Burns & Trauma, 2021, 9, tkab007
doi: 10.1093/burnst/tkab007
Research Article

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Minimizing treatment complexity of combat-related soft tissue injuries using a dedicated tension relief system and negative pressure therapy augmented by high-dose *in situ* antibiotic therapy and oxygen delivery: a retrospective study

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Received 9 July 2020; Revised 28 September 2020; Editorial decision 1 March 2021

Abstract

Background: Following combat-related, extensive soft tissue injury from gunshot wounds or blasts, prolonged duration from injury to full wound closure is associated with infection, increased morbidity and mortality, failure to mobilize, poor functional outcome and increased cost. The purpose of this study was to evaluate a novel treatment enabling early primary closure of combat wounds.

Methods: This was a retrospective study of 10 soldiers and civilians with extensive combat-related soft tissue limb injuries (5 gunshot wounds, 5 blasts) treated using the TopClosure® Tension Relief System (TRS) with simultaneous administration of regulated oxygen-enriched and irrigation negative pressure-assisted wound therapy (ROINPT) via the Vcare α® device.

Results: Nine patients were treated during the acute phase of injury and one was treated following removal of a flap due to deep infection 20 years after injury and flap reconstruction. Two patients had upper limb injury and the rest lower limb injury. With the aid of the TRS and/or ROINPT, immediate primary closure during reconstruction was achieved in 6 patients and delayed primary closure in three. Only one patient required a skin graft to close a small area of the wound after most of the wound had been closed by delayed primary closure. Wound closure was achieved within 0–37 days (median: 12.5 days, interquartile range: 2.75–19.75) from injury.

Conclusions: The TRS is a novel device for effective, early skin stretching and secure wound closure through the application of stress relaxation and mechanical creep, achieving primary closure of large defects using a simplified surgical technique and reducing the need for closure using skin grafts and flaps and the use of tissue expanders. Delivering supplemental oxygen to the wound by ROINPT reverses the reduced oxygen levels inherent in conventional negative pressure-assisted wound therapy, mitigating anaerobic contamination and reducing infection. Irrigation may accelerate the evacuation of infectious material from the wound and provide a novel method for antibiotic administration. The combination of TRS and ROINPT devices allow for early primary closure with improved functionality of combat-related limb injuries.

Key words: Soft tissue injury, Combat injuries, Limb injuries, Stress relaxation, Mechanical creep, Tension relief systems

Highlights:

- TRS and CITA-ROINPT have been shown to allow early closure of combat-related wounds by simplifying surgery and applying an effective antisepsis regimen to circumvent the need for aggressive debridement.
- The method incorporates atraumatic tissue mobilization, antisepsis with continuous ultra-high concentration antibiotic irrigation, oxygen perfusion of the wound, vacuum therapy, and shielding of the wound from outside contamination.
- The time interval between initial damage control "war surgery" and definitive reconstruction is substantially shortened, facilitating early mobilization and rehabilitation.

Background

Limb injuries are frequent in combat, accounting for almost 40% of injuries in soldiers treated in Iraq and Afghanistan [1]. Most of these are either blast- or gunshot-related, while a minority are associated with blunt trauma—usually road traffic crashes [2].

High-energy gunshot wounds and blast wounds result in severe disruption of the skin, deep soft tissues and bone. Injury severity and time to definitive treatment are associated with wound infection that precludes reconstruction and primary closure [3]. Initial management is, therefore, conservative, comprising hemorrhage control, debridement of devitalized tissue, irrigation and dressing [4].

Delayed primary closure is usually attempted between 2 and 5 days later, after further wound inspection and/or debridement. Regulated negative pressure-assisted wound therapy (RNPT) is a commonly used adjunct and may be applied after wound hemostasis has been achieved. RNPT allows for wound decontamination, improved granulation tissue growth and gradual filling of the wound cavity [5]. Once the wound is clean, closure may be attempted by delayed primary approximation of the skin, skin graft or rotational or free flaps.

In this article, we describe the utility of the TopClosure® tension relief system (TRS) and regulated oxygen, irrigation (hydrodynamic or continuous *in situ* targeted ultra-high-concentration antibiotic (CITA) irrigation) with negative pressure-assisted wound therapy (ROINPT) through the Vcare α® device, which may facilitate the early decontamination and primary closure of a complex combat-related limb wound as a simplified surgical procedure. Both the TRS and the Vcare α® device were developed by the main author to solve problems previously encountered in the treatment of combat-related injuries and other hard to close wounds.

