26 Orthopaedic-Related Infections Resulting from Blast Trauma

Louise Robiati and A. Hamish R. W. Simpson

Abstract

Blast mechanisms are responsible for a large proportion of combat-related musculoskeletal injuries. These injuries include complex open fractures which are grossly contaminated and are at increased risk of developing wound infections, osteomyelitis, fracture non-union and the need for late amputation. With terrorist use of Improvised Explosive Devices on the increase globally, managing these injuries is no longer limited to the combat setting.

Eradication of infection is a key consideration when managing blast-mediated extremity injuries and is best achieved through a multidisciplinary approach. This review specifically considers the clinical factors associated with treating blast-mediated injury to extremities, focusing on strategies for minimising infection and directions for future research.

26.1 Introduction

Orthopaedic blast injuries result both directly, from high-energy waves passing through body tissues and penetration from ordinance components, and indirectly from displacement of the casualty and surrounding objects during the blast [1]. These mechanisms result in fractures, soft tissue damage and amputations which are grossly contaminated [2]. The physics and biomechanics of blast mechanisms are often more complex than those seen in the majority of reported civilian high-energy trauma, such as motor vehicle collisions, and therefore it may not be possible to directly extrapolate civilian research findings into the management of blast injuries (see Chap. 2).

Within the current literature, the focus for acutely managing blast-mediated injuries has mostly been confined to the military, with these injuries accounting for a large proportion of the clinical workload managed in this setting. During the conflicts in Afghanistan and Iraq (2003–2011), 81% of musculoskeletal combat injuries sustained were from explosive mechanisms [3–5]. However, with terrorist use of Improvised Explosive Devices (IEDs) on the increase globally, clinicians working in the civilian environment are increasingly being called upon to manage these injuries [6].

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26.2 Clinical Problem

A 2014 systematic review of the North Atlantic Treaty Organisation (NATO) coalition forces in Afghanistan and Iraq reported that 39% of battle casualties sustained extremity injuries [7]. Fractures were reported by recent studies to comprise 15–40% of these injuries, 82% of which were open fractures [5, 8, 9]. A well-recognised complication after this type of fracture is infection [10, 11]. For example, in combat-related Gustilo-Anderson grade III open tibia fractures (open fracture with extensive soft tissue damage) rates of infection were reported to range from 23 to 40% compared to 15% in civilian cohorts with the same grade of injury [11–15]. The increased rates of infection seen in the combat setting are believed to be due to both the local and systemic insults associated with blast mechanisms of injury, with long-term consequences including osteomyelitis, fracture non-union and late amputation [16].

26.2.1 Osteomyelitis

Osteomyelitis is an inflammatory process in the bone and bone marrow caused by an infectious agent which results in bone destruction and can be challenging to treat [17, 18]. After combat-related injuries, rates of osteomyelitis are reported as ranging from 6 to 25%, compared to 8% reported in the civilian population [13, 15, 19–21]. Due to the persistence of infection and requirement for further surgical intervention osteomyelitis has been shown to complicate orthopaedic care in both the early and late phases of rehabilitation after blast-mediated injuries [22].

26.2.2 Fracture Non-Union

Fracture non-union is covered extensively in Chap. 25. A non-union can be defined as a fracture that is 9 months post-injury and has shown no radiographic progression for 3 months [23]. However, from a clinical point of view, the term is often used to describe a fracture that has no potential to heal without further intervention. Fracture non-union has a devastating impact on a patient's quality of life and can result in limb loss as well as being an increased burden on the healthcare system [12, 24, 25].

The incidence of fracture non-union in the United Kingdom (UK) and the United States (US) has been estimated at around 11,700 and 100,000 per annum respectively, with rates of tibia non-union in the civilian literature reported at 12% for closed and 24% for open fractures [21, 25–28]. However, fewer proceed to fracture union in the military population, with rates of non-union for grade III open tibia fractures at 12 months ranging from 20 to 50% [12, 13]. The aetiology of non-union is multifactorial with infection reported as a contributory factor in 38% of cases in the civilian population [26, 29].

26.2.3 Late Amputation

Late, secondary or delayed amputations are considered to be amputations performed after an attempted limb salvage through reconstruction [30, 31]. While a range of time frames from injury to amputation are reported in the literature, several studies have used the Lower Extremity Assessment Project (LEAP) study definition of 3 months from time of injury to amputation [30, 32]. Rates of late amputation from limb-threatening injuries are reported as 5% in the civilian literature and 5–22% in the military literature for grade III open fractures [13, 21, 22, 31, 33]. Infection was cited as the main reason for performing a late amputation in both the civilian and military cohorts [21, 31, 33].

