The Use of Modalities in Wound Care Part 2: Hyperbaric Oxygen Therapy (An update on HBO Therapy coverage, NCD implications)

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INTRODUCTION

In the second installment of the use of modalities in wound care white paper, we will review the use of hyperbaric oxygen (HBO therapy) as a lever for reducing unwarranted clinical variability. This is the second part of three papers focused on the use of advanced modalities aimed at providing evidence and clinical guidance for providers managing complex wound patients. As in all previous white papers, the "CLEAR" (or Clinically Led, Evidenced-based, Analytically driven, Research-informed) process was used for the review of the literature and Healogics data was examined using a 2019 treated wound cohort.

In addition to updating our previously published results on the effectiveness of HBO therapy for the treatment of Wagner grades 3 and 4 wounds[1], this white paper provides information concerning the use of HBO therapy for radiation cystitis. In the appendix, we have included an important update and guidance on the retirement of two Medicare Local Coverage Determinations (LCDs) on HBO therapy and will give clarity to the Healogics community on our interpretation of the now universal National Coverage Determination (NCD).

The use of HBO therapy for diabetic foot ulcers (DFUs) has a long and controversial history. Early studies focused solely on complex DFU patients who were hospitalized. Investigators, over time, recognized the importance of conducting more robust randomized trials; however, many of these studies were handicapped by low patient enrollments. More recently, meta-analysis and systematic reviews have become more prevalent. Many of the original studies used the Wagner classification scheme, which was then adopted for randomized control trials (RCTs). While the Wagner classification is often used in clinical trials and for insurance claims, there are numerous limitations and more recent grading systems could potentially help unravel some of the confusion if used in future studies.

To begin, the physiological reasons to consider HBO therapy for the treatment of DFUs include increasing the oxygen gradient and macrophage recruitment, along with generating elevated levels of local growth factors.[2] On a systemic level, HBO therapy increases the recruitment and release of endothelial progenitor cells, which home to the area of injury and promote vasculogenesis and collagen formation[3]. The management of DFUs includes glucose control, offloading, debridement, local wound care and ensuring adequate tissue perfusion. HBO therapy should be considered as adjunctive care and as part of an overall comprehensive treatment plan.

EFFECTIVENESS OF HBO THERAPY: REVIEW OF LITERATURE

While there were a few small studies prior to 1987, the paper by Baroni et al. is referenced by most as the first prospective study of HBO therapy on the DFU[4]. Patients in this trial were admitted to the hospital and were aggressively debrided, and had rigid glucose control and culture-driven antibiotic therapy, in addition to HBO therapy. Healing rates improved and amputations were reduced in the HBO therapy group compared to controls; however, there were only 28 patients in the study. The same group updated their data and, retrospectively, reported on 80 patients in 1982 and a 10-year experience in 1990[5].

Randomized controlled trials began to reach the literature with Doctor et al., publishing one of the first in 1992[6]. Again, hospitalized patients were studied, (n=30), and culture-positive rates and amputations were decreased in the HBO therapy group. Interestingly, these investigators used a 3.0 Atmosphere Absolute (ATA) protocol four times over a two-week setting. Faglia reported on 68 hospitalized patients in a randomized trial in 1996[7]. This study included peripheral arterial disease (PAD) patients who were either bypassed or treated with endovascular techniques. This paper also used Wagner classifications to stratify and set the stage for many subsequent investigators to utilize this scoring system. Several authors followed with studies, each using different research primary endpoints, various inclusion and exclusion criteria and definitions of success, making meta-analysis extremely difficult[8-10].

Efforts to improve the quality of studies conducted on the use of HBO therapy continued over the years and, in 2003, the first randomized, double-blinded, placebo-controlled trial was published by Abidia et al[11]. While only including 18 patients, this study demonstrated improved healing at one year in the HBO treated group, establishing that HBO therapy can initiate a healing process early that is sustainable over time. Kessler and Duzgun followed with randomized trials that also showed positive effects for HBO therapy treated patients[12,13].

Additionally, a well-conducted trial, enrolling 75 patients with Wagner 2-4 ulcers and studied using a placebo compression with room air at 2.5 ATA, was published by Londahl and team in 2010[14]. In this study, the one-year intent-to-treat healing rate was 52% versus 29% for those treated with HBO therapy versus controls, respectively (p=0.03).

