NEGATIVE PRESSURE WOUND THERAPY IN WARTIME WOUNDS – CASE SERIES AND REVIEW OF THE LITERATURE

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ABSTRACT Introduction: For a long time, the military doctrine inarguably stated that wartime wounds must be managed by debridement, lavage, saline-soaked dressing and healing by secondary intention. However, the new reality of the changed warfare and medical support doctrine (improved prehospital care, a higher rate of survivors with extensive soft tissue loss, faster evacuation) forced the change of this paradigm and led to the rapid implementation of NPWT in the treatment of the complex combat wounds. Despite the large body of literature dealing with various aspects of the NPWT, there are few series reporting its use in wartime wounds. The aim of the present study is to report a part of our experience and to perform a state-of-art review of the available literature. Material and methods: A total of three well-documented cases managed by our team are presented – two with blast trauma and one with a gunshot injury. Literature search in PUBMED using the following keywords – combat/warfare wound/injuries. Additionally, a manual search was performed through cross-reference. All reports concerning NPWT of combat wounds of extremities and soft tissue except for case reports were included. The following variables were analysed: mechanism of injury (blast/gunshot), number of the patients and wounds, number of dressing changes, the average time to and type of closure, amputation rate, wound and flap complication rates. Results: A total of 1038 papers was found through PUBMED and additional manual search using cross-references. Of them, 17 titles were considered eligible. Two case reports and four reviews were excluded, whereas ten case series and one comparative study were included in the analysis. Conclusion: Currently, NPWT plays an essential role in the treatment of the combat wounds, but no evidence-based recommendations could be made at this stage. Based on the available literature, it is difficult to conclude that NPWT diminishes the rate of wound infection and amputation rate due to the low quality of the studies and the multifactorial determination of these variables. Nevertheless, except for the well-known benefits such as evacuation of fluids, stimulation of granulation tissue and preparation for definitive closure, in combat setting NPWT offers several significant advantages over the conventional dressings – the reduced need for dressing changes saves the precious and limited wartime resources such as manpower and time, provides safer evacuation with significantly improved patient’s and medical crew’s comfort.

KEYWORDS wartime, combat wounds, extremities, NPWT
INTRODUCTION

Unfortunately, every subsequent war notoriously corroborates the observation of the famous Russian military surgeon N. Pirogov that „The war is an epidemic of injuries”. It is particularly true for the recent conflicts which generated significantly more severely wounded survivors with devastating wounds because of the improved prehospital care. On the other hand, however, the war is also a potent driving force for the medical progress. In his landmark paper „Combat casualty care and the surgical progress”, B. Pruitt tried to delineate the factors influencing the progress [1]. He opposed the tyranny of surgical dogma and lack of knowledge as significant impediments vs the expansion of knowledge base and immediate application of new technology as the accelerators. It is entirely true for the rapid implementation of the negative pressure wound therapy (NPWT) in combat wounds.

Although the idea is not new, NPWT received its worldwide recognition after the essential experimental works of Argenta and Morykwas in 1997 and now is used in a variety of wounds, including as a temporary abdominal closure [2, 3]. For a long time, the military doctrine inarguably stated that wartime wounds must be managed by debridement, lavage, dressing and healing by secondary intention. The Third Edition of Emergency War Surgery (2004) recommended loose nonocclusive or saline-soaked dressings and stated that „soft-tissue war wounds heal well without significant loss of function through secondary intention” and „delayed primary closure may be difficult to achieve in war wounds”, without mentioning of the NPWT [4] as it was incorrectly stated by some authors [5, 6].

However, the new reality of the changed warfare and medical support doctrine (improved prehospital care, a higher rate of survivors with extensive soft tissue loss, faster evacuation and continuous medical care) forced the change of this paradigm and led to the rapid implementation of NPWT in the treatment of the complex combat wounds.

Despite the large body of literature dealing with various indications and aspects of the NPWT, there are few series reporting its use in wartime wounds. The present study aims to report a part of our experience and to perform a state-of-art review of the literature.

