CRUSH INJURIES AND SKELETAL MUSCLE-COMPARTMENT SYNDROMES

Michael B.Strauss

Rationale

Introduction and Definitions: Crush injuries represent a spectrum of injury to body parts as result of trauma. Presentations vary from minor contusions to limb threatening damage. Typically, the injury involves multiple tissues from skin and subcutaneous to muscle and tendons to bone and joints. In their most severe presentations, predictable complications including osteomyelitis, non-union of fractures, failed flaps and amputations occur in approximately 50 percent of the cases with "standard of practice" surgical and medical interventions.[1-3]

The skeletal muscle- compartment syndrome (SMCS) is another consequence of trauma, but in this situation the target tissues are muscles and nerve. Edema and/or bleeding within the confines of the fascial envelope increase the pressure within the skeletal muscle-compartment. When the tissue fluid pressure within the compartment exceeds the capillary perfusion pressure to the muscles and nerves in the compartment, these tissues are rendered ischemic and manifest the signs and symptoms of a SMCS. The SMCS, especially in its insipient stages before a fasciotomy is required, is a therapeutic challenge since no means to arrest its progression other than hyperbaric oxygen (HBO) exist.

Unfortunately, HBO is woefully neglected as an adjunct for managing crush injury and SMCS. Strong arguments for its use based on evidenced-based information and how HBO mitigates the pathology of these conditions exist.

Pathophysiology: Trauma plus tissue hypoxia are the common denominators of crush injuries and SMCS. This leads to two consequences; first, a continuum of injury from normal to irreversibly damaged, and second, a self-perpetuating (i.e. vicious circle) progression of edema contributing to tissue ischemia and vice versa. Consequences of trauma include visible damage to tissue, injury at the cellular level and biochemical alterations. If the trauma and consequent energy transfer to the tissues is great enough, the tissues will immediately die. The only options in these circumstances are debridement if the site of involvement is small or major limb amputation if large.

At the cellular level the self-perpetuating aspects of these injuries manifest themselves. Trauma to blood vessels, especially at the microcirculation level, leads to transudation of fluid (i.e. edema formation), interstitial bleeding, sluggish flow, stasis, slugging, rouleau formation, and obstruction. The consequences are ischemia and hypoxia to the tissues perfused by the damaged vasculature. When this occurs, cells are no longer able to maintain their metabolic functions such as retaining their intracellular water. This further contributes to edema and third spacing of fluid. If the edema occurs in a closed space the increased pressure will collapse the microcirculation, eliminate oxygen transfer across the capillary endothelium and further contribute to the hypoxic insult.

Events at the biochemical level, the ultimate determinants of outcome, are manifested in two ways. First, oxygen is required for all cellular metabolic functions. If oxygen tensions are insufficient, wound healing and angiogenesis responses as elaborated through the fibroblast and bacterial killing by the neutrophil are thwarted.[4-6] Oxygen tensions in the tissue fluids greater than 30 mmHg are required for these responses to occur[7]. The second biochemical event is that of the reperfusion injury.[8] Once perfusion is temporarily interrupted, occurring in varying degrees with crush injuries and compartment syndromes, the endothelium becomes sensitized to the hypoxic insult. This results in activation of adhesion molecules leading to the attachment of neutrophils to the endothelium. The consequence is a cascade of biochemical events arising from the neutrophil releasing its reactive oxygen species. These oxygen radicals damage tissue beyond repair and cause severe vasoconstriction, defining the reperfusion injury and the no reflow phenomenon associated with it.

