Adjuvant Hyperbaric Oxygen Therapy in the Management of Crush Injury and Traumatic Ischemia: An Evidence-Based Approach

LISARDO GARCIA-COVARRUBIAS, M.D.,* NORMAN E. McSWAIN, JR., M.D., F.A.C.S.,* KEITH VAN METER, M.D.,† RICHARD M. BELL, M.D., F.A.C.S.‡

*From the *Department of Surgery, Tulane University School of Medicine and Charity Hospital, New Orleans, Louisiana; †Department of Medicine, Section of Emergency Medicine, Louisiana State University School of Medicine and Charity Hospital, New Orleans, Louisiana; ‡Department of Surgery, University of South Carolina School of Medicine, Columbia, South Carolina*

Hyperbaric oxygen therapy (HBO) has been recommended as an adjunct treatment in acute traumatic ischemia and crush injury. Several animal models have shown better outcomes when HBO is used in crush injury and compartment syndrome. Animal and *in vitro* models have suggested that these beneficial effects may be mediated by attenuation of ischemia-reperfusion injury. We did a systematic review of the literature using the Eastern Association for the Surgery of Trauma (EAST) recommendations for evidence-based reviews. An electronic search using Medline, OVID technologies, and the Cochrane database was performed. Only clinical papers published between 1966 and December 2003 with at least five patients that included enough information to evaluate were selected. A group of trauma experts reviewed the selected articles and scored them applying the instrument developed by the EAST practice management guidelines committee. Nine documents fulfilled the inclusion criteria for a total of approximately 150 patients. Most documents were retrospective, uncontrolled, and case series lacking a standardized methodology (class III). There was one prospective controlled randomized trial with some limitations on its design. We determined that eight of nine studies showed a beneficial effect from HBO with only one major complication. We concluded that adjunctive HBO is not likely to be harmful and could be beneficial if administered early. Well designed clinical studies are warranted.

THE USE OF HYPERBARIC OXYGEN THERAPY (HBO) as an adjunct to the management of surgical disease is controversial.[1] Nevertheless, crush injury and acute traumatic ischemia are considered approved indications for HBO.[2] The Agency for Healthcare Research and Quality reported on a systematic review of the literature that found HBO to be beneficial in severe chronic wounds.[3] Extrapolating this consensus to acute traumatic ischemia and crush injury is inappropriate, as the pathophysiology is different.[4, 5]

The pathophysiology of crush injury and compartment syndrome involves ischemia and hypoxia followed by free oxygen radical formation upon reestablishment of perfusion. Changes in the microcirculation develop progressively during the ischemic period and correlate with the duration of ischemia. These changes result in increasing vascular permeability to plasma proteins and progressive interstitial edema mediated by leukocyte-endothelium interactions.[6]

Several animal models have shown significant reduction in loss of muscle function, edema, and muscle necrosis when HBO is used in crush injury and compartment syndrome, even in the presence of hypovolemic shock.[7, 8] HBO preserves ATP levels and attenuates glutathione depletion when administered immediately after reperfusion.[9] It also attenuates ischemia-reperfusion injury that appears to be mediated by downregulation of key adhesion molecules such as intercellular adhesion molecule-1 and beta-2 integrins.[10, 11]

Considering the pathophysiology of acute traumatic ischemia and crush injury along with the beneficial effects of HBO, it has been hypothesized that adding HBO to the management of these injuries may result in a better outcome.

Evidence-based recommendations for the management of the injured extremity have been developed by

Address correspondence and reprint requests to Lisardo Garcia-Covarrubias, M.D., 1430 Tulane Avenue, Department of Surgery SL-22, New Orleans, LA 70112.

The Eastern Association for the Surgery of Trauma (EAST) Ad Hoc Committee on Practice Management Guidelines.[12, 13] This review was undertaken to evaluate the clinical experience with HBO in the management of crush injury and/or acute traumatic peripheral ischemia following the EAST recommendations for evidence-based reviews.

