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Jury Review Paper

Open Fractures and Crush Injury

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Background

Open Fractures are associated with elevated risks of deep infection and delayed or non-union of the fracture, with the risks rising with increasing severity of associated soft tissue injury. The most commonly used severity score for fracture associated soft tissue injury is the Gustilo score (see Figure 1), with the highest categories of injury, Gustilo 3B and 3C fractures, reported as being associated with complication rates from 30-100%.(1–4)

As the highest risk open fractures are those associated with severe crush injuries, this 2016 ECCHM review of the utility of HBOT considers both crush injury and open fractures together.

Most traumatic injuries involve at least some degree of crushing of tissue, from minor contusions through to massive tissue damage. Hyperbaric Oxygen Therapy is widely accepted by hyperbaric clinicians as having a role in crush injury, with the 2004 European Consensus Conference recommending HBOT for Gustilo 3B and 3C open fractures and the American UHMS Hyperbaric Oxygen Therapy Indications report listing “Crush Injuries” as an “Approved Indication”. (5,6) There is, however, little consensus on whether HBOT might be justified in less severe injuries or in crush injury not involving an open fracture. Certainly no-one would suggest that all injuries should receive HBO - most hospital based hyperbaric centres would probably reserve HBOT for only severe soft tissue crush injuries where tissue viability is at risk or perhaps where infection risk is high. Anecdotally, there is significant utilisation of HBOT for relatively minor soft tissue injuries in elite athletes but this has not been systematically reported.(7)

It is important to note that outside of the hyperbaric community, HBOT is not generally considered part of the standard of care for trauma and even within the hyperbaric community, HBOT utilisation rates for crush injuries are negligible outside of a small number of centres that have taken a particular interest. (8,9)

Worldwide, trauma is responsible for a major burden of mortality and morbidity, often affecting relatively young persons. It is estimated that an EU citizen dies every two minutes, with 25 persons hospitalised for every death. (10) In the USA, one estimate places the annual treatment costs of injury at over US$80 Billion and when lost productivity is taken into account the total financial burden of trauma was estimated at $406 Billion per annum. (11) In addition to the immediate impact of acute injury and the treatment and recovery process that follows, there is often residual disability as a result of imperfect healing or secondary to complications of the injury or of its treatment.(12,13)

It is difficult to provide estimates for the incidence of crush injury, given the lack of a clear definition but fractures are the most common reason for hospitalization following trauma. Data from Australia has fractures accounting for 36% of all injury hospitalizations and this seems likely to be representative of developed countries. (14) The detailed epidemiology of orthopaedic injury is complex, with widely varying incidences reported for various fracture types, with some real geographical differences as well as methodological reasons for this. Robust Australian data has fractures accounting for 36% of all injury hospitalisations and this is probably representative of developed nations. While the majority of fractures are closed, open fractures are of particular importance as they present more complex management challenges, and are associated with higher risks of complications. Open fractures are also more frequently associated with higher energy trauma and more severe soft tissue injury. The overall incidence of open long bone fractures has been reported as 11.5/100 000 persons per year with the majority of these being severe tibial fractures.(15)

It therefore is an important matter to evaluate the strength of evidence for the role of HBOT in this field, given the potential demand for HBOT that would result if HBOT was to become considered as standard care within the trauma community.

Termininology

Although widely used, the term Crush Injury is not well defined and can have different meanings depending upon context and author. Crush Injury needs to be distinguished from Crush Syndrome – the condition that can follow massive crush injuries when the circulation is contaminated with sufficient tissue breakdown products, cytokines and electrolyte disturbance to create potentially life-threatening organ failure.(16)

Although the term Crush Injury can be used merely to describe the mechanism of injury, it more usually describes the consequences to tissues as a result of crushing. Some limit the use of the term Crush Injury to compression or “squeezing” type injuries as may happen in industrial accidents when a person is crushed under a heavy weight, or entrapped between solid objects, or trapped by distorted motor vehicle structures following a car crash. A much more widely inclusive interpretation of Crush Injury arises from considering that any blunt trauma to soft tissues will result in some degree of tissue crushing. Even some “penetrating trauma” will result in tissue crushing, such as happens around the bullet pathway in gunshot injuries. According to this very inclusive view of Crush Injury, nearly all trauma involves some degree of crush and from a pathophysiological point of view and it is probably only a surgically sharp knife wound that truly has a truly negligible crush component. (16-17)

Given a broad spectrum of severity and of consequences of crushing injuries to tissue but no clear threshold that divides minimal injury from severe, it follows that any proven therapy for crush injury could be used with at least some benefit to a large proportion of all injured persons. The major consideration in less severe crush injuries would be whether the impositions and cost of therapy could be justified in terms of the amount of benefit available, noting that minor crush injuries such as simple contusions usually heal well without specific therapy and with minor sequelae if any. In most cases, it would be hard to justify the costs and practicalities of HBOT merely for an acceleration of recovery rate without a functional outcome difference.