Mechanisms of HBO: The immediate justifications for using HBO in crush injuries and compartment syndromes are twofold: First, HBO supplements oxygen availability to hypoxic tissues during the early post-injury period when perfusion is most likely to be inadequate. Second, HBO increases tissue oxygen tensions to sufficient levels for the host responses mentioned above to function. Hyperbaric oxygen exposures at two atmospheres absolute (ATA) increase the blood oxygen content (the combination of hemoglobin and plasma carried oxygen) by 125 percent. The oxygen tensions in plasma as well as tissue fluids is increased 10-fold (1000 %).[9-11] Sufficient oxygen can be physically dissolved in plasma under HBO conditions to keep tissues alive without hemoglobin-borne oxygen.[11] Increased tissue oxygen tensions result in a three-fold "driving force" (mass effect) for oxygen to diffuse through tissue fluids.[12,13] This helps to compensate for the hypoxia resulting from the increased oxygen diffusion distance from the capillary to the cell through the surrounding edema.

Edema reduction is a secondary effect of tissue hyperoxygenation. Hyperbaric oxygen induces vasoconstriction which reduces blood flow by 20 percent.[10,14] Since inflow is decreased by 20 percent through vasoconstriction while outflow is maintained, the net effect is edema reduction of 20 percent.[14-18] Edema reduction occurs because of decreased filtration of fluid from the capillary to the extracellular space as a consequence of vasoconstriction while resorption of fluid at the capillary level is maintained. Hyperoxygenation of the plasma maintains oxygen delivery to tissues in the presence of HBO-induced vasoconstriction.[10,19,20] Another consequence of decreasing the interstitial fluid pressure through edema reduction is improved blood flow through the microcirculation. The reason for this is that once the interstitial fluid pressure is reduced below the capillary perfusion pressure, the collapsed microcirculation can again open-up and allow perfusion to resume. By reducing edema while supplementing tissue oxygenation, HBO interrupts the self-perpetuating, edema-ischemia "vicious circle" cycle to prevent progression of the injury.

Mitigation of the reperfusion injury is another effect of HBO for crush injuries and compartment syndromes.[21-23] It interrupts the interactions between toxic oxygen radicals and cell membrane lipids by perturbing lipid peroxidation of the cell membrane and inhibiting the sequestration of neutrophils on post-capillary venules.[24-26] The biochemical mechanism that accounts for this latter effect is that HBO interferes with the adherence of neutrophils elaborated through the $Beta_2$ integrin (Cluster-Designation-11) on the sensitized capillary endothelium.[22] The result is

interruption of the superoxide anion interaction with nitric oxide that produces the highly reactive peroxynitrite radical.[27] Another benefit of HBO for reperfusion injury is the help in providing an oxygenated environment for the generation of oxygen radical scavengers (such as superoxide dismutase, catalase, peroxidase and glutathione) that detoxify reactive oxygen species.[28,29]

Patient Selection Criteria

Crush Injuries: Objective criteria coupled with accepted grading systems should be used to make decisions when to use HBO for crush injuries and compartment syndromes. Not only must the seriousness of the injury be considered, but the ability of the host to respond to the injury needs to be factored into the decision making process. Obviously better criteria for using HBO in crush injuries must be employed than saying the injury is very severe or HBO is needed because a complication such as sloughing of a flap has arisen. This objective can be met by utilizing the internationally accepted Gustilo open-fracture crush injury grading system coupled with an innovative five criteria 0-to-10 point objective host evaluation (Tables 1 and 2).[2,3, 30] For the host evaluation, five assessments considered most useful for making decisions whether or not the patient's physiological status warrants using interventions to avoid amputation are graded on a 2 (best)-to-0 (worst) analogue scale. The Mangled Extremity Severity Score can also be used to provide objective criteria for HBO decision making with crush injuries, but will not be discussed further in this guideline in light of the almost exclusive utilization of the Gustilo system in the orthopaedic community.[31-33] Unfortunately, too often HBO is requested only after complications from a crush injury have arisen such as slough of a flap, wound dehiscence, threatened flap after delayed coverage/and or closure is done, muscle necrosis from residuals of a skeletal muscle-compartment syndrome, and/or osteomyelitis. The time to start HBO is with the initial management in those crush injuries where complications are predictable such as the Gustilo III-B and C fractures and in lesser Gustilo grades in impaired and decompensated hosts (Table 2).

