

## **Clinical Experience With Hyperbaric Oxygen Therapy in the Salvage of Ischemic Skin Flaps and Grafts**

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Bowersox JC, Strauss MB, Hart, GB. Clinical experience with hyperbaric oxygen therapy in the salvage of ischemic skin flaps and grafts. *J Hyperbaric Med* 1986; 1(3):141-149—We reviewed the records of 105 patients with ischemic skin flaps or grafts who received hyperbaric oxygen therapy as an adjunctive treatment. Sixty-three percent of the patients with skin flaps and 90% of the patients with skin grafts had risk factors that were considered to be poor prognostic indicators of flap or graft survival. Eighty-nine percent of threatened flaps and 91% of threatened skin grafts were salvaged. All but 2 of the patients treated were able to tolerate hyperbaric oxygen therapy: minimal side effects of barotrauma and confinement anxiety were easily managed. Nine patients with histories of impaired wound healing or underlying diseases (diabetes mellitus, peripheral vascular disease) received hyperbaric oxygen treatments before skin grafting. There was greater than 95% take of the skin grafts in this group. Treatment failures in the patients in this series were associated with older age, delay in initiation of treatment, and the presence of underlying factors associated with poor wound healing.

*HBO therapy, skin flaps, skin grafts, survival, diabetes mellitus, peripheral vascular disease*

### **Introduction**

Improved operative techniques and perioperative wound management have reduced the incidence of skin flap and graft failures. In certain patients, however, underlying diseases and infections are associated with dysvascularity and impaired wound healing. It is these patients, in particular, in which complications after covering procedures remain a formidable problem.

Tissue hypoxia is a common denominator in the pathogenesis of edema, ischemia, and infection, factors leading to skin flap and graft necrosis. Therefore, hyperbaric oxygen treatments have been advocated as an adjunctive therapy in salvaging compromised flaps and grafts. In animal studies using pedicle flaps (1-6), skin grafts (7), and island skin flaps (8), intermittent treatments with 100% oxygen at 2 to 3 ATA resulted in significantly increased tissue survival when compared to controls treated at sea level atmospheric pressure. Several case reports also attest to the benefits of hyperbaric oxygen

therapy in improving skin flap and graft survival (9–11). Perrins (12, 13) reported improved viability of skin flaps and grafts in a small series of patients treated with hyperbaric oxygen postoperatively.

No clinical data are available, however, detailing treatment protocols and outcomes in more than a small series of patients. For this reason, we undertook a retrospective analysis of 105 patients treated with hyperbaric oxygen for the threatened failure of skin flaps and grafts.

### Methods and Patient Selection

We reviewed the records of all patients who received hyperbaric oxygen treatments at Memorial Medical Center, Long Beach, CA, for the threatened failure of skin flaps or grafts from 1976 through 1983 ( $n = 105$ ). Sixty-five patients had skin flaps, 31 had split thickness skin grafts, and 9 patients had both flaps and grafts for 6 procedures or conditions (Table 1). Anatomical locations of the grafts and flaps included the trunk, head and neck, upper extremities, and lower extremities (Table 2). The median patient age was 53

**Table 1: Procedures or Conditions Creating Skin Flaps or Grafts**

| Procedure                                     | Number of Patients |                     |                  |
|-----------------------------------------------|--------------------|---------------------|------------------|
|                                               | Flaps,<br>$n = 65$ | Grafts,<br>$n = 31$ | Both,<br>$n = 9$ |
| Tumor resection                               | 28                 | 3                   | 2                |
| Ulcerations                                   | 11                 | 11                  | 1                |
| Amputations                                   | 9                  | 4                   | 1                |
| Soft tissue injuries                          | 7                  | 8                   | 2                |
| Osteomyelitis                                 | 2                  | 5                   | 2                |
| Anesthetic and reconstructive plastic surgery | 8                  | 0                   | 0                |

<sup>a</sup>All pedicle.

<sup>b</sup>All split thickness.

