Int J Clin Exp Med 2017;10(8):12259-12267
www.ijcem.com /ISSN:1940-5901/IJCEM0047199

Original Article

New protocol to treat Chinese patients with wound-derived acute severe illness

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Received December 23, 2016; Accepted March 27, 2017; Epub August 15, 2017; Published August 30, 2017

Abstract: Background and aim: Treatment of severe acute wounds caused by major injury or infection remains challenging. These wounds are often accompanied by comorbidities such as septic shock or multiple organ failure, in which the prognosis is poor. In China, patients with wound-derived acute severe illness are usually treated by conventional salvage approach, in which life support measures are prioritized before vital organ protection and wound repair. To improve patients' prognosis and quality of life after treatment, our institute established a new salvage protocol that simultaneously provided life-support measures and wound care for patients with wound-derived acute severe illness. This study provided a retrospective review on the outcomes of patients treated with the new salvage protocol. Methods: Records from 2011 to 2013 at Peking Union Medical College Hospital in Beijing, China were reviewed to identify patients with wound-derived acute severe illness treated with the new salvage protocol. The protocol included the proactive wound treatment using negative pressure wound therapy (NPWT). During the treatment with NPWT, emergency department and ICU administered adjunctive therapies as needed. Results: Fifty-six patients were treated with the new protocol. All patients had septic shock and 29/56 (51.8%) required mechanical ventilation. Of patients treated according to the new protocol, 21/56 (37.5%) fully recovered and 29/56 (51.8%) improved sufficiently to be transferred to a general ward. Six patients (10.7%) died of causes unlikely related to NPWT. Conclusion: The new salvage protocol implemented in our institute provided wound care proactively and is beneficial to patients with wound-derived acute severe illness.

Keywords: Wound, emergency treatment, critical, salvage treatment mode, NPWT

Introduction

Acute or chronic wounds affect millions of people around the world and represent a major health problem. It has been estimated that persistent wound affected nearly 1% of the global population and cost around 5% of all medical expenses [1, 2]. To date, treatment of complex acute wounds resulting from injury, infection, or iatrogenic factors remains a challenge in clinical practice.

In China, conventional salvage treatment always provides life-saving measures first, while wound treatment is the last to be performed. Patients who have a wound that is the primary cause of their critical illness are classified as "patients with wound-derived acute severe illness". These patients are often hospitalized in an emergency department or an intensive care unit (ICU); their wounds are mostly resulted from major injury or infection. For patients who have wounds caused by iatrogenic factors, they usually have an underlying disease as well as a history of surgeries. These patients are mostly critically ill with septic shock and organ failure. The treatment strategies of patients with wound-derived acute severe illness are determined by physicians across different specialties. Most of the time, complex surgeries, such as amputation, are needed for patients with significant morbidities. These patients, unfortunately, usually have poor clinical outcomes. Under the conventional treatment strategy, patients with complex acute wounds often missed the best, earliest opportunities for wound treatment. The delayed healing of the wound resulted in a vicious cycle of new infections, fluid loss, etc, which led to increased treatment time, higher medical expenses, and reduced quality of life due to a poor prognosis.

Negative pressure wound therapy (NPWT) is a technology that has significantly advanced the treatment of wounds throughout the past 2 decades. NPWT, also called "vacuum-assisted wound closure", is an integrated system (V.A.C.® Therapy) [3, 4] that involves placing a polyurethane foam dressing (V.A.C.® Granu Foam™) into an open wound, sealing the area with an adhesive film, and connecting a tube attached to the dressing to a therapy unit that provides continuous or intermittent negative pressure (monitored by Sensa T.R.A.C.™ technology) at the wound site. Exudate is collected into an attached canister. NPWT is intended to create an environment that promotes wound healing by secondary or tertiary (delayed primary) intention by preparing the wound bed for closure, reducing oedema, promoting granulation tissue formation and perfusion, and by removing exudate and infectious material [5, 6].

During the period from 2011 to 2013, the plastic surgery department collaborated with the emergency department and ICU team at Peking Union Medical College Hospital (PUMCH; Beijing, China) to establish a new salvage treatment protocol. The protocol included proactive wound treatment using NPWT, as well as inter-departmental efforts to provide life-saving measures. The purpose of this retrospective review is to report our experiences of the use of this new protocol to treat patients with wound-derived acute severe illness.