Methods

Literature searches were conducted using Medline, OVID technologies, and the Cochrane database. Survey parameters included studies written in the English language using human subjects and the following search terms: "hyperbaric oxygen" and "limb trauma"; "hyperbaric oxygenation" and "limb trauma"; "hyperbaric oxygenation" and "musculoskeletal trauma"; "hyperbaric oxygen" and "musculoskeletal trauma"; "hyperbaric oxygen" and "vascular trauma"; and "hyperbaric oxygen" and "vascular injury." We only considered original papers published between 1966 and December 2003 with at least five human subjects that included enough information for evaluation of HBO regimen and clinical outcome. Current review articles were reviewed for relevant bibliography. Abstracts from meetings were included only if they met the above criteria and were included in a Medline-indexed journal supplement.

The quality of the references selected was assessed by applying the instrument developed by the EAST Practice Management Guidelines Committee.[14] Articles were classified as class I, II, or III according to the following definitions:

Class I: A randomized controlled trial.
Class II: A prospective, noncomparative clinical study or a retrospective analysis derived from reliable data.
Class III: A retrospective case series or database review.

A level of recommendation was established based on the documents evaluated as follows:

Level I: Based on prospective, randomized controlled trials.
Level II: Based on prospective, noncomparative clinical studies or a retrospective analysis derived from reliable data.
Level III: Based on retrospective case series or database review.

Each article was reviewed by at least two trauma experts (see Acknowledgments section). The articles selected were mailed to the trauma experts along with a scoring form (Appendixes 1, 2) and a self-addressed stamped envelope. Differences of opinion with regard to classification or question about the article's relevance or quality were addressed by the first three authors (L.G-C., N.E.M., and K.V.M.).

We extracted the following data from each original study and summarized it in an evidentiary table: author(s), study design, patient traits including number of subjects and type of injury, HBO protocol, outcome, and data class.

Results

Our electronic search yielded 47 articles for "hyperbaric oxygen" and "limb trauma; 40 for "hyperbaric oxygenation" and "limb trauma"; 6 for "hyperbaric oxygenation" and "musculoskeletal trauma"; 6 for "hyperbaric oxygen" and "musculoskeletal trauma"; 47 for "hyperbaric oxygen" and "vascular trauma"; and 48 for "hyperbaric oxygen" and "vascular injury." Only eight of them met the inclusion criteria.[15–22] We also found one meeting abstract[23] that provided enough information for evaluation. Eight of the nine documents evaluated were class III and one was class I (Table 1). The second search conducted in December 2003 yielded no new information that met the inclusion criteria for this review.

Most of the articles failed to include a scoring system for severity of injury. Cases included complex vascular injuries, although one report included only patients with limb compartment syndrome.[19] The timing for HBO was difficult to assess, as some reports did not include this information. The HBO protocol was variable, and pressure ranged between 2 to 3 atm absolute. The duration of each treatment was also variable, but the most common were 90-minute sessions. Total number of HBO treatments ranged between 1 and 21. Among the nine documents, only one "serious complication" was mentioned,[15] but it was not specified.

Székely et al.[15] reported on 19 cases including severe injury to the upper or lower extremities, vascular trauma, extensive skin loss, and anaerobic infections associated with open fractures. However, only five cases included enough detail to assess, and the authors acknowledged difficulty in evaluation of the role of HBO in overall results of treatment. Measurement of skin temperatures in the injured limb and the intact limb were recorded and compared, and a favorable prognostic sign was considered when the temperature in the affected site rose during HBO and did not drop significantly after treatment. The authors explain that this rise in temperature may have been secondary to the oxygen received by the tissues promoting metabolism. The authors concluded that HBO has a role in some cases of severe limb damage. However, our assessment based on the five patients with complete in-

TABLE 1. *Evidentiary Table: Hyperbaric Oxygen in Crush Injury and Acute Traumatic Ischemias*