The threshold for application of HBOT is thus a critical issue in crush injury.

Open Fractures are well recognised as a distinct category of orthopaedic injury, and involve a breach in the integrity of the skin cover over a fracture, wether or not there is actual exposure of bone. There are a number of systems available for scoring severity of the combined soft tissue and bony injury involved in an open fracture, of which the Gustilo (or Gustilo and Anderson) Score is the most widely used and the one utilised in this review.(18)

Note: Although the hyperbaric medical community has traditionally considered Crush Injury as the indication for HBOT and therefore the most appropriate title for an HBO Indication, with or without the term "fracture" appended, it is suggested that the Jury consider titling this indication for HBOT in the reverse order – that is "Open Fractures and Crush Injury", as this may lead to more frequent consideration by orthopaedic and trauma surgeons who might not consider this document and its recommendations relevant except if they only think of "Crush Injury" in the most limited way.

Pathophysiology

The pathophysiology of crush injury has been well described, with good examples in the hyperbaric literature. (6,17) In summary, the initial injury causes tissue disruption at macroscopic through to microscopic levels, with cell wall, intra-cellular and microvascular damage in addition to any larger scale anatomical disruption. There is a gradient of injury from severe disruption or even non-viability to less severe tissue injury further from the point of impact or of maximum crush. It should be noted that very similar pathophysiology can also result from trauma that might not be classified as "crush injury", such as the shearing forces involved in creating soft tissue tears or traumatic flaps. The severity of tissue injury will be greatly exacerbated if there has been ischaemia as a result of vascular damage or if there is localised circulatory compromise during prolonged compression or entrapment.

The severity of tissue injury progresses over the hours and days following the initial trauma, due to a complex interaction of secondary injury processes. It is this secondary injury period that offers the best "window of opportunity" for therapies, including HBOT – which may minimise or prevent secondary injury. Secondary injury factors include biochemical disturbance, excito-toxicity, energy deprivation, pro-inflammatory cytokines and cell signalling disturbances, with subsequent cell wall leak, vascular leak, oedema accumulation and inflammatory changes that increase swelling and energy demand. Increased tissue volume elevates tissue pressures, compressing the microvasculature and decreasing blood flow, exacerbating cellular hypoxia and diminishing clearance of cellular debris and toxins. Intravascular sludging can progress to thrombosis, especially if haemo-concentration and shock is present. A "vicious circle" results that makes the initial injury worse, risking loss of tissue viability that can be progressive. After several days, this critical secondary injury phase starts to resolve, with endangered tissues either surviving, or becoming necrotic.(19,20)

If there was significant ischaemia during the injury event, there will be a component of ischaemia-reperfusion injury following restoration of circulation at the time of rescue, or during resuscitation and blood volume restoration, or as a result of surgical repair in the case of macro-vascular injury. Ischaemia reperfusion injury can also complicate the primary injury if a tourniquet is used to facilitate surgical procedures for limb injury. Although reperfusion is usually considered to occur

over a short period of time after correction of ischaemia, for instance after release of a tourniquet or vascular clamp, it is probable that ischaemia-reperfusion injury can also be an ongoing phenomenon in crushed tissue when heterogeneously impaired tissue perfusion is slowly restored over the course of some hours of resuscitation and subsequent tissue blood flow improvements.