Previous skin stretching devices allowed stretching of the skin through low-tension mechanical creep only [6,7]. The TRS may apply both mechanical creep and extreme tension using stress relaxation by tension sutures. After initial debridement, primary closure of a large soft tissue defect may be achieved by placing tension across the wound away from the skin edges. The skin edges are most vulnerable to pressure-induced ischemia; thus, placing pressure away from the skin edges reduces ischemia and facilitates healing and early wound closure.

The Vcare α® is an innovative advanced RNPT system that allows the incorporation of regulated oxygen flow and simultaneous negative pressure therapy. Low oxygen partial pressures develop in wounds treated using conventional negative pressure wound therapy (NPWT) systems, restricting their suitability for wounds with significant anaerobic contamination [8]. Supplemental oxygen reverses the reduced oxygen partial pressure in the wound and may inhibit anaerobic bacterial growth [9,10]. Concurrent hydrodynamic irrigation accelerates the evacuation of infectious material from the wound [11]. Irrigation also may provide a means for regulated antibiotic administration directly into the wound. CITA therapy has been found to be of value in the management of infected permanent pacemakers and implantable cardioverter–defibrillators [12]. Empirical antibiotics are used initially until microbiological culture and sensitivity results are known. It is the high concentration of antibiotics achieved in the wound, rather than hydrodynamic (mechanical) cleansing, that forms the basis for CITA irrigation [13]. The initial daily dose of antibiotic prescribed is similar to the recommended daily intravenous dose.

The combination of regulated oxygen, antibiotic irrigation and negative pressure with TRS is currently only commercially available through the Vcare α® device (Figure 1). The device performs three functions: it detects excessive bleeding, it alarms once bleeding is detected and it helps control the extent of the bleeding by ceasing the negative pressure. These features are missing in other NPWT devices [14].

The aim of this retrospective study of 10 patients is to demonstrate the evolution of the application of the TopClosure® TRS combined with oxygen and antibiotic wound irrigation through ROINPT as a concept in combat-related soft tissue injury and as a novel method for early and simplified closure of combat-related wounds to promote early mobilization and rehabilitation of patients.

Through three exemplar cases, we demonstrate how the technique has evolved, how the TRS and CITA–ROINPT were applied and how wound closure may be expedited.

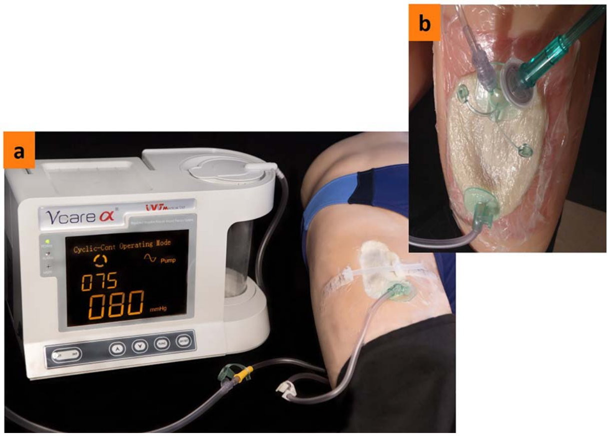

Figure 1. Regulated oxygen-enriched and irrigation negative pressure-assisted wound therapy applied by **(a)** Vcare $\alpha^{®}$ device applied to a wound model. **(b)** Note the application of the irrigation sources most distal to the vacuum outlet

Methods

Study population

Ten consecutive patients with combat-related limb injuries resulting in extensive skin and soft tissue damage were treated with TRS and ROINPT by the main author at the request of the admitting surgical teams in 3 different public hospitals in Israel between 2013 and 2017. As Israel has no military hospitals, both military and civilian casualties are treated in public hospitals. The wounds of patients discussed in this manuscript were deemed unsuitable for simple sutured primary closure after initial primary debridement by the admitting surgeons due to the extent of skin and soft tissue loss and contamination of their wounds. Timing of wound closure during reconstruction was defined as either immediate or delayed depending on whether closure was achieved during the first reconstructive surgical procedure or following additional surgical procedures, respectively. Patient characteristics are shown in Table 1. Of the 10 patients, 9 had acute injuries. One patient presented with an acute infection involving a latissimus dorsi flap applied 20 years earlier for coverage of an extensive combat injury to his knee.

Ethics

This retrospective study was conducted with institutional ethics approval of the hospitals where the patients were treated: Hillel Yaffe Medical Center and the Sheba Rehabilitation Center in Israel (protocols HYMC-19-0099 and SMC-17-3907).

