Compromised skin graft and flap

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Background (to be completed)

- Incidence
- Clinical presentation (summary)
- Standard management (summary) and outcome (HBO excluded)

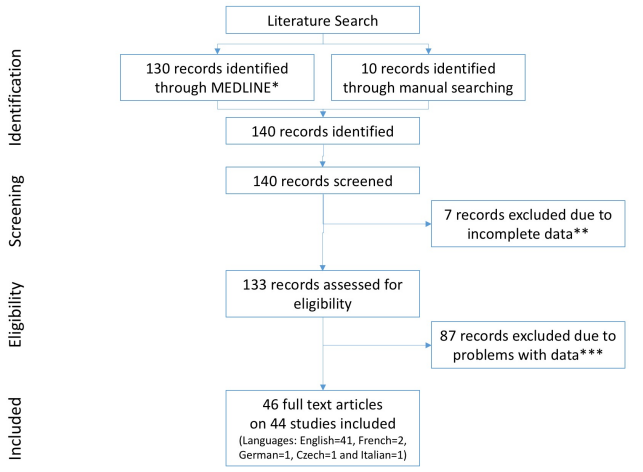
Rationale for HBO use (to be completed)

- Pathophysiology
- Animal study (if any)

Evidence

The MEDLINE was searched with the query: ("Skin Transplantation"[Mesh] OR "Surgical Flaps"[Mesh]) AND ("Humans"[Mesh] AND "Hyperbaric Oxygenation"[Mesh]) with exclusion of reviews (NOT "Review"[pt]). The output included 130 records, which have been extended by additional 10 records, found in the reference list of above mentioned papers and not included in the MEDLINE. All records were searched for the full text with exclusion of abstracts from the conference. In 133 cases we succeeded, but in 7 records there was no possibility to get the full text. From those 133 full papers, we excluded 87 papers as they were presenting any reliable information for the problem (no clinical data, lack of information about HBOT in relation to skin grafts/flaps, using bone components in flaps).

For analysis, we have included 46 papers reporting 44 studies enlisted in the following Table. This list includes papers in English (N=41), French (N=2), German (N=1), Czech (N=1) and Italian (N=1). The search strategy is presented in the following Figure.



* Query: ("Skin Transplantation"[Mesh] OR "Surgical Flaps"[Mesh]) AND ("Humans"[Mesh] AND "Hyperbaric Oxygenation"[Mesh]) AND (NOT "Review"[pt])
** No possibility to get the full text
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The only blinded, prospective, randomized controlled trial (RCT) was conducted by Perrins in 1967 (Perrins 1967) (Perrins 1966). In this paper he reported 48 patients (half of the patients treated with HBOT, half - without) referred for split skin grafts. Interestingly there was no exclusion in this study, and every patient that presented for split grafting was included, regardless of age (except infants), sex and thickness, size, or situation of the graft, or the underlying cause of the lesion. Patients were allotted randomly to either treatment or control group; surgical procedure was done by the same surgeon who did not know if the case was subsequently to be treated. HBOT was conducted at 2 ATA for 120 minutes, time for starting HBOT was short, as first session was conducted on the evening of operation and thereafter in the morning and evening for three consecutive days. For patch grafts the number of patches applied to the raw area were counted at operation and then on the 7^{th} day, when the second dressing was performed; for sheet grafts the area was measured and percentage survival was obtained. Complete survival, defined as 95% or more that survived, occurred in 64% in HBOT group as opposed to 17% of the controls ($p<0.01$). Over 80% of the grafted area survived in nearly twice as many of the treated cases as in the controls; while in none of the treated cases was less than a 60% of survived area obtained. In the paper there is no information whether those grafts were compromised before starting HBOT but low success rate in the controls is intriguing. Nevertheless, to date, this remains the single prospective and blinded RCT evaluating HBOT for grafts strongly supporting its use.