26.2.4 Organisms

In combat-related open fractures, microorganisms initially cultured from the wounds have been predominantly gram-negative and include organisms such as *Acinetobacter, Enterobacter,* *Pseudomonas, Bacillus* and *Klebsiella* [13, 19]. These are consistent with findings from a UK civilian study which reported on open fractures sustained overseas, 50% of which were caused by gunshot or blast mechanisms, and repatriated to a UK level 1 trauma centre [34]. However, these findings differ from the predominantly gram-positive cultures reported in a study undertaken in German major trauma centres [35]. The time delay to culture sampling in the military and UK papers, as well as any variance between the microorganism flora prevalent in different countries may explain this finding.

Of note culture samples taken later in the military cohorts' clinical course were predominantly gram-positive and included organisms such as *Staphylococcus aureus* [13, 19, 33]. This change in flora may be nosocomial due to repeated surgeries and prolonged hospital stays [13]. Identifying these differences and changes in microbiological flora are essential for guiding changes in antibiotic regimens. They also demonstrate the importance of tissue sampling to avoid broad-spectrum therapies which contribute to multidrug resistance [36]. There is a lack of consensus amongst nations on which antibiotics to use in blast-mediated injuries however a wider range of bacterial and fungal infections should be anticipated in blast injuries compared to high-energy civilian trauma requiring additional antimicrobial cover [13, 16, 35].

26.3 Current Treatment and Management Strategies

When treating these complex injuries, clinicians are faced with the difficult decision of whether to attempt to salvage the limb or perform an early amputation. Long-term outcome studies have reported that rates of post-operative wound infections were 23% in limb salvage and 34% in amputation cohorts [21]. Burns et al. (2012) identified that 64% of culture specimens taken at initial surgery in military grade III open fractures were positive for bacterial growth, with those patients significantly more likely to go on and develop deep post-operative infections, osteomyelitis and require late amputations [13]. Given the complex nature of blast-mediated extremity injuries, increased risk of infection and the considerable complications potentially resulting from this, one of the main goals for managing these injuries in the acute setting is eradication and prevention of infection [16].

26.3.1 Antibiotics

Antibiotic administration has long been described in the literature as a critical factor in the prevention of infection in open fractures [11, 37]. There remains a lack of consensus around the optimal timing of administration after injury, duration and delivery of these antibiotics [38].

Historically it has been recommended that antibiotics be administered within 3 h from the time of injury [39]. However, a recent study demonstrated reduced rates of infection if antibiotics were delivered within 66 min from the time of injury, with these findings supporting previously reported preclinical in vivo research [39–41]. The UK national guidelines now recommend that antibiotics are administered ideally within 1 h of injury [42]. Therefore, given the potentially protracted casualty evacuation timelines in a combat setting, there is an argument for training medical personnel to provide antibiotics safely pre-hospital [43, 44]. However, the self-administration of oral antibiotics remains contentious due to concerns regarding inappropriate administration, potential adverse reactions and increased risk of contributing to antibiotic resistance [45, 46].

Antibiotics for open extremity injuries are generally administered intravenously (IV) but, in the combat casualty environment, establishing and maintaining venous access can be challenging and intramuscular (IM) or intraosseous (IO) methods may be required [16, 44, 47]. It remains unclear whether adequate therapeutic levels of antibiotics are achieved when administered IM, IO or IV in a limb with disrupted vascularity [16, 48]. Within the literature, some consideration has also been given to the efficacy of using locally delivered antibiotics through powder, liquid or antibiotic-impregnated bead formulations [16]. A meta-analysis identified that patients with grade III open fractures who received local and systemic antibiotics had infection rates of 7% compared to 27% if they received systemic antibiotics alone [48]. However, this meta-analysis identified several limitations, including the clinical heterogeneity of the studies concerning their study population, interventions, follow up and, crucially, the definition of infection [48].

Concerning the duration of antibiotic therapy, current guidelines recommend that antibiotics are continued for 72 h or until wound closure, whichever is sooner [39]. However, a meta-analysis reported that rates of infection in grade III injuries did not increase if antibiotics were only given for 24 h [49]. In the context of blast-mediated injuries, these findings should be interpreted with caution as they were based on two studies using civilian populations. They also did not take into consideration the International Committee of the Red Cross (ICRC) recommendations of continuing antibiotics for 5 days until definitive closure [49, 50].

