maintenance debridement is often required for chronic wounds to reduce the progressive necrotic burden (eg, necrotic tissue, excess exudate, biofilm, and planktonic bacteria within dead tissue) that may impede healing.^{19,44,55} This lets the

Table 4. Methods of Debridement*

Debridement	Application	Advantages	Disadvantages
Autolytic	Uses moist dressings (eg, hydrocolloids or transparent films) over the wound in conjunction with the body's natural enzymes to soften and liquefy the necrotic tissue	<ul style="list-style-type: none"> • Selective • Safe and easy to use • Painless 	<ul style="list-style-type: none"> • Requires close monitoring of wound for signs of infection • Not recommended for use with infected wounds or exposed tendon/bone
Sharp/surgical	Uses instruments (eg, scalpels, scissors, forceps, or curettes) to remove necrotic tissue from the wound	<ul style="list-style-type: none"> • Fast and highly selective • Can be performed at bedside 	<ul style="list-style-type: none"> • Can be painful • Can be costly (eg, use of special equipment or if operating room is required) • Risk of hemorrhage/complications • Patient must be able to tolerate surgical intervention
Enzymatic	Uses enzymes (eg, collagenase) to digest and dissolve the necrotic tissue	<ul style="list-style-type: none"> • Can be selective • Can be used on infected wounds 	<ul style="list-style-type: none"> • Patient can be allergic to enzyme • Requires a prescription • Can be costly • Inflammation or discomfort may occur around the wound
Mechanical	Uses force to remove the damaged and necrotic tissue (eg, wet-to-dry dressings, pulsed lavage, ultrasound, and hydrotherapy)	<ul style="list-style-type: none"> • Can be used with larger wounds • Cost of dressing (ie, gauze) is low 	<ul style="list-style-type: none"> • Non-selective • Can be painful • Bleeding can occur • Force can cause trauma to the wound • Cost of ultrasound and hydrotherapy can be high
Biosurgery	Uses maggot larvae (eg, <i>Lucilia sericata</i> , green bottle fly) to consume necrotic tissue and bacteria	<ul style="list-style-type: none"> • Selective and rapid • Can be painless • Decreases bacterial load • Can be used for various wound types 	<ul style="list-style-type: none"> • Can be costly and time-consuming • Potential for allergic reactions • Can cause psychological distress

*Adapted from Kirshen et al.⁵⁷

treating physician maintain the wound bed in a state of readiness to heal.⁶³ Not all wounds are suitable for debridement, especially wounds that show little capacity to heal.^{59,63} For instance, sometimes stable, non-infected heel ulcers with poor circulation should not be debrided except when signs of infection are present.^{59,63} Debridement should also be delayed for wounds with inadequate blood flow if there is no acute infection or inflammation present.^{47,59}

NPWT/ROCF may serve as a bridge between debridements or between debridement and delayed primary closure.^{47,64,65} It can also be used as an adjunct to debridement when treating contaminated soft tissue injuries. Leininger et al reported that the use of NPWT/ROCF with aggressive debridement and pulsed lavage for the treatment of high-energy war injuries in 77 patients resulted in a 0% wound infection rate and 0% overall wound complication rate.⁶⁶

Infection

The continuum of wound infection consists of the contaminated wound, the colonized wound, the critically colonized wound, and the infected wound. Contamination is the presence of non-replicating microorganisms within a wound that do not impair healing. Colonization indicates that replicating microorganisms have attached to the wound surface but do not impede healing.^{44,54} Critical colonization refers to bacterial burden in the wound that is between being colonized

and infected. A critically colonized wound is accompanied by non-healing, friable granulation tissue, tunneling, and odor. Critically colonized wounds are slow to heal but do not display typical signs of infection (eg, erythema, warmth, swelling, pain, fever, and loss of function). Infected wounds have delayed healing and are accompanied by systemic symptoms, such as pain, swelling, pus, odor, increased exudate, color change in the wound bed, and atypical granulation tissue formation.^{44,54}

Based on the Infectious Disease Society of America (IDSA) diabetic foot infection guidelines, two signs of inflammation or other clinical signs (eg, excessive drainage, purulence, cellulitis, and significant pain) are needed to indicate infection because the level of colonization is difficult to determine.⁶⁷ Reliable cultures are optimally obtained after a debridement in the operating room. A qualitative deep culture appears to be more beneficial than a surface swab culture. A surface swab culture is not clinically reliable, often reflecting only surface contaminants.⁶⁸ In cases of traumatic wounds, if osteomyelitis is suspected, a bone biopsy should be obtained for culture and pathology. A true-cut needle biopsy is helpful in this regard.