Compartment Syndromes: The skeletal muscle-compartment syndrome, like the crush injury, represents a continuum of severities divided into suspected, impending, and established stages. The unifying pathophysiological feature of compartment syndromes is the self-perpetuating edema-ischemia cycle. In the suspected stage, the compartment syndrome is not actually present, but the severity of the injury or the circumstances (i.e. prolonged ischemia time) raise suspicions that a compartment syndrome could develop. In this stage HBO is not recommended, but frequent neurocirculatory checks of the injured extremity are required to recognize the earliest possible progression to the impending stage.

If the edema-ischemia cycle perpetuates itself, the condition may evolve into the impending stage. In this stage signs include: 1) Increasing pain, 2) Hypesthesias, 3) Muscle weakness, 4) Discomfort with passive stretch and /or 5) Tenseness in the compartment. If any of these signs exist, compartment pressure measurements should be made. If the compartment pressure(s) and clinical finding are such that fasciotomy is not required at this time, HBO should be started to prevent progression from the impending stage to the established stage. If pressure testing is not available and the compartment syndrome is not in the established stage, three or more clinical findings is sufficient indication to initiate HBO treatments (Figure 1-a). A second indication for

HBO in the impending stage, if pressure testing is available, is increasing compartment pressures with repeated measurements. As in crush injuries, the host-function status needs to be considered when making decisions to use HBO for the impending stage of the SMCS.

In the established stage of the SMCS, symptoms, signs and/or pressure measurements confirm the diagnosis and dictate immediate fasciotomy be done (Figure 1-b). Hyperbaric oxygen must not be used as reason to defer surgery in the above situations. However, after fasciotomy HBO should be used as an adjunct to wound management if significant residual problems remain, such as ischemic muscle, threatened flaps, unclear demarcation between viable and non-viable muscle, residual neuropathy, massive swelling, prolonged (more than 6 hours) ischemia time and/or significant host impairment as determined by the Host-function Score. The term "lag phase" refers to the time interval from the injury or insult to the time symptoms of a SMCS are severe enough to make the diagnosis. It may vary from an hour or two with bleeding into the compartment to 24 hours or more with blunt trauma. The lag phase is a manifestation of the self-perpetuating events that precede the impending and established phases of the SMCS.

Clinical Management

Crush Injuries: The early application of HBO, preferably within four to six hours of the injury, is recommended. Treatment schedules for crush injuries should be tailored to mitigate the suspected pathophysiology. For example three or more treatments in a 24 hour period for critical ischemias, twice a day for threatened flaps and oxygenating an environment so host factors can function and once a day for dealing with infections, remodeling or resorption of calcified tissues (Table 3). For the isolated reperfusion injury after revascularization or thrombectomy of an extremity that otherwise has sustained minimal physical trauma, a single HBO treatment, based on animal studies and limited clinical observations, is probably adequate.[22,26] Typically, treatment pressures range from 2 ATA in monoplace chambers to 2.4 ATA in multiplace chambers with oxygen breathing periods of 90 minutes for two or more treatments a day to 120 minutes for single daily treatments.

Compartment Syndromes: For the impending stage of the SMCS, HBO treatments should be given twice a day for 24 to 36 hours, the time that the self-perpetuating edema-ischemia cycle would be expected to end. Symptoms and signs of pain reduction, absence of neurological abnormalities, and less tautness in the compartment should be used in deciding to stop HBO. For residual complications after fasciotomy has been performed for an established compartment syndrome, HBO should be given twice a day for a seven to ten day period or when the problems have stabilized enough that no benefit is being realized from HBO. Treatment durations and pressures are the same for crush injuries; that is 90 to 120 minute durations at 2.0 to 2.4 ATA.