CONTROVERSIAL STUDIES OVER TIME

There have also been some studies that reported negative results for HBO therapy when treating DFUs. Margolis et al. published a retrospective paper in 2013 based on a database of 6,259 patients from the National Healing Corporation[15]. This paper found that patients had lower healing rates and higher amputations when HBO therapy was utilized. Numerous letters to the editor and conversations at national meetings followed its publication. One point of concern was that many patients with Wagner 2 ulcers, who typically are not deemed appropriate for HBO treatment, were included in the analysis. The Margolis study raises some of the potential issues when comparing population data and clinical trial results. The study should not have been interpreted to imply that HBO therapy does not work, as almost half of the patients did improve; however, there was no statistical difference between the overall comparison groups. Due to the study design, these findings are more likely driven by patient selection and analysis inclusion criteria versus actual treatment efficacy. This is not uncommon as there have been many oncological protocols that fail in initial trials, and then sub-group analyses are later performed and a specific cancer type is found to be highly responsive. Taken in the opposite direction, a highly significant clinical RCT may fail when the drug or device is utilized on a broader population than those in the initial trial. We have discussed the patient/population pivot in prior publications, and we need to remind ourselves of this concept as we read and interpret data and clinical papers.

Another known study to show negative results of HBO therapy was conducted by Fedorko and associates.[16] They published a double-blinded, placebo-controlled RCT looking at 107 patients with Wagner 2-4 DFUs. Patients with peripheral arterial disease were excluded and 30 HBO treatments were planned for all participants. One limitation of the study was that only 61% of the HBO patient group; however, received their full treatment course. Additionally, while one of the main study outcomes was amputation, this was determined not by actual amputation procedures, but rather by a decision that amputation was indicated based only on a photograph. This highly unusual protocol resulted in many letters to the editors and comments from the HBO community seeking clarification. Interestingly, the Canadian government commissioned this study and, despite the results, they continued to pay for HBO therapy, with limited coverage to Wagner grade 3 and higher, after this publication.

Most recently, Santema et al. published an RCT on ischemic patients comparing standard of care (SOC) to SOC with HBO therapy[17]. However, in an unconventional move while the clinical trial was underway, the study design was changed, and the power calculation was modified by increasing the expected improvement in HBO therapy due to poor enrollment. In addition, many patients enrolled failed to complete their planned number of HBO treatments. Of note; however, there was a sub-group of patients that did complete HBO therapy who achieved significant healing and amputation-free survival. Again, due to these issues in study design, many letters to the editor were generated and the author responded by stating that additional studies looking at a narrower group of patients that complete their HBO treatments might render different results[18].

HBO THERAPY UTILIZATION IN REAL-WORLD DATA

So, where does this leave us? We wanted to better understand the impact of HBO therapy utilization by examining Wagner 3 and 4 diabetic foot ulcers using Healogics comprehensive wound database. To better isolate the treatment effect, we limited the population to those with only a single wound located on the foot. The rationale for this criterion was to be able to compare our findings with those of many of the initial studies that focused only on diabetic foot ulcers and not more broadly on diabetic wounds of the lower extremity.

In 2017, we initially published an overall Comprehensive Healing Rate (CHR) for the company using a modified intent to treat methodology[19]. In that paper, we established the industry norm, allowing comparisons and opportunities for performance management for Centers and providers in the future using a transparent, honest reporting method. Only patients with no wound identified, who were seen for a consult only, or who were still in active therapy at the time of data collection were excluded. This modified intent to treat (mITT) healing rate for all wound types was 74.6%, which represented 1,006,690 wounds. At the time of publication, there were questions raised about the potential for bias, given that 10% of the wounds reported in the study were still in treatment- and, therefore, excluded when the data collecting was stopped for the research. To answer this concern, in the second paper, we used the same database, which was continuously adding patients and reported a mITT healing rate of 74.2% on then 2,651,878 wounds[1]. This still represents the largest healing outcomes paper published and shows the consistency and data integrity that we have achieved over time. We then focused in on the mITT for various wound etiologies and noted that if a wound was classified as diabetic, there was little difference in the healing rate from the mean.

In Table 1 from that publication, seen below, healing rates by etiology were described. Using the general term “diabetic,” it was noted that there was not a large difference in the healing rate compared to the overall healing rate, 71% vs. 74%, respectively.

Table 1. Wound Healing rates by etiology and aggregate

mITT 2014-2018	Arterial	Diabetic	Pressure	Venous	All Wound Types
Total no. of healed wounds	34,745	328,158	190,832	296,219	1,408,871
Total no. of wounds	89,469	605,102	447,064	475,203	2,651,878
% Healed at population level	38.83	54.23	42.69	62.34	53.13
Exclude - no. of active treatments at study conclusion	4,516	8,544	32,406	8,331	87,098
% of total	5.05	1.41	7.25	1.75	3.28
No. of remaining wounds	84,953	596,558	414,658	466,872	2,564,780
% Healed at level	40.90	55.01	46.02	63.45	54.93
Exclude - no. of without wound documented	24	320	349	402	6,277
% of total	0.03	0.05	0.08	0.08	0.24
No. of remaining wounds	84,929	596,238	414,309	466,470	2,558,553
% Healed at level	40.91	55.04	46.06	63.50	55.07
Exclude - no. of consult and with days first to last assessment ≤ 7 days	22,049	133,350	116,073	99,078	658,735
% of total	24.64	22.04	25.96	20.85	24.84
Final - no. of remaining wounds	62,880	462,888	298,236	367,392	1,899,818
% Healed at level mITT	55.26	70.89	63.99	80.63	74.16
% Amputation at level mITT	2.99	2.42	0.5	0.11	0..94

mITT, modified intent-to-treat.