MATERIAL AND METHODS


All reports except for case reports reporting outcome after NPWT treatment of combat wounds of the extremities were included. The following variables were analysed: mechanism of injury (blast/gunshot), number of the patients and wounds, number of dressing changes, the average time to and type of closure, amputation rate, wound and flap complication rates.

An informed consents were obtained from the patients or their relatives for the publication of the cases. The Institutional Ethics Committee approved the study.

Case reports

Three well-documented cases are presented.

Case 1:
A 56-years-old female after blast trauma with traumatic amputation of the left forearm and traumatic decollement of the left breast (Figs. 1, 2).

She underwent two dressing changes with split skin grafting four days after trauma (Figs. 3, 4). Unfortunately, she died due to severe primary pulmonary blast trauma.

Case 2:
A 22-years-old soldier suffered blast trauma in Afghanistan by secondary injury from a fragment of rocket grenade. The entry wound was in the left groin without iliac/femoral vessels injury, whereas the exit wound was found in left gluteal area with a concomitant rectal injury.

He underwent damage control laparotomy with sigmectomy and hemostasis with subsequent evacuation to Landsthul and subsequently to our country. NPWT treated the entry wound and closed by the delayed stepwise closure for ten days (Figs. 5, 6).

The exit wound was managed by antibiotic beads and NPWT with six dressing changes and secondary healing after 40 days (Figs. 7-11). Sigmostomy reversal was performed after six months.

Case 3:
A 45-years-old male with GSW. The entry wound was in a sacral area with a fracture of S2-4, injury of the sigmoid colon and rectum, left ureter and urinary bladder. The patient underwent Hartmann procedure, suture of bladder and ureter with bilateral.

He developed postoperative necrotising fasciitis and partial fascial dehiscence (Figs. 12, 13). The wounds were managed by serial debridements and NPWT (Figs. 14-17). The abdominal wound was closed after ten days, whereas the sacral one after 20 days (Figs. 18, 19).

RESULTS

A total of 1038 papers were found in PUBMED and after an additional manual search using cross-references. Of them, 17 titles were considered eligible. Two case reports [7, 8] and four reviews [5, 6, 9, 10] were excluded, whereas ten case series [11-16, 18-22] and one comparative study [17] were included in the analysis. The included studies are summarised in Table 1.

DISCUSSION

The extremities injuries were reported in 52% of the wounded in Iraq and Afghanistan during 2005-2009 according to an extensive
Table 1 The results from the included studies.

<table>
<thead>
<tr>
<th>Author Year</th>
<th>Country</th>
<th>N pts./wounds</th>
<th>Blast/ GSW %</th>
<th>N dressing changes</th>
<th>Days with NPWT</th>
<th>Wound infection</th>
<th>Amputation rate</th>
<th>Flap/graft complications</th>
<th>LOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leninger, 2006 prospective [11]</td>
<td>Iraq 332nd Air Force Theater Hospital</td>
<td>77/88 local residents</td>
<td>63/37</td>
<td>2.2</td>
<td>4.2</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>7.4</td>
</tr>
<tr>
<td>Ullmann, 2006 retrospective [12]</td>
<td>Israel</td>
<td>8 NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Peck, 2007 retrospective [13]</td>
<td>Iraq, 332nd Air Force Theater Hospital</td>
<td>134 vascular injuries, local residents</td>
<td>NA</td>
<td>3.3</td>
<td>NA</td>
<td>3.7</td>
<td>3</td>
<td>4.5</td>
<td>15</td>
</tr>
<tr>
<td>Machen, 2007 NA [14]</td>
<td>CSH, Iraq</td>
<td>over 50 mixed</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Helgeson, 2007 retrospective [15]</td>
<td>USA Walter Reed</td>
<td>16 blast</td>
<td>changing every 3-4 day</td>
<td>19</td>
<td>0</td>
<td>NA</td>
<td>18.7</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Geiger, 2008 retrospective [16]</td>
<td>USA</td>
<td>68 soldiers</td>
<td>55/19</td>
<td>NA</td>
<td>12 in the beginning</td>
<td>Four days at the end of the study</td>
<td>NA</td>
<td>4.8</td>
<td>7/11 pedicle/free flaps</td>
</tr>
<tr>
<td>Penn-Barwell, 2011 retrospective [18]</td>
<td>UK</td>
<td>37 militaries</td>
<td>2.8</td>
<td>15.5</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td># Mansoor, 2013 retrospective [19]</td>
<td>Pakistan</td>
<td>85/106 soldiers</td>
<td>75/25</td>
<td>4.3</td>
<td>12.5</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Maurya, 2016 prospective [20]</td>
<td>India</td>
<td>17 soldiers</td>
<td>blast</td>
<td>3-6</td>
<td>16.5</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Kovalchuk, 2017 prospective [21]</td>
<td>Ukraine</td>
<td>49/37</td>
<td>68/32</td>
<td>1.9 change every 48-96 h</td>
<td>NA</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Trukhan, 2018 NA [22]</td>
<td>Belarus</td>
<td>6</td>
<td>83/17</td>
<td>1-3 devices</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA– non-addressed, CSH – Combat Support Hospital (Role III), LOS – the length of stay,