When Crush Injury affects one of the areas of the body that is anatomically susceptible, Compartment Syndrome can result. The pathophysiological cascade of injury involved is then greatly accelerated and exacerbated by an acute rise in tissue pressure in the compartment, with early collapse of capillaries and post capillary venules leading to progressive cessation of flow in the microcirculation and the potential for severe ischaemic damage. Although crush injury is often involved as a causative factor for compartment syndrome, this condition requires a special treatment: urgent surgical fasciotomy to release pressure and restore circulation. Although HBOT has been proposed as a treatment for incipient compartment syndrome and as an adjunct to fasciotomy closure, these indications are not specifically considered further in this review.(6)

Fracture healing is significantly dependent upon the physiological support provided to the fracture by the surrounding muscles which provide nutrient blood supply after disruption of the normal bone circulation. Bones which are partly sub-cutaneous with incomplete muscle cover, such as the ulna and the distal tibia, are prone to delayed union and non-union at least in part because of limited muscular coverage after injury. Whenever there is severe crush injury to soft tissues surrounding a fracture, this problem of compromised soft tissue support for the fracture exists. (3,18,21)

Open fractures represent a special category of orthopaedic injury that is associated with increased risk of poor outcomes compared with closed fractures. This is a result of several factors including the soft tissue injury being typically more severe, contamination during the injury event, prolonged exposure of the fractured bone ends secondary to tissue loss, or as a result of later tissue loss should crushed skin, fascia or muscle become necrotic due to the progression of crush injury. Open fractures are nearly always associated with some degree of crush injury and the highest risk fractures, Gustilo Grade 3 injuries, are those with the most severe crush injuries (3A and 3B) and those with vascular disruption causing ischaemia (3C)(21,22)

Standard Management

There have been few reviews and guidelines published which are specific to crush injury as it is usually considered just one component of an orthopaedic or soft tissue injury. In 2002, Greaves et al published the findings of a British multi-society, multi-disciplinary Consensus Conference on Crush Injury and Crush Syndrome(8). The focus of some of the most comprehensive literature on severe crush injuries and open fractures has been upon the choice of whether to amputate or attempt limb salvage, as reviewed by Scalea et al (2013) in their publication on the Western Trauma Association's algorithm for management of the "Mangled Extremity" (23)

If crush injuries are extensive but limb salvage is the aim, then therapy is initially focussed on measures to avoid or minimise crush syndrome, including active resuscitation with sufficient fluids to force a diuresis along with correction of electrolyte and acid base disturbances. (8) Haemofiltration may be required as acute renal failure is common following extensive crush injuries. For minor crush

injuries such as simple contusions, ice packs are often used to limit swelling but in the more extensively injured patient, management of the soft tissue crush injury component of their trauma is essentially supportive and expectant. When open injuries are present, wound cleansing is carried out and non-viable tissue is surgically debrided. Prophylactic antibiotics are administered to reduce infection risk. In severe injuries, serial debridements may be necessary as non-viable tissues declare themselves over the days following injury.(24–26)

When open fractures are present with significant associated crush injury, the most common approach involves early surgical cleansing and debridement and either temporary or definitive fracture immobilisation without wound closure. (27) Vacuum dressings are now frequently used where available. (27,28) A recent review suggests the primary controversies in management of open fractures are the nature and duration of antibiotic prophylaxis, what time is acceptable from injury to first surgery, and the issue of early closure versus delayed closure. (29) Important trends relevant to adjunctive therapies such as HBOT are that some hours of delay to surgery are now usually seen as acceptable if this enables transfer to a more expert centre, and that some days of delay in soft tissue closure is generally accepted as not risking higher infection rates provided there is adequate early antibiotic prophylaxis and wound cleansing. (29–33) Delayed closure offers the advantage of limiting early debridement to only clearly non-viable tissue, leaving “marginal” tissues in situ and hence offering an opportunity for salvage.

Rationale for HBOT use

Hyperbaric oxygen offers prevention or minimization of both soft tissue necrosis and infection plus beneficial reductions of oedema, injury related inflammation and ischaemia-reperfusion injury. (34–38) Minimisation of swelling, improvement in tissue viability and reduction in infection risk may provide opportunities to change surgical practice towards more conservative debridements, simpler soft tissue closure with longer time to achieve this and the maybe also the ability to utilize internal fixation earlier than usual in some cases. HBOT probably accelerates acute wound healing and may speed the healing of bone and soft tissues and possibly improve the quality of healing in certain tissues, most importantly ligament, tendon and peripheral nerve. (39-52)

Were any or all of these actions significant in reducing injury complications, accelerating recovery or improving outcomes following severe acute musculoskeletal trauma of then HBOT would be a powerful adjunct to present standard care for trauma. Given the limited number of trauma centres with hyperbaric facilities, and the logistic difficulties managing major trauma, it would, however, be necessary for there to be significant proven benefit to justify routine use of HBOT, especially in the first few days after injury when the logistics are most difficult and when patient tolerance can be a limiting factor.(9,53)