Materials, surgical procedure and rehabilitation

Both the TopClosure® TRS (IVT Medical Ltd, Israel) and the Vcare $\alpha^{®}$ system (IVT Medical Ltd, Israel) have been previously described [15,16]. The TRS is comprised of two malleable polymer attachment plates. These are optimally placed 2–4 cm from the wound edges so that tension is placed away from the wound margins. The plates are secured to the skin by means of adhesive and regular skin staples. Several pairs of plates may be placed along the wound edges, depending on the length of the wound and the anticipated tension across the wound edges. The system includes interconnecting approximation straps that allow incremental advancement of the wound edges through mechanical creep by advancing each strap through a lock/release ratchet mechanism.

After initial debridement, the TRS allows for a slow approximation of even damaged tissues by mechanical creep through gentle tissue apposition or relatively fast manipulation of intact viable well-vascularized wound edges under extensive tension by stress relaxation. By pulling together the tension sutures placed through the opposing plates, the skin edges and subcutaneous tissue are approximated en bloc towards each other. Repeated application of tension using stress relaxation results in an incremental and rapid approximation of the opposing tissues. Tension is applied for 30 seconds followed by 1–2 minutes of relaxation on alternating tension sutures. Once the wound margins are approximated, the tension sutures are tightened and locked above the attachment plates.

The ROINPT system is applied to provide simultaneous irrigation of oxygen and CITA to the wound while the vacuum is maintained. A soft, compressible, open-cell sponge (IVT Medical Ltd, Israel) is placed directly on to the wound beneath the outer tension sutures and the TopClosure® straps. The second layer of sponge is placed above these. The wound is sealed with an adhesive drape and connected to the vacuum system. Unlike other NPWT systems, the Vcare $\alpha^{®}$ is compatible with the continuous supplemental oxygen and irrigation delivery system by means of separate tubes placed within the wound. This allows simultaneous irrigation of the wound with high volumes (0.5–2.0 L per day) of saline or antiseptic solution resulting in a hydrodynamic cleansing effect. Irrigation volumes are gradually lowered. Alternatively, it allows simultaneous irrigation of the wound with low volumes (25–200 mL per day) of concentrated antibiotic solution in order to achieve a local ultra-high concentration antibacterial effect. We typically use gentamicin or vancomycin until microbiological culture and sensitivities are known. Placing the oxygen and irrigation tubes on one side of the wound, while placing the vacuum port most distally at the other side of the wound, creates a unidirectional, three-dimensional flow of the irrigation solution and oxygen through the entire wound cavity.

The surgical concepts applied in every case involved the following: extensive copious irrigation of the open wound with 1.5% hydrogen peroxide and 5% povidone-iodine solutions; conservative debridement; avoidance of tissue undermining; meticulous hemostasis; and application of mechanical creep to damaged tissues for slow stretching while applying stress relaxation to non-undermined, intact tissues only. ROINPT was applied after full hemostasis was achieved.

Mobilization and rehabilitation were initiated soon after injury, facilitated by immediate or early closure and securing, of even large wounds, using the TRS.

Table 1. Patients with combat-related limb injuries

Patient	Age (years)	Wound location and dimensions (width × length × depth in cm)	Mechanism of injury	Closure method (time until complete wound closure for delayed primary closure)	Commencing rehabilitation activity following surgery	Length of stay in hospital/rehabilitation center
1	22	Arm 6 × 8 × 3	GSW	TRS and RNPT: delayed primary closure (12 days)	1 day	27 days/18 days
2	23	Leg 8 × 18 × 3.5	GSW and compartment syndrome	TRS and ROINPT: delayed primary closure and skin graft (6 weeks)	1 day	128 days/0 days
3	40	Ankle/foot 5 × 8 × 4	GSW	TRS and CITA–ROINPT: delayed primary closure (31 days)	5 days	42 days/0 days
4	27	Shoulder/arm 6 × 8 × 4	Blast injury	TRS and CITA–ROINPT: delayed primary closure (14 days)	2 days	31 days/0 days
5	20	Hand 2 × 5 × 2	GSW	TRS and CITA–ROINPT: immediate primary closure	8 days	8 days/missing data
6	21	Distal thigh/knee 4 × 7 × 3	Multi-fragment injury	TRS and CITA–ROINPT: immediate primary closure	2 weeks	6 days/8 weeks
7	21	Knee 9 × 12 × 2	Multi-fragment injury	TRS and CITA–ROINPT: immediate primary closure	2 weeks	6 days/6 weeks
8	22	Leg 10 × 18 × 2.5	GSW fasciotomy	TRS and CITA–ROINPT: delayed primary closure (21 days)	2 weeks	9 days/6 weeks
9	44	Distal thigh/knee 8 × 12 × 4	Late infection of latissimus dorsi flap of a multi-fragment injury	TRS and CITA–ROINPT: immediate primary closure	10 days	10 days/0 days
10	32	BK amputation 10 × 18 × 2	Multi-fragment injury	TRS and CITA–ROINPT: immediate primary closure	3 weeks	3 weeks/5 weeks