By limiting the diabetic etiology group to those with only a single wound, located on the foot or toe, with a diagnosis of diabetes, compared to the total population, we note a significant difference in the healing rate, 56% vs. 74%, respectively.

Table 2. Modified intent-to-treat healing rate and amputatoin rate: diabetic single wound Wagner grade 3/4 on foot or toe

	All Single Wound 3/4
Total no. wounds	25,562
% Healed at population level	43.65
Exclude - no. of active at study conclusion	1,877
% of total	7.34
No. of remaining wounds	23,685
% Healed at level	46.39
Exclude - no. of without wound documented	0
% of total	0
No. of remaining wounds	23,685
% Healed at level	46.39
Exclude - no. of consult and with days first to last assessment ≤ 7 days	4,624
% of total	18.10
Final - no. of remaining wounds	19,057
% Healed at level mITT	56.04
% Amputated at level mITT	4.09

This places the diabetic patient with a foot or toe wound at the same healing rate, on a percentage healing basis, as those with peripheral arterial based ischemic wounds, which are known to be extremely difficult to heal and in which limb loss is a constant threat.

We then analyzed those patients in which HBO therapy had been ordered and used at least for a single treatment session. The healing rate for those with one or more HBO treatments versus the population was calculated as 60% vs. 74%, respectively.

Table 3. Modified intent-to-treat heeling rate and amputation rate

	HBO THERAPY	No HBO THERAPY
Total no. of wounds	6,616	18,946
% Healed at population level	53.30	40.29
Exclude - no. of active at study conclusion	490	1,387
% of total	7.41	7.32
No. of remaining wounds	6,126	17,559
% Healed at level	56.58	42.83
Exclude - no. of without wound documented	0	0
% of total	0	0
No. of remaining wounds	6,126	17,559
% Healed at level	56.58	42.83
Exclude - no. of consult and with days firs to last assessment ≤ 7 days	382	4,242
% of total	5.77	22.39
Final - no. of remaining wounds	5,742	13,315
% Healed at level mITT	60.01	54.33
% Amputated at level mITT	4.16	4.06
9.47% delta	9.47% delta	

Hyperbaric oxygen vs. nonhyperbaric oxygen diabetic Wagner grade 3/4 single wound located on the foot or toe.
HBO, hyperbaric oxygen

Using the lessons learned from the papers by Fedorko and Santema, which studied patients who completed HBO treatments, we analyzed the results of patients who completed their HBO treatments. We found that only 45.2% of patients for whom HBO therapy is ordered, however, complete the entire prescribed course.

Table 5. Modified intent-to-treat by hyperbaric oxygen therapy course completion hyperbaric oxygen therapy group only

	Healed (%)	Not Healed (%)	Total (%)	N
Complete HBOT treatment course	75.24	24.76	45.23	2,597
Incomplete treatment course	47.44	52.56	54.77	3,145
Total	60.01	39.99	100	5,742

HBOT, hyperbaric oxygen therapy.

Looking at these results graphically, we can see that the use of HBO therapy has an effect, but the completion of HBO therapy can allow patients with Wagner grade 3 or 4 wounds to achieve parity with the healing rate of the overall population (75% vs. 74%, respectively).

As there has been a tremendous amount of skepticism surrounding HBO therapy data, we repeated this entire process using the 2019 data set we have used for all the recent white papers. This allowed us to compare equal time periods and see if the results are consistent over time.