Biofilm refers to a community of organisms encapsulated within a self-made polymeric matrix (exopolymeric substance) attached to an available surface, including wound surfaces. Biofilm plays a significant role in a large number of infections and is much more resistant to antibiotics.^{46,69,70} In addition, the colonies within it periodically send out new bac-

teria (planktonic bacteria) to further populate the wound with new biofilm colonies. When biofilms are present in wounds, supplemental therapy, such as ultrasound, biofilm solvents, or debridement, is required to remove it.

Previous studies have shown antibiotics effectively treat infections in chronic wounds.^{71,72} Systemic antibiotics may not always be the best option for reducing bacterial burden.¹⁹ Topical antimicrobials, in conjunction with systemic antibiotics, may provide the greatest benefit when used in chronic wounds with active but localized infection.^{19,73} Once the bacterial burden is decreased to an acceptable level, both topical and systemic antibiotics should be discontinued and an appropriate dressing treatment should be started. The panel recommends the IDSA guidelines as an excellent resource for infection management.

NPWT/ROCF is increasingly being used in the management of complex infected wounds as part of an overall treatment plan after debridement and appropriate antibiotic therapy has been initiated. Morykwas et al initially demonstrated its ability to effectively reduce bacteria levels in a porcine animal study.³⁰ One study using NPWT/ROCF did show an increase in bacterial colonization during treatment, but in most cases wounds still rapidly healed.⁷⁴ NPWT/ROCF's ability to maintain a closed wound environment protects the wound from external contaminants.^{13,33,75}

Newer NPWT/ROCF technologies have been successfully used on infected wounds. A pilot study by Gabriel et al



reported on the use of the V.A.C.[®] GranuFoam Silver™ Dressing in a 5-patient case series.⁷⁶ The initial treatment results showed a reduction in clinical infection and wound closure time when compared to the institution's past use of moist wound therapy (MWT) for infected wounds.

Other studies have used V.A.C. Instill[®] WoundTherapy, which combines the traditional NPWT/ROCF system and the ability to intermittently instill topical wound treatment solutions into the wound bed; this combined therapy may be beneficial on highly infected wounds that may be limb-threatening if located on an extremity.⁷⁷⁻⁸⁰ The use of GranuFoam Silver™ Dressings or V.A.C. Instill[®] Therapy does not reduce the need for initial aggressive debridement of healthy tissue.

Exudate Management

The important characteristics of exudate are viscosity, volume, and odor. Another factor to consider is the origin of the exudate, such as surface exudate (ie, biofilm) or deep exudate. A key distinction should also be made between an exudate that is associated with an infection versus an exudate associated with edema and loss of perfusion. The main objectives of exudate management include optimizing the wound environment, controlling bioburden, maintaining the integrity of the surrounding skin, and preserving quality of life by minimizing leakage, odor, and wound pain.⁸¹

A moist environment is critical to optimal healing, and a delicate balance needs to be achieved so that excessive fluid does not cause maceration or exces-

sive desiccation result in slow epidermal regeneration.^{44,55} Exudate management is extremely important in chronic wounds because the fluid contains high levels of MMPs (eg, collagenases and elastases), high levels of inflammatory cell types, and other inhibitory factors that impair wound healing.^{13,81,82}

Argenta and Morykwas first demonstrated in 1997 that large exudate volumes (up to 1000 mL) were safely removed from large NPWT/ROCF-treated ulcers.¹³ DeFranzo et al reported that ≤ 500mL exudate in a 24-hour period was removed from lower-extremity wounds with exposed bones with NPWT/ROCF use.⁸³ Kamolz et al had similar results, removing up to 500 mL of exudate from a partial-thickness burn wound.³²

Wound Margin/Epidermal Edge

The condition of the wound margin is another important aspect of wound healing. Slow-advancing or non-advancing epidermal margins signal chronic wounds with non-migrating keratinocytes and non-responsive wound cells.⁵⁴ Undermining, which may indicate infection, may be present at the wound edge, preventing cells from proliferating and migrating normally during wound healing.⁴⁴ Thus, debridement of the entire wound, including the epidermal edges, is vital for wounds to heal.