Supporting Literature and Evidence-based Indications

Crush Injury Literature Review: More than 600 clinical cases reported in over 20 publications attest to the usefulness of HBO in crush injuries.[33,34] Although most of the reports describe the benefits of HBO in subjective terms such as HBO treatments were "helpful," "good results" were achieved, or from "past experiences" problems of similar magnitude would have resulted in amputations, overall outcomes were positive in about 80 percent of the reports.[35]

The more important observation was as the frequency of treatments increased, the outcomes improved.[36-38] Specifically, in traumatic ischemias, Schramek reported 100 percent salvage rates with six HBO treatments a day, Loder reported 80 percent complete or partial recoveries with three HBO treatments a day and Slack reported 59 percent responded well with one HBO treatment a day. In 2005 Lisardo, et al. published an evidenced-based approach regarding the use of HBO in the management of crush injuries and traumatic ischemias.[39] They found nine reports comprising approximately 150 patients that met their inclusion criteria. Eight of nine studies showed a beneficial effect of HBO with only one reported major complication. They concluded that HBO as an adjunct to managing crush injuries and traumatic ischemias is not likely to be harmful and could be beneficial if administered early. The one randomized controlled trial in their report was that of Bouachour's crush injury-fracture study.[40] Bouachour and his co-authors reported complete healing in 94 percent of the HBO group versus 33 percent in the controls ($p < 0.01$) while the need for additional surgeries was six percent in the HBO group as compared to 33 percent in the controls ($p < 0.05$). The hyperbaric oxygen arm also demonstrated benefits when age was used as a marker for host-function status.

Compartment Syndromes Literature Review: In the 1980's the effects of HBO on the SMCS were reported in a series of articles using a canine model.[15-17,42,42] The HBO treated group had significantly less skeletal muscle necrosis than the controls when radiopharmaceutical and histological methods were used to study outcomes. When HBO treatments were delayed, more injury was observed in the HBO group, but was still significantly less than the controls. In animals rendered shocky by exsanguination, HBO provided protective benefits as measured by muscle necrosis and edema reduction as compared to the controls. Nylander's studies with tourniquet ischemia showed similar benefits in the HBO treated animals.[14] Bartlett, et al. reported significantly improved electrophysiological muscle function in a canine SMCS with a combination of fasciotomy and HBO versus the fasciotomy group alone.[43] These findings are consistent with several hundred reported clinical experiences using HBO for SMCS.[44-46]

American Heart Association Level of Classification: When the American Heart Association (AHA) criteria are used for crush injuries, HBO meets the criteria for a 1-b evidenced-based indication. This is based upon a high benefit to complication ratio, the mechanisms of HBO are appropriate for mitigating the pathophysiology, and a published randomized control trial exists. If SMCS are considered as a separate entity rather than in the traumatic ischemia group, the indication drops to a 2-a level because of the absence of a randomized control trial.

Rational-based, Evidence-Appropriate Indications: With less than 20 percent of the decisions made in clinical medicine meeting the criteria of evidenced-based indications, a more pragmatic system is recommended for making decisions whether or not to use HBO in general and crush injuries and compartment syndromes in particular.[47] Consequently, a rational-based, evidence-appropriate (RBEA) evaluation system is recommended[48] (Table 4). Five assessments considered most useful for making RBEA decisions whether or not to use interventions to avoid amputation are graded on a 2 (best)-to-0 (worst) analogue scale. This generates a 0-to-10 score. Scores of five or greater are considered justification for using the intervention. For crush injuries the RBEA score is 7 and for compartment syndrome it is 6.

Utilization Review

Crush Injuries: Recommendations for utilization review have been listed previously (Table 3). Because of the various timelines in the progression of complications that arise from open-fractures and crush injuries, utilization review must be carefully considered. For crush injuries and compartment syndromes, utilization review should be initiated by the consulting hyperbaric medicine physician, and the decision whether to extend HBO treatments or stop them should be a joint opinion of the hyperbaric physician, the trauma/orthopaedic surgeon, the plastic/reconstructive surgeon and/or the primary care physician.