Author (Ref.)	Study Design/ Data Class	Patient Traits	HBO Protocol	Outcome	Beneficial
Székely (15)	Case series. No control/III	5 cases with severe injury to the limbs including 3 with associated fractures.	2 ATA. Variable duration.	2 died; 3 had primary amputation. A serious complication from HBO is mentioned but not specified.	No
No author (16)	Case series. No control group/III	21 patients with traumatically amputated limbs/fingers.	2–3 ATA q.d.–b.i.d. for about 1 week.	14 were successfully re-implanted.	Yes
Monies-Chass (17)	Case series. No control group/III	7 patients with severe vascular trauma and associated fractures to the lower extremities. All treated surgically. All had signs of ischemia postoperatively.	2 h at 2.8 ATA every 4 h postoperatively. Mean 9.5 treatments.	Ischemia disappeared in 6 cases. Dry gangrene of toes that required amputation in one patient. No HBO complications.	Yes
Shupak (18)	Case series. No controls/III	13 patients with traumatic injuries to lower limbs; 10 had major arterial injury and had associated fractures.	90 min at 2.4 ATA b.i.d. after surgery. Mean 5 treatments.	Complete limb salvage in 8 patients. In 4 patients, ischemia level was lowered distally. 3 patients had BKA. 1 patient had AKA, and 1 showed no improvement. No oxygen toxicity.	Yes
Strauss (19)	Case series. No controls/III	20 patients with compartment syndrome. First group, 10 patients compartment pressure ranged from 15 to 48 mm Hg. Second group, 10 patients compartment pressure not reported.	First group 90 min at 2 ATA b.i.d.–t.i.d. Mean 12 treatments. Second group had HBO after fasciotomy. Mean 36 treatments.	None of the first group of patients required fasciotomy, and all recovered without sequel. Second group "difficult to quantitate objectively the benefits of HBO."	Yes
Radonic (20)	Retrospective case series/III	13 patients with crural arteries injury. 10 had associated fractures. All treated surgically in conjunction with HBO.	7–21 sessions of 60–120 min at 2.18 ATA	In HBO patients, outcome (function) was very good 2, good 3, fair 7, and one had BKA. In non-HBO patients, outcome was very good 4, good 3, fair 4, BKA 3 patients. AKA 2 (one had BKA initially).	Yes
Bouachour (21)	PRCT/I	36 patients with Gustillo type II–III injury. Patients with peripheral arterial occlusive disease were excluded. All patients underwent surgical management within 6 h of injury.	After surgery, 18 patients received HBO 90 min at 2.5 ATA b.i.d. for 6 days, and 18 received placebo.	Complete wound healing without necrosis requiring excision in 17 patients of HBO group *vs.* 10 of placebo group ($P < 0.01$). Repetitive procedures in 33% placebo group *vs.* 6% in HBO group ($P < 0.05$). There were no complications from HBO.	Yes
Kiyoshige (22)	Small series. No control/III	6 patients, 10 amputated digits Treatment replantation and HBO.	HBO 2 ATA 1 h for 5 days.	7 survived.	Yes
Matos (23)	Case series. No control group/III	23 patients with type III crush injuries; grade IIIA (7), grade IIIB (13), grade IIIC (3). All patients except two had surgery within 24 h of injury and HBO within 72 h.	2.36 ATA for 90 min b.i.d.–q.d. Average of 12 HBO treatments.	20 had preservation of the threatened limb. The 3 failures underwent transtibial amputation.	Yes

ATA, atmosphere absolute; HBO, hyperbaric oxygen; q.d., every day; b.i.d., twice a day; t.i.d., three times a day; BKA, below the knee amputation; AKA, above the knee amputation.

formation did not reveal an obvious benefit from HBO.

Twenty-one traumatic amputations or near amputations of the limbs and fingers were reported from the Shangai Sixth People's Hospital.[16] Eighteen cases involved the upper extremities, two cases involved single finger injuries, and one the lower extremity. The average time of limb ischemia was 16 hours (range,

6–36 hours). All patients received HBO after replantation. Limb survival occurred in 10 of 15 detached limbs, including 1 of 2 fingers, ischemic for less than 10 hours, and in 4 of 6 patients with ischemic time longer than 20 hours.