Despite the practical difficulties involved, HBO has been routinely used as a treatment for crush injury and compartment syndromes in a limited number of centres, in some cases for decades with almost universal reports of positive outcomes, albeit often published in very general terms. (54) HBOT is usually recommended for Crush Injury in hyperbaric medicine-specific literature and by nearly all professional hyperbaric medical societies. (54–60) The basis for this and clinical experience published to date have been systematically reviewed by others in recent years(5,6). Whilst the

literature reports promising results, the broader trauma community consensus seems to be that further clinical investigation is required before HBO could be endorsed strongly enough for changes to be made to existing trauma systems and trauma centre infrastructure.(8,53,61)

Pre-Clinical and Animal Studies

There have been few animal studies that have attempted to create the large, heterogeneous and multi-tissue injuries associated with major blunt trauma, crush injury and open fractures. There are significant animal research ethics concerns involved in injuring animals; creating consistent major injuries is technically difficult and outcomes are hard to measure objectively and consistently, as is the case in human trauma(63,64). There have, however, been many relevant animal studies looking at specific injuries to individual tissues. Many of these studies involve surgically created ischaemia or crushing of individual structures rather than blunt trauma but there is probably reasonable generalizability of animal research findings to human injury, at least for musculo-skeletal structures and skin. It can be noted that there have been centuries of largely successful experience in translating soft tissue and orthopaedic procedures practiced on animals into human surgical practice.

A large variety of animal models of soft tissue flap ischaemia have demonstrated the ability of HBOT to preserve acutely ischaemic tissue and improve flap survival. (65-70) HBOT has also been demonstrated to substantially accelerate and improve the quality of healing of muscle, ligament, tendon, peripheral nerve and bone. (39–41) HBOT can actively reduce post-trauma oedema, favorably modulate inflammatory processes and upregulate various endogeneous antioxidant systems. (71,72) HBOT during or immediately after ischaemia can inhibit ischaemia-reperfusion injury via mechanisms that include inhibition of ß2 integrin-mediated neutrophil adhesion during reflow. (34,71) This effect does not inhibit neutrophil-mediated bacterial killing which is, by contrast, enhanced. (34,72-74) Bacterial killing is known to be highly oxygen dependent, and HBO can maximise endogeneous and pharmacological antibacterial activity via neutrophils as well as by directly inhibiting anaerobes and augmenting the action of antibiotics, such as aminoglycosides which are impaired in hypoxic conditions. (38,75-77) HBOT greatly reduces bacterial colony counts when administered in conjunction with antibiotics following bone contamination.(75-78) HBO also accelerates angiogenesis and fibroblast function to improve healing of problem wounds. (34,79) All these actions are attractive in the setting of orthopaedic and soft tissue trauma.

Questions to be addressed

Informal Question:

What is the role of Hyperbaric Oxygen Therapy in Crush Injuries and Open Fractures

Summary of PICO Questions:

Patient population	- patients with open (site) fracture/soft tissue/crush injury
Intervention	- HBOT plus standard treatment
Comparator	- standard treatment
Outcome	- acute/chronic complications

Long form Individual PICO Questions

1. In patients who have suffered an open fracture, does the delivery of a course of HBOT in addition to standard trauma care during the acute care phase, compared with standard trauma care alone, reduce the risk of acute complications such as wound necrosis or infection
2. In patients who have suffered an open fracture, does the delivery of a course of HBOT in addition to standard trauma care during the acute care phase, compared with standard trauma care alone, reduce the risk of late complications such as deep soft tissue or bone infection, delayed or non-union of the fracture, or pain and disability.
3. In patients who have suffered a significant soft tissue crush injury without an open fracture, does the delivery of a course of HBOT in addition to standard trauma care during the acute care phase, compared with standard trauma care alone, prevent tissue necrosis or otherwise improve outcomes.
4. In patients who have suffered a significant crush injury, does the delivery of a course of HBOT in addition to standard trauma care during the acute care phase, compared with standard trauma care alone, reduce the risk of Crush Syndrome or alter its course

Supplementary threshold and dose questions:

- Are there selection criteria for who will benefit, such as host status or injury severity?
- What HBOT dose is appropriate?