For blast trauma, the current recommendations for antibiotic use in UK military deployed hospital facilities is Co-amoxiclav within 1 h of injury and a one-off dose of Gentamicin at the time of surgery [51]. These are mirrored by Public Health England guidelines for bomb blast victims which recommend for open fractures, ‘through and through fractures’ or intra-articular injuries intravenous Co-amoxiclav or Cefuroxime/Metronidazole should be administered until first surgical debridement and continued until wound closure with conversion to oral Co-amoxiclav for 6 weeks as well as a dose of Gentamicin at the time of initial surgery [52].

26.3.2 Irrigation

When managing open, infected or contaminated injuries, the adage ‘the solution to pollution is dilution’ is often heard. With guidelines providing recommendations on the volume of irrigation which should be used, depending on the grade of the open fracture [44]. However, in practice, wounds are irrigated with as much fluid as the operating surgeon deems necessary. Research has been undertaken to investigate whether the constituents and pressure of the irrigation alter post-operative infection outcomes [53].

Preclinical studies identified that use of irrigation fluids containing additives such as castile soap, bacitracin, benzalkonium and chlorhexidine initially resulted in reduced bacterial numbers post-operatively when compared to normal saline [54, 55]. Forty-eight hours post-operatively these studies observed a rebound effect with increasing rates of infection for those solutions containing additives [54, 55]. Authors attributed this observation to the additives having an irritant effect on the local healthy tissues resulting in them becoming necrotic, and, therefore, a favourable environment for bacterial growth [54, 55].

The Fluid Lavage of Open Wounds (FLOW) study was a clinical multicentre randomised controlled trial (RCT) with 2447 participants comparing irrigation of open fractures with castile soap or normal saline and very-low, low and high irrigation pressure rates (1–2, 5–10 or > 20 psi) [56]. They reported a significant reduction in infection rates in the normal saline group when compared to the soap group but no difference in pressure rates [56]. However, it was noted that some patients also received Negative Pressure Wound Therapy (NPWT) post-operatively which, in post-publication analysis, the authors reported increased rates of infection in these patients [56, 57]. However, they did not report any sub-group analysis for solution type or pressure or time to wound closure which may have biased their findings [56, 57].

26.3.3 Debridement

Surgical debridement excises devitalised soft tissue and bone and removes any foreign material which may become a nidus for infection [16, 39]. The ‘six-hour rule’ for time from injury to debridement is reportedly borne from animal experiments undertaken in 1898 which demonstrated a positive correlation between higher rates of infection and delay to surgical debridement and is often quoted in the literature and historical guidelines for the management of open fractures [39, 58]. A 2012 systematic review concluded that an association between time to surgery and rates of subsequent infection had not been demonstrated [59].

The LEAP study, a prospective observational study, identified no difference in the rate of infection when comparing time of injury to debridement of fewer than 5 h (28%), 5–10 h (29%) and more than 10 h (26%) in 315 open fractures [60]. However, they did find that a delay of greater than 2 h from the time of injury to admission to a definitive trauma centre was associated with a greater risk of infection. Brown et al. [19] also reported that time to surgery did not affect infection-related complications in military casualties with the most severely damaged extremities. Neither of these studies reported on the timing of antibiotic administration. This is an important factor as animal studies have demonstrated that a delay in antibiotic delivery (despite early surgical debridement at 2 h) resulted in higher rates of infection [40]. Although present guidance does not currently specify a time-frame, immediate debridement for highly contaminated wounds or those associated with vascular compromise is recommended, which is in keeping with military practice for blast trauma [42].

26.3.4 Compartment Syndrome

The majority of current combat extremity injuries are from explosions [3]. The resulting forces cause fractures, tissue loss and vascular injury which all contribute to the risk of developing compartment syndrome in the injured limb [61]. Compartment syndrome arises when pressure increases within a limited space and compromises the circulation and function of the tissues within that space and requires emergent decompression [62, 63]. Delays in diagnosis or inadequate decompression through fasciotomies lead to complications and poor functional outcomes [64, 65].