Monies-Chass et al.[17] reported on seven young healthy patients suffering severe vascular trauma to the lower extremities. The average time between the injury and vascular repair was 9 hours (range, 4–20 hours). All patients underwent standard vascular repair, but after operation the limbs remained severely ischemic with cyanosis and swelling. HBO was begun 1 to 2 days after operation. Ischemia reversed in six patients, and progression of early gangrene of the toes was halted in one patient after HBO therapy, limiting amputation to the toes. Functional outcome of these cases was not mentioned.

Shupak et al.[18] reported on 13 patients with trauma to the lower extremities from the Israel Naval Hyperbaric Institute. Penetrating trauma accounted for five injuries and blunt trauma for eight. All patients had extensive soft tissue involvement and peripheral neurologic compromise. Ten patients had associated major arterial injury. All patients underwent surgical treatment before HBO. Early fasciotomies were routinely performed in all the cases. The indication for HBO was aggravation of ischemia after surgery. The time delay from the time of injury to HBO is not mentioned. Surgical repair was performed in average 11.5 hours (range, 0.5–36 hours) after the time of injury. The injured extremity was examined (skin color, edema, motor and sensory function, palpation of peripheral pulses, and skin temperature at the edge of the ischemia demarcation line) before and after each HBO treatment. HBO was discontinued when no further improvement was noted after two successive treatments. Complete limb salvage was achieved in eight patients. Outcome did not vary between penetrating *versus* blunt trauma. The authors conclude that HBO should be indicated after surgical treatment as soon as doubt exists about the viability of the injured extremity.

Strauss and Hart[19] reported on 20 patients that received HBO. The authors diagnosed all the 20 patients with "skeletal-muscle compartment syndrome," but etiology is not specified. The patients were divided in two groups of ten. Compartment pressures in group I ranged from 15 to 48 mm Hg but were not mentioned in group II. None of the patients in group I needed surgical decompression. In contrast, all patients in group II received fasciotomy. The authors felt that in group I administration of HBO during the lag phase (time from injury to the development of symptoms of compartment syndrome) may have halted the progression of the process to the point that fasciotomy was not necessary. In group II, the authors acknowledge the difficulty to quantitate objectively the benefits from HBO. Nevertheless they made the following observations: rapid reduction of edema, improvement in marginally viable tissue thus eliminating the need for further surgeries, and recovery of nerve function in two patients.

Radonic et al.[20] presented their experience of 28 patients with combat-related crural vascular injuries during the Croatian war. The mechanism was penetrating in all cases. All the patients underwent vascular, orthopedic, and plastics repair. Fasciotomy was performed in all patients. Thirteen patients with extensive bony and soft tissue injuries in addition to a prolonged ischemic period (greater than 6 hours before admission) received adjuvant HBO. Increase in blood pressure, improved skin color, rise in temperature on the injured side, and maintenance of temperature were considered good prognostic signs after HBO. Outcome results were assessed at discharge from the hospital and were described as very good, good, or fair. The authors feel that HBO helped to decrease amputation rate.

The only PRCT (class I) was published by Bouachour et al.[21]: a total of 36 patients with crush injury of the limb excluding patients with history of peripheral vascular disease. Eighteen patients were randomized to receive adjuvant HBO and 18 received placebo. The authors concluded that HBO improved complete healing and reduced repetitive surgery in severely injured patients. This study was deemed to have poor design/methodology as scored by the validity scale described by Jadad.[24] Specifically the authors failed to describe the randomization process, and no description of withdrawals or dropouts was given.

Kiyoshige et al. reported his own experience on ten replanted digits of six patients who sustained crush, avulsion, and degloving amputations. The author used a color monitoring system to assess postsurgical circulation before and after HBO. The color monitor patterns were divided into uneventful, congestion to survival, congestion to necrosis, and necrosis. These patterns are described elsewhere.[25] Seven replants survived and three failed. The failed three digits demonstrated remarkable color changes during HBO. No color changes were observed in six of the seven surviving digits under HBO. The author concludes that the difference in color reaction to HBO may be helpful in early decisions to employ salvaging procedures.