GSW gunshot wound, *TRS* tension relief system, *RNPT* regulated negative pressure-assisted wound therapy, *ROINPT* regulated oxygen-enriched and irrigation negative pressure-assisted wound therapy, *CITA* continuous *in situ* targeted ultra-high concentration of antibiotic treatment, *BK* below knee

Results

Ten patients were treated (median age: 27 years, range: 20–44 years). Mangled extremity severity scores were less than 7 in all patients. One patient suffered from hypothyroidism. None of the other patients had chronic comorbidities and none had life-threatening acute physiological disorders. Primary closure was achieved during reconstruction in 8 of 10 patients. One patient had delayed primary closure. In another patient, most of the wound was closed by delayed primary closure while a small area was covered by a partial-thickness skin graft. All patients returned to full active lives. None of them have required additional surgical procedures for their wounds so far.

From these 10, we describe three representative cases in detail to illustrate the evolution of the combined TRS and ROINPT approach used by the main author over several years.

Representative case 1: early delayed primary closure enabled by mechanical creep with the aid of the TRS

A 22-year-old patient aged in the early twenties was admitted with a high-energy gunshot injury to the trunk and the extremities. The intraoperative assessment of the arm injury included fluoroscopy to exclude bone injury and clinical assessment of distal perfusion. Surgery included conservative debridement of the wound resulting in a 6 × 8 × 3 cm (width × length × depth) soft tissue defect represented in schematic illustration (Figure 2a). Wound edges were gently approximated by the application of two TRS sets secured using skin staples to avoid retraction of the wound margins (Figure 2b). A compression dressing was applied over the wound to prevent oozing. The wound was inspected two days later by releasing the approximation straps through the lock/release mechanism of the TRS. After thorough lavage and hemostasis, the RNPT was applied (without supplemental oxygen or irrigation). A sponge was placed on the wound and the TRS straps further tightened (Figure 2c). Repeated dressing changes were performed in the operating room. The wound was gradually closed by maintaining tension away from the skin edges through progressive tightening of the TRS straps. The wound was kept clean using RNPT dressings and edges were completely approximated by the TRS in stages. Early delayed primary closure was achieved on the 12th postoperative day (Figure 2d). The patient was discharged from the rehabilitation center 18 days after initial injury with the left upper limb fully functional.

Representative case 2: immediate primary closure aided by stress relaxation, TRS and CITA–ROINPT

A 21-year-old patient presented with a combat-related multi-fragment injury to the lateral aspect of the right

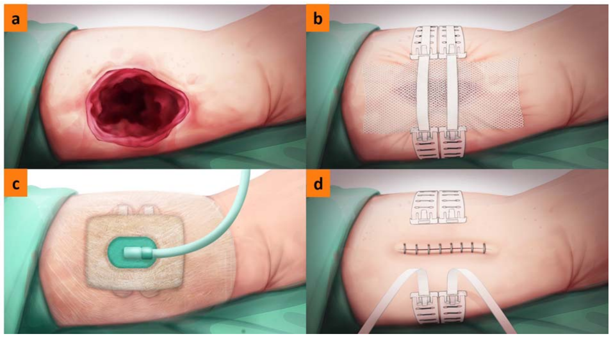

Figure 2. Schematic picture showing management of gunshot wound of the arm of patient 1. **(a)** Wound after initial debridement; **(b)** immediate approximation of wound edges; **(c)** skin approximation by tension relief system and wound coverage by regulated negative pressure-assisted wound therapy; **(d)** complete wound closure by mechanical creep at day 12

Figure 3. A 21-year-old combatant following multi-fragment injury to the lateral aspect of the right knee. **(a)** A large soft tissue defect with an open capsule; **(b)** closure of capsule and placement of 3 TopClosure® sets with tension sutures; **(c)** immediate primary closure of the wound within 44 minutes; **(d)** note the irrigation catheter placed in the wound prior to complete closure

knee (Figure 3a). The joint capsule was open. The wound was lavaged and debrided on the day of injury leaving a $9 \times 12 \times 2$ cm soft tissue defect. Two days following injury, under general anesthesia, the wound was inspected, thoroughly lavaged and meticulous hemostasis was achieved. The joint capsule was closed and three TopClosure® sets applied in combination with three pairs of one nylon tension sutures to the skin (Figure 3b, c). An irrigation catheter for CITA therapy was placed at the base of the wound. Using stress relaxation, the wound edges were totally approximated within 45 minutes, achieving immediate primary closure (Figure 3d). The wound was sealed using the ROINPT system. The postoperative course was uneventful, and the CITA–ROINPT was removed three days later (Figure 4a). The patient was discharged to the orthopedic rehabilitation center 7 days after injury. Continuous passive motion manipulation of the knee was started two weeks after surgery (Figure 4b).