Wound Reconstruction

Role of NPWT/ROCF in Reconstruction

Once a healthy wound bed is

achieved, the next step is to determine the appropriate method of wound closure to successfully preserve a limb. Table 5 lists the various devices and products used in wound treatment during limb preservation. Although several options exist, the literature has shown that NPWT/ROCF is a proven advanced therapy system for treating acute and chronic wounds, as it results in rapid wound bed preparation and earlier wound closure,^{13,16,84,85} which makes it a viable option to assist in limb preservation. NPWT/ROCF can be used to help preserve a limb because it promotes both a healthy wound bed and shrinks the wound size.

Limb Preservation

To support the use of NPWT/ROCF in limb preservation, Frykberg and Williams compared its use to traditional wound therapies (control) in reducing the incidence of lower extremity amputations in DFU patients.⁸⁶ This retrospective study analyzed a large set of payer claims data (commercial and Medicare claims) to compare amputation rates. Overall, the data showed that NPWT/ROCF-treated patients had a lower incidence of amputations compared to control-treated patients, with significantly fewer amputations performed within the Medicare claims data set (12.1% versus 16.6%, respectively; $P=0.0494$).⁸⁶

Additionally, Armstrong and Lavery investigated whether NPWT/ROCF improved the proportion and rate of wound healing after partial foot amputation as compared to MWT in dia-

Table 5. Devices and Products Used in Wound Treatment During Limb Preservation

Devices/products
NPWT/ROCF
Hyperbaric oxygen therapy
Biologics/dermal substitutes
Growth factors (eg, platelet-derived growth factor, fibroblast growth factor)
Ultrasound

betic patients.¹⁴ The results of this RCT demonstrated that more patients healed in the NPWT/ROCF group as compared to the MWT group. The rate of wound healing and granulation tissue formation (ie, 76% to 100% formation) in the wound bed was significantly greater in the NPWT/ROCF group over the 16-week study period. The authors concluded that it was an effective treatment for diabetic foot wounds, which could translate into potentially fewer re-amputations than standard care.¹⁴ This conclusion was further supported by an economic analysis by Apelqvist et al based on data from this RCT.⁸⁷ Their results showed that fewer re-amputations occurred in the NPWT/ROCF group than in the MWT group (2 versus 7, respectively) with all major amputations occurring in the MWT group.⁸⁷

A second RCT, performed by Blume

et al, showed that a significantly greater percentage of foot ulcers achieved complete ulcer closure with NPWT/ROCF than with Advanced Moist Wound Therapy (AMWT) within the 112-day active treatment phase (43.2% versus 28.9%, respectively; $P=0.007$).³⁵ More importantly, NPWT/ROCF patients experienced significantly fewer secondary amputations as compared to AMWT patients (7/169 [4.1%] versus 17/166 [10.2%], respectively; $P=0.035$).³⁵ Subsequently, the limb preservation team at Yale–New Haven Hospital, New Haven, Conn, has incorporated NPWT/ROCF into an algorithm for treatment of the at-risk limb. This has enabled the team to preserve length and function, thereby improving limb preservation outcomes.

Secondary Intention

NPWT/ROCF can be useful when healing a wound by secondary intention. The ideal indication for such a treatment is a small, superficial wound with a well-vascularized bed. When healing by secondary intention, NPWT/ROCF provides a means of promoting granulation tissue formation, removing exudate, and drawing the wound edges together for better approximation.^{13,14,20,28,30} The patient's ability to heal should also be used as a criterion for when and how long to use NPWT/ROCF for healing by secondary intention. Patient history is the strongest predictor of ulceration, amputation, and healing. A history of difficulty in healing may prompt extended use of NPWT/ROCF before definitive

closure. Under those circumstances, it is critical to regularly measure the wound to ensure forward progress. Reevaluate continued treatment if the wound stalls.