The only abstract included in our review reported 23 patients with crush injuries of the extremities treated with adjunctive HBO at the University of Miami/Jackson Memorial Medical Center during 2 years (1997–1998).[23] All injuries were type III according to the Gustillo classification. Subclassification was as follows: IIIA = 7, IIIB = 13, and IIIC = 3. Most

patients received surgical treatment within 24 hours of injury and HBO within 72 hours. Twenty patients had a successful outcome with preservation of the limb. Subclassification of the outcomes is not mentioned.

Discussion

The EAST management guidelines for patients with crush injury and acute traumatic ischemia are based on class II and class III data including more than 7000 patients.[12, 13]

Although several publications favor using HBO in the management of these patients,[26–28] only nine documents fulfilled the inclusion criteria for our study. The existence of only 8 class III studies and one class I article for a total of approximately 150 patients confirms the need for controlled studies.

The lack of well-designed, prospective, randomized controlled trials including HBO in this topic is not surprising, as neither class I articles were found in the EAST guidelines for management of these injuries. Although in the hierarchy of research designs prospective randomized controlled trials are considered to be evidence of the highest grade, a recent publication suggested that well designed observational studies could be as valid as PRCTs.[29]

A major problem with some of the HBO reports is variability in mechanisms of injury, which influence outcomes. The first case report on the successful use of HBO in crush injury was published in 1961.[30] A 16-year-old male sustained a severe compound fracture-dislocation of the left ankle with significant soft tissue involvement and laceration of the three major arteries (Gustillo III-C injury). Likewise, some other anecdotal reports have included patients with severe injuries treated with HBO that reported encouraging results, including a decrease in the amputation rate.[31, 32] However, severity of injury and functional outcome postinjury are not clear. One wonders if some of the severely injured patients treated with HBO would have been better served with an early amputation.

The ability to reconstruct and save severely injured limbs has improved in the past two decades.[33–35] Nevertheless, a large cohort of patients from eight level I trauma centers who sustained high-energy trauma below the distal femur showed no significant difference in functional outcome between the amputation and the reconstruction group.[36] Furthermore, the reconstruction group had a higher risk of complications, additional surgeries, and rehospitalization. Bouachour's[21] prospective randomized controlled trial showed a reduction in repetitive surgery in patients older than 40 years that were treated with HBO. However, functional outcome was not mentioned.

Some studies have suggested that in traumatized limbs, transcutaneous oxygen measurements in hyperbaric oxygen may be valuable in predicting poor outcome, including patients who may need amputations.[37] Mathieu et al.[38] found that patients with a bilateral perfusion index (transcutaneous oxygen of the injured limb/transcutaneous oxygen of the uninjured limb) lower than 0.20 predicts the necessity of amputation with a specificity of 100 per cent. They also found that transcutaneous oxygen measurements in normobaric oxygen are not sufficiently discriminative. If this is reproduced by other groups, it may become a significant objective method to triage traumatized limbs, as injury severity scoring systems have limited usefulness to predict amputations.[39]

Prophylactic fasciotomy has been associated with a higher complication rate, such as tissue necrosis, wound dehiscence, skin graft failure, and infection.[40] Strauss and Hart suggested that HBO may halt the progression of compartment syndrome to the point where surgical decompression is not needed. The same authors found that HBO reduced muscle edema and necrosis after compartment syndromes in the canine hind limb.[41]

Gold et al.[42] reported on a case of compartment syndrome of the hand secondary to a rattlesnake bite. The patient refused to have a fasciotomy, and he was managed with antivenom, mannitol, and HBO. On the third hospital day, the patient was discharged and was reported recovered with no sequelae. It is difficult to draw meaningful conclusions from noncontrolled studies and isolated case reports. Therefore, until further therapeutic modalities are well established, early fasciotomy should be regarded as the standard of care in acute compartment syndrome. Adjunctive HBO may help to decrease muscle damage. Ideally, HBO should be administered early, as Nelson et al. showed that delayed application of HBO 16–18 hours postinjury is not effective.[43]

Adjunctive HBO is not likely to be harmful in the management of crush injury and acute traumatic ischemia. Pathophysiologic mechanisms, animal data, and clinical studies (level I and III evidence) suggest it may be helpful. If available, HBO should be administered early. Transcutaneous oximetry may prove to be useful as an objective measure to triage patients needing amputations. Surgery should never be delayed, and prophylactic fasciotomies should be the standard of care in acute compartment syndrome.