There were two retrospective controlled cohort studies evaluating adjunctive HBOT in compromised flaps. A 2008 study published by Roje et al (Roje, Roje et al. 2008) reported effects of HBOT on short-term complications for war injury reconstructions. Of a total of 1220 patients with war wounds treated in one centre in Croatia between 1991 and 1995, only 388 with more complex wounds of Gustilo type III A, B, and C to the upper or lower extremities, or both, were included in the study. The outcome of 99 patients treated with HBOT at pressure between 2.2 and 2.8 ATA (with frequency and number of sessions based on clinical picture) was compared with 289 controls treated without use of HBOT. Authors recorded deep infections, osteomyelitis, skin grafts lyses, and flap necrosis. Additionally, stratification by wound severity taking into account complexity, severity, and primary characteristics of the war wound, was introduced. In patients receiving HBOT, deep soft tissue infections and skin graft lyses were twice less frequent, and flap necrosis more than three times less frequent than in those not receiving HBOT ($p<0.001$). Osteomyelitis was also less frequent in patients receiving HBO therapy, but only by 15% ($p=0.03$). Median time to granulation formation was shorter by 25% in patients receiving adjuvant HBOT ($p<0.001$). In 2014 D'Souza et al. (D'Souza, Lowe et al. 2014) reported results of treatment of osteonecrosis of the mandible. Out of 71 patients reported there were 28 patients where free flaps were used for reconstruction. Healing rate of osteoradionecrosis (including flap survival) was 93% (14 out of 15 patients) in HBOT group and 85% (11 out of 13 patients). Clearly there is no difference between those two groups. Unfortunately there is no clear data neither on HBOT details (pressure, time, frequency, number of sessions) nor relation between HBOT and flaps procedure, so results are inconclusive when concerning direct effect of HBOT on survival of flaps in compromised patients. Nevertheless, this is one of few papers in the subject, so it should be included in the analysis.

There were 18 papers reporting case series including 326 patients in total. Out of them, 16 papers concerning clinical observations of 308 patients with skin grafts and soft tissue flaps clearly favour HBOT. Only 2 papers, concerning 18 patients, do not give any clear conclusion concerning final results of the treatment and their relations with HBOT.

There were also 24 papers reporting observation of 31 clinical cases, all favouring HBOT.

Table:

(authors, year)	Type	Nb patients	Evaluation criteria		(pressure, time, nb of session)	Results	comment
(Perrins 1967) (Perrins 1966)	Blinded, prospective, randomized, controlled trial	48 (24 HBOT vs 24 control)	Complete survival of the graft (means >95% total surface survival)	Every patient that presented for split skin grafting was included, regardless of age (except infants), sex and thickness, size, or situation of the graft, or the underlying cause of the lesion.	HBOT @ 2 ATA for 120 minutes bid for 3 days	1) 64% complete graft survival in HBOT group vs 17% in controls ($p<0.01$) 2) increase in survival of 29% of the surface area of the grafts	Blinded, prospective, randomized, controlled trial. Favours HBOT.
(Roje, Roje et al. 2008)	Retrospective controlled cohort study	388 (289 control vs 99 HBOT)	Deep infection, osteomyelitis, skin grafts lyses, and flap necrosis; additional stratification by wound severity.	Short-term complications for war injury reconstructions.	HBOT @ 2.2-2.8 ATA with frequency and number of sessions based on clinical picture	1) Skin graft lyses 52% in control vs 23% in HBOT ($p<0.001$) 2) flap necrosis 51% in control vs 15% in HBOT ($p<0.001$) 3) In all severity groups, deep soft tissue infections, flap necrosis, and skin graft lysis were less frequent in patients who received HBOT.	Retrospective controlled cohort study. Favours HBOT.
(D'Souza, Lowe et al. 2014)	Case series	28 (15 with HBOT and 13 without)	Healing	Skin free flaps for surgical reconstruction in ORN	No data	Healing rate in 14 out of 15 patients in HBOT group (93%) and in 11 out of 13 patients without HBOT (85%)	Controlled case series. No difference between HBOT and controls. No clear data on relation between HBOT and flaps procedure
(Larson, Steensma et al. 2013)	Case series	15	Flap survival	91 patients screened, included patients were those who underwent HBOT for a failing post-reconstructive flap, regardless of flap design or classification. Cases were excluded if the patient underwent HBOT treatment for a different clinical indication, received prophylactic HBOT prior to flap reconstruction, suffered flap compromise due to a traumatic etiology, or if the interval between surgical creation of the flap and initiation of HBO2 was longer than three weeks.	HBOT 2.4 ATA for 90 min, once daily for 14 pts, bid for 1 pt, avg 27 HBOT (3-60) in avg 43/5 days (6-113)	Threatened flaps were salvaged in 11 patients (73.3%) treated with HBOT and failed in 4 cases (26.7%). Of the successfully salvaged flaps, four (36.4%) healed completely, and an additional seven (63.6%) demonstrated marked improvement.	Controlled case series. Favours HBOT.
(Gonnering, Kindwall et al. 1986)	Case series	6	Survival of compromised flaps and grafts	Periorbital reconstruction	HBOT @ 2 ATA for 120 min bid for 5 days	Complete survival of 2 ischemic random flaps and 4 composite grafts	Case series. Favours HBOT.
(Friedman, Stonerock et al. 2003)	Case series	5	Graft survival	Using composite earlobe grafts for repairing of cleft lip-nasal asymmetries and nasal defects both in children and adults	HBOT, usually bid of 90 minutes each on an outpatient basis for 5 days after composite graft placement	100% composite graft takes, although in one instance, the patient with a large graft (1.5 cm) did have epidermolysis of a portion of the graft.	Case series. Favours HBOT.