Compartment Syndromes: For the impending stage of compartment syndromes, utilization review is recommended after three HBO treatments. For managing complications post-fasciotomy, utilization review should be done after 7 days or 14 HBO treatments.

Threatened Flaps or Grafts: If subsequent skin grafting or delayed closure is done for the fasciotomy site, and the graft or flaps are threatened, then HBO treatments should be instituted per these latter protocols.

Cost-Impact

Crush Injuries: The additional expenses associated with HBO treatments when used in crush injuries weigh favorably against the costs of dealing with 50 percent complication rates associated with Gustilo Type III-B and C open-fracture crush injuries.[1-3] In 1977 Brighton estimated that in the United States, $140,000 was the average cost per patient required to resolve the hundred thousand open fracture-crush injuries that failed to heal primarily each year.[49] The costs would be many-fold higher today. Even with new technologies, the complication rates are predictable for the most severe open-fracture crush injuries (Gustilo II-B and C).[2,3] Because of the large number of open-fracture crush injuries that occur in the United States each year, a reduction in complications and the morbidity associated with them could have a substantial impact on health care costs and far outweigh the additional expenses associated with HBO treatments. Not to be dismissed are the intangible benefits that primary healing and avoidance of amputations have for the patient's mental outlook, ability to function independently and return to gainful employment.[50] Experiences with HBO from the supporting literature and evidenced-based indications show when this modality is used as an adjunct for managing open-fracture crush injuries, complication rates of the severest injuries are approximately 20 percent. This compares favorably to the 50 percent complication rates reported in the literature when HBO was not used.[1-3]

Compartment Syndromes: In a review, total costs were reported to be 75 percent less when HBO was initiated in the impending stage of the SMCS and prevent its progression to the established stage (and the need for fasciotomy) than for treating complications with HBO after a fasciotomy had been done.[51]

Post-Script: Although frost bite injuries, burns, threatened flaps and grafts and in-jeopardy replantations are not specifically mentioned in this section, they all have the unifying factor of trauma plus tissue hypoxia. The insults are what differentiate this group; cold injury for frost

bite, heat injury for burns, etc from crush injuries and compartment syndromes. Their pathophysiology is similar to these two conditions with a continuum of injury responses and the self-perpetuating edema-ischemia "vicious" circle. Conditions such as burns and threatened flaps are discussed in other sections of this report. For other conditions HBO is indicated because they are, in reality, acute traumatic peripheral ischemias.[52,53]

Table 1: The Five Assessment Host-Function Score[30]

Grade / Assessment	2-Points	1-Point	0-Points
	Use ½ points if findings are mixed or intermediate between 2 findings		
Age	<40	40-60	>60
	Subtract ½ point if DM or CVD Present		
Ambulation	Community	Household	None
	Subtract ½ point if walking aids used		
Cardiac/Renal Status (Which ever gives the lower score)	OK	Impaired	Decompensated/ End-stage
Smoking/Steroid Use (Which ever gives the lower score)	None	Past	Current
Neurological Impairment	None	Some	Severe

Interpretation
Healthy Host 8-to-10 points
Impaired, but Compensated Host 4-to-7 points
Decompensated Host 0-to-3 points

Key: **CVD** – Collagen vascular disease, **DM** – Diabetes mellitus

Note: To determine Host-Function score add-up the points for each assessment; score interpretations are provided on the right

Table 2: Guide for the use of HBO in Open Fracture, Crush Injuries (ala the Gustilo classification)[2,3] **with Consideration for Host-function[30]**