Ritenour et al. (2008) reported on complications after fasciotomy in the US combat casualties. This study included 336 patients who underwent 643 fasciotomies and identified 17% who required revisions and 22% who had delayed fasciotomies after medical evacuation from Iraq or Afghanistan [61]. In both the revision and delayed fasciotomy cohorts, rates of muscle excision and mortality were statistically higher than in the early, non-revised group [61]. For the revision surgery cohort, the anterior and deep posterior compartments of the lower leg were the most commonly unopened [61]. In those patients who underwent a delayed fasciotomy, the amputation rate was twice compared to those undergoing in theatre fasciotomy [61].

In the combat environment, additional factors may impede a timely diagnosis and decompression of compartment syndrome. For example, patients presenting with multiple distracting injuries, use of analgesics and sedation, oedema or delayed bleeding into compartments following adequate resuscitation, application of constrictive splints and simultaneous arrival of multiple casualties contribute to the reduced ability to identify clinical signs and perform serial examinations [61, 66–68]. Therefore, there is a need to maintain a high level of clinical suspicion for compartment syndrome in severely injured patients and early use of complete and prophylactic fasciotomies in high-risk patients should be considered [61].

26.3.5 Skeletal Fixation

When managing open fractures the main goals for treatment are prevention of infection, fracture healing and good functional outcome [69]. During the First World War deployed forward hospitals managed ballistic femoral fractures with thorough debridement and skeletal stabilisation with traction or splintage and noted a reduction in mortality rates from 80% to 20% [70]. Traction and splintage have been shown to remain a viable option today and have been used successfully in both military conflicts and in austere environments [71, 72]. Fracture stabilisation confers a variety of additional benefits including protection against further damage to soft tissues, improved wound care and soft tissue healing [69, 73].

The use of external fixators in combat fracture management continues to be an area of controversy since Bradford first reported its use on ballistic fractures in the US military hospitals during World War II [9]. It was initially indicated in patients with multiple injuries, infected fractures, or to prevent complications during evacuation [74–76]. However, in a post-war report, its use was associated with a high percentage of both infection and delayed union and was therefore forbidden and removed from hospitals [75, 77]. External fixation fell out of favour until the conflict in Somalia, where a review of the literature and resources required for managing combat-related open fractures resulted in it once again becoming the preferred method of stabilisation for US forces [78]. The purported advantages of external fixation include facilitation of transportation of wounded patients with fractured extremities, permitting access to soft tissue wounds and rapid stabilisation of the skeletal system to facilitate revascularisation procedures [78, 79]. Temporary external fixation in multiply-injured casualties may also confer systemic benefits to patients undergoing ‘damage control orthopaedics’ [80, 81].

Use of external fixators in ballistic trauma is not without complications. Clasper and Phillips (2005) prospectively followed up on 15 external fixators applied in the management of war injuries during the 2003 Gulf conflict. They identified that 13 (86.7%) required early revision or removal due to complications of the injury or the fixator; 10 (67%) had instability of the fixator; 3 (20%) developed pin site infections refractory to intravenous antibiotics and 5 (33%) developed pin loosening [82]. Due to the high rate of early complications, when using external fixators, this study cautioned against its universal application in war injuries [82]. Where, clinically, external fixators are favoured the authors recommended configuring a more rigid construct by using multiple pins and bars and to avoid using them for bridging fractures and if necessary acute limb shortening should be considered [83].

In a blast or combat setting use of internal fixation has been discouraged due to increased rates of infection in animal and civilian open fracture models [84, 85]. The limited availability of equipment, appropriate access to imaging and the unconfirmed sterility of theatres in a combat environment also dissuade clinicians from using this method of fixation [86].

26.3.6 Negative Pressure Wound Therapy

Surgical debridement of blast-mediated injuries can leave large wounds which may be unsuitable for primary closure. Sterile dressings are typically applied to protect the wound, but an alternative treatment is the application of Negative Pressure Wound Therapy (NPWT) [87]. NPWT are suction devices that create a partial vacuum drawing fluid which may have collected away from the wound and, in turn, encourage soft tissue healing [87].

There is contradictory and limited research reporting on the effect of NPWT on rates of infection after high-energy explosive injuries. For example, Warner et al. (2010) identified increased rates of infection in those treated with NPWT compared to those treated with NPWT and antibiotic bead pouches. However, this study was retrospective and had small study numbers [88]. Leininger et al. (2006) reported 0% of infection at 2 weeks in casualties treated with vacuum dressings. This study was also retrospective and did not undertake long-term follow up [89].