Existing Cochrane Reviews

Whilst there are no Cochrane reviews specifically oriented towards Crush Injuries or Open Fractures, there are two reviews within which the topics of Open Fractures and Crush Injury might be seen to be included:

Hyperbaric oxygen therapy for treating surgical and traumatic wounds, Eskes et al, updated 2013(80)

Hyperbaric oxygen therapy for promoting fracture healing and treating fracture non-union, Bennett et al, updated 2012(62)

These two reviews identify only the 1996 study of Bouachour et al as relevant to the question of Crush Injury and Open Fractures. (81) A 1998 publication of a randomised controlled trial of HBO in 20 participants undergoing intramedullary nailing of tibial shaft fracture reported improved perfusion parameters but these were simple closed fractures and clinical outcomes were not reported.(82)

Searching revealed no additional RCT's published to date that would update the findings of these two reviews

Other Systematic Reviews

Garcia-Covarrubias et al (2005) undertook a systematic review titled “Adjuvant Hyperbaric Oxygen Therapy in the Management of Crush Injury and Traumatic Ischemia: An Evidence-Based Approach”(61)

Eight case series were identified by this 2005 review in addition to Bouachour’s RCT however none included controls. Two of these involved traumatic amputations/reimplantations but the remainder have been included in this report.(61, 83-89)

Review methodology for this report

Literature search was conducted using Medline, Ovid, Embase and Cochrane resources using search terms hyperbaric oxygen and the MESH term hyperbaric oxygenation (limited to human studies) PLUS the search words trauma, musculoskeletal, crush and fracture. Correlation of the references found was performed with the references included within the two Cochrane Reviews and the review by Garcia-Covarrubias. Other valid references were searched for within the reference lists for recent non-systematic reviews including the UHMS Committee Reports, previous ECHM Consensus Reports, and chapters in relevant textbooks. Selective searches were also performed using the Rubicon Foundation database.

References were then reviewed for relevance, with only those reporting outcomes from case series of 5 patients or more included in the table of results attached.

Research in Progress

Three relevant randomised controlled trials are registered as having concluded enrolments but without publication to date. These are designed to investigate the role of HBOT in severe open fractures of the lower limb, in internal fixation of fractures of the calcaneum, and in radial fractures respectively. Only the first of these addresses open fractures and injuries that would conventionally be considered to involve significant crush injury, however a positive finding from any well designed study considering orthopaedic injury would add significantly to the literature, given the very limited amount of prospective research undertaken to date, with only two relevant randomised trials completed, both with significant limitations.

Literature Review Findings

The hyperbaric medicine textbook chapters reviewed were found to reference literature that in most part overlaps with the studies listed by Garcia Covarrubias but with some additions and with reports within the text of hundreds of other cases having been treated successfully, in particular in Russia, at the Long Beach Memorial Hospital in the USA and at the Galeazzi Institute in Milan, Italy. (90,91) These textbook chapter reports were felt to be to general and limited to include in the appended literature table.

The references published by Garcia-Covarrubias were found with the search methodology used, plus a second paper describing in more detail the set of injured patients from which were drawn the cases reported by Monies-Chass, (84,92) Three additional relevant post 2005 publications were identified by the search strategy used. Two relevant conference abstracts were also identified which have been included as they both contain some comparator group information in the published abstract. No new randomised controlled trials were identified.

Huang et al report preliminary results of a prospective study of 16 patients with complex open elbow injuries (Gustilo Grades 3A, B and C) where HBOT was used in association with early internal fixation. (93) The main focus on this study was the use of HBOT as an enabler of early internal fixation rather than following the more tradition approach of initial external fixation. No deep infections occurred and 12 month functional outcomes were categorised as "satisfactory" in 75% of cases. Although a specific comparison group was not reported, the absence of any deep infections despite early internal fixation was considered significant and the functional outcomes were regarded as very good, given the severity of the injuries.

Roje et al reported on 388 patients with upper and lower extremity war injuries treated in Croatia between 1991 – 1995. (94) 310 of these were treated according to the NATO recommended surgical strategy, and of these, 25% received hyperbaric oxygen. HBOT was associated with reduced rates of deep soft tissue infection, osteomyelitis, skin graft lysis and flap necrosis. Granulation of wounds was observed to occur earlier. The effects of HBOT appeared even stronger in those patients with comparable injuries not treated according to NATO emergency war surgery guidelines. This report contains the largest number of relevant cases reported in detail and it appears that the HBOT group and comparator group had injuries of similar severity, making this report a very significant contribution.

Yamada et al report a historic cohort study of 29 patients with Gustilo Grade 3 crush injury fracture cases – 13 treated without HBOT followed by 16 patients treated with HBOT. (95) There were no infections and no requirement for additional surgical debridement after initial surgery in HBOT cases versus 6 infections (46%) and 5 additional debridements (38%) in control cases.