Type (Gustilo)	Injury Characteristics	Anticipated Outcomes in Healthy Hosts	Indications for HBO vs Host Status[1]		
			Healthy	Impaired	Decompensated
I	Small (<1 cm wide) puncture wound from inside to out	Usually no different from a closed fracture			Yes
II	Laceration with minimal deep soft tissue damage	Same as above		Yes	Yes
III	**Crush Injuries**	**Depends on Sub-type**			
A	Sufficient soft tissue to close the wound	Complications[2] ~ 10%		Yes	Yes
B	Flaps needed for coverage	~ 50% incidence of complications[2]	Yes	Yes	Yes[3]
C	Major vascular injury		Yes	Yes	Yes[3]

Notes: [1]Refer to Table 1, the Host-Function Score

[2]Complications include infection, failed flaps, delayed/non-union, intractable pain, non-function and amputation

[3]Consider primary amputation in decompensated hosts with Grade III-B and C open fracture, crush injuries; Hyperbaric oxygen may be needed to help with primary healing of the amputation flaps

Table 3: Treatment Recommendations and Peer Review when Using HBO for Crush Injury and Compartment Syndrome

Condition	HBO Treatments and Peer Review[1]	Comments
Primary Conditions		
1. Reperfusion Injury	1	Minimal tissue trauma; e.g. after revascularizations, free flaps and transient ischemias
2. Crush Injury	8 (TID 2 days, BID 2 days and daily 2 days)	If deterioration noted when HBO treatments are decreased, resume the previous schedule
3. Compartment Syndrome	3 (BID day 1 and a single HBO Rx day 2)	HBO is not a substitute for fasciotomy; use HBO for the impending stage of the SMCS
Residual Problems and/or Complications		
1. Threatened flaps and grafts	10 (BID for 5 days)	If site remains tenuous, consider daily HBO treatments an additional 5 days
2. Problem wounds/infected wounds	21 (BID for 7 days; daily for 7 days)	See problem wounds section
3. Refractory osteomyelitis	21 (Daily for 3 weeks)	HBO must be integrated with a combined antibiotic and surgical strategy
4. SMCS post-fasciotomy concerns	14 (BID for 7 days)	Concerns include massive swelling, threatened flaps, unclear demarcation, neuropathy, etc..(see text)

Notes: [1]Peer review should be done by two or more of the following: 1) HBO consulting physician, 2) Trauma/orthopaedic surgeon, 3) Plastic/reconstructive surgeon and/or 4) Primary care physician

Abbreviations: BID = Twice a day, e.g. = for example, **HBO** = Hyperbaric Oxygen, **SMCS** = Skeletal muscle-compartment syndrome, **TID** = Three times a day

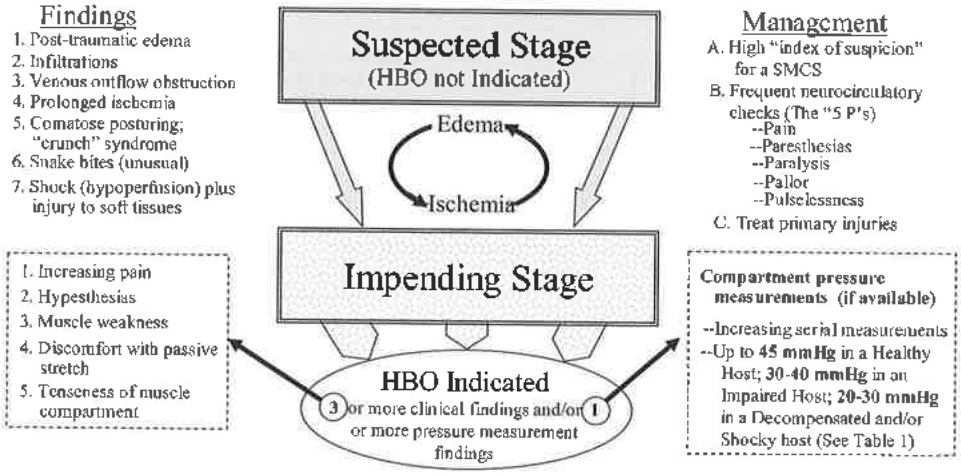
Table 4: Rational-based, Evidence-Appropriate (RBEA) Evaluation to Guide Decision Making for Selecting Treatment Interventions