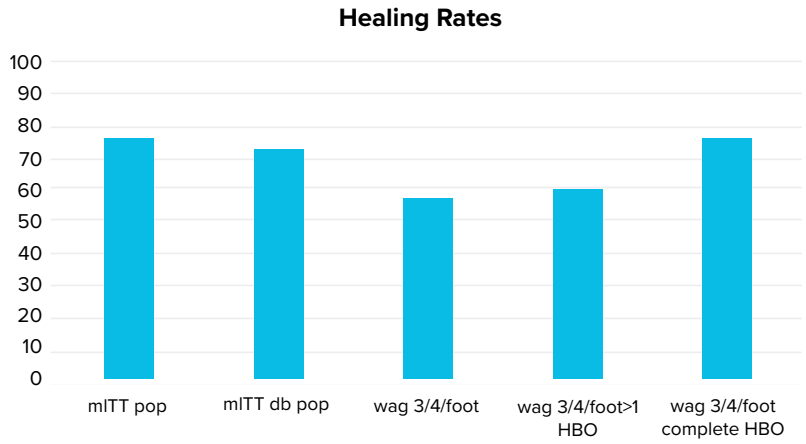
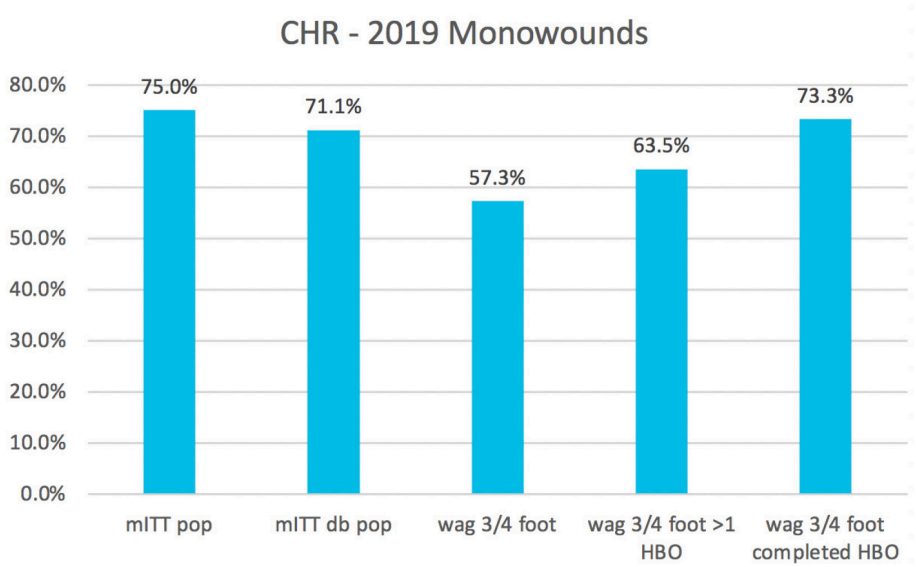


Figure 1. Healing Rates. mITT pop: modified intent-to-treat populatoin level. mITT db pop: modified intent-to-treat diabetic population. wag 3/4/foot: Wagner Grade 3 or 4 on foot. wag 3/4/foot> 1 HB O: Wagner Grade 3 or 4 on foot incompelte HBOT. wag 3/4/foot complete HBO: Wagner Grade 3 or 4 on foot completed HBOT treatment course. HBOT, hyperbaric oxygen therapy; mITT, modified intent-to-treat.

We, again, see a similar pattern in the mITT healing rates. The designation of a patient with a single wound, Wagner 3 or 4 on the foot or toe, places them at high risk of non-healing. HBO therapy can help, but the patient needs to complete their treatment course. If you remember the Visit Frequency white paper, we clearly demonstrated that blood pressure control, glucose levels, lipid levels and various other clinical conditions had improved outcomes with increased provider contact and adherence to treatment. This should, therefore, not come as a surprise. These results also help us understand the results from Margolis and others who included Wagner grade 2 wounds in their analysis.