Figure 4. Follow-up course of patient 2. **(a)** First dressing change at 3 days after surgery. With no signs of infection or ischemia, the regulated oxygen-enriched and irrigation negative pressure-assisted wound therapy was terminated. **(b)** Early start of rehabilitation by continuous passive movement at 14 days after the injury is allowed by the 3 TopClosure® sets, securing wound closure. **(c, d)** Healing at 6 weeks following injury with an almost full range of motion

Figure 5. Follow-up at 5.5 years after initial injury of patient 2. This patient engages in vigorous-intensity physical activity. (**a**,**b**) Demonstrating minimal residual visual deformity

The TRS sets were removed in stages over 4–5 weeks, with the patient achieving full range of motion of the knee within 6 weeks. The wound healed with no complication, as determined at follow-up assessment 6 weeks after surgery (Figure 4c, d). Five-and-a-half years later, this patient is engaged in vigorous-intensity physical activity (Figure 5).

Representative case 3: immediate primary closure aided by stress relaxation, TRS and CITA–ROINPT

A 44-year-old patient presented with acute infection of a latissimus dorsi free flap fashioned 20 years previously to cover a combat injury to the right knee (Figure 6a). The cause of acute infection remains unknown. Evaluation of the knee included plain-film X-ray followed by an ultrasound and a bone scan. These confirmed a soft tissue abscess with no bone involvement. Intravenous vancomycin was administered with

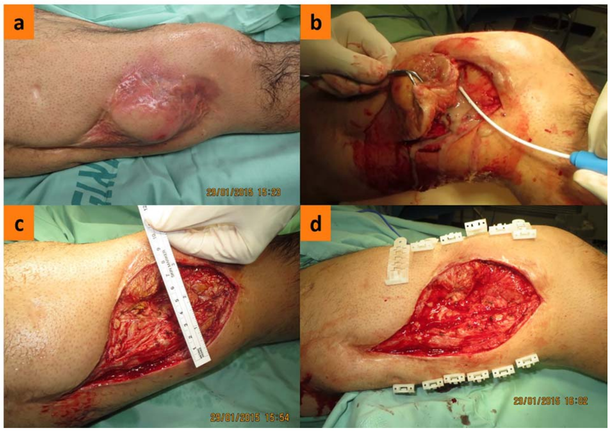

Figure 6. A 44-year-old presenting with latissimus dorsi free flap covering a soft tissue defect of the right knee following a combat injury 20 years previously. **(a)** Infected flap; **(b, c)** evacuation of pus and resection of the entire fibrotic flap resulting in a huge defect; **(d)** application of 6 TopClosure® sets for wound approximation and closure

no clinical improvement. The decision was taken to proceed to surgery. During surgery, a significant amount of pus was drained and hard, scarred tissue comprising the entire latissimus dorsi flap was excised resulting in a soft tissue defect measuring 8 × 12 × 4 cm (Figure 6b, c). The wound was thoroughly lavaged with dilute hydrogen peroxide and povidone-iodine solution. Meticulous hemostasis was achieved. The skin defect was approximated using 6 sets of TopClosure® TRS, with 1 pair of 1 nylon tension sutures applied across each set (Figure 6d). An antibiotic irrigation catheter was placed at the base of the wound. Following stress relaxation over 50 minutes the wound edges were fully approximated, achieving immediate primary closure (Figure 7a, b). Compartment syndrome was excluded by confirming adequate distal pulses. The wound was sealed with the ROINPT system (Figure 7c). CITA irrigation, compromising 160 mg gentamicin in 100 mL saline was administered continuously over 24 hours through the ROINPT for 4 days until bacterial culture and sensitivity revealed *Staphylococcus aureus* with wide sensitivity. Wound antibiotic concentrations were 3 orders of magnitude higher than serum levels. Measured serum levels during treatment and after the termination of therapy are presented in Figure 8. These show that serum levels did not exceed recommended peak levels. ROINPT was applied for a total of 9 days allowing continuous oxygen flow into the wound (Figure 7d). The patient was able to walk 10 days after surgery and was discharged home on the 10th postoperative day. He returned to preoperative regular activity as revealed at follow-up at 3.5 months and over 5 years after surgery (Figure 9a, b, c, d).