Evidence is limited but warrants additional clinical studies that include an accepted injury scoring system, mechanism of injury, delay to treatment, standardized HBO protocol, amputation and wound infection rate, healing time, long-term function, and cost-effectiveness.

Acknowledgments

Diana M. Barratt, M.D., M.P.H., Department of Neurology, Louisiana State University and Baromedical Research Institute, New Orleans, LA (for critical revision and editorial assistance); Juan A. Asensio, M.D., Department of Surgery, University of Southern California, Los Angeles, CA; Michael J. Bosse, M.D., Department of Orthopedic Surgery, Carolinas Medical Center, Charlotte, NC; Eric R. Frykberg, M.D., Department of Surgery, University of Florida, Jacksonville, FL; John P. Hunt, M.D., Department of Surgery, Louisiana State University, New Orleans, LA; Brent E. Krantz, M.D., Department of Surgery, University of South Carolina, Columbia, SC; Fred Luchette, M.D., Department of Surgery, Loyola University, Maywood, IL; Patrizio Petrone, M.D., Department of Surgery, University of Southern California, Los Angeles, CA; Michael C. Townsend, M.D., Department of Surgery, Tulane University, New Orleans, LA (for reviewing and scoring the articles selected for critical analysis).

REFERENCES

1. Sheridan RL, Shank ES. Hyperbaric oxygen treatment: A brief overview of a controversial topic. J Trauma 1999;47:426–35.

2. Feldmeier JJ (chairman and editor). Hyperbaric Oxygen 2003: Indications and Results: The Hyperbaric Oxygen Therapy Committee Report. Kensington, MD: Undersea and Hyperbaric Medical Society, 2003.

3. Wang C, Schwaitzberg S, Berliner E, et al. Hyperbaric oxygen for treating wounds. A systematic review of the literature. Arch Surg 2003;138:272–9.

4. Stadelmann WK, Digenis AG, Tobin GR. Physiology and healing dynamics of chronic cutaneous wounds. Am J Surg 1998;176(Suppl 2A):26S–38S.

5. Blaisdell FW. The pathophysiology of skeletal muscle ischemia and the reperfusion syndrome: a review. Cardiovasc Surg 2002;10:620–30.

6. Zimmerman BJ, Granger DN. Reperfusion injury. Surg Clin North Am 1992;72:65–83.

7. Skyhar MJ, Hargens AR, Strauss MB, et al. Hyperbaric oxygen reduces edema and necrosis of skeletal muscle in compartment syndromes associated with hemorrhagic hypotension. J Joint Bone Surg 1986;68-A:1218–24.

8. Haapaniemi T, Nylander G, Sirsjo A, et al. Hyperbaric oxygen reduces ischemia-induced skeletal muscle injury. Plast Reconst Surg 1996;97:602–9.

9. Haapaniemi T, Sirsjo A, Nylander G, et al. Hyperbaric oxygen treatment attenuates glutathione depletion and improves metabolic restitution in postischemic skeletal muscle. Free Rad Res 1995;23:91–101.

10. Buras JA, Stahl GL, Svoboda KKH, et al. Hyperbaric oxygen downregulates ICAM-1 expression induced hypoxia and hypoglycemia: the role of NOS. Am J Physiol Cell Physiol 2000; 278:C292–302.

11. Zamboni WA, Roth AC, Russell RC, et al. Morphological analysis of the microcirculation during reperfusion of ischemic skeletal muscle and the effect of hyperbaric oxygen. Plast Reconstr Surg 1993;91:1110–23.