Favalli et al (conference abstract only) reported a case series of 16 patients who received HBOT for Gustilo Grade 2 and 3 fractures compared with their hospital's past experience with such cases without HBOT. (87) No significant difference was seen in fracture consolidation time or non-union, but they saw no soft tissue or bone infection compared with their previous experience of a 20.8% infection rate for Gustilo 3 injuries.

Data relevant to the question of HBOT and Crush Syndrome has been provided by publications on patients treated with HBOT following the 1999 earthquake in Marmara, Turkey. Kazancioglu et al report that 16 cases received HBOT for crush injuries following a mean of 9.4 hours of entrapment under rubble, with 8 of these requiring haemodialysis. Control data was available from 29 patients not receiving HBOT. It was reported that HBOT contributed to avoidance of amputations but the need for haemodialysis was not reduced in the HBOT patients.(96)

Evaluation

There appears to be a consistent finding since HBOT was first used for traumatic ischaemia in the 1960's that the provision of HBOT during the acute care phase of managing severe soft tissue trauma can reduce secondary tissue necrosis and wound infection, with a consequent reduction in the rate of late or persistent deep wound infection including osteomyelitis. It seems likely the reduction in complications of trauma is applicable to open crush injuries with or without an underlying fracture.

It is not clear to what extent HBOT can assist in crush injury without a skin wound, but where skin or underlying tissue viability is compromised, it is likely that the same salvage effects are possible. It is

consistently reported that visibly ischaemic tissue can visibly improve with tissue survival, provided there has been macro-vascular reconstruction of any proximal traumatic vascular disruption.

It is important to note that all of the above applies only to the use of HBOT commencing in the first few days after injury or surgery for injury.

With respect to long term results, it appears that early use of HBOT can reduce the risk of late deep soft tissue infections and post-traumatic osteomyelitis and there is some suggestion that the avoidance of complications, tissue preservation and facilitation of early definitive fracture fixation may improve functional outcomes in certain injury types. There is little support for the contention that HBOT might accelerate fracture union in humans, despite promising results in small animal studies.

The recent conference abstract on the use of HBOT for earthquake rubble entrapment injuries suggests that the delivery of HBOT to victims of severe crush injuries does not reduce the need for haemofiltration when crush syndrome has resulted.

Although some of the references reviewed propose the use of HBOT as an adjunct to the management of post-acute trauma wound healing problems or infections, these indications were considered outside the scope of this review.

Patient Selection

Most reports relate to higher severity / higher risk crush injuries such as Gustilo Grade 3B and 3C open fractures, and less severe injuries where there is a compromised host or some other special risk factor. It would seem likely that these severe injuries should stand to gain the greatest benefit from HBOT but is must be noted that there is a paucity of data related to HBOT use with injuries of lesser severity.

Mathieu (1990) demonstrated that transcutaneous oxygen monitoring at pressure but not at 1ATA was predictive of whether amputation would be required. (97) It follows that whilst TCOM during HBOT may assist in monitoring therapy and predicting futility, it is not helpful in the decision as to whether to initiate HBOT in the first place.

It is clear that it is feasible to treat major trauma patients with hyperbaric oxygen, at least in experienced and suitably equipped centres. It should be noted that all reports reviewed come from experienced centres and any recommendation regarding wider use of HBOT in crush injury and open fractures should consider limiting the application of the recommendation to experienced trauma centres which have hyperbaric facilities. The literature to date does not provide sufficient support for HBOT to justify transporting a trauma patient away from a trauma centre.

HBOT Protocol

HBOT dosing and timing has been very variable in both animal work and in human studies. Both monoplace and multiplace chambers have been successfully used. Pressures have ranged from 2.0 to 2.8 ATA and session durations from 60 to 120 minutes. Treatment has commenced anywhere from within a few hours of injury through to several days later and treatment was most usually

delivered either once or twice daily, for a variable period until tissue demarcated or skin closure or fracture coverage was achieved. In the recent report on open elbow injuries, just two sessions post operatively was associated with the avoidance of infection in the cases treated.