Materials and methods

Patients and treatments

All the patient data were identified and collected in accordance with institutional guidelines. Patients gave consent on the use of identified wound photos and clinical data for medical research. Patients with wound-derived acute severe illness were admitted to the hospital and had consultation with the physicians from plastic surgery department. All of the patients had their wounds treated in the following procedures: 1) Wounds were cleansed, disinfected, and debrided at the bedside: 2) A polyurethane foam dressing (V.A.C.® Granu Foam™, KCI, an Acelity company, San Antonio, TX, USA) was applied, and an adhesive drape and tubing were used to cover the wound: 3) NPWT (V.A.C.® Therapy; KCI, Acelity company, San Antonio, TX, USA) was used at the wound, with pressure at -125 mmHg to -200 mmHg. Since NPWT was a key step in the treatment for patients in this study, the procedure was discontinued only when sepsis was under control or shock was reversed. During the treatment with NPWT, emergency department and ICU administered adjunctive therapies as needed.

Statistical analysis

Categorical data was reported as frequency (%) and continuous data was reported as mean ± sd. ANOVA or Kruskal-Wallis test were used to compare continuous data among patients with different outcome, the row mean scores different method of Cochran-Mantel-Haenszel test were used to compare the categorial data among patients with different outcome. Statistical analysis was performed using SAS 9.3. Give that sample size of this study was small, multivariate analysis was abandon. A value of $P<0.05$ was considered as statistically significant.

Results

The patient cohort included fifty-six patients with wound-derived acute severe illness, in which 29 (51.8%) were male and 27 (48.2%) were female. Their ages ranged from 17 to 82 years old; the median age was 45, with two patients under the age of 20. None of the patients had their first visit at the plastic surgery department. Their underlying diseases included diabetes (32.1%), bed-ridden/immobile (17.9%), organic heart disease (16.1%), tumor (14.3%), psoriasis (3.6%), familial benign Pemphigus (1.8%), and Behcet's disease (1.8%). Wounds were of various aetiology, including iatrogenic invasive manipulation (32.1%), acute open wound (23,2%), skin and soft-tissue infection (19.6%), skin and soft-tissue defect (17.9%), crush injury of lower limb (5.4%), and blast injury (1.8%). Patients presented multiple comorbidities. All of the patients had septic shock, and more than half of them had bacteraemia (67.9%) and mechanical ventilation (51.8%). The detail of the demography and clinical characteristics of patients were summarized in **Table 1**.

All of the patients were treated with NPWT with the treatment duration ranging from 3 to 29 days (median 11.5 days). During the use of NPWT, majority of the patients (38/56) received

Table 1. Demography and clinical characteristic of patients treated with NPWT (n=56)

Characteristics	Value	Characteristics	Value
Gender, n (%)		Wound aetiology, n (%)	
Female	27 (48.21)	Iatrogenic invasive manipulation	18 (32.14)
Male	29 (51.79)	Acute open wound	13 (23.21)
Age (year)		Skin and soft-tissue infection	11 (19.64)
Mean ± sd.	45.02 ± 16.50	Skin and soft-tissue defect	10 (17.86)
Min	17	Crush injury of lower limb	3 (5.36)
Max	82	Blast injury	1 (1.79)
Underlying Diseases, n (%)		Comorbidities, n (%)	
Diabetes	18 (32.14)	Septic shock	56 (100.00)
Bed-ridden/immobile	10 (17.86)	Bacteremia	38 (67.86)
Organic heart disease	9 (16.07)	Mechanical ventilation	29 (51.79)
Tumor	8 (14.29)	Poor circulation	24 (42.86)
Psoriasis	2 (3.57)	Unconsciousness	19 (33.93)
Familial benign Pemphigus	1 (1.79)	Renal failure	13 (23.21)
Behcet's disease	1 (1.79)	Limb defect	8 (14.29)
		Exposure of viscera	6 (10.71)

Table 2. Other therapeutic measures and outcome of patients treated with NPWT

Characteristics	Value
Other therapeutic measures	
Split-thickness skin grafting	17 (30.36)
Skin flap transfer	9 (16.07)
Debridement only	6 (10.71)
Debridement and suture	6 (10.71)
No	18 (32.14)
Duration of NPWT (day)	
Mean ± sd.	11.50 ± 7.85
Min	3
Max	39
Outcome	
Recovered	21 (37.50)
Improved*	29 (51.79)
Death	6 (10.71)

*Transferred to general ward for further treatment.

other therapeutic measures such as debridement, primary suture, split-thickness skin grafting, and skin flap transfer. Eighteen patients were treated only with NPWT (with regular dressing changes), and no other therapeutic measures were given (**Table 2**). The clinical outcome of the patients were encouraging; most of them improved considerably, either in terms of general physical condition or local condition of the wound. Fifty out of fifty-six patients had the wounds recovered or improved (**Table 2**).