(Saber, Yahya et al. 2005)	Case series	27	Survival of grafts, measurement of TCOM	Chronic leg ulcers (36 ulcers in 27 patients).	HBOT 2 ATA with 120 min; 12 sessions preoperative, followed by 12 postoperative	At 18 months, 18 skin grafts (50%) showed complete take, 15 (41.7%) demonstrated partial take and 3 (8.3%) failed	Case series. Favours HBOT.
(Assaad, Chong et al. 2011)	Case series	39	Survival of grafts	Limbal conjunctival autografting for recurrent pterygium (40 eyes in 39 patients). 18 eyes had previously undergone beta radiation or chemotherapy with mitomycin C	HBOT 2 ATA for 90 minutes for initial 5 sessions, than extended based on clinical judgement	All grafts were taken. No recurrences have been recorded.	Case series. Favours HBOT.
(Ueda, Kaneda et al. 1987)	Case series	26	Survival and improvement	23 axial and 3 random flaps, all compromised	No info	Average improvement 92.1%	Case series. Favours HBOT.
(Mathieu, Neviere et al. 1993)	Case series	15	Survival, TCOM	Pedicle musculocutaneous flaps; traumatic, burns, osteomyelitis, radionecrosis	HBOT 2.5 ATA	7 flaps survived and 8 flaps failed. Positive correlation between TCOM over 50 mmHg and flaps survival	Case series. Favours HBOT.
(Waterhouse, Zamboni et al. 1993)	Case series	16	Survival	14 free flaps & 2 replantations. Compromised by prolonged ischemia, a secondary ischemia or radiation history	No info in the abstract	The benefit of HBOT was related to the time to initiation of treatment, with 89% of pts (8/9) treated within 24 hours having complete salvage, and partial necrosis (<25%) occurring in one patient.	Case series. Favours HBOT.
(Chan, Koh et al. 2014)	Case series	4	Flap survival	Musculocutensous flap, all patients had previously failed multiple (5 to > 35) surgical procedures.	HBOT preoperatively in all 4, 2.2-2.4 ATA for 90 min, five times per week for 5-6 weeks, up to total 30 sessions; postoperatively in 2 pts 10 further sessions within 2 weeks	Complete healing occurred in all patients at a median (range) follow-up of 2.5 (2–3) months. There were no further hospital admissions for PPS at a median (range) follow-up of 35 (8–64) months	Case series. Favours HBOT.
(Nolen, Cannady et al. 2014)	Case series	12	Flap survival	89 patients observed (39 with HBO vs 50, without) Free flap reconstruction for ORN of the mandible; 12 (13%) did not contain a bone component	No info	No info comparing HBOT vs no HBOT in boneless flaps	Case series. Not conclusive.
(Gevorgyan, Wong et al. 2013)	Case series	14 (8 with HBOT)	Flap survival	In 6 patients there were free flaps	HBOT 2.0 or 2.4 ATA for 90 minutes; 30 sessions preoperatively and 10 postoperatively	There were no flap failures encountered in this series.	Case series. Favours HBOT.
(Gehmert, Geis et al. 2011)	Case series	6	Flap survival	Flap transplantation was performed to cover tissue defects of the lower limb caused by trauma in all patients.	The first day after surgery the patients underwent hyperbaric oxygen therapy (HBOT). The HBOT regimen consisted of treatment over 90 minutes with 100% O2 (FiO2 1.0) at 240 kPa	No info on flap outcome	Case series. Not conclusive.