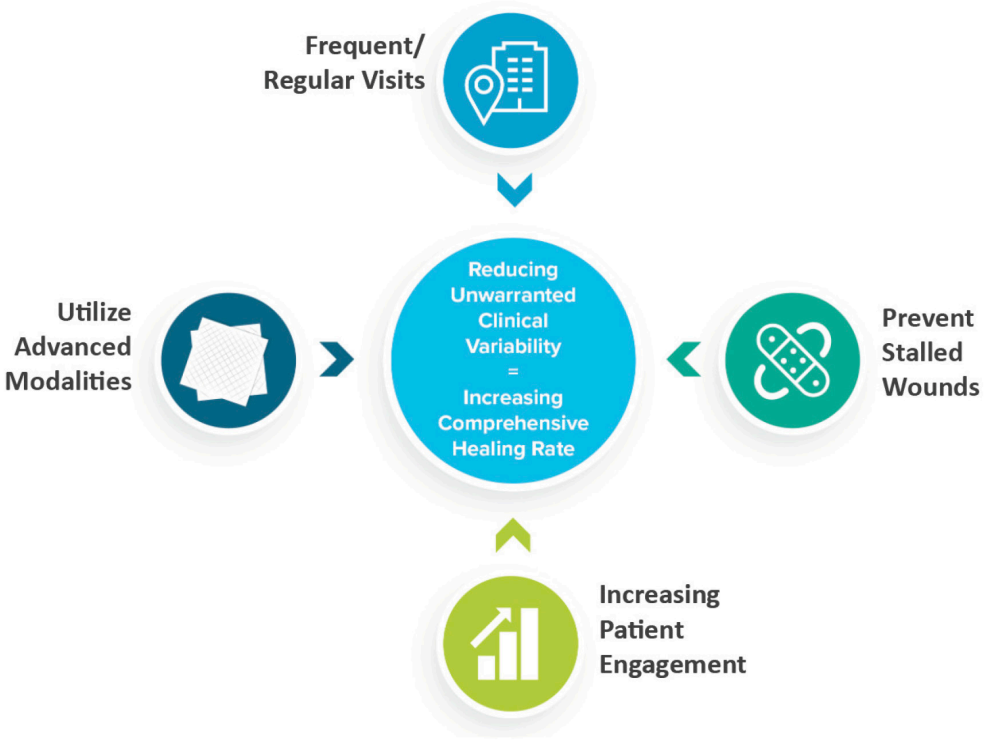


ANOTHER IMPORTANT USE CASE FOR HBO THERAPY: RADIATION CYSTITIS

Most publications report that between 5 to 18% of patients who received pelvic radiation will be affected by radiation cystitis and that it can occur anywhere from six months post-irradiation to as long as 20 years later[20]. There are; however, widespread discrepancies in the reported literature with some papers quoting between 20 and 80%[21]. It is safe to state that the problem is common and affects patients clinically and while also impacting their quality of life. Clinical signs include hematuria, frequency, anemia and if severe, urinary obstruction due to clot retention. Conservative treatment options include bladder irrigation, fulgaration and, in end-stage situations, cystectomy. HBO therapy addresses the hypoxic, hypocellular, and hypovascular tissue. HBO therapy has been utilized as a treatment option for radiation cystitis, but urologists are often unaware of this treatment option. Degener et al. studied 15 patients at 2.4 ATA for an average of 34 treatments with an overall success rate of 93%[22]. Another study reported complete resolution in 52% of a cohort of 71 patients[23]. A common question and concern from urology refer to activation of latent prostate cancer or activation of tumor growth when using HBO therapy. There is no evidence to support those claims in the literature[24,25]. Recently a study was conducted to evaluate the effectiveness of two different HBO treatment protocols for radiation cystitis[26]. This was a retrospective study evaluating the outcomes of using 2.0 ATA versus 2.4 ATA. Overall, 75% of patients saw good responses, with another 16% having a partial response. The two treatment protocols appeared to offer equivalent results, although there were more treatments required at 2.0 and more barotrauma-related complications at 2.4; however, neither of these findings were statistically significant. One important finding; however, was the fact that when patients were advanced and had blood transfusions in the past, there was less success with HBO therapy. The authors conclude that patients should be referred early in the course of their disease to maximize the clinical effects of HBO therapy. As with many studies, the retrospective nature of this publication warrants additional prospective studies to be conducted.

SUMMARY AND CONCLUSIONS

We will achieve our best outcomes for patients when we see them frequently with high-quality visits, identify wounds that are falling off their trajectory, intervene with modalities and engage them in their own care.



When we do that, in addition to evaluating the 9 essential elements every visit, we give our patients their best chance for a positive outcome. HBO therapy can be extremely effective for patients with Wagner 3 and 4 when used early in the treatment course and when all treatments are delivered. HBO therapy is a powerful treatment option for radiation cystitis and hemorrhagic cystitis and should be considered early in the patients who present with symptoms consistent with this diagnosis.

There are many diagnoses that we know HBO therapy can significantly impact, such as soft tissue radiation necrosis, chronic refractory osteomyelitis and osteoradionecrosis. This paper singles out Wagner 3 and 4 DFUs and radiation cystitis as more common conditions that should receive consideration for treatment options when treating these patients. Our data focuses on DFUs specifically and brings additional evidence for providers when creating their treatment plans. As always, HBO therapy is an adjunctive treatment and attention must be paid to the vascular status, nutrition, glucose control, infection and offloading. However, the research gathered through our Wound Science Initiative, to improve patient outcomes and the Nine Essential Elements of our clinical plan already indicate these as necessary.

We will continue to share our outcomes and the evidence to support our best practice recommendations.

APPENDIX:

Changes in HBO therapy coverage: The elimination of two Local Coverage Determination (LCD) and the National Coverage Determination (NCD) interpretation by Healogics.

As many of you have by now heard, Novitas and First Coast retired their LCDs pertaining to HBO therapy in August 2020. This means that the NCD is the prevailing Medicare coverage determination for the country. The LCDs had some specific, rigorous requirements that are not included in the NCD. Given the ambiguity in the NCD, we felt it important to outline our recommendations for providers to use when considering HBO treatments for their patients. These recommendations are based on best practice, medical society guidelines and published literature when available. This document will list the specific regulatory changes and our recommendations for interpretation. As always, medical decision-making is determined by the treating provider, and these recommendations are meant to inform, guide and act as additional input when prescribing HBO therapy for those patients the provider feels would benefit from the treatment.