**Table 2: Anatomical Location of Skin Flaps and Grafts**

| Site              | Number of Patients |                     |                  |
|-------------------|--------------------|---------------------|------------------|
|                   | Flaps,<br>$n = 65$ | Grafts,<br>$n = 31$ | Both,<br>$n = 9$ |
| Trunk             | 23                 | 3                   | 5                |
| Head and neck     | 17                 | 2                   | 1                |
| Upper extremities | 0                  | 3                   | 1                |
| Lower extremities | 25                 | 23                  | 2                |

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yr (range = 3 to 88 yr); there were 56 males and 49 females. Patients were referred for hyperbaric oxygen therapy after the history, clinical appearance, or both of the flap or graft suggested they were at risk. This was based on three criteria: Clinical judgment, previous failure of the graft or flap, and/or recognized factors compromising wound healing, infection control, or both in the host (Table 3). Nine patients received hyperbaric oxygen treatments before skin grafting because underlying diseases (diabetes mellitus, peripheral vascular disease, or both) placed them at high risk for graft failure. The mean number of preoperative treatments was  $26 (\pm 5)$  for  $40.0 (\pm 7.6)$  h. Eleven patients in our series were referred from other medical centers for treatment after tissue ischemia was noted intra- or postoperatively.

All patients were treated in monoplace hyperbaric chambers (Sechrist Industries, Inc., Anaheim, CA) at 2.0 ATA (29.4 psi) in a 100% oxygen atmosphere. Patients were continuously monitored by critical care, registered nurses under the supervision of physicians; all were full-time staff in the Baromedical Department. Initially, treatments were for 90 min twice daily, 6 to 10 h apart, until sustained clinical improvement was noted (5 to 7 d); treatments were then continued for 120 min, once daily. Postoperatively the patients received  $16 (\pm 4)$  HBO treatments for a total of  $25.7 (\pm 5.3)$  h. All patients received appropriate wound management, including careful dressing changes as well as debridement and parenteral antibiotics as needed. During the course of HBO therapy, smoking was proscribed. In general, vasodilators, sympathetic blocks, dextran, or anticoagulants were not used. The response to therapy was judged on the appearance of the flap or graft and categorized as complete healing (no flap necrosis or greater than 95% surface area survival of skin grafts), marked improvement (minimal flap necrosis or 70 to 90% survival of skin grafts), or a failed procedure (flap necrosis requiring a further

**Table 3: Risk Factors for Flap or Graft Failure**

| Risk Factor                            | Number of Patients      |                          |                       |
|----------------------------------------|-------------------------|--------------------------|-----------------------|
|                                        | Flaps,<br><i>n</i> = 65 | Grafts,<br><i>n</i> = 31 | Both,<br><i>n</i> = 9 |
| Soft tissue infections                 | 19                      | 15                       | 5                     |
| Radiation therapy                      | 14                      | 3                        | 2                     |
| Peripheral vascular disease            | 13                      | 7                        | 2                     |
| Diabetes mellitus                      | 11                      | 7                        | 0                     |
| Osteomyelitis                          | 4                       | 4                        | 1                     |
| Spinal cord injury/paralysis           | 4                       | 1                        | 0                     |
| History of poor wound healing          | 1                       | 4                        | 0                     |
| Patients with one or more risk factors | 44/65                   | 28/31                    | 8/9                   |
| Percentage of patients                 | 68                      | 90                       | 89                    |

covering procedure or extensive healing by secondary intention or less than 70% survival of skin grafts).

Hyperbaric oxygen treatments were terminated prematurely in 12 patients (after 1 to 3 treatments). There were 7 patients with flaps and 5 patients with skin grafts in this group. Patient refusal to refrain from smoking during the course of therapy was the most common reason that treatments were discontinued (8 patients). Two patients had barotrauma to the ears not relieved by medication or by myringotomy tubes. One patient with extensive metastatic disease died after 1 treatment and 1 patient had only 3 treatments because of logistical complications. These patients were excluded from further evaluation. Thus, the results of 67 skin flaps and 35 skin grafts were analyzed in 93 patients.