12. Dunham CM, Bosse MJ, Clancy TV, et al. Practice management guidelines for the optimal timing of long-bone fracture stabilization in polytrauma patients: the EAST practice management guidelines work group. J Trauma 2001;50:958–67.

13. Arrillaga A, Bynoe R, Frykberg ER, et al. Practice management guidelines for penetrating trauma to the lower extremity. The EAST Practice Management Guidelines Work Group. Available at: http://www.east.org/tpg.html. Accessed April 12, 2003.

14. EAST Ad Hoc Committee on Practice Management Guideline Development 2000. Utilizing Evidence Based Outcome Measures to Develop Practice Management Guidelines: A Primer. Available at: http://www.east.org/tpg.html. Accessed April 12, 2003.

15. Székely O, Szánto G, Takats A. Hyperbaric oxygen therapy in injured subjects. Injury 1973;4:294–300.

16. No authors. Hyperbaric oxygen therapy in replantation of severed limbs. A report of 21 cases. Chin Med J 1975;1:197–204.

17. Monies-Chass I, Hashmonai M, Hoerer D, et al. Hyperbaric oxygen treatment as an adjuvant to reconstructive vascular surgery in trauma. Injujry 1977;8:274–7.

18. Shupak A, Gozal D, Ariel A, et al. Hyperbaric oxygenation in acute peripheral posttraumatic ischemia. J Hyperbaric Med 1987;2:7–14.

19. Strauss MB, Hart GB. Hyperbaric oxygen and the skeletal muscle-compartment syndrome. Contemp Orthop 1989;18: 167–74.

20. Radonic V, Baric D, Petricevic A, et al. War injuries of the crural arteries. Br J Surg 1995;82:777–83.

21. Bouachour G, Cronier P, Gouello JP, et al. Hyperbaric oxygen therapy in the management of crush injuries: A randomized double-blind placebo-controlled clinical trial. J Trauma 1996;41: 333–9.

22. Kiyoshige Y. Effect of hyperbaric oxygen therapy as a monitoring technique for digital replantation survival. J Reconstr Microsurg 1999;15:327–30.

23. Matos LA, Hutson JJ, Bonet H, et al. HBO as an adjunct treatment for limb salvage in crush injuries of the extremities. Undersea Hyperb Med 1999;26(Suppl):66–7.

24. Jadad AR, Moore RA, Carroll D, et al. Assesing the quality of reports of randomized clinical trials: Is blinding necessary? Control Clin Trials 1996;17:1–12.

25. Kiyoshige Y, Tsuchida H, Watanabe Y. Color monitoring after replantation. Plast Reconstr Surg 1996;97:463–8.

26. Porcellini M, Bernardo B, Capasso R, et al. Combined vascular injuries and limb fractures. Minerva Cradioangiol 1997;45: 131–8.

27. Zonis Z, Weisz G, Ramon Y, et al. Salvage of the severely injured limb in children: a multidisciplinary approach. Pediatr Emerg Care 1995;11:176–8.

28. Schramek A, Hashmonai M. Vascular injuries in the extremities in battle casualties. Br J Surg 1977;64:644–8.

29. Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. N Engl J Med 2000;342:1887–92.

30. Smith G, Stevens J, Griffiths JC, et al. Near-avulsion of foot treated by replacement and subsequent prolonged exposure of patients to oxygen at two atmospheres pressure. Lancet 1961;2: 1122–3.

31. Schramek A, Hashmonai M. Vascular injuries in the extremities in battle casualties. Br J Surg 1977;64:644–8.

32. Radonic V, Baric D, Petricevic A, et al. Military injuries to the popliteal vessels in Croatia. J Cardiovasc Surg 1994;35: 27–32.

33. Alexander JJ, Piotrowski JJ, Graham D, et al. Outcome of complex vascular and orthopedic injuries of the lower extremity. Am J Surg 1991;162:111–6.