The Wound management of Open Lower Limb Fractures (WOLLF) study was a prospective multicentre RCT comparing standard dressings to NPWT for grade II and III lower limb open fractures [87]. The authors reported rates of deep infection at 30 days as 7% and 8% in the NPWT and standard dressing cohorts, respectively, and therefore did not support the use of NWPT over standard dressings [87]. Unlike the military setting, patients in this study did not require medical evacuation to treatment facilities overseas. Therefore, there may be some benefits to using NPWT if protracted aeromedical evacuation is anticipated [90, 91]. Further prospective RCTs are required in order to evaluate this as well as assessing benefits in both the military blast and civilian terrorist setting.

26.4 Future Research Directions

26.4.1 Clinical

To date, the majority of clinical research reporting on infection after blast-mediated extremity injuries has been retrospective. These studies do have inherent limitations; they are unpowered, rely on data to be charted accurately, lack control groups and are deficient in randomisation of treatment intervention with researchers not blinded to intervention [92]. Therefore, to improve knowledge in this area, prospective, randomised longitudinal studies must be undertaken. In future military campaigns, robust and comprehensive databases will be required to allow for the collection of meaningful prospective data [93]. In order to facilitate the undertaking of comparable research, the research community must validate and build on the consensus for the definition of fracture-related infection to also include definitions for late amputation, as well as criteria for diagnosis, timing and methods for microbiology sampling [30, 94]. While findings from civilian high-energy trauma research may influence clinical practice in future military campaigns, the complex nature of blast injury means it may not be possible to directly extrapolate these to combat trauma.

In addition to the areas of potential research discussed earlier in this review, an area warranting further investigation is antibiotic pharmacokinetics and pharmacodynamics. Limb injuries from blast are often associated with vascular injuries, managed with tourniquet application and resuscitated with substantial blood transfusions [3, 95]. What remains unclear is the extent to which this has an impact on the delivery of systemic antibiotics to open wounds and fracture site. Improving knowledge in this area may alter current management guidelines. For example, to ensure adequate antibiotic penetration into tissues, alternative methods of administration, higher initial antibiotic dosing or re-dosing may be required, but this has yet to be established [11, 16, 37].

26.4.2 PreClinical

On reviewing deep tissue microbiology samples from the time of revision surgery in military patients 26% had at least one organism which was the same as that cultured from samples taken at the time of injury [13]. These findings demonstrate that a proportion of deep post-operative infections are caused by the original inoculating organism [13]. Therefore, an area for further research would be to clarify if persistence of the original microorganisms could be attributed to inadequate irrigation and debridement at the time of injury or due to latent infection. With latent infection resulting from intracellular bacteria, multidrug-resistant organisms or presence of biofilms on hardware applied or inserted at the time of injury [96–98].

Translational preclinical research to date investigating interventions such as irrigation, debridement and antibiotic delivery on bacterial loads have been undertaken in animal models with critical defects [40, 55, 99]. However, a review of UK military personnel sustaining open tibia fractures on operations identified that the majority had non-critical size defects, so an alternative model is required [12]. Preclinical in vivo studies often assess an intervention in isolation and therefore do not reflect the complexity of damage control surgery. Casualties from blast mechanisms are often multiply-injured; there would be a benefit in using a poly-traumatised model such as that described by Claes et al. (2011) for investigating therapeutic interventions, although this model does not incorporate infection [100].

26.4.3 Novel Therapies

To date, research has focused on optimal strategies for local antibiotic administration, tissue decontamination and fracture stabilisation, as described above. However, other directions to consider include novel therapies such as the use of mesenchymal stromal cells (MSC). MSCs have been shown to have therapeutic potential in preclinical fracture non-union models as well as antibacterial effects in acute respiratory distress syndrome (ARDS) and biofilm models [101–103]. Therefore, their therapeutic potential in the context of orthopaedic, blast-mediated infections warrants further investigation.

26.5 Summary

Eradication of infection is a key consideration when managing blast-mediated extremity injuries and is best achieved through a multidisciplinary approach. Initial treatment strategies include early administration of antibiotics, timely and adequate irrigation and debridement of wounds, skeletal stabilisation and wound closure or dressing until definitive fixation and closure can be achieved.

Further research is required in both clinical and preclinical settings to develop best practice guidance as well as to identify potential novel therapies. These studies should endeavour to be designed and reported following the recent consensus published on fracture-related infection to facilitate the comparison of study findings.

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