Sixty-three percent of the patients with skin flaps and 90% of the patients with skin grafts had risk factors that were considered to be poor prognostic indicators of flap or graft survival. These factors included soft tissue infections ( $n = 39$ ), peripheral vascular disease ( $n = 22$ ), previous radiation therapy to the flap or graft bed ( $n = 19$ ), diabetes mellitus ( $n = 18$ ) (Table 3).

All data are expressed as the mean  $\pm$  SE of the mean. The data were analyzed by two-way analysis of variance or using Student's  $t$  test for unpaired data. Significant difference in values was considered to be  $P \leq 0.05$ .

## Results

Overall, threatened skin flaps and grafts were salvaged in approximately 90% of patients treated with hyperbaric oxygen (Table 4). Of those with compromised skin flaps, 37 (55%) healed completely, whereas an additional

**Table 4: Outcome of Threatened Flaps and Grafts in Patients Treated with Hyperbaric Oxygen**

| Treatment Outcome                             | No. of<br>Flaps | Percent | No. of<br>Grafts | Percent |
|-----------------------------------------------|-----------------|---------|------------------|---------|
| Complete healing<br>(greater than 95% take)   | 37              | (55)    | 19               | (54)    |
| Marked improvement<br>(70–90% take)           | 23              | (34)    | 13               | (37)    |
|                                               |                 | 89      |                  | 91      |
| Failure<br>(less than 70% take)               | 7               | (11)    | 3                | (9)     |
| Total number of flaps and<br>grafts evaluated | 67              |         | 35               |         |
|                                               |                 | 100     |                  | 100     |

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23 (34%) showed marked improvement. Similar results were obtained in patients with skin grafts: 19 (54%) had greater than 95% take and 13 (37%) had between 70 and 90% take of their grafts. In this latter group virtually all wounds were allowed to heal-in by secondary intention. There were 9 patients with histories of poor wound healing or previous skin graft failures because of underlying diseases who received hyperbaric oxygen treatments pre- and postoperatively. No treatment failures occurred in this group.

Those patients with skin flaps who were treated unsuccessfully had a mean age 12 yr older than those with favorable outcomes ( $60 \pm 8$  vs.  $48 \pm 2$  yr,  $P < 0.01$ ); furthermore, the latency period (the time from flap production to the onset of hyperbaric oxygen therapy) was 15.2 d longer in those whose flaps failed ( $19.8 \pm 7.8$  vs.  $4.6 \pm 1.1$  d,  $P < 0.01$ ). The patients with failed flaps received a greater number of hyperbaric oxygen treatments extending over a longer period of time (Table 5). Of the 7 patients with failed flaps, 6 involved the lower extremities and 1 involved the lip. In contrast to patients with skin flaps, patients whose skin grafts failed had no significant differences in age from those who were treated successfully ( $53 \pm 9$  vs.  $53 \pm 4$  yr). No differences in the latency periods were noted between the skin graft patients with regard to treatment outcome when data from the 9 patients who received pre- and postoperative treatments were included. Excluding these patients, the latency period was actually longer in those who had favorable treatment outcomes ( $7.8 \pm 4.4$  vs.  $0.5 \pm 0.2$  d,  $P < 0.05$ ). There were, however, only 3 patients whose skin grafts failed. All these patients had grafts to the lower extremities. Patients whose flaps or grafts failed despite hyperbaric oxygen therapy had a greater number of risk factors associated with poor wound healing (Table 6). In fact, the 3 treatment failures in the skin graft group all