34. Schlickewei W, Kuner EH, Mullaji AB, et al. Upper and lower limb fractures with concomitant arterial injury. J Bone Joint Surg Br 1992;74:181–8.

35. Isenberg JS, Sherman R. Zone of injury: a valid concept in microvascular reconstruction of the traumatized lower limb? Ann Plast Surg 1996;36:270–2.

36. Bosse MJ, MacKenzie EJ, Kellam JF, et al. An analysis of outcomes of reconstruction or amputation of leg-threatening injuries. N Engl J Med 2002;347:1924–31.

37. Mathieu D, Neviere R, Pellerin P, et al. Pedicle musculocutaneous flap transplantation: prediction of final outcome by transcutaneous oxygen measurements in hyperbaric oxygen. Plast Reconstr Surg 1993;91:329–34.

38. Mathieu D, Wattel F, Bouachour G, et al. Post-traumatic limb ischemia: prediction of final outcome by transcutaneous oxygen measurements in hyperbaric oxygen. J Trauma 1990;30: 307–14.

39. Bosse MJ, MacKenzie EJ, Kellam JF, et al. A prospective evaluation of the clinical utility of the lower extremity injury-severity scores. J Bone Joint Surg Am 2001;83-A:3–14.

40. Velmahos GC, Theodorou D, Demetriades D, et al. Complications and nonclosure rates of fasciotomy for trauma and related risk factors. World J Surg 1997;21:247–53.

41. Strauss MB, Hargens AR, Gershuni DH, et al. Delayed use of hyperbaric oxygen for treatment of a model anterior compartment syndrome. J Orthop Res 1986;4:108–11.

42. Gold BS, Barish RA, Dart RC, et al. Resolution of compartment syndrome after rattlesnake envenomation utilizing non-invasive measures. J Emerg Med 2003;24:285–8.

43. Nelson AG, Wolf EG, Li B. Influence of delayed hyperbaric oxygenation on recovery from mechanically induced damage. Undersea Hyperbar Med 1994;21:185–91.

Appendix 1

Scoring Sheet for Class I Papers on HBO and Crush Injury

Class I: Prospective, randomized controlled trials.
Class II: Clinical studies in which the data was collected prospectively and retrospective analyses that were based on clearly reliable data. Types of studies so classified include observational studies, cohort studies, prevalence studies, and case control studies.
Class III: Studies based on retrospectively collected data. Evidence used in this class indicate clinical series, database or registry review, large series of case reviews, and expert opinion.

Paper title _____

*The article is graded on a 5-point system:

1. Was the study described as randomized (0 or 1) _____
2. Was the study described as double-blind (0 or 1) _____
3. Was there a description of withdrawals and dropouts (0 or 1) _____
4. Was the randomization appropriate (−1 or 1) _____
5. Was the binding appropriate (−1 or 1) _____

TOTAL _____

Articles scored less than 3 are considered to have poor design and/or methodology.
*Based on the Eastern Association for the Surgery of Trauma (EAST) Ad Hoc Committee on Practice Management Guideline Development 2000.)

Appendix 2

Scoring Sheet for Papers on HBO and Crush Injury

Class I: Prospective, randomized controlled trials.
Class II: Clinical studies in which the data was collected prospectively and retrospective analyses that were based on clearly reliable data. Types of studies so classified include observational studies, cohort studies, prevalence studies, and case control studies.
Class III: Studies based on retrospectively collected data. Evidence used in this class indicate clinical series, database or registry review, large series of case reviews, and expert opinion.

"For class II and class III articles, objective validation scales do not exist, and as such each article should be read by at least 2 members of the panel in order to evaluate design and method."

Please evaluate the quality of this paper by assessing if a hypothesis is set forth, the methods are well described and adhered to, the results are accrued according to the described methods, and the conclusions are supported by the results and address the hypothesis.

1. Paper title _____

2. Based on the above information this paper is:
   (Circle one)

   Class II **Class III**

3. Comments:
   (quality of the journal, methods, results and paper overall; use the back of the sheet if necessary)