Assessment	Scoring[1,2] (For justifying the intervention)	RBEA Evaluation for Using HBO	
		Crush Injury	Compartment Syndrome
1. Treating physician's **experiences** based on outcomes	2 Points (Overwhelming evidence)	1	1
2. **Mechanisms** and **lab studies** of the intervention appropriate for the pathophysiology of the condition		2	2
3. **Literature reports**	1 Point (Evidence is consistent)	1 ½	1
4. **No other treatments available** (Failures with interventions or poor outcomes with management)		1	2
5. **Randomized control trials** and/or head-to-head studies (2 or more reports).	0 Points (No information, no benefit or possible harm	1 ½	0
		7 Points	6 Points

Notes: [1]Use half points if the information is between two scoring criteria

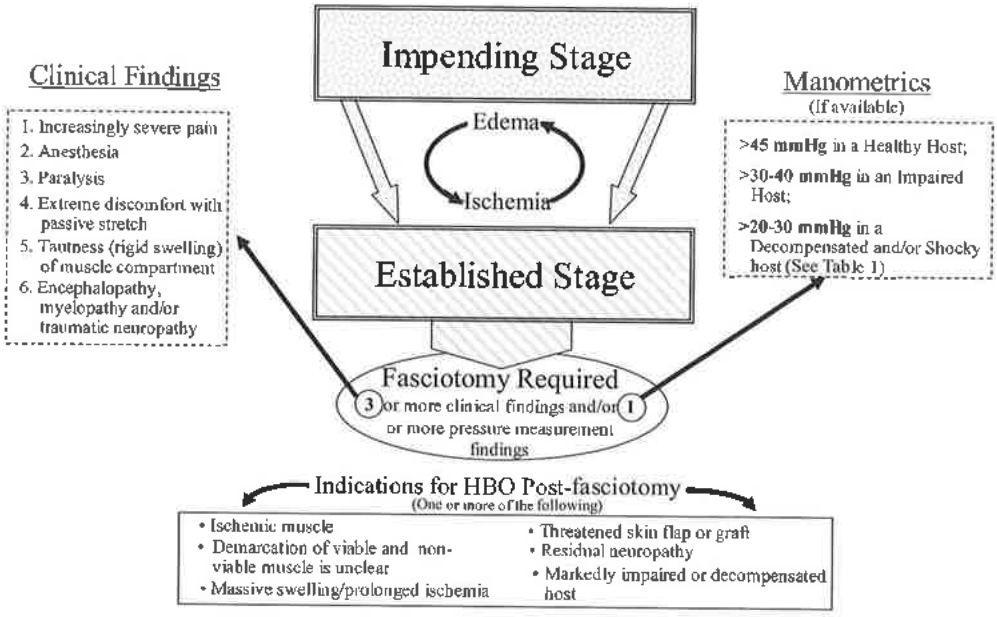
[2]Six or more points qualifies the intervention as a rational-based, evidence-appropriate indication

Figure 1-a: Indications for Hyperbaric Oxygen (HBO) in the Skeletal Muscle-Compartment Syndrome



Legend: The Skeletal muscle-compartment syndrome starts with an injury or an insult (see findings above). If the edema-ischemia "vicious circle" progresses, the Suspected Stage evolves into the Impending Stage. Hyperbaric oxygen is the only known intervention that will mitigate the edema-ischemia "vicious circle" progression

Figure 1-b: Requirements for Fasciotomy in the Skeletal Muscle-Compartment Syndrome and Indications for HBO Post-fasciotomy



Legend: If the Impending Stage progresses onto the Established Stage, HBO must not be used as a substitute for fasciotomy. However, HBO should be used post-fasciotomy if one or more residual findings are present.

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