Discussion

Both the TRS and the ROINPT have been used previously by the authors to achieve closure of challenging large soft

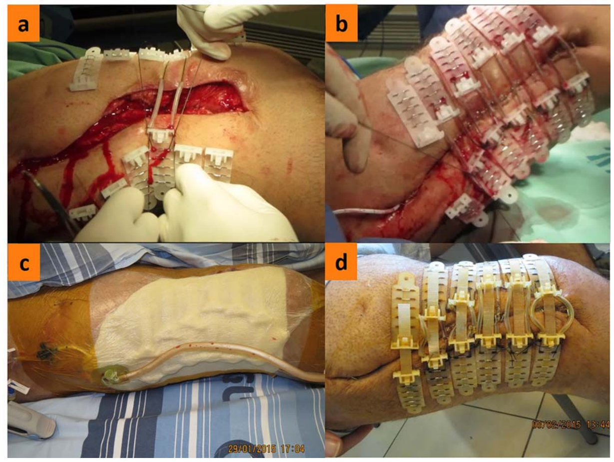

Figure 7. Operative stages and early follow-up of patient 3. **(a)** Staged approximation of wound edges by intraoperative stress relaxation; **(b)** immediate primary closure of the wound; **(c, d)** wound coverage by regulated oxygen-enriched and irrigation negative pressure-assisted wound therapy (ROINPT) and removal on the 10th postoperative day

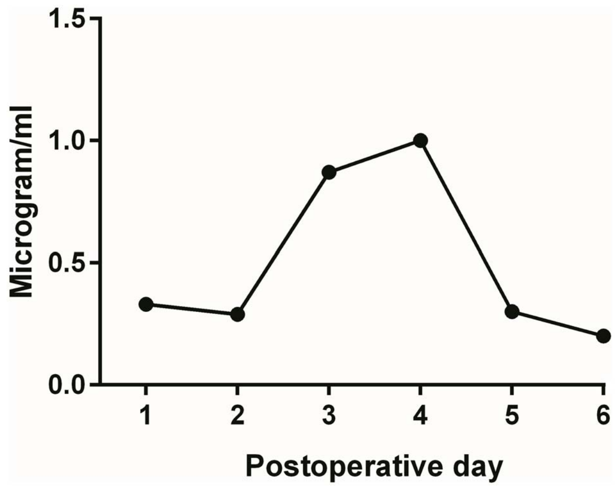

Figure 8. Measured serum gentamicin following continuous *in situ* targeted ultra-high-concentration antibiotic (CITA) administration indicating effective antibiotic absorption

tissue defects following trauma, iatrogenic surgical complications, extensive tumor resections and pressure ulcer excisions [9,15,16]. In the case series presented in this article, we describe our experience of applying combined TRS and CITA–ROINPT in patients with high-energy combat-related soft tissue injuries of the limbs.

The central importance of the procedure is the rapid recovery of the patient that ensures early ambulation and rehabilitation. This is crucial for combat-related injuries in low-resource settings with limited rehabilitation facilities as morbidity and disability increases with delayed ambulation and recovery. Hybrid TRS and CITA–ROINPT revolutionize the concept of wound closure in the presence of actual or potential local sepsis. In another study performed in the orthopedic rehabilitation department at the Sheba Medical Center in Israel, 30 patients treated during 2017–2019 for hard to close, complicated, soft tissue limb wounds with TRS

Figure 9. Early follow-up and long-term outcome of patient 3. **(a)** Mobilization on the 10th postoperative day. **(b, c)** Wound at 3-month follow-up; note that skin elasticity was regained at 3 months. **(d)** Wound at over 5 years after surgery

and CITA–ROINPT were compared with a historical cohort of 20 patients treated during 2014–2017 in the same department with the aid of conventional vacuum and dressing technologies [17]. Most of the patients in that study were diabetic. No differences between the two groups were noted in age, other comorbidities and time between wound formation and treatment. Wounds treated included diabetic ulcers, infected amputations and pressure ulcers, among others. At the end of their hospitalization, 66.7% (20/30) of the study group achieved complete wound closure, while only 25% (5/20) achieved wound closure in the control group ($p = 0.004$). The median time until wound closure in these patients was 29 days in the study group, which was shorter that the median of 102 days in the control group ($p < 0.001$). Similar to our current results in patients with combat-related injuries, this study shows that hard to close, complicated, soft tissue limb wounds benefit from a combined treatment approach that incorporates the TRS and CITA–ROINPT.