Biologics/Dermal Substitutes

Dermal substitutes are collagen matrices applied to the wound site that become vascularized by the underlying tissue, forming a neodermis. Biologics are cultured skin cells that secrete the necessary growth factors to promote healing. These substitutes are used on patients who may not have good donor sites for a split-thickness skin graft (STSG) or whose wounds are not ready for an STSG.⁸⁸ Espensen et al described the use of NPWT/ROCF with bioengineered tissue grafting in diabetic foot wounds.⁸⁹ When used over a dermal matrix (ie, Integra[®]), it creates an environment to promote perfusion for revascularization and acts as a platform for subsequent STSGs. These recommendations are supported by a study that used it in combination with Integra on patients with complex wounds.⁹⁰ The results showed that the time to vascularization utilizing Integra was improved compared to previous results by Burke et al.^{90,91} In addition to the retrospective study and case series previously discussed, a RCT by Jeschke et al further showed that patients with large defects who received fibrin glue-anchored Integra and postoperative NPWT/ROCF had a shorter mean period from Integra coverage to skin grafting as compared to the conventional treatment group (10 ± 1 day versus 24 ± 3 days, respectively; $P<0.002$).⁹²



Furthermore, Steinberg presented 3 case studies using NPWT/ROCF in conjunction with dermal substitutes and found that the combination of therapies helped prepare the wound for other treatment modalities (ie, STSGs) and facilitated granulation tissue formation in the wound bed.⁸⁸

Skin Grafts and Flaps

The success of skin grafts and flaps is vital for limb preservation. Several studies, including RCTs, have already been published regarding the use of NPWT/ROCF for the management of skin grafts and as a bolster to enhance graft take.⁹²⁻⁹⁷ Scherer et al showed that the NPWT/ROCF group required significantly fewer repeated STSGs as compared to the bolster dressing group (1 out of 34 versus 5 out of 27 patients, respectively; $P=0.04$), suggesting more effective support of graft survival than traditional bolsters.⁹³ In a prospective RCT, Moisisidis et al showed that the NPWT/ROCF group had significantly better qualitative graft take ($P<0.05$) as compared to the standard group.⁹⁸ The use of NPWT/ROCF over STSGs minimizes shear forces and prevents seroma, hematoma, and final skin graft slough.

NPWT/ROCF also helps manage flaps,³⁰ a quality important for limb preservation. Dr. Attinger presented data in a series in which 17 consecutive local flaps used to cover ankle wounds were initially covered with NPWT/ROCF for the first 3 postoperative days. All flaps completely survived, and all wounds went on to heal. NPWT/ROCF has

also been used to successfully secure STSGs on free muscle flaps with no compromise to free-flap viability.⁹⁹ NPWT/ROCF is a useful adjunct in flap surgery and for the success of limb preservation surgery.

Cost Implications

Treatment costs must be considered when using a multidisciplinary approach to limb preservation. The costs of amputations and subsequent care far outweigh the costs of using different therapies to preserve a limb. For example, treating an uncomplicated diabetic foot ulcer has been estimated to cost approximately \$8,000. An infected ulcer increases the cost to \$17,000. Finally, if an amputation is necessary to treat the infected ulcer, the cost increases dramatically to \$45,000.¹⁰⁰ Another report calculated the cost of a lower extremity amputation to be \$70,434, with estimated annual US expenditures for diabetes-related amputations to be approximately \$11.7 billion.¹⁰¹

Additional costs are incurred with reamputations, especially those related to dysvascular limbs. Dillingham and colleagues examined reamputations, mortality rates, and costs among a large cohort of patients with dysvascular amputations over 12 months using data from the Centers for Medicare and Medicaid Services claims files for 1996 and 1997.¹⁰² The data showed that 26% of patients (N=3565) with a lower-limb amputation required a second amputation within 12 months and more than one-third died within 1 year. When

costs for 5% of the study sample were extrapolated to the entire Medicare populations of dysvascular amputees, the medical care costs exceeded \$4.3 billion.¹⁰²

A multidisciplinary approach for limb preservation needs to be more cost-effective than amputations in treating patients and returning them to function in the shortest amount of time. Thus, optimizing wound management options will be beneficial for the patient (eg, improving time to wound closure and preventing amputation) and the healthcare system (ie, providing cost savings).¹⁶