* All except two were traumatic amputations, # The authors used Chariker-Jeter nonadhesive gauze instead of the commercially available foams.
cohort study based on the Joint Theater Trauma Registry [23], but in some series, they reached up to 70% [13]. It is probably a consequence of the standard use of Kevlar vests by the soldiers leaving the extremities unprotected [24]. Approximately 74% of the wounds in the modern warfare are caused by blast trauma, whereas GSWs accounts for 20%. Our experience in Afghanistan showed the significantly more frequent involvement of the extremities in blast vs GSWs (85% vs 42%) [25]. Despite the lack of recommendation in the literature, the implementation of NPWT in a combat setting started at the beginning of 2003 in Iraq. Unfortunately, RCTs and comparative trials are still lacking, and most of the published studies are of poor quality. Five of the included eleven studies deserve particular comment.

In 2006 Leninger et al. published the first series with 88 wounds in 77 patients admitted within 24 hours after the wounding [11]. The study included local nationals and reported successful definitive wound closure in all cases for average 4.2 days without infectious complications.

Geiger et al. from the Naval Medical Center, San Diego reported 68 cases of wounded militaries [16]. During the 31-months study period, they found significantly increased usage of NPWT from 46% in 2003 to 90% in 2005, along with a decrease of the time to definitive closure from 12 days to 4 days respectively. In contrast, the authors reported 17 days to closure in non-NPWT cases. The rates of acute and chronic osteomyelitis were 24% and 1.6%. Additionally, lower amputation rate in comparison to historical controls (5% vs 45% in Vietnam war) was reported. It, however, may be attributed to the rapid evacuation to tertiary facilities, improved wound care and the earlier coverage of the open fractures. On the other hand, usually, not enough information is available about the late amputations rate due to lack of follow-up.

In a more recent study from Pakistan, Mansoor et al. reported no infectious and flap complications in 105 wounds after average 12.5 days with NPWT. Of them, 49% were closed by delayed primary suture, 25% by split-thickness skin grafts, 11% by flaps and 6% healed by secondary intention. Interestingly, due to financial reasons, the authors used the Chariker-Jeter technique with home-made non-adhesive gauze impregnated with povidone and fenestrated silicone drain instead of the commercially available sets. The last includes gauze impregnated with Polyhexamethylene Biguanide (Kerlix® AMD, Covidien) which has antimicrobial properties against Gram-positive and Gram-negative bacteria, including MRSA.

Helgeson et al. published a series of 16 complex wounds with an average size of defect 87 cm² managed by NPWT and Integra® (Plainsboro, NJ, USA) [15]. The patients underwent a mean 8.5 debridements with subsequent placement of Integra® and NPWT at -125 mmHg for average 19 days followed by split-thickness skin grafting plus NPWT for five days at -75 mmHg. The authors reported successful closure in 81% without infectious complications and highlighted the importance of dermal substitute in cases with large defects and exposed tendons and bones, where NPWT alone yields unsatisfactory results.