We further analyzed the clinical characteristics of the patients with different outcomes (recovered, improved, and death) (**Table 3**). For patients who were recovered (37.5%), they were mostly young and middle-aged (mean: 35.7 years old). A total of 29/56 (51.8%) patients had the conditions improved and were transferred to general wards for further treatment. These patients were generally older (mean: 46.5 years old). Six patients (10.7%), all over the age of 40 (mean age at 70.67), died of causes unlikely related to NPWT. These 6 patients were all bed-ridden/immobile (P=0.000), and no other therapeutic measures were performed on these 6 patients during the NPWT treatment period (P=0.000), suggesting the importance of receiving adjunctive therapy in combination with the NPWT.

Case studies

The following 2 cases demonstrated the successful use of the new salvage treatment protocol with NPWT which were worth to be described in details.

Case 1: necrotising soft tissue infection on forearm:

A 38-year-old male presented with furuncles on his right forearm that were rapidly developing into severe skin and soft-tissue infections, nec-

Table 3. Comparison of clinical characteristics of patients with different clinical outcomes

Characteristics	Recovered n=21	Improved n=29	Death n=6	*P*
Age (year), mean ± sd.	35.71 ± 12.28	46.45 ± 14.47	70.67 ± 7.23	0.000
Duration of NPWT (day), mean ± sd	10.1 ± 5.46	9.62 ± 5.52	25.5 ± 11.15	0.003
Gender				0.119
Female	12 (57.14)	14 (48.28)	1 (16.67)	
Male	9 (42.86)	15 (51.72)	5 (83.33)	
Other therapeutic measures				0.000
Skin flap transfer	4 (19.05)	5 (17.24)	0 (0.00)	
Debridement only	1 (4.76)	5 (17.24)	0 (0.00)	
Debridement and suture	6 (28.57)	0 (0.00)	0 (0.00)	
No	2 (9.52)	10 (34.48)	6 (100.0)	
Split-thickness skin grafting	8 (38.10)	9 (31.03)	0 (0.00)	
Bacteremia	15 (71.43)	21 (72.41)	2 (33.33)	0.212
Mechanical ventilation	10 (47.62)	15 (51.72)	4 (66.67)	0.465
Poor circulation	9 (42.86)	13 (44.83)	2 (33.33)	0.811
Unconsciousness	3 (14.29)	11 (37.93)	5 (83.33)	0.002
Renal failure	4 (19.05)	7 (24.14)	2 (33.33)	0.468
Limb defect	6 (28.57)	2 (6.90)	0 (0.00)	0.023
Exposure of viscera	5 (23.81)	1 (3.45)	0 (0.00)	0.023
Diabetes	4 (19.05)	10 (34.48)	4 (66.67)	0.033
Bed-ridden/immobile	0 (0.00)	4 (13.79)	6 (100.0)	0.000
Organic heart disease	0 (0.00)	7 (24.14)	2 (33.33)	0.013
Tumor	2 (9.52)	5 (17.24)	1 (16.67)	0.500
Wound aetiology				0.052
Blast injury	1 (4.76)	0 (0.00)	0 (0.00)	
Skin and soft-tissue defect	3 (14.29)	6 (20.69)	1 (16.67)	
Acute open wound	9 (42.86)	4 (13.79)	0 (0.00)	
Skin and soft-tissue infection	2 (9.52)	6 (20.69)	3 (50.00)	
Crush injury of lower limb	0 (0.00)	3 (10.34)	0 (0.00)	
Iatrogenic invasive manipulation	6 (28.57)	10 (34.48)	2 (33.33)	

rotizing fasciitis, and septic shock. The skin swelled prominently, resulting in tension blisters all over its surface. Despite incision and drainage performed previously in a different hospital, the patient was not improving. While being transported to PUMCH, the patient was conscious but indifferent, and his non-invasive blood pressure was not detected. At the emergency room, anti-shock and other life support systems were administered. Peripheral blood leukocytes were 60×10^9/L at peak, and leukemoid reactions occurred. The culture of a sample taken from the deep forearm wound (**Figure 1A** and **1B**) as well as a blood culture revealed pan-drug resistant *Acinetobacter baumannii*. Systemic antibiotics were administered.