Studies have demonstrated that NPWT/ROCF can be a cost-effective treatment in relation to the overall cost of treating and closing a wound.¹⁰³⁻¹⁰⁵ In regard to limb preservation, Apelqvist et al reported on the resource utilization and economic costs of care for the diabetic patients with post-amputation wounds based on the RCT conducted by Armstrong and Lavery.^{14,87} Not only did NPWT/ROCF patients have fewer reamputations as compared to MWT in the study period, the average total cost to achieve healing was lower (\$25,954 versus \$38,806, respectively).⁸⁷

Additionally, Dr. Vickie Driver presented economic data at the 2008 World Union Wound Healing Society based on inpatient data from the multicenter RCT evaluating the safety and clinical efficacy of NPWT/ROCF compared to advanced moist wound therapy for the treatment of diabetic foot ulcers and reported a cost savings with its use, which was associated with

a decrease in amputations.^{35,100}

Limitations

Because there is a limited number of RCTs reporting the use of NPWT/ROCF, data from Level III or Level II studies have been referenced in discussions of wound types for which Level I evidence is not available. For example, NPWT/ROCF evidence cited in sections on infection and exudate management consists of Level III or II studies.

Conclusion

A panel of experts convened to discuss their experience using a multidisciplinary approach to limb preservation and the role of NPWT/ROCF in the treatment of these complex wounds. The inclusion of various disciplines and/or skill sets is critical to optimize chances for limb preservation. The disciplines that should be available include vascular, podiatric, orthopedic, and plastic surgeons, and infectious disease specialists, endocrinologists, and wound specialists. Without those specialty sets available, limb preservation can be severely hampered and may require transfer of the patient to a facility where those skills are available. NPWT/ROCF may be a useful temporary bridge dressing until the needed expertise becomes available. Effective debridement, aggressive infection management, exudate management, and wound edge approximation along with correction of biomechanical abnormalities, offloading, and good vascularization are extremely important for limb preservation. Once the wound has been

converted to a healing wound, it can be closed through a variety of methods, including healing by secondary intention, delayed primary closure, skin graft, or flap closure. Special attention should always be paid to reconstructing a biomechanically viable limb to minimize the risk of recurrent ulceration. Based on personal experience and published evidence, the panel concluded that the use of NPWT/ROCF during the various stages of healing and reconstruction can be a very useful adjunct to augment the multidisciplinary approach needed for successful limb preservation.

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Descriptions of Panel Members' Limb Preservation Centers

One of the clinics in the United States offering multidisciplinary limb preservation is the Center for Wound Healing at Georgetown University, in Washington, DC. Drs. Christopher Attinger, John Steinberg, Richard Neville, Paul Cooper, and Francis McGuigan have developed an integrated team to treat patients at risk for amputation. The clinic can treat 20 to 40 limb preservation patients at a time. Dr. Attinger, founder and lead plastic surgeon, says a coordinated, multidisciplinary team using established treatment protocols can "heal wounds that no single specialist can." His center saves 97% of diabetic limbs from full amputation.

Yale University School of Medicine in New Haven, CT, houses a limb preservation center with a strong podiatry and vascular surgery team. Drs. Bauer Sumpio and Peter Blume use vascular, podiatric, and plastic surgery interventions to preserve at-risk limbs. The center collaborates with endocrinologists and infectious disease specialists to coordinate patients' medical management.

At Boston University Medical Center (BUMC), vascular surgeon Dr. Gary Gib-

bons was taught by Dr. Joslin, who was the first to combine vascular and podiatric surgeries to decrease amputations. Dr. Gibbons says the Boston site is unique because it is patient-centered and evidenced-based. Dr. Vickie Driver, who started a US Army limb preservation center 14 years ago, is now part of BUMC. She was recruited to develop the center's research and education arm. It now has a multidisciplinary, dedicated fellowship and international scholars program that focuses on cutting-edge research in limb preservation and tissue repair. The center is dedicated to improving amputation rates in underserved sectors by increasing affordable access to state-of-the-art wound care.

Scott & White Hospital in Temple, TX, offers a multi-specialty limb preservation physician group. Dr. Lawrence Lavery, a podiatrist at Scott & White, says that defects in specialty care, such as lack of plastic surgeons, lead to less desirable and more time-consuming reconstructive techniques. The group recently added a plastic surgeon who specializes in reconstructive techniques for wound coverage.