Warner et al. conducted the only comparative study in which NPWT is compared with antibiotic bead pouch – Simplex cement with 2 g Vancomycin and 1 g Tobramycin (DePuy, Warshaw, Indiana) [17]. Although the sample size is small the results were in favour of the antibiotic beads thus questioning the “undisputable” advantage of NPWT – 2.2 vs four dressing changes, 8 vs 12 days until definitive closure, 0 vs 30% wound infections and lower cost with approximately 12 000$.

The potential of NPWT to cure the wound infection is widespread, but not yet proven claim. It is a well-known fact that wartime wounds are heavily contaminated and carry a high risk of wound infection. Geiger et al. found a higher rate of A. baumannii and S. aureus which urged them to change the antibiotic policy starting with carbapenems at the admission [16]. In a series from Ukraine, Kovalchuk et al. showed positive bacterial growth in 78% of the wounds (monoinfection in 88%) [21]. An important finding from a practical point of view is the marked shift from Gram-positive growth in the first week (74%) after trauma to the predominance of Gram-negative flora at the third week (89%), of which A. baumannii (53%) and P. aeruginosa (15%) were the most frequent. The authors pointed out the significant change of the microbiological profile in contrast to the wounds during Soviet-Afghan war (predominance of Staphylococcus sp. and Enterobacteriaceae without A. baumannii). Another military series from Iraq showed Gram-positive bacteria in 93% of the cultures [26]. Sheppard et al. found that most of the wounds were not colonised or infected (69%) upon arrival at Role 5, whereas 31% had positive growth [27]. The authors reported the high cumulative prevalence of A. baumannii (63%), followed by E. faecium (4%) and E. coli (2.5%). The British experience showed clinically manifested infection in 24% of the wounds with early detection of Gram-negative flora, intermediate predominance (at the second week) of Enterobacter and P. aeruginosa and later presence of S. aureus [28]. In a cohort with 110 soldiers with osteomyelitis, Yun et al. also reported an early predominance of Gram-negative pathogens (Acinetobacter spp., K. pneumoniae and P. aeruginosa) with a subsequent shift toward Gram positive flora (mainly S. aureus) [29]. In a review paper Murray et al. stated: “although Gram-negative pathogens often complicate initial infections, many of the late relapses are Gram-positive bacteria, commonly methicillin-sensitive S. aureus and MRSA” [30]. This early detection of Gram-negative flora differs from the previous wars and is in contrast to the expected dominance of Gram-positive bacteria. The explosive devices and antipersonnel landmines lead to higher rate of wound infection because they are usually placed under the ground, and after detonation, they produce multiple secondary projectiles not only from their fragmentation, but also soil, stones, nails etc. including pieces of the dirty clothing, all of which are embedded in into the wounds. In fact, Gram-positive flora (Staphylococcus, Enterobacteriaceae spp.) resides in all of these secondary projectiles [28]. The Ukraine series also reported Gram-negative profile similar to those in Iraq and Afghanistan despite the different terrain (soil vs sand) [21]. Taken together, these findings do not support the specific causative role of the types of injury (blast vs GSW) and the terrain.

Despite the heterogeneity and the paradox of the results mentioned above, the recent guidelines recommend Gram-positive antibiotic coverage as an initial step with a subsequent change of the therapy according to the bacterial culture. The recent US guideline for prevention of combat wound infections recommends an initial therapy with Cefazolin 2 g 3-4 times daily starting within 3 hours after injury or Clindamycin 600 mg per 8 h without coverage of Gram-negative flora [31]. In case of delayed evacuation single dose of Moxifloxacin 400 mg, Levofloxacin 500 mg or Cefotetan 2 g are recommended. Since 2008 the French guideline recommends amoxicillin and clavulanic acid (2 g IV, three times daily) and Clindamycin as an alternative, whereas Gram-negative coverage is suggested for complicated fractures and hollow viscera perforations [32]. Despite the retro-
spective design, on multivariate analysis, Brown et al. proved that „using just penicillin or flucloxacillin resulted in fewer infections” [28]. Anaerobic coverage seemed to be associated even with increased risk, whereas they also advise against the routine use of Gram-negative coverage, which may result in the selection of multidrug-resistant strains. The antibiotic policy in wartime wounds should be debated and is needed to be clarified in future researches.