The combined treatment achieves the following objectives:

1. It eliminates the need for aggressive, extensive and mutilating debridement.
2. It simplifies the surgical procedure for early wound closure.
3. It obviates wound healing by secondary intention that may take weeks or even months.
4. It obliterates the wound cavity, reducing bacterial contamination of wounds and actively preventing infection.
5. It promotes limb salvage.
6. It allows for early ambulation and rehabilitation.

All these factors have obvious significance for patients, military and civilian personnel and national economies—with reduced consumption of medical resources, reduced hospital lengths of stay, early rehabilitation and early reintegration of patients into society and employment [4].

All the patients in this case series had complex wounds with extensive soft tissue damage and actual or potential infection. The wounds were not amenable to standard sutured primary closure for two reasons: there is no real possibility to close large defects such as these with standard sutures without inducing ischemia and necrosis; and early flap reconstruction is precluded in contaminated or infected wound environments. Flap reconstruction requires highly trained medical specialists and well-equipped facilities. These are not available worldwide in limited-resource settings [18,19]. Thus, traditionally, the only recourse has been to wait until further inspection of the wound shows no evidence of infected or devitalized tissue before proceeding to suture only where wound edges come together easily (with excision of underlying bone or soft tissue to facilitate closure while substantially compromising limb function) or reconstruct by applying suitable flaps. Although NPWT allows an alternative to conventional cavity dressing, wound healing is by secondary intention or slow granulation with skin graft, with attendant delays in ambulation and rehabilitation.

The TRS and CITA–ROINPT system removes the need for initial overly aggressive debridement as the procedure incorporates anti-sepsis with high concentration continuous antibiotic irrigation and excludes the wound from outside contamination. Thus, the time interval between initial damage-control 'war surgery' and definitive reconstruction is substantially shortened. The benefit is not simply early wound closure, but simplification of the surgical procedure, early ambulation and the avoidance of morbidity associated with prolonged dressing changes, immobility, complex surgical reconstruction procedures and prolonged hospital stay.

The three cases presented above describe the evolution of our approach to the treatment of combat-related injuries. In the first case, the TRS was initially used to avoid skin retraction with a gentle, slow approximation of the wound edges over time. After meticulous hemostasis—essential before the application of NPWT, which has the potential to induce bleeding—delayed primary closure was achieved in stages over 12 days through mechanical creep alone. In subsequent cases, the closure was expedited through stress relaxation over a short period of time during surgery. Thus, in the second case, the TRS allowed immediate primary closure of a large wound in one stage using tension sutures to apply stress relaxation and CITA–ROINPT for wound oxygenation and hydrodynamic wound decontamination. In the third case, the TRS was applied to achieve immediate primary closure through stress relaxation across a large, heavily infected, purulent wound, previously requiring closure by a free flap. This case, in particular, demonstrates the importance of CITA with concomitant ROINPT to eliminate infection simultaneously with immediate wound closure. Figure 8 shows the measured serum antibiotic levels during the CITA treatment period, indicating systemic gentamicin absorption by gradient diffusion from the ultra-high concentration within the wound cavity (in the 100–1000 minimum inhibitory concentration range) to the surrounding tissues, resulting in a non-toxic trough range of serum levels (1 minimum inhibitory concentration). This is in line with significant experience accumulated in other scenarios, such as infected cardiovascular implantable electronic devices, where we used the same concepts of treatment, in which CITA successfully circumvented the need for device extraction while avoiding toxic antibiotic levels [20]. CITA treatment was applied in the last 7 cases in this group as the author adopted CITA over saline irrigation, favoring active wound anti-sepsis to reduce bacterial load over continuous hydrodynamic (mechanical) cleansing. The relatively slow process of angiogenesis and granulation under NPWT conditions alone results in the formation of scar tissue that is conventionally covered with a skin graft, which is inferior to the rapidly stretched normal tissue resulting from skin elongation by the TRS.