It is implicit in the aims of using HBOT to minimise or prevent necrosis and infection following trauma that the therapeutic intervention (HBOT) must commence before these problems become established. The progression of compromised tissue to necrosis starts within hours of trauma and is largely established within a first few days post injury. The transition from bacterial contamination towards early acute infection also probably happens within the first few days. It follows that HBOT should be started as early as possible in order to have a prophylactic effect against infection. In some centres, the "as early as possible" aim has led them to provide HBOT to patients immediately after initial surgery, in some cases whilst the patient is till anaesthetised and receiving artificial ventilation. Temporary tympanostomy tubes may be inserted to facilitate this. Others wait until the patient has recovered sufficiently to receive HBOT as an "awake" patient, although it is anecdotally not uncommon for some sedation or anxiolytic medication to be required in such patients.

Recommendations to be considered:

HBOT in Open Fractures with Crush Injury
We recommend that early application of HBOT following severe open fractures can reduce complications such as tissue necrosis and infection. Gustilo 3B and 3C injuries are considered indications for HBOT and less severe injuries should be considered for treatment when host or injury related risk factors are present.

HBOT in Open Crush Injury without fracture
We suggest that HBOT may offer benefit in crush injuries with open wounds but without fracture, where tissue viability is at risk or where there is significant risk of infection

HBOT in Closed Crush Injury without fracture
It could be reasonable to provide HBOT for closed crush injuries where tissue viability is clinically judged to be at risk.

It could be reasonable to provide HBOT for closed crush injuries where there is a potential for compartment syndrome, but where compartment syndrome requiring fasiotomy is not established and where it is possible to monitor progress and response to treatment either clinically or via compartment pressure or oxygenation monitoring (It must be noted that TCpO2 is not suitable for this as it does not monitor the viability of muscle).

HBOT and Crush Syndrome
We suggest that HBOT is not indicated purely for the purposes of prophylaxis or treatment of Crush Syndrome, however HBOT can be used for treatment of associated soft tissue crush injuries by centres which have suitable hyperbaric and critical care services

Commencement of HBOT
We suggest that HBOT should be commenced as soon as reasonably possible after resuscitation and initial surgical management of any open wounds and fractures. The greatest benefit is probably associated with commencement within 24 hours of injury and it could be reasonable for experienced and suitably equipped and staffed centres to provide the first session of HBOT immediately following initial surgery, even where this required artificial ventilation of the patient during HBOT.

Dose of HBOT
There is no adequate evidence of superiority to support any particular HBOT dose within the range of HBOT dose commonly used in hospital practice, including pressures between 2.0 and 2.8 ATA and times at maximum pressure from 60 – 90 minutes. It is suggested that twice daily HBOT be considered in severe cases, at least initially.

Number of HBOT treatment sessions
Between 2 and 12 sessions have been used successfully in different studies without sufficient information to determine superiority. It is recommended that the clinical judgement of experienced trauma surgeons be utilised to monitor apparant changes in tissue viability.

We recommend that HBOT centres treating Crush Injury should have equipment for monitoring TcPO2 under pressure as this has predictive value in some situations.

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Table 1: Gustilo classification of open fractures

Classification	Description
Type 1	Puncture wound of less than or equal to 1cm with minimal soft tissue injury
Type 2	Wound is greater than 1cm in length Moderate soft tissue injury Soft tissue coverage of bone is adequate Comminution is minimal
Type 3a	Extensive soft tissue damage Includes massively contaminated, severely comminuted, or segmental fractures Soft tissue coverage of bone is adequate
Type 3b	Extensive soft tissue damage with periosteal stripping and bone exposure Usually severely contaminated and comminuted Flap coverage is required to provide soft tissue coverage
Type 3c	Associated with a vascular injury requiring repair for limb salvage

Note: Farm injuries with soil or farm animal matter contamination, open fractures with neurovascular injury, gunshot wounds, any open fractures over 8 hours old and any segmental fractures should be classified as Grade 3 regardless of wound size.