None of the wounds in the Ukraine series became infected during the NPWT and 100% delayed closure was achieved [21], whereas the others reported rates of 0-4% [11, 15, 19] in contrast to approximately 30% infection rate generally reported in the recent conflicts in Iraq and Afghanistan [28]. This, however, may be a result from the earlier evacuation and the improved care as whole or may reflect a bias due to the low quality of the included series. This is particularly true on the background of the finding of Warner et al. who reported infection rate of 30% in NPWT (Methycillin-resistant S. aureus) vs 0% in the antibiotic bead group [17]. It is also in unison with other authors reporting no change of the bacterial load in NPWT in comparison to the conventional dressing, along with a decrease of non-fermentative Gram-negative and a selective increase of S. aureus when black foam was used [33]. These contradictory results are by the lack of evidence for the antibacterial role of NPWT in the current literature [34, 35]. The debridement and pulse lavage remain the mainstay of the therapy of combat wounds with the primary aim to prevent the evolution of the contamination into a clinically manifested infection. In the light of prevention, a possible beneficial role of NPWT may be considered owing to the imperious outer sheet, which precludes the bacterial superinfection with multidrug-resistant hospital strains. The change of NPWT dressing in the sterile environment of operating theatre may also play such role in contrast to the bed-side changes of the conventional ones. Presumably, an essential step toward the improved antibacterial efficacy of NPWT is its combination with instillation therapy (NPWTi). The initial results are promising, but further high-quality studies are needed before its validation, including to determine the subset of wounds which may receive maximal benefit and also the type of the instilled solution [36]. NPWTi should not be placed on skin flaps or grafts because of the negative influence on the healing process [36].

Despite the early implementation of NPWT in a combat setting in 2003, the commercial set of KCI (San Antonio) was approved for aeromedical evacuation in December 2006. There are two studies with 240 patients which reported that NPWT is feasible and safe during intercontinental evacuation [37, 38]. In the pilot study of Fang et al., all patients arrived with intact NPWT system [37]. Pollak et al. reported functional problems during the flight in 4.5% of the cases after average 30 hours between the dressing application and arrival at Role 4 [38]. In nine cases leak of the dressing (n=6), ongoing bleeding (n=2) and necrosis of wound base (n=1) were observed. NPWT virtually eliminated the need for dressing change during the long transportation and was significantly associated with improved patient’s comfort and reduced tasks of the medical crew. Limitations of the present study are related to the low quality of the included papers - descriptive case series and lack of high quality comparative or randomised control trials. The significant risk for publication bias regarding the NPWT literature due to lack of access to the unpublished data (data for only 30% of the patients are available) should also be taken into account [39]. This is also probably true regarding its use in wartime wounds. The future researches are needed to assess the antibacterial clearance of NPWT, and the effectiveness of the instillation therapy or the combination NPWT plus antibiotic beads in combat setting may be by the creation of prospective trauma registries with uniform reporting of the outcome.

Nevertheless, the US Prevention of Combat-Related Infections Guidelines Panel and French guideline recommend its use as an adjunctive tool in the complex combat wounds [30, 32].

CONCLUSION

In fact, NPWT plays an essential role in the treatment of the combat wounds, but no evidence-based recommendations could be made at this stage. It cannot be concluded that NPWT diminishes the rate of wound infection and amputation rate due to the low quality of the published studies and the multifactorial determination of these variables.

Nevertheless, except for the well-known benefits such as evacuation of fluids, reducing of edema, stimulation of granulation tissue and better preparation for definitive closure (either by delayed primary suture or skin grafts/flaps), in combat setting NPWT offers several significant advantages over the conventional dressings – the reduced need for dressing changes saves the precious and limited wartime resources (manpower and time), provides safer evacuation throughout the different echelons of care with significantly improved patient’s and medical crew’s comfort. The changing microbiological spectrum of the combat wounds flora during the treatment requires closer surveillance with dynamic adaptation of the antibiotic regimens. Future studies exploring the effectiveness of NPWTi and combination NPWT/antibiotic beads are warranted.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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