Dr. Warren Joseph of Roxborough Memorial Hospital in Philadelphia notes that limb preservation centers are different

from wound care centers, which typically concentrate on non-lower-extremity issues such as decubitus ulcerations and surgical wounds. Though these are vitally important services, many centers do not have enough advanced specialists with appropriate levels of interest in saving limbs.

Dr. Allen Holloway manages an outpatient clinic focused on burns at Maricopa Medical Center in Phoenix. He has previously managed this institution's stand-alone wound clinic with limited access to specialists.

The Limb Preservation Clinic at Madigan Army Medical Center in Tacoma, WA, developed by Drs. Driver and Charles Andersen, has continued to develop by adding Dr. Thomas S. Roukis. The clinic has four vascular surgeons, a vascular PA, a non-invasive vascular laboratory with three RVTs, a wound care clinic, and two limb preservation fellows, and offers an accredited 2-year limb preservation fellowship.

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Contributor Participation

Contributors	Affiliation	Specialization	Limb Preservation Approach
Dr. Christopher Attinger	Georgetown University Hospital	MD, FACS, Director	<ul style="list-style-type: none"> Part of multidisciplinary team at the Center for Wound Healing at Georgetown University that includes vascular surgery, plastic surgery, orthopedic surgery, podiatry, infectious disease, rheumatology, hematology, endocrinology, hyperbaric medicine, pedorthetist, prosthetist, and physical therapy.
Dr. John Steinberg	Georgetown University School of Medicine, Department of Plastic Surgery	DPM, FACFAS, Assistant Professor	
Dr. Francis McGuigan	Georgetown University Hospital	MD, Orthopedic Surgery	
Dr. Bauer Sumpio	Yale University School of Medicine, Department of Surgery	MD, PhD, FACS, Professor and Section Chief, Vascular Surgery	<ul style="list-style-type: none"> Part of a limb preservation center offering podiatry, vascular, and plastic surgery.
Dr. Peter Blume	Yale School of Medicine, Department of Orthopaedics Section of Podiatric Surgery	DPM, FACFAS, Assistant Clinical Professor of Surgery, Anesthesia and Orthopedics and Rehabilitation	
Dr. Gary Gibbons	Quincy Medical Center; Boston University School of Medicine	MD, Executive Director of Foot-care, Vascular, and Endovascular Specialists of Quincy Medical Center; Professor of Surgery	<ul style="list-style-type: none"> A multidisciplinary limb preservation clinical and research team at the Boston University Medical Center. It includes vascular, podiatric and plastic surgery, cardiology, vascular medicine, infectious disease, endocrinology, pedorthetist, prosthetist, and both vascular and limb preservation/tissue repair fellowship programs.
Dr. Vickie Driver	Boston Medical University, Department of Surgery, Clinical Research Foot Care, Endovascular and Vascular Services	DPM, MS, FACFAS, Director, Clinical Research: Wound Care, Foot Care, Endovascular and Vascular Services, Associate Professor of Surgery	
Dr. Lawrence Lavery	Scott and White Hospital; Texas A&M Health Science Center	DPM, MPH, Professor of Surgery	<ul style="list-style-type: none"> Part of a multispecialty physician group.
Dr. Warren S. Joseph	Roxborough Memorial Hospital, Department of Podiatric Surgery; Veterans Administration Medical Center, Coatesville, PA	DPM, FIDSA, Podiatric Medicine, Infectious Diseases	<ul style="list-style-type: none"> Part of a diversified wound center that includes an infectious disease physician, internists, and a podiatric surgeon.
Dr. Allen Holloway	Arizona Burn Center, Department of Surgery, Maricopa Medical Center	MD, Director of Burn Outpatient Services; Director, Vascular Lab	<ul style="list-style-type: none"> Part of a multidisciplinary team at a major burn center.
Dr. Charles A. Andersen	Madigan Army Medical Center, Wound Care Clinic	MD, FACS, FAPWCA, Chief and Medical Director	<ul style="list-style-type: none"> Part of a vascular, endovascular, limb preservation surgery service.