(Metselaar, Dumans et al. 2009)	Case series	5	Flap survival	One-stage surgical repair of the meatal skin defect in patients with long-lasting osteoradionecrosis of the outer ear canal, using a postauricular, inferiorly pedicled skin flap.	HBOT 2.5 ATA for 80 minutes both preoperatively (from 17 to 30) and postoperatively (from 10 to 11)	Success in 4 out of 5 patients, negative in 1 out of 5.	Case series. Favours HBOT.
(Svehlik, Zabavnikova et al. 2007)	Case series	3	Flap survival	Wounds after injury	HBOT 2 ATA every second day for 90 minutes on working days (without weekends); 8 sessions before grafts (6-10) and 16 after (10-20)	Healed by the end of HBOT (48 days on average)	Case series. Favours HBOT.
(Cordova, Corradino et al. 2005)	Case series	10	Flap survival	Musculocutaneous pectoralis major flap. Previous surgery and radiotherapy with recurring or pluri-recurring pharyngostomes	HBOT before and after operation, no more data	All flaps taken; min. 1 year follow-up	Case series. Favours HBOT.
(Maynor, Moon et al. 1998)	Case series	20 patients / 28 flaps	Monitoring of drainage-free interval	Patients that received free vascularized muscle flaps; of the 28 flap procedures done, 9 were skin-muscle rotation flaps (SMR) and 19 were microsurgical free tissue transplant (FTT). Individually, 15 patients received FFT, 9 received SMR flaps and 4 received FTT and SMR flaps. Six patients had initial failure, 1 started HBO simultaneous HBO and the rest began HBO therapy at various times after flap failure (2, 5, 5, 8 and 29 months, respectively). 12 pts received flaps before the initiation of HBO, 5 received them concurrently, and 3 received HBO before their flap procedures.	HBOT 2 ATA for 120 minutes, 6 days per week; mean HBO sessions 35 (6-99)	Drainage-free interval after HBO; follow-up of 84 months; pts who had received flaps were more likely to be drainage free than those who had not received flaps; using life-table analysis this difference approached but did not reach statistical significance (p=0.074).	Case series. Favours HBOT.
(Davis, Landeen et al. 1987)	Case series	4	Graft survival	Patients with pyoderma gangrenosum	HBOT 2.4 ATA once daily for 90 minutes as preparation for grafts (27, 31, 76 and 82 days) plus postgraft HBOT until graft take was secure	16 pre + 9 post = 100% take with 25 months follow-up demonstrating no recurrence; 75 pre + 7 post = 90% take at 9 days and 100% take after 21 days; 12 pre + 11post = 50% graft take plus 16 HBOT plus mesh split-thickness skin grafts plus HBOT up to 37 total with 2-year follow-up showing healing; 24 pre + 3 post =100% take after 3 days and healing persisted for 1 year	Series of consecutive patients. Favours HBOT.
(Bowersox, Strauss et al. 1986)	Case series	105	Flap and graft survival	Compromised grafts or ischemic skin flaps, 90% pts had risk factors	HBOT @ 2 ATA for 90 min bid for 5-7 days followed by 120 min daily once sustained clinical improvement was noted (avg 16+4 treatments)	89% of compromised flaps and 91% od threatened skin grafts were salvaged. Failed flaps and grafts were associated with 2 or more risk factors for poor wound healing and compromised flap failure was associated with a	Case series. Favours HBOT.