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Study (first author, year)	Type	Nb patients (HBOT/ Comparator	Aim(s) / Evaluation criteria	Inclusion / Exclusion criteria	HBO protocol (start urgency Press / time Sessions)	Results	Conclusion / comment
Székely O 1973	Case series	16 (within 19) (16 vs "past experience")	Limb salvage	Limbs likely to be lost due injury	2-2.5ATA/ 2 hrs Average 10 sessions	"Beneficial" in 12 of 16 cases	Note: 19 patient reported upon but included 2 treated for anaerobic infection and one finger reimplantation
Monies-Chass I 1977	Case series (subset of the cases reported by Schramek)	7 (7 vs "expected outcome")	Limb salvage / disappearance of visible ischaemia	Repair of vascular trauma with post op ischaemia.	Start 1-2 days post op 2.8ATA/2 hrs 4-18 sessions	Disappearance of ischaemia in all cases. Dry gangrene of toes in one	"Last Resort" treatment – in all cases judged that expected outcome was gangrene and high amputation
Schramek A 1977	Case Series	7 (within 51) (7 vs expectations of gangrene)	Limb Salvage	51 war injured with vascular trauma HBOT for the 7 with "imminent gangrene" despite revasularisation	2.8ATA/2 hrs Initial treatments as close as 2 hours apart	No major amputations. Toes required ablation in 1 of 7	Includes tha Monies-Chass patients 54 arterial and 28 venous injuries.
Loder R 1979	Case series	71	Resolution of Ischaemia / visual	HBOT for a range of acute trauma with obvious ischaemia	2.5ATA / 1 hr Up to 3 daily then reduce to daily	53 complete recovery 10 partial 8 not helped	53/71 had major injuries with ischaemia (33skin, 20 whole limb)
Shupak A 1987	Case series	13 (13 vs "expected outcome"	Limb salvage / Observation of ischaemia progression, amputation	Post traumatic lower limb ischaemia Gustilo 3C (vascular repair required)	Start @ 6.6 hrs (1.5-24) post op 2.4ATA/90mins Twice daily for 2-8 sessions (mean of 5)	8 pts complete salvage 4 patients improved but BKA required 1 non response	Very severe injuries. Ventilated pts included.

Favalli A 1990	Case series	16 (16 vs ”previous experience”)	Assess fracture union and infection rates	Open tibial shaft fractures Gustilo 2 & 3	From 2nd day post trauma. 2.5ATA/60mins daily Mean 20 sessions	No soft tissue or bone infections vs 20.8% infection in past experience with Gustilo 3. No difference in fracture union	Conference abstract only
Radonic V 1995	Case Control	28 (13/15)	Limb salvage	War injuries to crural arteries. 20 had fractures. HBO given if >6 hrs ischaemia	Start ”immediately” post op. 2.2ATA/60-120mins 7-21 sessions	Decreased amputation rate (1/13 vs 4/15	HBO used only in patients with higher risk due long ischaemia
Bouachour G 1996	Blinded RCT	36 (18/18)	Number of operative procedures, healing of wound without secondary necrosis.	Crush Injuries Gustilo 2 & 3	”After Surgery” 2.5ATA Twice daily 6 days / 12 sessions	”Complete healing’ without necrosis in 17/18 vs 10/18 Additional procedures in 6% vs 33%	The only relevant RCT to date. Longer term outcomes not reported.
Matos L 1999	Case series	33	Limb preservation Limb function	Gustilo 3 crush injuries (7 x 3A, 23 x 3B, 3 x 3C)	Start within 48 hrs of injury 2.36ATA/90 mins Mean 15 sessions	Soft tissue infection ”minimised” No osteomyelitis 4 failures (amputation)	Conference abstract only
Huang KC 2007	Case series, Prospective, consecutive	16	Reduce infection & enable early internal fixation/infection, Mayo elbow function score at 12 months	Open elbow injuries Gustilo 3 75% required flaps or grafts	2 sessions within 48hrs of surgery. 2.5ATA/120mins with air breaks	No deep infections 3 superficial infections resolved OK 75% excellent or good outcomes	Good anti-infection result with only 2 HBO Early fixation achieved without significant problems

Roje Z et al 2008	Retrospective single centre case/control	388 (99/289)	Reduce complications - improve outcomes/infection, graft loss, flap necrosis, time to granulation	Gustilo 3 war injuries	3-10 sessions 2.2ATA(92 pts) 2.8 ATA (7 pts)	Deep infection 35%/68% Osteomylitis 63%/74% Graft lyses 23%/52% Flap necrosis 15%/51% Granulation time 9/12 days All p<0.001	Detailed HBO experience published in Croatian (Kovacevic 1996, Petri 1999) HBO chamber not always available.
Yamada N 2014	Historic Cohort / Case Series	29 (16/13)	Reduce complications / Infection, additional surgery, length of stay	Open fractures Gustilo 3 / ventilated pts no included	Post op day 1 2.0/60min/daily 2-12 sessions	Infection 0%/46% p.003 Added debridement 0%/38% p.0.013 LOS no difference	Well matched severity and procedures but HBO group more current so maybe some trauma practice improvements