The plastic surgery and orthopaedics departments were invited to an emergency consultation, during which emergency department surgeons proposed to remove the focus of infection with an immediate amputation to help control the septic shock. Because this patient was a manual labourer and the only able-bodied person in his household, both the patient and his family expressed a strong desire for limb salvage. During physical examination, the plastic and orthopaedic surgeons observed relatively good sense and mobility of the distal end of the limb, great vessels and nerves exposed on the wound surface, some necrotic muscle and skin, and copiously draining exudate (over 2000 mL every 24 hours).

The multidisciplinary team ultimately decided to initiate NPWT (**Figure 1C**) and postpone the amputation. After 2 weeks of NPWT, the wounds were filled with beefy red granulation tissue

Figure 1. Necrotising soft tissue infection on radialis (A) and ulnaris (B) at presentation to emergency room. V.A.C.® Therapy was initiated over the wounds at -125 mmHg (C). Wound at 2 weeks after V.A.C.® Therapy was initiated (D). After 4 weeks of V.A.C.® Therapy, the wound was ready for closure via STSG (E). Patient was discharged with healed forearm at 3 weeks post STSG (F).

and considerably smaller (**Figure 1D**). After 3 weeks of NPWT, the drainage volume significantly decreased to 100 mL every 24 hours, and the tension blisters disappeared. With a gradual decrease in the dosage of vasoactive drugs, the patient's vital signs were stable, and the number of the peripheral blood leukocytes returned to the normal level. At 4 weeks, the wound was ready for a split-thickness skin graft (STSG) (**Figure 1E**) and NPWT was discontinued. After the wound was surgically debrided, an STSG was applied. The patient fully recovered and was discharged with a healed forearm 3 weeks post STSG application (**Figure 1F**).

Figure 2. Lateral (A) and medial (B) lower leg wounds at presentation to ICU. One V.A.C.® Therapy system was applied to both wounds using a bridging technique (C and D). Two weeks after V.A.C.® Therapy was initiated, both wounds (E and F) were ready for skin graft closure; split-thickness skin grafts were applied on this day. At the 4-month follow-up post STSG, both wounds (G and H) were closed.

Case 2: osteofascial compartment syndrome and crush syndrome in lower leg, plus acute renal failure:

A 31-year-old female noticed that her left lower leg was swollen and numb and reported sensory and movement disturbance below the knee joint after she arrived home intoxicatedly. She fell down and slept for 22 hours. Patient was diagnosed with osteofascialcompartment-syndrome. Incision, drainage, and debridement were performed in a different hospital, but the patient's condition was not improved. When admitted to PUMCH, the patient suffered from hypovolaemic shock, metabolic acidosis, hyperpotassemia, anuria (volume of the deep red urine was less than 100 mL for 24 hours), and the levels of serumcreatinine, myoglobin and creatine kinase were significantly increased.

On the patient's swollen left shank, two symmetrical incisions were made, each approximately 30 cm long touching the muscular layers (**Figure 2A** and **2B**). Below the knee joint, there was a significant weakness of deep and superficial sensibility, myodynamia of grade 0, and foot drop. Blood and wound secretion cultures revealed *Escherichia coli* infection. A diagnosis of crush syndrome with acute renal failure was clear.

Soon after her hospitalization, the patient was sent to an ICU where bedside renal replacement therapy and anti-infective therapy were administered. After consultation, the plastic surgery department immediately applied NPWT at the bedside (**Figure 2C** and **2D**). As a large amount of deep red drainage was discharged into the canister, the urine colour gradually lightened, and serum myoglobin and creatine kinase levels decreased. Within 2 weeks of NPWT application, the urine volume gradually increased, the amount of serumcreatinine gradually returned to the normal level, and both the sensibility and myodynamia of the limb were recovered to some extent. At approximately 2 weeks post initiation of NPWT, granulation tissue covered the wound surface (**Figure 2E** and **2F**). At this time, NPWT was discontinued, surgical debridement was performed, and an STSG was applied for wound repair. After the surgery, physical therapy was administered. Two weeks later patient was discharged and could already walk on crutches. **Figure 2G** and **2H** show the healed wounds 4 months after placement of the STSG.