**Table 5: Patient Characteristics by Treatment Outcome**

| Treatment Outcome                             | No. of<br>Procedures | Age, yr    | Latency<br>Period, d    | No. of<br>Treatment          | Time, h                      |
|-----------------------------------------------|----------------------|------------|-------------------------|------------------------------|------------------------------|
| Skin flaps                                    |                      |            |                         |                              |                              |
| Successful                                    | 60                   | $48 \pm 2$ | $4.6 \pm 1.1$           | $28 \pm 3$                   | $43 \pm 5$                   |
| Failed                                        | 7                    | $60 \pm 8$ | $19.8 \pm 7.8$          | $42 \pm 8$                   | $59 \pm 9$                   |
| Skin Grafts                                   |                      |            |                         |                              |                              |
| Successful (postoperative<br>treatments only) | 23                   | $54 \pm 4$ | $7.8 \pm 4.4$           | $32 \pm 4$                   | $47 \pm 6$                   |
| Successful (pre/postoperative<br>treatments)  | 9                    | $48 \pm 9$ | N.A.<br>$0.4 \pm 0.1^b$ | $26 \pm 5^a$<br>$16 \pm 4^b$ | $40 \pm 8^a$<br>$26 \pm 5^b$ |
| Failed                                        | 3                    | $53 \pm 9$ | $0.5 \pm 0.2$           | $53 \pm 22$                  | $66 \pm 26$                  |

<sup>a</sup>Values are for preoperative hyperbaric oxygen treatments.

<sup>b</sup>Values are for postoperative hyperbaric oxygen treatments.

**Table 6: Association of Risk Factors with Successful Treatment Outcome**

| Risk Factor                  | Successful Outcome/Total Number of Patients<br>With Indicated Risk Factor, % Successful |                          |
|------------------------------|-----------------------------------------------------------------------------------------|--------------------------|
|                              | Flaps,<br><i>n</i> = 67                                                                 | Grafts,<br><i>n</i> = 35 |
| Soft tissue infections       | 18/24 (75)                                                                              | 17/20 (85)               |
| Radiation therapy            | 15/16 (94)                                                                              | 5/5 (100)                |
| Peripheral vascular disease  | 12/15 (80)                                                                              | 7/9 (78)                 |
| Diabetes mellitus            | 6/11 (55)                                                                               | 6/7 (80)                 |
| Osteomyelitis                | 5/5 (100)                                                                               | 3/5 (60)                 |
| Spinal injury with paralysis | 4/4 (100)                                                                               | 1/1 (100)                |
| Hx of impaired wound healing | 1/1 (100)                                                                               | 4/4 (100)                |
| No associated risks          | 21/21 (100)                                                                             | 3/3 (100)                |

**Table 7: Number of Risk Factors vs. Treatment Outcome**

| No. Risk Factors<br>Per Patient | Flaps          |            | Grafts         |            |
|---------------------------------|----------------|------------|----------------|------------|
|                                 | No. Successful | No. Failed | No. Successful | No. Failed |
| None                            | 21             | 0          | 3              | 0          |
| One                             | 20             | 1          | 15             | 0          |
| Two                             | 10             | 0          | 8              | 2          |
| Three or more                   | 9              | 6          | 6              | 1          |

had 2 or more associated risk factors (Table 7). None of these treatment failures had preoperative HBO.

Complications of hyperbaric oxygen therapy were minimal. Fifteen patients experienced barotrauma to the ear that was relieved by medications and pressure-relieving maneuvers in all but 2 patients. Both of these elderly patients underwent the placement of myringotomy tubes but were still unable to tolerate treatments. The other readily managed side effect that we observed was that of confinement anxiety, the result of being enclosed in the relatively small monoplace treatment chambers. Usually, these symptoms resolved after the first several treatments and with patient education and counseling. Occasionally, diazepam was used. Twelve patients reported these symptoms. All completed the full course of therapy. One patient with a seizure history experienced a generalized seizure during hyperbaric oxygen treatment. He was treated with anticonvulsants and completed all subsequent hyperbaric oxygen treatments without sequelae. This was the only episode of central nervous system toxicity observed. No sign or symptom of pulmonary toxicity was observed in any of the patients treated.