1. **Number of HBO treatments allowed**

    a. Novitas and/or FCSO limited a patient to 60 treatments in a rolling 12-month period.

    b. The NCD does not specify the number of treatments allowed and will rely on provider MDM and the 30-day assessment documentation to make determinations for coverage.

    c. Healogics interpretation

        i. There are no published papers that set upper limits for HBO therapy. Treatments for soft tissue radiation necrosis, for example, can require up to 60 treatments to achieve positive outcomes. If a patient presents later in the same 12-month period with another indication for HBO, the provider should consider the previous exposure and weigh the risk/benefits prior to ordering additional therapy. A detailed history surrounding the prior HBO course of therapy should be analyzed including any complications or side effects that may have occurred. While there are no formal guidelines to cite, 60 treatments should serve as an upper limit for any individual treatment course in most cases, and careful consideration should be given to any patient who has an additional condition that might warrant HBO therapy within a rolling 12-month period.

2. **Soft tissue radionecrosis**

    a. Novitas and/or FCSO required that the signs and symptoms of the late effects of radiation must not have appeared until at least 6 months from the last radiation treatment.

    b. The NCD does not specify a timeframe between signs/symptoms and the last date of radiation. HBO therapy is approved as an adjunct to conventional treatments with evidence of failure to demonstrate healing.

    c. Healogics interpretation

        i. The tissue damage that occurs after radiation depends on several clinical variables including the type, dose and duration of the radiation therapy[27]. The quality and overall health of the patient's skin/tissue/organ is another variable that results in a wide range of damage and a variable timeframe between dosing and subsequent damage. There is published support for soft tissue damage between a three-to-six month timeframe from the radiation therapy[28,29]. Many reports simply describe variable timeframes, such as months to years[30]. Additionally, infection or trauma (i.e. surgery) to previously radiated tissue can exacerbate the process[31].

In summary, without firm guidelines to direct our recommendations, the provider should carefully document the dose, type, dates and duration of the prior radiation. While there is documentation to support a timeframe between three-to-six months, earlier considerations could be made in the face of infection or recent surgery. As always, the providers narrative report will be the most important aspect of the medical decision-making process and ultimately will be the most critical aspect of a payer's review for a treatment claim. While we have not set forth a specific timeframe, skin damage immediately following radiation therapy is more likely to be an acute radiation injury/burn and therefore would not qualify for HBO therapy.

ii. There have been rare cases in which a request has been made to use HBO therapy shortly after a surgical procedure, such as Mohs surgery. Unusual cases in which Mohs surgery was used for ORN and recurrent cancer have been reported in the literature[32]. In certain high-risk cancers, post Mohs radiation has been utilized, although it is extremely rare[33]. These atypical cases should be considered on a case-by-case basis. Risk/benefit analysis would be critical, as well as a multi-disciplinary meeting with all involved clinicians.

3. Osteoradionecrosis

a. Novitas and/or FCSO had similar requirements for a six-month interval between the signs and symptoms of ORN and the date of the last radiation treatment. In addition, coverage was limited to cases in which there was an overt fracture or bone resorption.

b. The NCD does not have any language regarding either requirement but does mention that HBO therapy should be adjunctive to conventional treatment.

c. Healogics interpretation: Interestingly, the literature in this area refers to a formal definition of ORN as exposed irradiated bone that fails to heal over a three-month period of time and does not identify a specific time from the last radiation treatment[34,35]. Exposed bone or imaging demonstrating involved necrotic bone should; however, still be documented. The provider should discuss what standard treatments have been utilized, and what the overall comprehensive treatment plan will be beyond just the addition of HBO therapy to ensure that the appropriate documentation is available for coverage. A patient that fails to show any sign of improvement at the end of three months of standard of care should trigger the team to create a treatment plan that includes contacting the surgical team, medical specialists and for the consideration of HBO therapy. The process of setting up these plans often takes a long time and wasted time can be avoided by not waiting until the end of six months to initiate the goals of treatment.

4. Diabetic wound of the lower extremity (DWLE)

a. Novitas and/or FCSO required an ankle brachial index (ABI) of not less than 0.6 to demonstrate vascular optimization. They also required debridement/excision of the infected nidus of bone for osteomyelitis underlying a chronic ulcer, or mal perforans ulcer, as part of standard of medical/surgical treatment. This was a very confusing rule as the ABI is often a poor marker in diabetic patients given the false values generated by vascular calcifications. In addition, patients that are revascularized to the best level possible often still have decreased tissue perfusion despite post-operative changes in the ABI. It is those specific patients that could benefit the most from the use of HBO therapy.

b. The NCD states that documentation of efforts to support vascular optimization should be present but does not specify an ABI value. Specifically, DWLE must meet the following criteria stated in the NCD in order for HBO therapy to be considered appropriate.

i. Presence of type 1 or 2 diabetes

ii. A wound with a diagnosis of Wagner grade 3 or higher AND

iii. ailed an adequate (30 day) course of standard wound therapy without measurable signs of healing. Standard of care is defined as addressing the following items. It should be noted that the "standard of care" can be performed by the referring provider or previous specialist as long as both the treatmnets and time frames are clearly delineated in the medical record.