						delay in HBOT initiation over 2 weeks (19.8 days post-op for failed flaps vs 4.6 days for salvaged, p<0.01)	
(Pistorio, Leslie et al. 2015)	Case report	1	Flap survival	Living bilayer skin substitute, for non-operative salvage of a traumatic degloving injury in 70-year-old female on chronic steroids for sarcoidosis	HBOT 2.2 ATA for 90 minutes, bid for 9 days than continued for a total of 20 sessions to prepare the wound bed for grafting	Success	Low level of evidence. Favours HBOT.
(Fredman, Wise et al. 2014)	Case report	1	Flap survival	Skin flap ischemia after skin-sparing mastectomy	HBOT 2 ATA for 90 minutes, starting day of surgery, until POD 3 days; in total 5 sessions	Full resolution	Low level of evidence. Favours HBOT.
(Araujo, Kondo et al. 2013)	Case report	1	Graft survival	Pyoderma gangrenosum, immunosuppression,	HBOT before skin grafts and after skin grafts	Success	Low level of evidence. Favours HBOT.
(Ratnagobal and Sinha 2013)	Case report	1	Graft survival	Pyoderma gangrenosum, split-thickness skin grafting	HBOT 45 sessions without improvement of the wound; after preparation of the wound bed and skin graft a “course” of HBO was given “immediately following the skin graft	Complete healing with significant reduction in pain	Low level of evidence. Favours HBOT.
(Baltacioglu, Bagis et al. 2015)	Case report	1	Flap survival	Failure of the first mucoperiosteal flap sutured over two dental implants; than gingival graft used to cover exposed bone surface followed by HBOT	HBOT three 30 minute sessions @ 2.4 ATA over 5 days, total 15 sessions	Two weeks after completion of HBO the implant are was corrected with laser; complete healing; observation 1 year	Low level of evidence. Favours HBOT.
(Chong, Ooi et al. 2011)	Case report	1	Graft survival	Two burn wounds on both knees in diabetic patient, covered by skin grafts	HBOT 2.4 ATA for 90 minutes; 10 sessions preoperatively plus 5 sessions postoperatively	Graft take was 100% on left knee and and 90% on right knee at postoperative day 26.	Low level of evidence. Favours HBOT.
(Martella, Agazzi et al. 2009)	Case report	1	Flap survival	Severe skin necrosis after breast reconstruction with a transverse rectus abdominis musculocutaneous flap in methylenetetrahydrofolate reductase deficiency.	HBOT starting after operation, lasting for 10 days	Overall success including flaps	Low level of evidence. Favours HBOT.
(Niezgoda, Cabigas et al. 2006)	Case report	1	Graft survival	Pyoderma Gangrenosum treated unsuccessfully with immunosuppression, antibiotics, vacuum assisted closure (VAC) and HBOT. Split-thickness skin grafting followed by HBOT.	HBOT 11 sessions at 2.4 ATA, continuation of VAC	Complete recovery, follow up to 24 months	Low level of evidence. Favours HBOT.
(Leach, Kruger et al. 2005)	Case report	1	Flap and graft survival	Cochlear implantation with infections (antibiotics plus HBOT before operation). Scalp flap and a split-thickness skin graft.	HBOT 2.4 ATA for 90 minutes once daily for 17 sessions; than operation; resuming HBOT the following day for 4 more days	Full recovery; follow-up 6 months	Low level of evidence. Favours HBOT.

(Grundmann, Jaehne et al. 2000)	Case report	2	Implant survival	One nose replantation (after dog bite) and one lobe necrosis with fistula following laryngopharyngectomy	HBOT 2.4 ATA fo 90 minutes every day (6 days a week); 10 sessions for nose replantation and 14 pre-operation with 10 post-operation after musculoskeletal flap with pectoris major	Successful	Low level of evidence. Favours HBOT.
(Emmerova, Barcal et al. 1994)	Case report	1	Graft survival	Trophic ulcer of the lower leg after years of unsuccessful therapy. Skin graft.	HBOT 2. 5 ATA for 90 minutes, once daily; after 15 HBOT sessions, the autograph was done plus 21 HBOT sessions	Full recovery	Low level of evidence. Favours HBOT.
(Schweitzer and Burtka 1991)	Case report	1	Flap and graft survival	Failure of natural scalp flap after cochlear transplantation. Secondary scalp transposition flap and split thickness skin graft	HBOT 2.4 ATA for 75 minutes once daily for 11 days and immediate postoperative HBOT for additional 4 days	Full recovery	Low level of evidence. Favours HBOT.
(Longoni, Viotti et al. 1982)	Case report	1	Graft survival	Skin graft for repair of wound after severe Fournier disease	HBOT 2.5 ATA for 60 minutes; 27 sessions in 60 days for treating infection, than inguinal skin graft plus 3 HBOT session in one day.	Full graft take	Low level of evidence. Favours HBOT.
(Gal, Yueh et al. 2003)	Case series	3	Flap survival	Free flaps to cover surgical wound after treatment of osteoradionecrosis of mandibula	HBOT 90 minutes in post-operative time	Full take of the free flap (3 out of 3), but the rest of patients with free flaps (27 of 30 patients) were also successful	Low level of evidence. Favours HBOT.
(Abbes, Demard et al. 1975) (Abbes, Demard et al. 1977)	Case report	1	Flap survival	Patient after subglossopharyngectomy. Delto-pectoral flap, compromised at 5th day, reconstruction and HBOT	HBOT 2-3 ATA (?), 120 minutes, 17 sessions, resection of flap, new graft plus 6 HBOT sessions	Success	Low level of evidence. Favours HBOT.
(Hart, O'Reilly et al. 1974)	Case report	5	Graft survival	Patients after burn, 2 pts breathing air required skin grafting, 3 pts breathing HBOT required grafting	HBOT 2 ATA for 90 minutes bid (no info on session numbers)	3 pts on HBOT: full take of graft, 1 pt on air: full take of graft 1 pt on air 90% graft loss	Low level of evidence. Favours HBOT.
(Szekely, Szanto et al. 1973)	Case report	1	Graft survival	Skin graft was used to cover injury wound in 11-year-old boy after septic shock	HBOT 2 ATA 120 minutes, pre- and post- operative	Success	Low level of evidence. Favours HBOT.
(Moffat, Weaver et al. 2015)	Case report	1	Flap survival	Breast flap, combined treatment with leech therapy, hyperbaric oxygen, pentoxifylline and topical nitroglycerin	HBOT 2 ATA, starting 22 hours after surgery, 3 sessions of 110 minutes once daily, than 4 sessions of 100 minutes once daily	Flap improved and completely healed by week 8 without need for further surgery	Low level of evidence. Favours HBOT.