## Discussion

The immediate effects of hyperbaric oxygen on ischemic tissues are hyperoxygenation and vasoconstriction. At 2 ATA, oxygen tensions in blood increase 10-fold (14). According to Peirce (15), the diffusion of oxygen into tissues is directly proportional to the square root of the oxygen tension. Thus, the amount of oxygen available to poorly perfused tissues was increased by a factor of approximately 3 in our patients during the HBO exposures. This increase correlated well with the observations of Perrins (13), who reported a threefold decrease in the necrotic area of the distal portion of pedicle skin flaps in patients who received hyperbaric oxygen therapy immediately upon recognition of circulatory compromise.

Wells et al. (16) have demonstrated sustained hyperoxygenation for 2 to 4 h after each hyperbaric oxygen treatment. The importance of this posttreatment hyperoxygenation is in maintaining a metabolic environment conducive to collagen synthesis, fibroblast proliferation, and oxidative leukocyte killing, all of which require tissue oxygen tensions of 30 to 40 mmHg (17, 18). In experimental wounds, hyperbaric oxygen increases the rate of epidermal cell migration (19). Enhanced fibroblast differentiation and collagen synthesis, resulting in a greater tensile strength of healing skin wounds, also occur in response to hyperbaric oxygen therapy (20).

Hyperbaric oxygen also acts directly as a vasoconstrictor reducing blood flow by approximately 20% in normal tissues (21, 22). Vasoconstriction is useful in reducing vasogenic edema associated with hyperemic states. Once flow is reduced, fluid resorption is shifted to favor the movement of fluid from the interstitium to the microcirculation. This vasoconstrictive effect seems to be counterproductive in ischemic conditions. However, the hyperoxygenation component compensates for the reduced flow and resultant decreased oxygen delivery by the red blood cell. The secondary effects of vasoconstriction are twofold. First, edema is reduced in the ischemic tissues, resulting in improved microcirculation as the interstitial pressures are reduced (23). The second effect is that of decreasing the diffusion distance of oxygen from the capillaries to perivascular tissues as the extracellular fluid is resorbed.

Our results substantiate the use of hyperbaric oxygen in treating patients with threatened failure of skin flaps or grafts: 90 to 91% of procedures were salvaged, despite most of the patients having serious risk factors for impaired wound healing. Early recognition of flap or graft ischemia by physicians with experience in the use of hyperbaric oxygen as an adjunctive form of therapy probably contributed to the excellent results that we observed. This is supported by the observation that those patients whose skin flaps were salvaged had hyperbaric oxygen therapy initiated sooner than those whose flaps failed. Furthermore, preoperative treatment with hyperbaric oxygen to prepare flap or graft sites seems justified in patients who have a history of failed covering procedures or in the presence of risk factors associated with impaired wound

healing. There were no treatment failures in 9 high-risk patients treated with hyperbaric oxygen before grafting.

In conclusion, we believe that hyperbaric oxygen is a useful adjunct in the management of ischemic skin flaps and grafts and confirms in a retrospective clinical study the observations made by others (1-3, 5-10, 12, 13). Certainly, not every patient requires this therapy; it should be reserved for those patients with recognized risk factors, clinical compromise, or a history of impaired wound healing. The mechanisms of hyperbaric oxygenation directly counteract the factors contributing to flap or graft compromise, including hypoxia, edema (which increases the diffusion distance of oxygen from the capillary to the cell), and wound infections. The side effects of hyperbaric oxygen treatments observed in this series were sufficiently low and easily managed to present no contraindications to using hyperbaric oxygen as an adjunctive form of therapy. The fact that 90% of the patients who presented with threatened skin flaps or grafts demonstrated sustained clinical improvement with the adjunctive use of hyperbaric oxygen supports the value of this therapy. An additional factor of increasing importance is the effectiveness of hyperbaric oxygen in reducing the hospital stay, morbidity, and repetitive surgeries that occur when compromised flaps and grafts fail.

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