1. Assessment of the vascular status and correction if possible
2. Optimization of nutrition
3. Optimization glucose control
4. Debridement by any means to remove devitalized tissue
5. Maintenance of a clean, moist bed of granulation tissue with appropriated moist dressings
6. Appropriate offloading
7. Use of necessary treatment to resolve infection

c. Healogics interpretation: Again, the most important thing the provider can do is to clearly describe the narrative and to tell the patients story. All of the seven items described above must be addressed and documented in the EMR. These seven factors are part of all published diabetic foot guidelines and should be part of all providers standard approach to manage these patients[36-38].

i. Assessment of the vascular status

This should be done with a formal study in a vascular lab. It is important to assess waveforms and toe pressures as the ABI is often falsely elevated in diabetic patients. The ultimate decision; however, on how to assess the vascular status should be made by the treating provider. There are many situations in which a revascularization is impossible (endovascular or open bypass) or in which revascularization has occurred but the tissue perfusion is still sub-optimal. If these efforts were made and the patient is still not progressing, HBO therapy might be indicated[36].

ii. Optimization of glucose and nutrition.

This requires the provider to either work on these items directly or to coordinate the care with the PCP or specialist. There are no specific values that describe optimization for any individual patient; however, the goal is to improve the status of both variables from the patient's baseline. Optimization of glucose and nutrition is rarely achieved with a single intervention or treatment, but with a coordinated plan throughout the entire episode of care. Patients will also have intermittent set-backs along their journey. The focus should be on achieving a continuous improvement over time. Addressing these items does not mean patients will achieve normalized values; however, it does mean that progress needs to be made and documented[39,40].

iii. Appropriate offloading

This recommendation is also a very patient specific concept. While total contact casting is best for one patient, an offloading extra-depth shoe is better for another. The provider

needs to make an individual assessemnt and provide the patient with the offloading method that will work best for them. As with the other items, the provider must document that offloading has been reviewed, prescribed and encouraged[36].

iv. Debridement and maintaining a clean wound bed with granulation tissue

These two concepts are intergrally connected and therefore discussed together. Debridment can be conducted by several means and should be used to remove non-viable tissue. Debridement is not a one-time event and the need to debride should be assessed with each patient encounter. Debridment is often described in two categories. First, an initial debridment is conducted to remove non-viable tissue, accurately stage the wound, identify infection and to begin to create a plan of care. Following the initial debridement is often a series of "maintenance debridements". These procedures might be less aggressive than the initial debridement, but when a patient's wound deteriorates, the cycle may have to be started again. Like glucose optimization, maintaining a clean wound bed can require ongoing efforts at debridement. Using dressings that provide a moist healing environment are considered standard of care and, while there is no data supporting one dressing over another, matching the wound bed characteristics with the specific properties of the dressing is considered standard of care[40,41]. It is imperative that the provider describes, in a narrative form, how, when, why and which type of debridement was performed, as well as the results of the process.

v. Use of necessary treatment to resolve infection

1. Again this is also an ongoing process that should be considered at each visit.[42-44] The infectious disease society of America (IDSA), under the leadership of Dr Ben Lipsky have published evidenced based guidelines on how to treat and when not to treat the diabetic foot ulcer patient[42-44]. The provider must discuss the specific findings that led to the diagnosis of a an infection and the steps taken to treat either with a topical or systemic approach. When attempting to classify using the Wagner system, the difference between a grade 2 and 3 is the presence of an abcess, tendonitis, cellulitis or osteomyelitis. However IDSA and the International Working Group on the Diabetic Foot (IWGDF) have separate classification systems to specifically diangose infection which the Wagner scale is not ideally suited to perform. The mere presence of organisms on a culture of a diabetic foot ulcer does not by itself constitute infection[45]. Simply swabbing the wound is not recommended, but obtaining a sample of tissue post debridment and irrigation would be of more value[45]. Jeandrot et al. suggested the use of C-reactive protein to assist in differentiating infected from non-infected diabetic foot ulcers[46]. The IWGDF published a review of the current guidelines in an attempt to help providers determine the best system to identify infection or establish the contribution of the vascular status[47]. Despite the acceptance by many of the IDSA guidelines, a recent paper recommended another revision by adding another tier[48].

Given the conflicting reports and possible options, we are suggesting the following approach. Prior to any assessment of a diabetic foot ulcer, determine the vascular status of the leg involved. Assuming perfusion is adeqate, evaluate the depth of the wound, palpate and probe for bone. Debride non-viable tissue, irrigate and consider tissue culture of the deepest extent of the debrided wound if signs of infection are present locally or ystemically. Consider obtaining a CRP, Sed rate, CBC and/or procalcitonin level to aide in

your diagnotic approach. Use imaging, which could consist of an X-ray, MRI, Wbc scan, and/or obtain a bone biopsy depending on the clinical situation. Remember to assess recent glucose control as often this might be the first sign of infection in a patient who is unable to mount a local inflammatory response. If you arrive at a diagnosis of a Wagner grade 3, recognize that an aggressive approach is warranted. This could include, oral or systemic antibiotics, a more aggressive debridement of tissue and/or bone, NPWT, cellular and tissue-based wound products and a consideration for hyperbaric oxygen therapy. Consultation with infectious disease, podiatry, vascular surgery and endocrinology might be required. No one algorithm will work in all cases, and the provider needs to operate with a heightened sense of urgency in all cases of diabetic foot ulcers.