(Mermans, Tuinder et al. 2012)	Case report	1	Flap survival	Full thickness breast skin flap	HBOT 20 sessions @ 2.4 ATA for 90 minutes from POD 4 till POD 19	Success	Low level of evidence. Favours HBOT.
(McCrary 2007)	Case report	1	Survival	Failing facial flap in 4-year-old girl after dog attack	HBOT US Navy Table 9 at 2.46 ATA for 90 minutes, bid for 2 days, than once more	Success	Low level of evidence. Favours HBOT.
(Cantarella, Mazzola et al. 2005)	Case report	1	Survival	Nose replantation after a dog bite in adult	HBOT 2.5 ATA for 70 minutes, 8 hours after surgery, once daily for 12 sessions	Success	Low level of evidence. Favours HBOT.
(Nichter, Morwood et al. 1991)	Case report	1	Survival	Nose replantation in 2-year-old girl	HBOT 90 minutes, bid for 8 days followed by 1 session per day for 3 days	Success	Low level of evidence. Favours HBOT.
(Rapley, Lawrence et al. 2001)	Case report	1	Survival	Nasal tip reconstruction after avulsive dog-bite injury in 5-year-old boy	HBOT 1 ATA for 90 minutes, bid for 3 days	Success	Low level of evidence. Favours HBOT.
(Khandelwal, Wall et al. 2008)	Case report	1	Flap survival	Complete scalp degloving injury in adult. Microsurgical replantation of the scalp, leech therapy	HBOT 2.5 ATA for 90 minutes bid for 7 days and then once daily for 30 days	Success	Low level of evidence. Favours HBOT.

Patients selection for HBOT

Patients at high risk for compromised graft/flap (eg. immunocompromised or having irradiated or infected wound bed) or with already compromised graft/flap that do not have any contraindication for HBOT should be considered for selection for kind of treatment. In most cases, the skin graft or flap is not life-saving procedure, so risk-to-benefit ratio of using HBOT as adjunctive treatment should be analysed with the highest priority of patient safety and availability of resources (access to the hyperbaric unit).

Current protocol

Standard HBOT session should be used.

Cost impact

As depending on the site and size of grafts/flaps, the cost of repetitive operation can be very high and result in significant distress for both the patient and the surgeon. HBOT can reduce the cost of treatment by reducing the risk for reoperation.

Conclusion / Recommendation

We recommend that HBOT should be used in all cases of compromised skin grafts and flaps. As time plays role in reviving impaired tissues, HBOT should be started as soon as possible after diagnosis of compromised grafts/tissues. The preferred protocol should include HBOT at pressure between 2 and 2.5 ATA for at least 60 minutes per session (preferably 90-120 minutes), repeated two or three times in first day, then twice per day or once daily until tissues declared alive or necrotic. Tissue viability can be accessed by clinical judgement or by using more objective methods including measurement of TcpO2 or assessment of capillaries by laser Doppler.

In cases when there is as increased risk for compromised skin grafts and flaps, eg. irradiated or infected wound bed, immunocompromised patient, we recommend that HBO should be used both preoperatively (usually up to 20 HBOT sessions given once or twice per day should be enough) and post-operatively (as depending on clinical judgement, usually 10 sessions given once or twice per day should be enough).

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