Discussion

The top priority in the conventional salvage treatment for patients with wound-derived acute severe illness is to save life and then conserve limb function. The purpose of the new salvage protocol evaluated in this study is to provide life saving measures as well as wound healing treatment that ultimately improve the quality of life of the patients. In patients with wound-derived acute severe illness, wound treatment is particularly important as it is the primary cause of the illness. Better wound treatment generally results in improved physical condition for these patients. Wound treatment should therefore be incorporated early into the whole treatment paradigm, and proceed simultaneously with life support measures. To implement such strategy, plastic surgeons will need to cooperate with other departments to proactively ameliorate local areas, and to provide other treatments as needed.

In the Case Study #1 reported, if traditional salvage treatment methods at PUMCH had been followed, the patient would have received an amputation. Consequently, the amputation might have been expanded because of tissue oedema, obscured boundary of necrosis, and other issues. Primary closure of the wound would have been highly unlikely, and wound repair would have been the last work to be conducted by the plastic surgery department. In addition, the patient would have run the risk of a surgery during the acute phase and would have suffered from great pain and loss, as acute necrotizing fasciitis is often accompanied by whole-body toxic shock with a mortality rate of 30%-43% with late diagnosis and treatment [7]. The key to proper treatment for this patient was to immediately remove the focus of infection, ease tissue oedema, and reduce circulatory burden.

In Case Study #2, the patient was diagnosed with relatively uncommon osteofascial compartment syndrome, crush syndrome, and acute renal failure. Since crush syndrome is commonly seen in construction accidents, traffic accidents, and earthquakes, it was speculated that the patient, who was not overweight and did not likely suffer from her own body pressure while she was lying down, may have been under pressure for a long period of time beneath tables, chairs or other pieces of furniture that

were knocked down and not removed by anyone else. There are three severity grades for crush syndrome [8], and with evident myoglobinuria, shock, hyperkalaemia and kidney failure, this patient was critically ill with crush syndrome of grade III with a survival chance of approximately 50% [9]. Considering such rapid deterioration, some surgeons in the PUMCH multi-disciplinary team believed that such severe case with evident myonecrosis that cannot be eased by incision and drainage, amputation should be administered immediately to eliminate the pathologic and physiological cascade reactions resulted from widespread myonecrosis [10]. Since amputation was unacceptable to the patient, the keys to proper treatment in this case were elimination of her internal necroses, quick restoration of renal function, and maximum preservation of her affected limb.

To play an active role in improving treatment procedures for patients, the plastic surgery department implemented the use of porous foam dressings with NPWT that provided stable and controllable negative pressure [3, 11]. NPWT (V.A.C.® Therapy, KCI, Acelity company, San Antonio, TX, USA) was approved for commercialization in China in October 2010. Although it has widely been used for wound treatment in many countries, it is not commonly used in China. In addition, most of the reports addressed the use of NPWT in chronic wound treatment, yet published data on the use of NPWT in complex acute wound are still limited. For an instance, there are questions on whether adjunctive NPWT should be applied on infected wounds. Based on our experience, patients with infected wounds could be treated with NPWT, but it is important to have debridement and appropriate antibiotics administered. We found NPWT allows sufficient drainage and reduction of tissue oedema, which is in accordance with other clinical reports [5, 6]. The use of NPWT to treat crush syndrome has been reported [12]. Compared with open incision and drainage, NPWT appears to remove infectious materials more effectively. Additionally, NPWT is simple to operate and monitor; it can be applied at the bedside without the risks of anaesthesia and surgery. Also, NPWT does not typically affect the therapies given by other departments.

The approach of treating the wound last for patients with wound-derived acute severe illness is changing in China, although many clinical settings still use the conventional treatment approach. It is important to consider the beneficial effect of treating the local areas (primary cause of the illness) and implement the treatment early on. This strategy will need cooperative efforts from physicians across multiple departments in a hospital. For patients with wound-derived acute severe illness, wound healing is the most important step in the whole treatment. The early healing of the wounds will likely improve the survival of patients. The longer the wound remains open, the greater the risk for infection. Amputation may be needed or life-threatening illness may occur at this stage [13]. In conclusion, NPWT appears to be beneficial for patients with wound-derived acute severe illness and can be adapted in clinical settings in China.

Acknowledgements

The authors thank Karen Beach (Acelity) for editorial assistance in preparation of this paper.

Disclosure of conflict of interest

None.

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