There are several rules which guide us when employing the TRS and CITA–ROINPT system in these types of injuries:

1. Combat-related injuries demand early debridement. We perform conservative debridement, avoiding resection of viable tissue.
2. Approximation of wound edges by undermining or raising the skin and subcutaneous flaps is avoided at all cost. Dissection of superficial tissue from deep tissue only serves to further damage the blood supply to the wound edges. This aggravates wound ischemia under conditions of tension. Furthermore, the approximation of the skin together with the attached underlying soft tissue allows closure of the wound with minimal to no dead space, avoiding subsequent seroma formation and infection.
3. Early approximation of skin edges, even by temporary placement of the TopClosure® interconnecting straps, inhibits tissue retraction which would eventuate if nothing other than dressings were applied to the wound. Gradual pull by the straps allows slow advancement and approximation of tissue through mechanical creep. This substantially reduces ischemia as conditions of acute tension are absent or substantially reduced. When vascularity to the wound edges is preserved, early or immediate closure may be achieved by stress relaxation (as was demonstrated in representative cases two and three). The TRS attachment plates serve as a platform through which tension sutures are applied, allowing the dispersion of tension over a wide area and away from the wound edges to an area of superior perfusion. The decision of whether to apply stress relaxation and primarily close the entire wound or close the wound in stages is based on an assessment of the vulnerability of the wound edges to ischemia and effective diminution of bacterial load within the wound.
4. Compartmentalized wound irrigation with CITA allows for early closure of contaminated wounds in combination with ROINPT. We begin with conventional daily doses of the antibiotic and adjust treatment as per culture and sensitivity results. Serum antibiotic levels are monitored in order to determine drug absorption and adjustment of the dosage.
5. The conventional application of NPWT for enhancing granulation tissue growth to fill up the wound cavity or cover internal structures is counterproductive if early skin stretching is feasible. The rate of skin stretching is faster than the process of granulation. Thus, early definitive wound closure is achieved with higher quality skin coverage.

A limitation of this study is that relatively few combat-related trauma patients were treated with the combined approach. In the small cohort described, there were no substantial complications and no device failures were observed. Failure of our simple surgical method still allows for flap reconstruction, ascending the reconstructive ladder. Further study of more patients with high-energy blunt and penetrating wounds is warranted, especially where there is gross contamination or established infection—circumstances where existing techniques are less effective and where limb salvage is less likely. More comparative data is needed to compare this technique with more conventional closure techniques such as flap reconstruction. While results in terms of time to wound closure and mobilization are encouraging, comparisons of time taken for application of the device at the primary damage-control surgery, the learning curve in device use in the general/trauma surgical arena and the need for specialist flap reconstruction (with donor site morbidity during flap reconstruction and potential loss of flap, as in representative case three) will be important in the evaluation of the effectiveness and role of this technique in trauma surgery and as a crucial first option in the reconstructive ladder.

Conclusions

The TRS and CITA–ROINPT method work together to reduce the time interval between initial damage-control surgical toilet and debridement of contaminated or infected high-energy cavitating combat-related injuries and definitive closure of these wounds. A simplified primary closure may be achieved early during reconstruction, achieving complete closure with only a short delay. In selected patients we achieved immediate closure during reconstruction, rendering reconstructive surgery a one-stage procedure. Early wound closure is revolutionary in the management of combat-related wounds and affords crucial benefits to patients who can mobilize and rehabilitate into normal daily activity sooner. Further, we propose that traditional damage-control surgery in all fields incorporates TRS approximation of skin and soft tissues with CITA–ROINPT during initial surgery after surgical toilet and debridement. This method institutes active combined treatment of actual and potential infection rather than extensive debridement and delayed closure that impedes wound closure and rehabilitation.

Authors' contributions

Study concept and design: MT and IA. Acquisition, analysis, or interpretation of data: all authors. Drafting of the manuscript: MT, IA and SB. Critical revision of the manuscript for important intellectual content: all authors. Final approval: all authors.

Acknowledgments

The authors wish to acknowledge Mr Itamar Cohen and Ms Shikma Drutman for their technical support.

Abbreviations

CITA: continuous *in situ* targeted ultra-high-concentration antibiotic; NPWT: negative pressure wound therapy; RNPT: regulated negative pressure-assisted wound therapy; ROINPT: regulated oxygen-enriched and irrigation negative pressure-assisted wound therapy; TRS: tension relief system

Funding

None to declare.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Ethics approval and consent to participate

This retrospective study was conducted with institutional ethics committee approval of the hospitals where the patients were treated (protocols HYMC-19-0099 and SMC-17-3907). This statement is included in the Methods section. Since this was a retrospective study, informed consent from each patient to participle in the study was not required but full informed consent for treatment was obtained.

Consent for publication

The two patients whose pictures appear in this manuscript were contacted and written consent for publication of the images was obtained. These consent forms are available to the journal editor upon request. The pictures are anonymized.

Conflicts of interest

MT is the developer and patent holder of TopClosure® Tension Relief System and the Vcare α® system described in this manuscript. MT heads IVT Medical, the producer of these devices, and holds shares in the company. All other authors have no conflict of interest to declare.

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