2. Chronic refractory osteomyelitis

a. Novitas and/or FCSO used several criteria that were required in order to label a patient as having chronic refractory osteomyelitis. First, there needed to be a documented four-to-six week course of antibiotic therapy which was unsuccessful. Bone needed to be debrided and if not, an explanation as to why the patient did not receive bone debridement was required. Lastly, a bone culture was required, and if not done, again, an explanation as to why this was not performed.

b. The NCD does not specify a timeframe for failed antibiotic therapy and there are no specific bone debridement or culture requirements.

c. Healogics interpretation: Given the significant differences between the LCDs and NCD, Healogics is offering a series of evidence-based suggestions.

i. A diagnosis of osteomyelitis should be documented initially based on imaging or bone biospy/culture. There are situations when bone debridment/biopsy/culture are not possible and the provider then relies on probe to bone and imaging[43].

ii. A course of four-to-six weeks of antibiotics has been given without a response. The diagnosis of CRO is made by history, exam, lab testing and imaging[49]. A trial of four-to-six weeks of antibiotics for osteomyelitis is considered standard of care, and the absence of a defined timeframe in the NCD should not encourage the use of HBO therapy prior to this accepted guideline. Recurrence rates of osteomyelitis despite prolonged antibiotics approaches 30% at one year, and up to 50% in cases involving pseudomonas[50] There have been positive results with median remission rates up to 89% reported in the literature using HBO therapy for CRO[51-53]. These recommendations pertain specifically to diabetic wounds of the lower extremity and diabetic foot ulcers. Recent evidence surrounding pelvic osteomyelitis, both acute and chronic, will be described in future communications, and there are very different recommendations and evidence for those anatomic sites[54].

iii. The provider needs to create the narrative that describes what has been done, what imaging and labs continue to suggest osteomyelitis despite standard of care, and provide a description of the wound and the implications/risk of not resolving the chronic osteomyelitis for the patient. The overall treatment plan should be included, as HBO therapy is considered adjunctive therapy.

SUMMARY OF COVERAGE CHANGES:

There has been some clarity provided to the HBO therapy community, as now we are all operating under a single National coverage determination (NCD). There were several confusing and, at times, difficult to achieve requirements in the prior LCDs that had the effect of limiting HBO therapy for many patients in several categories and which are not present in the NCD. The shift to the NCD; however, does not change the indications or appropriate work-up and treatment for patients under consideration for HBO therapy. Briefly, the following statements serve as an executive summary.

1. The number of treatments a patient receives should be based on the clinical response and how the patient tolerated the therapy. Should there be a second condition within a one-year period that HBO therapy might offer benefit, the provider should review the prior HBO episode and determine risk/benefits of considering an additional course of HBO therapy.

2. Soft tissue radionecrosis can present within three-to-six months from the time of radiation therapy. Damage might present sooner if surgery is performed in the region or an infection develops. Rare cases of radiation following Mohs procedures require a case-by-case review.

3. Osteoradionecrosis can occur after a history of radiation therapy (three-to-six months). Exposed or involved bone noted on imaging that has failed to heal over three months should be approached with a comprehensive treatment plan that might include HBO therapy.

4. Diabetic wounds of the lower extremity that are of a Wagner grade 3 or 4 achieve higher healing rates when HBO therapy is included in the treatment plan based on our published data[19]. HBO therapy is an adjunctive therapy and glucose, nutrition, vascular status, wound bed and offloading must all be addressed as part of a comprehensive treatment plan.

5. Chronic refractory osteomyelitis is defined as persistent infection despite four to six weeks of antibiotic therapy. Many cases of acute osteomyelitis recur within the first year of treatment and HBO therapy has proven effective in providing remission based on case studies. Pelvic osteomyelitis represents a different approach compared to DWLE and DFU cases.

6. While not explicitly mentioned in this review, a current review of HBO therapy for failed grafts and flaps does not specifically mention a timeframe in which HBO therapy needs to be initiated. A review of this recent paper; however, describes in both animal models and humans, that HBO therapy must be started as soon as the graft/flap shows evidence of compromise. We would be unable to justify anything beyond two weeks based on the current evidence at this time. As a point of clarity, we are referring to the failure of an existing graft/flap, not the preparation of any tissue for future reconstruction.

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